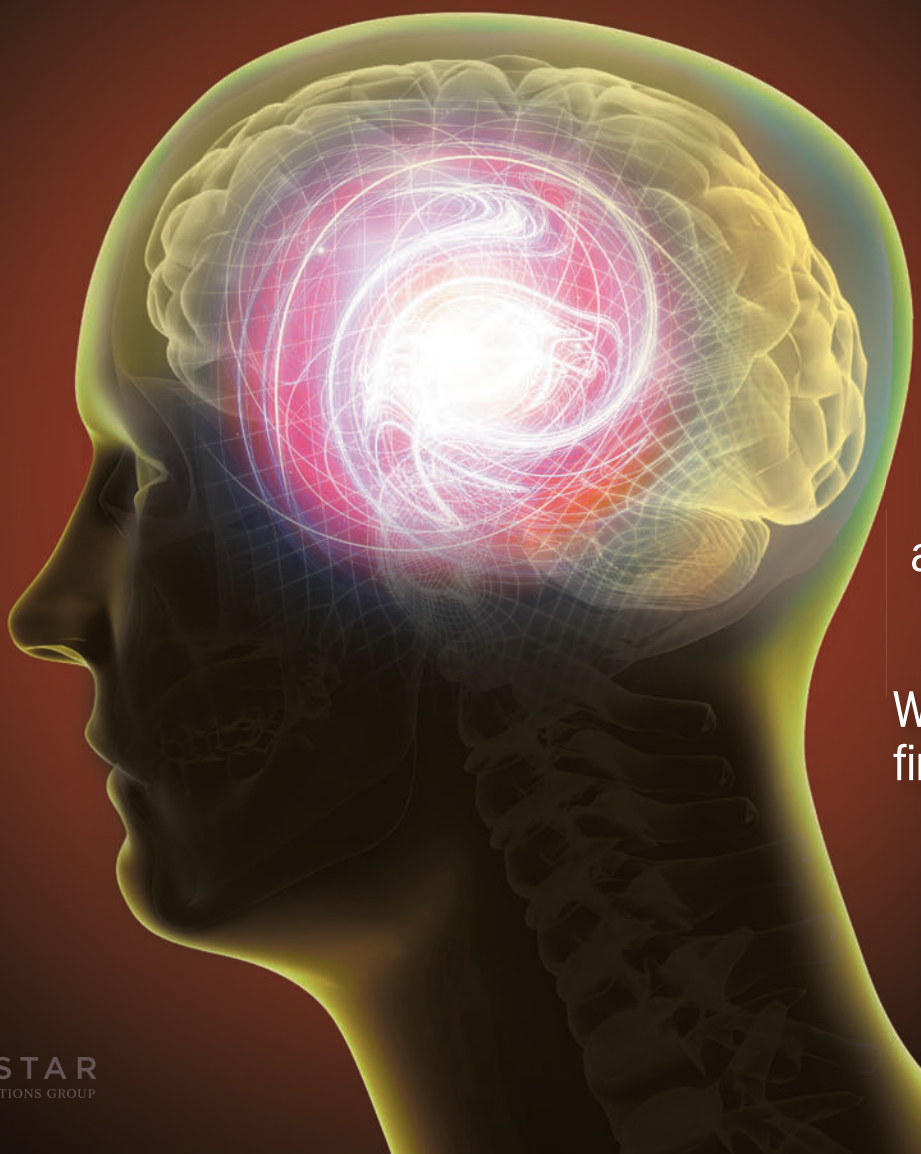
MANAGED HEALTHCARE EXECUTIVE®
For Decision Makers in Healthcare
ManagedHealthcareExecutive.com
VOL. 23 | NO. 5
MAY 2013

THE STATE OF Mental Healthcare

PAYERS // PROVIDERS // POLICY



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Don't assume providers are onboard with new focus

Providers are understandably anxious about mechanisms that reduce their income

BY JULIE MILLER

Julie Miller is editor-in-chief of MANAGED HEALTHCARE EXECUTIVE. She can be reached at julie.miller@advanstar.com

You might have missed the introduction of the Partnership for Sustainable Health Care and its whitepaper outlining a roadmap to affordability and quality. While the group does bring some diverse stakeholders together, the recommendations are pretty much the same-old same-old.

Ascension Health, the Pacific Business Group on Health, Families USA, the National Coalition on Health Care and America's Health Insurance Plans basically rehash the key reform themes of value-based payment, evidence and patient-centeredness. It's interesting to note that no major provider organization is really onboard with the group, although the American College of Surgeons apparently joined some of the discussions.

I suspect the reason why providers aren't enthusiastic about the proposal is because it calls for a reduction in per-capita spending, which translates to a smaller pie from which they can cut their slice of revenue and profits. Even the best-performing providers should be prepared for possible pay reductions under a system that expects less spending on health services overall.

Providers aren't shy about the fact that, yes, they want to make more money. Solo practitioners especially want to recoup their education costs and maintain enough revenue to pay staff and make investments in technology, all while putting a decent salary in their own pockets.

Too many observers and policymakers operate on the assumption that providers are willing—even begrudgingly—to adopt value-based payment for one reason or another. Perhaps they envision that providers believe in a new system of equity that will reward excellence. Perhaps they assume that the top performers are going to successfully champion the cause across the entire industry.

Everyone wants to see less spending on healthcare, including federal and state governments. But let's not be too quick to believe that providers are okay with the idea.

The *Journal of the American Medical Association* notes in a recent analysis of 34,000 surgical patients that hospitals gain $17,000 of profit for privately insured patients without complications compared with $56,000 in profit for patients with complications. That's not to say hospitals don't want to ensure safety and quality, but rather that new payment mechanisms will need to address real dollars-and-cents propositions.

TIME IS MONEY

So what can be done to entice providers to participate in the cost-cutting programs?

At best, stakeholder groups can work on strategies to make the provider's day-to-day operations easier or less costly. Time is money.

Health plans are increasingly partnering with providers to share data and help them manage risk, for example. Consider as many solutions as you can possibly dream up to help them make the most of their time.

The Partnership for Sustainable Health Care does point out that administrative processes should be streamlined to reduce waste, noting that 14% of total health spending in the United States is attributed to administration. But that seems to be the only point that addresses practical support for providers beyond the concept of incentives.

A consistent set of measurements, simplified data collection and uniform transactional activities are critical changes that can't be discounted. However, it still might not be enough to win over reluctant providers that have devoted all of their attention and anxiety to the inevitability of reduced income. **MHE**

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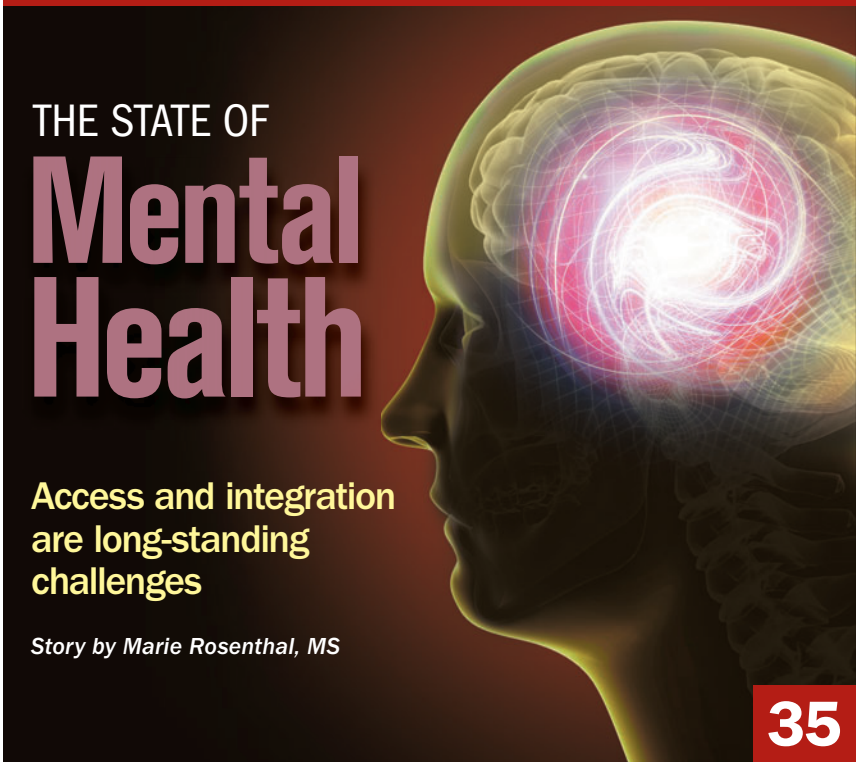

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Printed in U.S.A.

MANAGED HEALTHCARE EXECUTIVE (ISSN 1533-9300, Digital ISSN 2150-7120) is published monthly by Advanstar Communications Inc., 131 W First St., Duluth MN 55802-2065. Subscription rates: 1 year $99.00, 2 years $145.00 in the United States & Possessions; 1 year $122.00, 2 years $173.25 in Canada and Mexico; 1 year $192.00, 2 years $295.00 in all other countries. For air-expedited service, include an additional $87.00 per order annually. Single copies (prepaid only): $9.00 in the United States, $22.00 all other countries. Back issues, if available: $15.00 in the U.S.; $17.00 all other countries. Include $6.85 per order plus $2 per additional copy for U.S. postage and handling. If shipping outside the U.S., include an additional $10 per order plus $3 per additional copy. **Periodicals postage paid** at Duluth MN 55806 and additional mailing offices. **POSTMASTER:** Please send address changes to Managed Healthcare Executive, P.O. Box 6178, Duluth, MN 55806-6178. Canadian GST number: R-124213133RT001, PUBLICATIONS MAIL AGREEMENT NO. 40612608, Return Undeliverable Canadian Addresses to: IMEX Global Solutions, P. O. Box 25542, London, ON N6C 6B2, CANADA. Printed in the U.S.A.

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MANAGED HEALTHCARE EXECUTIVE
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VOLUME 23 | NUMBER 5

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Anticipate revisions to health reform

The comprehensive context of PPACA will change as more information comes to light

JULIE MILLER | EDITOR-IN-CHIEF

NATIONAL REPORTS—Experts believe the provisions of the Patient Protection and Affordable Care Act (PPACA) could undergo some alterations once the industry gets through practical implementation in 2014. A bit of trial and error could be in order.

One consequence to consider is the effect on hospitals in states that do not expand Medicaid, which will see a reduction in federal disproportionate share hospital (DSH) payments. The pay cut will be further exacerbated by higher uncompensated care costs. PPACA reduces DSH payments by $18 billion through 2020.

For example, Texas, a longtime opponent of PPACA and a state with 6.2 million uninsured, will not expand Medicaid. Its DHS pay will be reduced nonetheless because PPACA's design originally assumed all states would expand. Expansion was meant to result in lower uncompensated care costs, and the DHS reduction would balance out.

"What you're going to find out is hospitals there are going to start getting reductions in DSH pay while not enjoying the rest of the health reform deal," says Lynn Shapiro Snyder, Esq., senior member of the healthcare and life sciences and litigation practices of Epstein Becker Green, who spoke at a web conference last month.

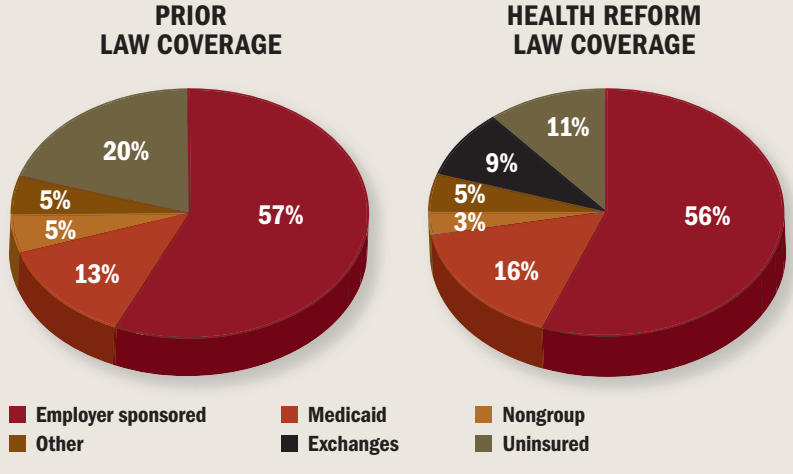
The comprehensive context of PPACA continues to change as more information comes to light. For example, the Congressional Budget Office (CBO) updated its estimate of the number of uninsured Americans. In 2010, CBO estimated 23 million uninsured or 8% of the under-65 population, but this year CBO is now estimating there are 29 million uninsured or 10% of the under-65 population.

The under-65 population also was adjusted by CBO to a total of 288 million people in the year 2023, up from 284 million in 2020.

"Prior to the law, we had 36 million people on Medicaid and about 13 million nongroup individuals," Snyder says. "What CBO thinks is going to happen with health reform implemented all the way out to 2023, is that we'll still have 31 million uninsured."

The 31 million uninsured will represent 11% of the under-65 population in 2023. Even with health reform, exchanges and Medicaid expansion, CBO notes a significant number of people will remain without coverage.

SOURCES OF COVERAGE AMONG 288 MILLION PEOPLE UNDER AGE 65



Source: Congressional Budget Office, February 2013

MILLIONS IN THE EXCHANGES

While the qualified health plans (QHPs) have just barely completed their initial product design for the insurance exchanges, the process is going to ripple through the industry between now and October 1 when enrollment begins.

Payers must reimburse fairly to maintain solid networks, but they also must price their products adequately to attract members and sustain their plans. More than 25 million people are expected to shop for private plans in the insurance exchanges.

However, the filing provisions re-

*See **CBO** on pg. 15*


Introducing a
NEW approach in
type 2 diabetes
treatment...

INVOKANA™ (canagliflozin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

INVOKANA™ is not recommended in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- History of a serious hypersensitivity reaction to INVOKANA™.
- Severe renal impairment (eGFR <30 mL/min/1.73 m^2), end stage renal disease, or patients on dialysis.

WARNINGS and PRECAUTIONS

- **Hypotension:** INVOKANA™ causes intravascular volume contraction. Symptomatic hypotension can occur after initiating INVOKANA™, particularly in patients with impaired renal function (eGFR <60 mL/min/1.73 m^2), elderly patients, and patients on either diuretics or medications that interfere with the renin-angiotensin-aldosterone system (eg, angiotensin-converting-enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs]), or patients with low systolic blood pressure. Before initiating INVOKANA™ in patients with one or more of these characteristics, volume status should be assessed and corrected. Monitor for signs and symptoms after initiating therapy.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information on the following pages.

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In adults with type 2 diabetes,

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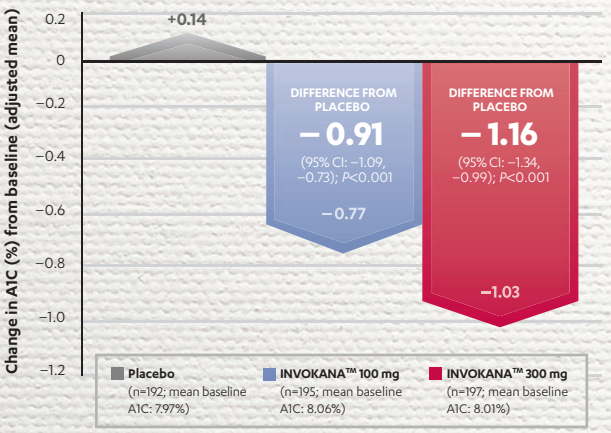
Introducing INVOKANA™—the first and only treatment option approved in the United States that reduces the reabsorption of glucose in the kidneys via sodium glucose co-transporter-2 (SGLT2) inhibition[1]

A1C Reductions as Monotherapy

INVOKANA™ monotherapy provided statistically significant A1C reductions vs placebo at 26 weeks[1]

A1C Change From Baseline With INVOKANA™ Monotherapy[1]



Effect on Weight*

Statistically significant weight reductions vs placebo at 26 weeks (*P*<0.001)[1]

» Difference from placebo†:
100 mg: −2.2%; 300 mg: −3.3%

Impact on Systolic Blood Pressure (SBP)*

Statistically significant SBP lowering vs placebo at 26 weeks (*P*<0.001)[2]

» Difference from placebo†:
100 mg: −3.7 mm Hg; 300 mg: −5.4 mm Hg

INVOKANA™ is not indicated for weight loss or as antihypertensive treatment.

***Prespecified secondary endpoint.**

†Adjusted mean.

A1C Reductions vs Sitagliptin

INVOKANA™ 300 mg demonstrated greater A1C reductions vs sitagliptin 100 mg, in combination with metformin + a sulfonylurea, at 52 weeks (*P*<0.05)[1]

» Difference from sitagliptin†: −0.37%

Incidence of Hypoglycemia

Monotherapy over 26 weeks:
100 mg: 3.6%; 300 mg: 3.0%; placebo: 2.6%[1]

With metformin and a sulfonylurea over 52 weeks:
INVOKANA™ 300 mg: 43.2%; sitagliptin 100 mg: 40.7%[1]

» Insulin and insulin secretagogues are known to cause hypoglycemia. INVOKANA™ can increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue

Convenient Once-Daily Dosing[1]

» Recommended starting dose: INVOKANA™ 100 mg

» Dose can be increased to 300 mg in patients tolerating 100 mg, who have an eGFR of ≥60 mL/min/1.73 m^2 and require additional glycemic control

The most common (≥5%) adverse reactions were female genital mycotic infection, urinary tract infection, and increased urination.

References: 1. Invokana [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals, Inc; 2013. **2.** Stenlöf K, Cefalu WT, Kim KA, et al. Efficacy and safety of canagliflozin monotherapy in subjects with type 2 diabetes mellitus inadequately controlled with diet and exercise. *Diabetes Obes Metab*. 2013;15(4):372-382.

Learn more at INVOKANAhcp.com/journal

Invokana™
canagliflozin tablets

IMPORTANT SAFETY INFORMATION *(continued from first page)*

WARNINGS and PRECAUTIONS *(cont'd)*

- **Impairment in Renal Function:** INVOKANA™ (canagliflozin) increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes. Renal function abnormalities can occur after initiating INVOKANA™. More frequent renal function monitoring is recommended in patients with an eGFR below 60 mL/min/1.73 m^2.
- **Hyperkalemia:** INVOKANA™ can lead to hyperkalemia. Patients with moderate renal impairment who are taking medications that interfere with potassium excretion, such as potassium-sparing diuretics, or medications that interfere with the renin-angiotensin-aldosterone system are more likely to develop hyperkalemia. Monitor serum potassium levels periodically after initiating INVOKANA™ in patients with impaired renal function and in patients predisposed to hyperkalemia due to medications or other medical conditions.
- **Hypoglycemia With Concomitant Use With Insulin and Insulin Secretagogues:** Insulin and insulin secretagogues are known to cause hypoglycemia. INVOKANA™ can increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue. Therefore, a lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with INVOKANA™.
- **Genital Mycotic Infections:** INVOKANA™ increases the risk of genital mycotic infections. Patients with a history of genital mycotic infections and uncircumcised males were more likely to develop genital mycotic infections. Monitor and treat appropriately.
- **Hypersensitivity Reactions:** Hypersensitivity reactions (eg, generalized urticaria), some serious, were reported with INVOKANA™ treatment; these reactions generally occurred within hours to days after initiating INVOKANA™. If hypersensitivity reactions occur, discontinue use of INVOKANA™; treat per standard of care and monitor until signs and symptoms resolve.
- **Increases in Low-Density Lipoprotein (LDL-C):** Dose-related increases in LDL-C occur with INVOKANA™. Monitor LDL-C and treat per standard of care after initiating INVOKANA™.
- **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with INVOKANA™ or any other antidiabetic drug.

DRUG INTERACTIONS

- **UGT Enzyme Inducers:** Rifampin: Co-administration of canagliflozin with rifampin, a nonselective inducer of several UGT enzymes, including UGT1A9, UGT2B4, decreased canagliflozin area under the curve (AUC) by 51%. This decrease in exposure to canagliflozin may decrease efficacy. If an inducer of these UGTs (eg, rifampin, phenytoin, phenobarbitol, ritonavir) must be co-administered with INVOKANA™ (canagliflozin), consider increasing the dose to 300 mg once daily if patients are currently tolerating INVOKANA™ 100 mg once daily, have an eGFR greater than 60mL/min/1.73 m^2, and require additional glycemic control. Consider other antihyperglycemic therapy in patients with an eGFR of 45 to less than 60 mL/min/1.73 m^2 receiving concurrent therapy with a UGT inducer and requiring additional glycemic control.
- **Digoxin:** There was an increase in the area AUC and mean peak drug concentration (C_{max}) of digoxin (20% and 36%, respectively) when co-administered with INVOKANA™ 300 mg. Patients taking INVOKANA™ with concomitant digoxin should be monitored appropriately.

USE IN SPECIFIC POPULATIONS

- **Pregnancy Category C:** There are no adequate and well-controlled studies of INVOKANA™ in pregnant women. Based on results from rat studies, canagliflozin may affect renal development and maturation. In a juvenile rat study, increased kidney weights and renal pelvic and tubular dilatation were evident at ≥0.5 times clinical exposure from a 300-mg dose.

  These outcomes occurred with drug exposure during periods of animal development that correspond to the late second and third trimester of human development. During pregnancy, consider appropriate alternative therapies, especially during the second and third trimesters. INVOKANA™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- **Nursing Mothers:** It is not known if INVOKANA™ is excreted in human milk. INVOKANA™ is secreted in the milk of lactating rats, reaching levels 1.4 times higher than that in maternal plasma. Data in juvenile rats directly exposed to INVOKANA™ showed risk to the developing kidney (renal pelvic and tubular dilatations) during maturation. Since human kidney maturation occurs in utero and during the first 2 years of life when lactational exposure may occur, there may be risk to the developing

human kidney. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from INVOKANA™, a decision should be made whether to discontinue nursing or to discontinue INVOKANA™, taking into account the importance of the drug to the mother.

- **Pediatric Use:** Safety and effectiveness of INVOKANA™ in pediatric patients under 18 years of age have not been established.
- **Geriatric Use:** Two thousand thirty-four (2034) patients 65 years and older, and 345 patients 75 years and older were exposed to INVOKANA™ in nine clinical studies of INVOKANA™. Patients 65 years and older had a higher incidence of adverse reactions related to reduced intravascular volume with INVOKANA™ (such as hypotension, postural dizziness, orthostatic hypotension, syncope, and dehydration), particularly with the 300-mg daily dose, compared to younger patients; more prominent increase in the incidence was seen in patients who were ≥75 years of age. Smaller reductions in HbA1C with INVOKANA™ relative to placebo were seen in older (65 years and older; -0.61% with INVOKANA™ 100 mg and -0.74% with INVOKANA™ 300 mg relative to placebo) compared to younger patients (-0.72% with INVOKANA™ 100 mg and -0.87% with INVOKANA™ 300 mg relative to placebo).
- **Renal Impairment:** The efficacy and safety of INVOKANA™ were evaluated in a study that included patients with moderate renal impairment (eGFR 30 to <50 mL/min/1.73 m^2). These patients had less overall glycemic efficacy and had a higher occurrence of adverse reactions related to reduced intravascular volume, renal-related adverse reactions, and decreases in eGFR compared to patients with mild renal impairment or normal renal function (eGFR ≥60 mL/min/1.73 m^2); patients treated with INVOKANA™ 300 mg were more likely to experience increases in potassium.

  The efficacy and safety of INVOKANA™ have not been established in patients with severe renal impairment (eGFR <30 mL/min/1.73 m^2), with end-stage renal disease (ESRD), or receiving dialysis. INVOKANA™ is not expected to be effective in these patient populations.
- **Hepatic Impairment:** No dosage adjustment is necessary in patients with mild or moderate hepatic impairment. The use of INVOKANA™ has not been studied in patients with severe hepatic impairment and it is therefore not recommended.

OVERDOSAGE

- There were no reports of overdose during the clinical development program of INVOKANA™ (canagliflozin).

  In the event of an overdose, contact the Poison Control Center. It is also reasonable to employ the usual supportive measures, eg, remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment as dictated by the patient's clinical status. Canagliflozin was negligibly removed during a 4-hour hemodialysis session. Canagliflozin is not expected to be dialyzable by peritoneal dialysis.

ADVERSE REACTIONS

- The most common (≥5%) adverse reactions were female genital mycotic infections, urinary tract infections, and increased urination. Adverse reactions in ≥2% of patients were male genital mycotic infections, vulvovaginal pruritis, thirst, nausea, and constipation.

K02CAN13149

Please see Brief Summary of full Prescribing Information on the following pages.

Invokana™
canagliflozin tablets

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April 2013 K02CAN13075

INVOKANA™

(canagliflozin) tablets, for oral use

Brief Summary of Prescribing Information.

INDICATIONS AND USAGE

INVOKANA™ (canagliflozin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus *[see Clinical Studies (14) in full Prescribing Information]*.

Limitation of Use: INVOKANA is not recommended in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

CONTRAINDICATIONS

- History of a serious hypersensitivity reaction to INVOKANA *[see Warnings and Precautions]*.
- Severe renal impairment (eGFR less than 30 mL/min/1.73 m^2), end stage renal disease or patients on dialysis *[see Warnings and Precautions and Use in Specific Populations]*.

WARNINGS AND PRECAUTIONS

Hypotension: INVOKANA causes intravascular volume contraction. Symptomatic hypotension can occur after initiating INVOKANA *[see Adverse Reactions]* particularly in patients with impaired renal function (eGFR less than 60 mL/min/1.73 m^2), elderly patients, patients on either diuretics or medications that interfere with the renin-angiotensin-aldosterone system (e.g., angiotensin-converting-enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs]), or patients with low systolic blood pressure. Before initiating INVOKANA in patients with one or more of these characteristics, volume status should be assessed and corrected. Monitor for signs and symptoms after initiating therapy.

Impairment in Renal Function: INVOKANA increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes. Renal function abnormalities can occur after initiating INVOKANA *[see Adverse Reactions]*. More frequent renal function monitoring is recommended in patients with an eGFR below 60 mL/min/1.73 m^2.

Hyperkalemia: INVOKANA can lead to hyperkalemia. Patients with moderate renal impairment who are taking medications that interfere with potassium excretion, such as potassium-sparing diuretics, or medications that interfere with the renin-angiotensin-aldosterone system are more likely to develop hyperkalemia *[see Adverse Reactions]*.

Monitor serum potassium levels periodically after initiating INVOKANA in patients with impaired renal function and in patients predisposed to hyperkalemia due to medications or other medical conditions.

Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues: Insulin and insulin secretagogues are known to cause hypoglycemia. INVOKANA can increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue *[see Adverse Reactions]*. Therefore, a lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with INVOKANA.

Genital Mycotic Infections: INVOKANA increases the risk of genital mycotic infections. Patients with a history of genital mycotic infections and uncircumcised males were more likely to develop genital mycotic infections *[see Adverse Reactions]*. Monitor and treat appropriately.

Hypersensitivity Reactions: Hypersensitivity reactions (e.g., generalized urticaria), some serious, were reported with INVOKANA treatment; these reactions generally occurred within hours to days after initiating INVOKANA. If hypersensitivity reactions occur, discontinue use of INVOKANA; treat per standard of care and monitor until signs and symptoms resolve *[see Contraindications and Adverse Reactions]*.

Increases in Low-Density Lipoprotein (LDL-C): Dose-related increases in LDL-C occur with INVOKANA *[see Adverse Reactions]*. Monitor LDL-C and treat per standard of care after initiating INVOKANA.

Macrovascular Outcomes: There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with INVOKANA or any other antidiabetic drug.

ADVERSE REACTIONS

The following important adverse reactions are described below and elsewhere in the labeling:

- Hypotension *[see Warnings and Precautions]*
- Impairment in Renal Function *[see Warnings and Precautions]*
- Hyperkalemia *[see Warnings and Precautions]*
- Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues *[see Warnings and Precautions]*
- Genital Mycotic Infections *[see Warnings and Precautions]*
- Hypersensitivity Reactions *[see Warnings and Precautions]*
- Increases in Low-Density Lipoprotein (LDL-C) *[see Warnings and Precautions]*

Clinical Studies Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to the rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Pool of Placebo-Controlled Trials: The data in Table 1 is derived from four 26-week placebo-controlled trials. In one trial INVOKANA was used as monotherapy and in three trials INVOKANA was used as add-on therapy *[see Clinical Studies (14) in full Prescribing Information]*. These data reflect exposure of 1667 patients to INVOKANA and a mean duration of exposure to INVOKANA of 24 weeks. Patients received INVOKANA 100 mg (N=833), INVOKANA 300 mg (N=834) or placebo (N=646) once daily. The mean age of the population was 56 years and 2% were older than 75 years of age. Fifty percent (50%) of the population was male and 72% were Caucasian, 12% were Asian, and 5% were Black or African American. At baseline the population had diabetes for an average of 7.3 years, had a mean HbA1C of 8.0% and 20% had established microvascular complications of diabetes. Baseline renal function was normal or mildly impaired (mean eGFR 88 mL/min/1.73 m^2).

Table 1 shows common adverse reactions associated with the use of INVOKANA. These adverse reactions were not present at baseline, occurred more commonly on INVOKANA than on placebo, and occurred in at least 2% of patients treated with either INVOKANA 100 mg or INVOKANA 300 mg.

Table 1: Adverse Reactions From Pool of Four 26–Week Placebo-Controlled Studies Reported in ≥ 2% of INVOKANA-Treated Patients*

Adverse Reaction	Placebo N=646	INVOKANA 100 mg N=833	INVOKANA 300 mg N=834
Female genital mycotic infections†	3.2%	10.4%	11.4%
Urinary tract infections‡	4.0%	5.9%	4.3%
Increased urination§	0.8%	5.3%	4.6%
Male genital mycotic infections¶	0.6%	4.2%	3.7%
Vulvovaginal pruritus	0.0%	1.6%	3.0%
Thirst#	0.2%	2.8%	2.3%
Constipation	0.9%	1.8%	2.3%
Nausea	1.5%	2.2%	2.3%

* The four placebo-controlled trials included one monotherapy trial and three add-on combination trials with metformin, metformin and sulfonylurea, or metformin and pioglitazone.

† Female genital mycotic infections include the following adverse reactions: Vulvovaginal candidiasis, Vulvovaginal mycotic infection, Vulvovaginitis, Vaginal infection, Vulvitis, and Genital infection fungal. Percentages calculated with the number of female subjects in each group as denominator: placebo (N=312), INVOKANA 100 mg (N=425), and INVOKANA 300 mg (N=430).

‡ Urinary tract infections includes the following adverse reactions: Urinary tract infection, Cystitis, Kidney infection, and Urosepsis.

§ Increased urination includes the following adverse reactions: Polyuria, Pollakiuria, Urine output increased, Micturition urgency, and Nocturia.

¶ Male genital mycotic infections include the following adverse reactions: Balanitis or Balanoposthitis, Balanitis candida, and Genital infection fungal. Percentages calculated with the number of male subjects in each group as denominator: placebo (N=334), INVOKANA 100 mg (N=408), and INVOKANA 300 mg (N=404).

Thirst includes the following adverse reactions: Thirst, Dry mouth, and Polydipsia.

Abdominal pain was also more commonly reported in patients taking INVOKANA 100 mg (1.8%), 300 mg (1.7%) than in patients taking placebo (0.8%).

Pool of Placebo- and Active-Controlled Trials: The occurrence of adverse reactions was also evaluated in a larger pool of patients participating in placebo- and active-controlled trials.

The data combined eight clinical trials *[see Clinical Studies (14) in full Prescribing Information]* and reflect exposure of 6177 patients to INVOKANA. The mean duration of exposure to INVOKANA was 38 weeks with 1832 individuals exposed to INVOKANA for greater than 50 weeks. Patients received INVOKANA 100 mg (N=3092), INVOKANA 300 mg (N=3085) or comparator (N=3262) once daily. The mean age of the population was 60 years and 5% were older than 75 years of age. Fifty-eight percent (58%) of the population was male and 73% were Caucasian, 16% were Asian, and 4% were Black or African American. At baseline, the population had diabetes for an average of 11 years, had a mean HbA1C of 8.0% and 33% had established microvascular complications of diabetes. Baseline renal function was normal or mildly impaired (mean eGFR 81 mL/min/1.73 m^2).

The types and frequency of common adverse reactions observed in the pool of eight clinical trials were consistent with those listed in Table 1. In this pool, INVOKANA was also associated with the adverse reactions of fatigue (1.7% with comparator, 2.2% with INVOKANA 100 mg, and 2.0% with INVOKANA 300 mg) and loss of strength or energy (i.e., asthenia) (0.6% with comparator, 0.7% with INVOKANA 100 mg and 1.1% with INVOKANA 300 mg).

In the pool of eight clinical trials, the incidence rate of pancreatitis (acute or chronic) was 0.9, 2.7, and 0.9 per 1000 patient-years of exposure to comparator, INVOKANA 100 mg, and INVOKANA 300 mg, respectively.

In the pool of eight clinical trials with a longer mean duration of exposure to INVOKANA (68 weeks), the incidence rate of bone fracture was 14.2, 18.7, and 17.6 per 1000 patient years of exposure to comparator, INVOKANA

100 mg, and INVOKANA 300 mg, respectively. Upper extremity fractures occurred more commonly on INVOKANA than comparator.

In the pool of eight clinical trials, hypersensitivity-related adverse reactions (including erythema, rash, pruritus, urticaria, and angioedema) occurred in 3.0%, 3.8%, and 4.2% of patients receiving comparator, INVOKANA 100 mg and INVOKANA 300 mg, respectively. Five patients experienced serious adverse reactions of hypersensitivity with INVOKANA, which included 4 patients with urticaria and 1 patient with a diffuse rash and urticaria occurring within hours of exposure to INVOKANA. Among these patients, 2 patients discontinued INVOKANA. One patient with urticaria had recurrence when INVOKANA was re-initiated.

Photosensitivity-related adverse reactions (including photosensitivity reaction, polymorphic light eruption, and sunburn) occurred in 0.1%, 0.2%, and 0.2% of patients receiving comparator, INVOKANA 100 mg, and INVOKANA 300 mg, respectively.

Other adverse reactions occurring more frequently on INVOKANA than on comparator were:

Volume Depletion-Related Adverse Reactions: INVOKANA results in an osmotic diuresis, which may lead to reductions in intravascular volume. In clinical studies, treatment with INVOKANA was associated with a dose-dependent increase in the incidence of volume depletion-related adverse reactions (e.g., hypotension, postural dizziness, orthostatic hypotension, syncope, and dehydration). An increased incidence was observed in patients on the 300 mg dose. The three factors associated with the largest increase in volume depletion-related adverse reactions were the use of loop diuretics, moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73 m^2) and age 75 years and older (Table 2) *[see Dosage and Administration (2.2) in full Prescribing Information, Warnings and Precautions, and Use in Specific Populations]*.

Table 2: Proportion of Patients With at Least one Volume Depletion-Related Adverse Reactions (Pooled Results from 8 Clinical Trials)

Baseline Characteristic	Comparator Group* %	INVOKANA 100 mg %	INVOKANA 300 mg %
Overall population	1.5%	2.3%	3.4%
75 years of age and older†	2.6%	4.9%	8.7%
eGFR less than 60 mL/min/1.73 m^2†	2.5%	4.7%	8.1%
Use of loop diuretic†	4.7%	3.2%	8.8%

***** Includes placebo and active-comparator groups

† Patients could have more than 1of the listed risk factors

Impairment in Renal Function: INVOKANA is associated with a dose-dependent increase in serum creatinine and a concomitant fall in estimated GFR (Table 3). Patients with moderate renal impairment at baseline had larger mean changes.

Table 3: Changes in Serum Creatinine and eGFR Associated with INVOKANA in the Pool of Four Placebo-Controlled Trials and Moderate Renal Impairment Trial

			Placebo N=646	INVOKANA 100 mg N=833	INVOKANA 300 mg N=834
Pool of Four Placebo-Controlled Trials	Baseline	Creatinine (mg/dL)	0.84	0.82	0.82
		eGFR (mL/min/1.73 m^2)	87.0	88.3	88.8
	Week 6 Change	Creatinine (mg/dL)	0.01	0.03	0.05
		eGFR (mL/min/1.73 m^2)	-1.6	-3.8	-5.0
	End of Treatment Change*	Creatinine (mg/dL)	0.01	0.02	0.03
		eGFR (mL/min/1.73 m^2)	-1.6	-2.3	-3.4
			Placebo N=90	**INVOKANA 100 mg N=90**	**INVOKANA 300 mg N=89**
Moderate Renal Impairment Trial	Baseline	Creatinine (mg/dL)	1.61	1.62	1.63
		eGFR (mL/min/1.73 m^2)	40.1	39.7	38.5
	Week 3 Change	Creatinine (mg/dL)	0.03	0.18	0.28
		eGFR (mL/min/1.73 m^2)	-0.7	-4.6	-6.2
	End of Treatment Change*	Creatinine (mg/dL)	0.07	0.16	0.18
		eGFR (mL/min/1.73 m^2)	-1.5	-3.6	-4.0

***** Week 26 in mITT LOCF population

In the pool of four placebo-controlled trials where patients had normal or mildly impaired baseline renal function, the proportion of patients who experienced at least one event of significant renal function decline, defined as an eGFR below 80 mL/min/1.73 m^2 and 30% lower than baseline, was 2.1% with placebo, 2.0% with INVOKANA 100 mg, and 4.1% with INVOKANA 300 mg. At the end of treatment, 0.5% with placebo, 0.7% with INVOKANA 100 mg, and 1.4% with INVOKANA 300 mg had a significant renal function decline.

INVOKANA™ (canagliflozin) tablets

In a trial carried out in patients with moderate renal impairment with a baseline eGFR of 30 to less than 50 mL/min/1.73 m^2 (mean baseline eGFR 39 mL/min/1.73 m^2) *[see Clinical Studies (14.3) in full Prescribing Information]*, the proportion of patients who experienced at least one event of significant renal function decline, defined as an eGFR 30% lower than baseline, was 6.9% with placebo, 18% with INVOKANA 100 mg, and 22.5% with INVOKANA 300 mg. At the end of treatment, 4.6% with placebo, 3.4% with INVOKANA 100 mg, and 3.4% with INVOKANA 300 mg had a significant renal function decline.

In a pooled population of patients with moderate renal impairment (N=1085) with baseline eGFR of 30 to less than 60 mL/min/1.73 m^2 (mean baseline eGFR 48 mL/min/1.73 m^2), the overall incidence of these events was lower than in the dedicated trial but a dose-dependent increase in incident episodes of significant renal function decline compared to placebo was still observed.

Use of INVOKANA was associated with an increased incidence of renal-related adverse reactions (e.g., increased blood creatinine, decreased glomerular filtration rate, renal impairment, and acute renal failure), particularly in patients with moderate renal impairment.

In the pooled analysis of patients with moderate renal impairment, the incidence of renal-related adverse reactions was 3.7% with placebo, 8.9% with INVOKANA 100 mg, and 9.3% with INVOKANA 300 mg. Discontinuations due to renal-related adverse events occurred in 1.0% with placebo, 1.2% with INVOKANA 100 mg, and 1.6% with INVOKANA 300 mg *[see Warnings and Precautions]*.

Genital Mycotic Infections: In the pool of four placebo-controlled clinical trials, female genital mycotic infections (e.g., vulvovaginal mycotic infection, vulvovaginal candidiasis, and vulvovaginitis) occurred in 3.2%, 10.4%, and 11.4% of females treated with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively. Patients with a history of genital mycotic infections were more likely to develop genital mycotic infections on INVOKANA. Female patients who developed genital mycotic infections on INVOKANA were more likely to experience recurrence and require treatment with oral or topical antifungal agents and anti-microbial agents *[see Warnings and Precautions]*.

In the pool of four placebo-controlled clinical trials, male genital mycotic infections (e.g., candidal balanitis, balanoposthitis) occurred in 0.6%, 4.2%, and 3.7% of males treated with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively. Male genital mycotic infections occurred more commonly in uncircumcised males and in males with a prior history of balanitis or balanoposthitis. Male patients who developed genital mycotic infections on INVOKANA were more likely to experience recurrent infections (22% on INVOKANA versus none on placebo), and require treatment with oral or topical antifungal agents and anti-microbial agents than patients on comparators. In the pooled analysis of 8 controlled trials, phimosis was reported in 0.3% of uncircumcised male patients treated with INVOKANA and 0.2% required circumcision to treat the phimosis *[see Warnings and Precautions]*.

Hypoglycemia: In all clinical trials, hypoglycemia was defined as any event regardless of symptoms, where biochemical hypoglycemia was documented (any glucose value below or equal to 70 mg/dL). Severe hypoglycemia was defined as an event consistent with hypoglycemia where the patient required the assistance of another person to recover, lost consciousness, or experienced a seizure (regardless of whether biochemical documentation of a low glucose value was obtained). In individual clinical trials *[see Clinical Studies (14) in full Prescribing Information]*, episodes of hypoglycemia occurred at a higher rate when INVOKANA was co-administered with insulin or sulfonylureas (Table 4) *[see Warnings and Precautions]*.

Table 4: Incidence of Hypoglycemia* in Controlled Clinical Studies

Monotherapy (26 weeks)	Placebo (N=192)	INVOKANA 100 mg (N=195)	INVOKANA 300 mg (N=197)
Overall [N (%)]	5 (2.6)	7 (3.6)	6 (3.0)
In Combination with Metformin (26 weeks)	**Placebo + Metformin (N=183)**	**INVOKANA 100 mg + Metformin (N=368)**	**INVOKANA 300 mg + Metformin (N=367)**
Overall [N (%)]	3 (1.6)	16 (4.3)	17 (4.6)
Severe [N (%)]†	0 (0)	1 (0.3)	1 (0.3)
In Combination with Metformin (52 weeks)	**Glimepiride + Metformin (N=482)**	**INVOKANA 100 mg + Metformin (N=483)**	**INVOKANA 300 mg + Metformin (N=485)**
Overall [N (%)]	165 (34.2)	27 (5.6)	24 (4.9)
Severe [N (%)]†	15 (3.1)	2 (0.4)	3 (0.6)
In Combination with Sulfonylurea (18 weeks)	**Placebo + Sulfonylurea (N=69)**	**INVOKANA 100 mg + Sulfonylurea (N=74)**	**INVOKANA 300 mg + Sulfonylurea (N=72)**
Overall [N (%)]	4 (5.8)	3 (4.1)	9 (12.5)
In Combination with Metformin + Sulfonylurea (26 weeks)	**Placebo + Metformin + Sulfonylurea (N=156)**	**INVOKANA 100 mg + Metformin + Sulfonylurea (N=157)**	**INVOKANA 300 mg + Metformin + Sulfonylurea (N=156)**
Overall [N (%)]	24 (15.4)	43 (27.4)	47 (30.1)
Severe [N (%)]†	1 (0.6)	1 (0.6)	0

Table 4: Incidence of Hypoglycemia* in Controlled Clinical Studies (continued)

In Combination with Metformin + Sulfonylurea (52 weeks)	**Sitagliptin + Metformin + Sulfonylurea (N=378)**		**INVOKANA 300 mg + Metformin + Sulfonylurea (N=377)**
Overall [N (%)]	154 (40.7)		163 (43.2)
Severe [N (%)]†	13 (3.4)		15 (4.0)
In Combination with Metformin + Pioglitazone (26 weeks)	**Placebo + Metformin + Pioglitazone (N=115)**	**INVOKANA 100 mg + Metformin + Pioglitazone (N=113)**	**INVOKANA 300 mg + Metformin + Pioglitazone (N=114)**
Overall [N (%)]	3 (2.6)	3 (2.7)	6 (5.3)
In Combination with Insulin (18 weeks)	**Placebo (N=565)**	**INVOKANA 100 mg (N=566)**	**INVOKANA 300 mg (N=587)**
Overall [N (%)]	208 (36.8)	279 (49.3)	285 (48.6)
Severe [N (%)]†	14 (2.5)	10 (1.8)	16 (2.7)

* Number of patients experiencing at least one event of hypoglycemia based on either biochemically documented episodes or severe hypoglycemic events in the intent-to-treat population

† Severe episodes of hypoglycemia were defined as those where the patient required the assistance of another person to recover, lost consciousness, or experienced a seizure (regardless of whether biochemical documentation of a low glucose value was obtained)

Laboratory Tests: *Increases in Serum Potassium:* Dose-related, transient mean increases in serum potassium were observed early after initiation of INVOKANA (i.e., within 3 weeks) in a trial of patients with moderate renal impairment *[see Clinical Studies (14.3) in full Prescribing Information]*. In this trial, increases in serum potassium of greater than 5.4 mEq/L and 15% above baseline occurred in 16.1%, 12.4%, and 27.0% of patients treated with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively. More severe elevations (i.e., equal or greater than 6.5 mEq/L) occurred in 1.1%, 2.2%, and 2.2% of patients treated with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively. In patients with moderate renal impairment, increases in potassium were more commonly seen in those with elevated potassium at baseline and in those using medications that reduce potassium excretion, such as potassium-sparing diuretics, angiotensin-converting-enzyme inhibitors, and angiotensin-receptor blockers *[see Warnings and Precautions]*.

Increases in Serum Magnesium: Dose-related increases in serum magnesium were observed early after initiation of INVOKANA (within 6 weeks) and remained elevated throughout treatment. In the pool of four placebo-controlled trials, the mean change in serum magnesium levels was 8.1% and 9.3% with INVOKANA 100 mg and INVOKANA 300 mg, respectively, compared to -0.6% with placebo. In a trial of patients with moderate renal impairment *[see Clinical Studies (14.3) in full Prescribing Information]*, serum magnesium levels increased by 0.2%, 9.2%, and 14.8% with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively.

Increases in Serum Phosphate: Dose-related increases in serum phosphate levels were observed with INVOKANA. In the pool of four placebo controlled trials, the mean change in serum phosphate levels were 3.6% and 5.1% with INVOKANA 100 mg and INVOKANA 300 mg, respectively, compared to 1.5% with placebo. In a trial of patients with moderate renal impairment *[see Clinical Studies (14.3) in full Prescribing Information]*, the mean serum phosphate levels increased by 1.2%, 5.0%, and 9.3% with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively.

Increases in Low-Density Lipoprotein Cholesterol (LDL-C) and non-High-Density Lipoprotein Cholesterol (non-HDL-C): In the pool of four placebo-controlled trials, dose-related increases in LDL-C with INVOKANA were observed. Mean changes (percent changes) from baseline in LDL-C relative to placebo were 4.4 mg/dL (4.5%) and 8.2 mg/dL (8.0%) with INVOKANA 100 mg and INVOKANA 300 mg, respectively. The mean baseline LDL-C levels were 104 to 110 mg/dL across treatment groups *[see Warnings and Precautions]*.

Dose-related increases in non-HDL-C with INVOKANA were observed. Mean changes (percent changes) from baseline in non-HDL-C relative to placebo were 2.1 mg/dL (1.5%) and 5.1 mg/dL (3.6%) with INVOKANA 100 mg and 300 mg, respectively. The mean baseline non-HDL-C levels were 140 to 147 mg/dL across treatment groups.

Increases in Hemoglobin: In the pool of four placebo-controlled trials, mean changes (percent changes) from baseline in hemoglobin were -0.18 g/dL (-1.1%) with placebo, 0.47 g/dL (3.5%) with INVOKANA 100 mg, and 0.51 g/dL (3.8%) with INVOKANA 300 mg. The mean baseline hemoglobin value was approximately 14.1 g/dL across treatment groups. At the end of treatment, 0.8%, 4.0%, and 2.7% of patients treated with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively, had hemoglobin above the upper limit of normal.

DRUG INTERACTIONS

UGT Enzyme Inducers: Rifampin: Co-administration of canagliflozin with rifampin, a nonselective inducer of several UGT enzymes, including UGT1A9, UGT2B4, decreased canagliflozin area under the curve (AUC) by 51%. This decrease in exposure to canagliflozin may decrease efficacy. If an inducer of these UGTs (e.g., rifampin, phenytoin, phenobarbital, ritonavir) must be co-administered with INVOKANA (canagliflozin), consider increasing the dose to 300 mg once daily if patients are currently tolerating INVOKANA 100 mg once daily, have an eGFR greater than 60 mL/min/1.73 m^2, and require additional glycemic control. Consider other antihyperglycemic therapy in patients with an eGFR of 45 to less than 60 mL/min/1.73 m^2 receiving concurrent therapy with a UGT inducer and require additional glycemic control *[see Dosage and Administration (2.3) and Clinical Pharmacology (12.3) in full Prescribing Information]*.

Digoxin: There was an increase in the area AUC and mean peak drug concentration (C_{max}) of digoxin (20% and 36%, respectively) when co-administered with INVOKANA 300 mg *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Patients taking INVOKANA with concomitant digoxin should be monitored appropriately.

USE IN SPECIFIC POPULATIONS

Pregnancy: Teratogenic Effects: Pregnancy Category C: There are no adequate and well-controlled studies of INVOKANA in pregnant women. Based on results from rat studies, canagliflozin may affect renal development and maturation. In a juvenile rat study, increased kidney weights and renal pelvic and tubular dilatation were evident at greater than or equal to 0.5 times clinical exposure from a 300 mg dose *[see Nonclinical Toxicology (13.2) in full Prescribing Information]*.

These outcomes occurred with drug exposure during periods of animal development that correspond to the late second and third trimester of human development. During pregnancy, consider appropriate alternative therapies, especially during the second and third trimesters. INVOKANA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known if INVOKANA is excreted in human milk. INVOKANA is secreted in the milk of lactating rats reaching levels 1.4 times higher than that in maternal plasma. Data in juvenile rats directly exposed to INVOKANA showed risk to the developing kidney (renal pelvic and tubular dilatations) during maturation. Since human kidney maturation occurs *in utero* and during the first 2 years of life when lactational exposure may occur, there may be risk to the developing human kidney. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from INVOKANA, a decision should be made whether to discontinue nursing or to discontinue INVOKANA, taking into account the importance of the drug to the mother *[see Nonclinical Toxicology (13.2) in full Prescribing Information]*.

Pediatric Use: Safety and effectiveness of INVOKANA in pediatric patients under 18 years of age have not been established.

Geriatric Use: Two thousand thirty-four (2034) patients 65 years and older, and 345 patients 75 years and older were exposed to INVOKANA in nine clinical studies of INVOKANA *[see Clinical Studies (14.3) in full Prescribing Information]*.

Patients 65 years and older had a higher incidence of adverse reactions related to reduced intravascular volume with INVOKANA (such as hypotension, postural dizziness, orthostatic hypotension, syncope, and dehydration), particularly with the 300 mg daily dose, compared to younger patients; more prominent increase in the incidence was seen in patients who were 75 years and older *[see Dosage and Administration (2.1) in full Prescribing Information and Adverse Reactions]*. Smaller reductions in HbA1C with INVOKANA relative to placebo were seen in older (65 years and older; -0.61% with INVOKANA 100 mg and -0.74% with INVOKANA 300 mg relative to placebo) compared to younger patients (-0.72% with INVOKANA 100 mg and -0.87% with INVOKANA 300 mg relative to placebo).

Renal Impairment: The efficacy and safety of INVOKANA were evaluated in a study that included patients with moderate renal impairment (eGFR 30 to less than 50 mL/min/1.73 m^2) *[see Clinical Studies (14.3) in full Prescribing Information]*. These patients had less overall glycemic efficacy and had a higher occurrence of adverse reactions related to reduced intravascular volume, renal-related adverse reactions, and decreases in eGFR compared to patients with mild renal impairment or normal renal function (eGFR greater than or equal to 60 mL/min/1.73 m^2); patients treated with INVOKANA 300 mg were more likely to experience increases in potassium *[see Dosage and Administration (2.2) in full Prescribing Information, Warnings and Precautions, and Adverse Reactions]*.

The efficacy and safety of INVOKANA have not been established in patients with severe renal impairment (eGFR less than 30 mL/min/1.73 m^2), with ESRD, or receiving dialysis. INVOKANA is not expected to be effective in these patient populations *[see Contraindications and Clinical Pharmacology (12.3) in full Prescribing Information]*.

Hepatic Impairment: No dosage adjustment is necessary in patients with mild or moderate hepatic impairment. The use of INVOKANA has not been studied in patients with severe hepatic impairment and is therefore not recommended *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

***CBO** from pg. 6*

main in effect for all rate increases and plans will have to justify subsequent premium hikes if they miscalculate prices early on.

"Pricing pressure is now a bully pulpit more than it is a cap," Snyder says.

Plans must file with the federal government as well as the states and be prepared for denial of rate increases—especially increases of more than 10%. Snyder says the pricing pressure is not just an issue for plans, it also trickles down to what plans can afford to pay providers. It's difficult to know right now what kind of allowable charges providers can expect when serving members of exchange products, she says.

And with the minimum essential benefits package and the excise tax on plans—meant to offset new costs associated with increased Medicaid coverage and subsidies—premiums are likely to be volatile the first few years of exchange operations.

Employers remain a key source of healthcare coverage in the United States with more than 160 million still obtaining insurance through their jobs by 2023, according to CBO. Snyder says the most concerning question is whether firms will keep offering coverage or send their employees to the exchanges.

"It's not a mathematical equation," she says. "There are union issues and employee-satisfaction issues around this."

Employers generally will keep their health benefits if they perceive that they can bend the cost curve. Some firms even bypass insurers by offering onsite health clinics for employees that emphasize wellness and prevention, for example.

One key issue remains for all stakeholders, however.

"The issue is whether you are going to have adequate margin to make a good living, have a return on your investment and not be too close to the line on losses or be so high on gains as to be a target for reductions," Snyder says. **MHE**

UNINSURED POPULATIONS TOP STATES

State	Uninsured	Participating in Medicaid Expansion	Challenged PPACA in Court
California	7.0 million	Yes	No
Texas	6.2 million	No	Yes
Florida	3.8 million	Leaning Toward	Yes
New York	2.7 million	Leaning Toward	No
Georgia	1.8 million	No	Yes
Illinois	1.7 million	Yes	No

U.S. total non-elderly uninsured = 49.9 million

Source: Kaiser Family Foundation; Advisory Board Company, as of March 13, 2013

Comprehensive benefit packages drive premiums 47% higher

Some plans must increase benefits and premiums to meet requirements

LISA SAMALONIS
MHE CONTRIBUTOR

NATIONAL REPORTS—The 2014 health reform provisions include the adoption of Essential Health Benefits as mandated by the Department of Health and Human Services (HHS) to provide more comprehensive coverage. Although designed to protect consumers, the package is expected to increase premium costs.

The recent "Cost of Comprehensive Health Benefits" report from Today eHealth, Inc., parent company of eHealthInsurance.com, shows that average monthly premiums for individual health insurance plans it evaluates are 47% higher than average when the plans cover comprehensive benefits. However, average deductibles for the plans are 27% lower than the average for all plans. Such comprehensive benefits generally parallel those in the essential benefit package.

Under the Patient Protection and Affordable Care Act (PPACA) major medical health insurance plans must cover 10 essential benefit categories at an actuarial minimum value of 60%. The full impact of the requirements will not be uniform across states.

"Health insurers are free to design plans of their choosing, so long as they are at minimum actuarially equivalent to the benchmark plan in the 10 required areas of service that must be covered," says Adam C. Powell, PhD, president of Payer+Provider Syndicate, a healthcare consulting firm in Boston.

In the case in which a health plan offers benefits of equal or greater value than the benchmark, no design changes are necessary. However, when a health plan does not offer a benefit, or offers one of lower actuarial value than the benchmark, the plan must add or enhance the benefit. In the short-term, doing so only has the potential to increase premiums, he says.

Some plans will increase the benefits and premiums to meet the requirements, and this will benefit some underinsured consumers, Powell says.

"For example, HHS has estimated that 62% of individual market health plans do not provide maternity coverage," Powell says. "Men and women not in the process of bearing children might prefer such plans when shopping on the individual market, as they do not need maternity coverage. As these plans likely siphon off a number of people not needing maternity benefits, the population insured by plans offering maternity benefits likely has a disproportionate number of pregnant mothers. By making maternity benefits a required benefit, pregnant mothers may become more evenly dispersed between health plans."

The dispersion of members could reduce the medical costs associated with plans that had previously offered maternity benefits, and increase the medical costs associated with plans that had previously not offered maternity benefits. It's too early to tell how prevalent adverse selection will be among plans, however, it will be a key issue.

The true costs and impact of the 2014 provisions are impossible to predict.

"The Essential Health Benefit requirements put in place by HHS offers many new services we're not used to or had available to us," says CJ Evrard, cofounder of Ihealthupdates.com, and IHU consulting group in Chicago. "Unfortunately because everything is occurring for the first time, there is no way to tell what will happen on October 1, 2013, when the exchange opens its doors for the first time, and how long it will take for all the kinks to be worked out." **MHE**

Campaign draws in uninsured

Marketing tools include bilingual websites

ROBIN DEMATTIA
MHE CONTRIBUTOR

NATIONAL REPORTS—Insurance companies are facing a rushed timetable to participate in Affordable Insurance Exchanges that will offer one-stop shopping to millions of Americans and small business. By October 1, they must have new products developed and approved, and a new way to sell products to a target audience that has likely never purchased insurance.

Their marketing departments are scrambling.

As one example, Blue Cross Blue Shield of Texas in March launched "Be Covered Texas," a grassroots campaign designed to work with community-based organizations such as schools, religious institutions and doctors to reach people where they live, work, learn, worship, text and tweet. Right now, the goal is to simply build awareness.

*See **Exchange** on pg. 23*


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THE NUMBERS STACK UP FOR

7
immune-mediated indications[1]

8
million U.S. prescriptions written*

15
years of clinical trial experience[2,†]

* IMS US NPA cumulative data, January 2003 through March 2012.
† First patient dosed April 1997.

Indications[1]

Rheumatoid Arthritis: HUMIRA is indicated, alone or in combination with methotrexate or other non-biologic DMARDs, for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis.

Juvenile Idiopathic Arthritis: HUMIRA is indicated, alone or in combination with methotrexate, for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 4 years of age and older.

Psoriatic Arthritis: HUMIRA is indicated, alone or in combination with non-biologic DMARDs, for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis.

Ankylosing Spondylitis: HUMIRA is indicated for reducing signs and symptoms in adult patients with active ankylosing spondylitis.

Crohn's Disease: HUMIRA is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy, and reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.

Ulcerative Colitis: HUMIRA is indicated for inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine. The effectiveness of HUMIRA has not been established in patients who have lost response to or were intolerant to anti-TNF agents.

Plaque Psoriasis: HUMIRA is indicated for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate. HUMIRA should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

Please see Brief Summary of full Prescribing Information on the last pages of this advertisement.

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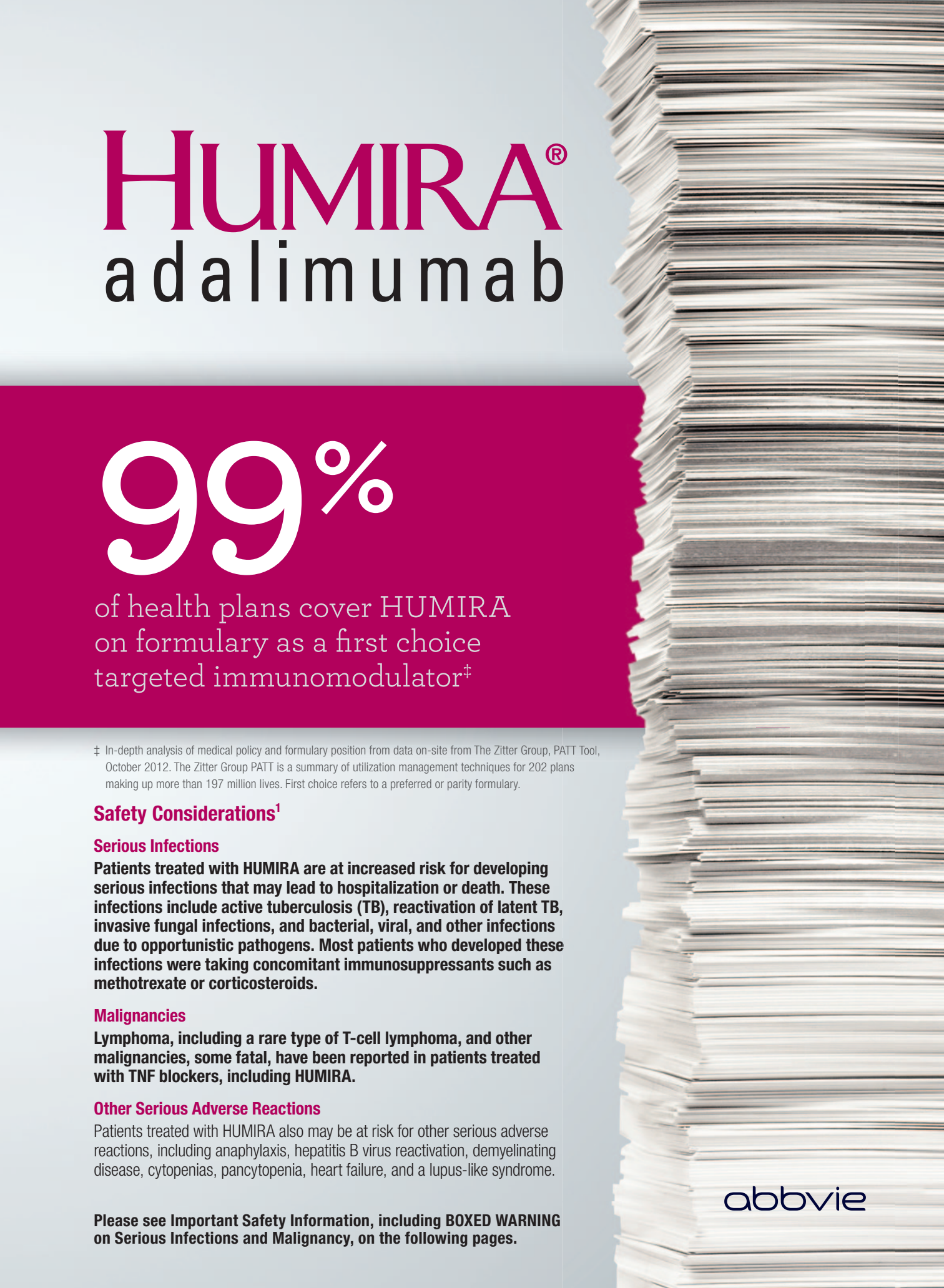

99%

of health plans cover HUMIRA on formulary as a first choice targeted immunomodulator‡

‡ In-depth analysis of medical policy and formulary position from data on-site from The Zitter Group, PATT Tool, October 2012. The Zitter Group PATT is a summary of utilization management techniques for 202 plans making up more than 197 million lives. First choice refers to a preferred or parity formulary.

Safety Considerations[1]

Serious Infections

Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death. These infections include active tuberculosis (TB), reactivation of latent TB, invasive fungal infections, and bacterial, viral, and other infections due to opportunistic pathogens. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Malignancies

Lymphoma, including a rare type of T-cell lymphoma, and other malignancies, some fatal, have been reported in patients treated with TNF blockers, including HUMIRA.

Other Serious Adverse Reactions

Patients treated with HUMIRA also may be at risk for other serious adverse reactions, including anaphylaxis, hepatitis B virus reactivation, demyelinating disease, cytopenias, pancytopenia, heart failure, and a lupus-like syndrome.

Please see Important Safety Information, including BOXED WARNING on Serious Infections and Malignancy, on the following pages.

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IMPORTANT SAFETY INFORMATION[1]

SERIOUS INFECTIONS

Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Discontinue HUMIRA if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before HUMIRA use and during therapy. Initiate treatment for latent TB prior to HUMIRA use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.**

Carefully consider the risks and benefits of treatment with HUMIRA prior to initiating therapy in patients with chronic or recurrent infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with HUMIRA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

- Do not start HUMIRA in patients with an active infection, including localized infections.
- Patients older than 65 years, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants may be at greater risk of infection.
- Consider the risks and benefits of treatment in patients with chronic or recurrent infection or with underlying conditions which may predispose them to infection, patients who have been exposed to TB, patients with a history of opportunistic infection, or patients who have resided or traveled in regions where TB or mycoses are endemic.
- Patients who develop a new infection should undergo a prompt and complete diagnostic workup, and appropriate antimicrobial therapy should be initiated.
- Drug interactions with biologic products: Concurrent use of anakinra or abatacept with HUMIRA is not recommended, as the combination of anakinra or abatacept with TNF blockers has been associated with an increased risk of serious infections. This risk has also been observed with rheumatoid arthritis patients treated with rituximab who received subsequent treatment with a TNF blocker.

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including HUMIRA. Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including HUMIRA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases has occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants.

- Consider the risks and benefits of HUMIRA treatment prior to initiating or continuing therapy in a patient with known malignancy.
- More cases of malignancies were observed among HUMIRA-treated patients compared to control patients in clinical trials.
- Non-melanoma skin cancer (NMSC) has been reported during clinical trials for HUMIRA-treated patients. Examine all patients, particularly those with history of prolonged immunosuppressant or PUVA therapy, for the presence of NMSC prior to and during treatment with HUMIRA.
- In HUMIRA clinical trials, there was an approximate 3-fold higher rate of lymphoma than expected in the general U.S. population. Patients with chronic inflammatory diseases, particularly with highly active disease and/or chronic exposure to immunosuppressant therapies, may be at higher risk of lymphoma than the general population, even in the absence of TNF blockers.
- Postmarketing cases of acute and chronic leukemia were reported with TNF blocker use.
- Approximately half of the postmarketing cases of malignancies in children, adolescents, and young adults receiving TNF blockers were lymphomas; other cases included rare malignancies associated with immunosuppression and malignancies not usually observed in children and adolescents.

HYPERSENSITIVITY

- Anaphylaxis and angioneurotic edema have been reported rarely following HUMIRA administration.
- If a serious allergic reaction occurs, stop HUMIRA and institute appropriate therapy.

HEPATITIS B VIRUS REACTIVATION

- Use of TNF blockers, including HUMIRA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases have been fatal.
- Evaluate patients at risk for HBV infection for prior evidence of HBV infection before initiating TNF blocker therapy.
- Exercise caution in patients who are carriers of HBV and monitor them during and after treatment with HUMIRA.
- Discontinue HUMIRA and begin antiviral therapy in patients who develop HBV reactivation.
- Exercise caution when considering resumption of HUMIRA therapy after appropriate treatment for HBV.

NEUROLOGIC REACTIONS

- TNF blockers, including HUMIRA, have been associated in rare cases with new onset or exacerbation of central nervous system and peripheral demyelinating diseases, including multiple sclerosis, optic neuritis, and Guillain-Barré syndrome.
- Exercise caution when considering HUMIRA for patients with these disorders.

HEMATOLOGIC REACTIONS

- Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia (e.g., thrombocytopenia, leukopenia) has been infrequently reported with HUMIRA.
- Consider stopping HUMIRA in patients with significant hematologic abnormalities.

CONGESTIVE HEART FAILURE

- Worsening or new onset congestive heart failure (CHF) may occur.
- Exercise caution in patients with CHF and monitor them carefully.

AUTOIMMUNITY

- Treatment with HUMIRA may result in the formation of autoantibodies and, rarely, in development of a lupus-like syndrome.
- Discontinue treatment if symptoms of a lupus-like syndrome develop.

IMMUNIZATIONS

- Patients on HUMIRA should not receive live vaccines.
- It is recommended that juvenile idiopathic arthritis patients, if possible, be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating HUMIRA therapy.

ADVERSE REACTIONS

- The most common adverse reactions in HUMIRA clinical trials (incidence >10%) were: infections (e.g., upper respiratory, sinusitis), injection site reactions, headache, and rash.

HUMIRA®
adalimumab

References: 1. HUMIRA Injection [package insert]. **2.** Data on file. AbbVie Inc.

Please see Brief Summary of full Prescribing Information on the following pages of this advertisement.

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HUMIRA® (adalimumab)

PROFESSIONAL BRIEF SUMMARY
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

WARNINGS: SERIOUS INFECTIONS AND MALIGNANCY
SERIOUS INFECTIONS

Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death *[see Warnings and Precautions]*. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Discontinue HUMIRA if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before HUMIRA use and during therapy. Initiate treatment for latent TB prior to HUMIRA use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.**

Carefully consider the risks and benefits of treatment with HUMIRA prior to initiating therapy in patients with chronic or recurrent infection.

Monitor patients closely for the development of signs and symptoms of infection during and after treatment with HUMIRA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy *[see Warnings and Precautions and Adverse Reactions]*.

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers including HUMIRA *[see Warnings and Precautions]*. Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including HUMIRA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases has occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all these patients had received treatment with azathioprine or 6-mercaptopurine (6–MP) concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants *[see Warnings and Precautions]*.

INDICATIONS AND USAGE

Rheumatoid Arthritis

HUMIRA is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. HUMIRA can be used alone or in combination with methotrexate or other non-biologic disease-modifying anti-rheumatic drugs (DMARDs).

Juvenile Idiopathic Arthritis

HUMIRA is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 4 years of age and older. HUMIRA can be used alone or in combination with methotrexate.

Psoriatic Arthritis

HUMIRA is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis. HUMIRA can be used alone or in combination with non-biologic DMARDs.

Ankylosing Spondylitis

HUMIRA is indicated for reducing signs and symptoms in adult patients with active ankylosing spondylitis.

Crohn's Disease

HUMIRA is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. HUMIRA is indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.

Ulcerative Colitis

HUMIRA is indicated for inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP). The effectiveness of HUMIRA has not been established in patients who have lost response to or were intolerant to TNF blockers.

Plaque Psoriasis

HUMIRA is indicated for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate. HUMIRA should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician *[see Boxed Warning and Warnings and Precautions]*.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Serious Infections

Patients treated with HUMIRA are at increased risk for developing serious infections involving various organ systems and sites that may lead to hospitalization or death *[see Boxed Warning]*. Opportunistic infections due to bacterial, mycobacterial, invasive fungal, viral, parasitic, or other opportunistic pathogens including aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, legionellosis, listeriosis, pneumocystosis and tuberculosis have been reported with TNF blockers. Patients have frequently presented with disseminated rather than localized disease.

The concomitant use of a TNF blocker and abatacept or anakinra was associated with a higher risk of serious infections in patients with rheumatoid arthritis (RA); therefore, the concomitant use of HUMIRA and these biologic products is not recommended in the treatment of patients with RA *[see Warnings and Precautions and Drug Interactions]*.

Treatment with HUMIRA should not be initiated in patients with an active infection, including localized infections. Patients greater than 65 years of age, patients with co-morbid conditions and/or patients taking concomitant immunosuppressants (such as corticosteroids or methotrexate), may be at greater risk of infection. Consider the risks and benefits of treatment prior to initiating therapy in patients:

- with chronic or recurrent infection;
- who have been exposed to tuberculosis;
- with a history of an opportunistic infection;
- who have resided or traveled in areas of endemic tuberculosis or endemic mycoses, such as histoplasmosis, coccidioidomycosis, or blastomycosis; or
- with underlying conditions that may predispose them to infection.

Tuberculosis

Cases of reactivation of tuberculosis or new tuberculosis infections have been observed in patients receiving HUMIRA, including patients who have previously received treatment for latent or active tuberculosis. Evaluate patients for tuberculosis risk factors and test for latent infection prior to initiating HUMIRA and periodically during therapy.

Treatment of latent tuberculosis infection prior to therapy with TNF blocking agents has been shown to reduce the risk of tuberculosis reactivation during therapy.

Consider anti-tuberculosis therapy prior to initiation of HUMIRA in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent tuberculosis but having risk factors for tuberculosis infection. Consultation with a physician with expertise in the treatment of tuberculosis is recommended to aid in the decision whether initiating anti-tuberculosis therapy is appropriate for an individual patient.

Strongly consider tuberculosis in the differential diagnosis in patients who develop a new infection during HUMIRA treatment, especially in patients who have previously or recently traveled to countries with a high prevalence of tuberculosis, or who have had close contact with a person with active tuberculosis.

Monitoring

Closely monitor patients for the development of signs and symptoms of infection during and after treatment with HUMIRA, including the development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy. Tests for latent tuberculosis infection may also be falsely negative while on therapy with HUMIRA.

Discontinue HUMIRA if a patient develops a serious infection or sepsis. For a patient who develops a new infection during treatment with HUMIRA, closely monitor them, perform a prompt and complete diagnostic workup appropriate for an immunocompromised patient, and initiate appropriate antimicrobial therapy.

Invasive Fungal Infections

If patients develop a serious systemic illness and they reside or travel in regions where mycoses are endemic, consider invasive fungal infection in the differential diagnosis. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider appropriate empiric antifungal therapy, taking into account both the risk for severe fungal infection and the risks of antifungal therapy, while a diagnostic workup is being performed. To aid in the management of such patients, consider consultation with a physician with expertise in the diagnosis and treatment of invasive fungal infections.

Malignancies

Consider the risks and benefits of TNF-blocker treatment including HUMIRA prior to initiating therapy in patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing a TNF blocker in patients who develop a malignancy.

Malignancies in Adults

In the controlled portions of clinical trials of some TNF-blockers, including HUMIRA, more cases of malignancies have been observed among TNF-blocker-treated adult patients compared to control-treated adult patients. During the controlled portions of 34 global HUMIRA clinical trials in adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), ulcerative colitis (UC) and plaque psoriasis (Ps), malignancies, other than non-melanoma (basal cell and squamous cell) skin cancer, were observed at a rate (95% confidence interval) of 0.6 (0.38, 0.91) per 100 patient-years among 7304 HUMIRA-treated patients versus a rate of 0.6 (0.30, 1.03) per 100 patient-years among 4232 control-treated patients (median duration of treatment of 4 months for HUMIRA-treated patients and 4 months for control-treated patients). In 47 global controlled and uncontrolled clinical trials of HUMIRA in adult patients with RA, PsA, AS, CD, UC, and Ps, the most frequently observed malignancies, other than lymphoma and NMSC, were breast, colon, prostate, lung, and melanoma. The malignancies in HUMIRA-treated patients in the controlled and uncontrolled portions of the studies were similar in type and number to what would be expected in the general U.S. population according to the SEER database (adjusted for age, gender, and race).

In controlled trials of other TNF blockers in adult patients at higher risk for malignancies (i.e., patients with COPD with a significant smoking history and cyclophosphamide-treated patients with Wegener's granulomatosis), a greater portion of malignancies occurred in the TNF blocker group compared to the control group.

Non-Melanoma Skin Cancer

During the controlled portions of 34 global HUMIRA clinical trials in adult patients with RA, PsA, AS, CD, UC, and Ps, the rate (95% confidence interval) of NMSC was 0.7 (0.49, 1.08) per 100 patient-years among HUMIRA-treated patients and 0.2 (0.08, 0.59) per 100 patient-years among control-treated patients. Examine all patients, and in particular patients with a medical history of prior prolonged immunosuppressant therapy or psoriasis patients with a history of PUVA treatment for the presence of NMSC prior to and during treatment with HUMIRA.

Lymphoma and Leukemia

In the controlled portions of clinical trials of all the TNF-blockers in adults, more cases of lymphoma have been observed among TNF-blocker-treated patients compared to control-treated patients. In the controlled portions of 34 global HUMIRA clinical trials in adult patients with RA, PsA, AS, CD, UC and Ps, 3 lymphomas occurred among 7304 HUMIRA-treated patients versus 1 among 4232 control-treated patients. In 47 global controlled and uncontrolled clinical trials of HUMIRA in adult patients with RA, PsA, AS, CD, UC and Ps with a median duration of approximately 0.6 years, including 23,036 patients and over 34,000 patient-years of HUMIRA, the observed rate of lymphomas was approximately 0.11 per 100 patient-years. This is approximately 3-fold higher than expected in the general U.S. population according to the SEER database (adjusted for age, gender, and race). Rates of lymphoma in clinical trials of HUMIRA cannot be compared to rates of lymphoma in clinical trials of other TNF blockers and may not predict the rates observed in a broader patient population. Patients with RA and other chronic inflammatory diseases, particularly those with highly active disease and/or chronic exposure to immunosuppressant therapies, may be at a higher risk (up to several fold) than the general population for the development of lymphoma, even in the absence of TNF blockers. Post-marketing cases of acute and chronic leukemia have been reported in association with TNF-blocker use in RA and other indications. Even in the absence of TNF-blocker therapy, patients with RA may be at a higher risk (approximately 2-fold) than the general population for the development of leukemia.

Malignancies in Pediatric Patients and Young Adults

Malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blockers (initiation of therapy ≤ 18 years of age), of which HUMIRA is a member *[see Boxed Warning]*. Approximately half the cases were lymphomas, including Hodgkin's and non-Hodgkin's lymphoma. The other cases represented a variety of different malignancies and included rare malignancies usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents. The malignancies occurred after a median of 30 months of therapy (range 1 to 84 months). Most of the patients were receiving concomitant immunosuppressants. These cases were reported post-marketing and are derived from a variety of sources including registries and spontaneous postmarketing reports.

Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including HUMIRA *[see Boxed Warning]*. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases has occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all of these patients had received treatment with the immunosuppressants azathioprine or 6-mercaptopurine (6–MP) concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants.

Hypersensitivity Reactions

In postmarketing experience, anaphylaxis and angioneurotic edema have been reported rarely following HUMIRA administration. If an anaphylactic or other serious allergic reaction occurs, immediately discontinue administration of HUMIRA and institute appropriate therapy. In clinical trials of HUMIRA in adults, allergic reactions overall (e.g., allergic rash, anaphylactoid reaction, fixed drug reaction, non-specified drug reaction, urticaria) have been observed in approximately 1% of patients.

Hepatitis B Virus Reactivation

Use of TNF blockers, including HUMIRA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. In some instances, HBV reactivation occurring in conjunction with TNF blocker therapy has been fatal. The majority of these reports have occurred in patients concomitantly receiving other medications that suppress the immune system, which may also contribute to HBV reactivation. Evaluate patients at risk for HBV infection for prior evidence of HBV infection before initiating TNF blocker therapy. Exercise caution in prescribing TNF blockers for patients identified as carriers of HBV. Adequate data are not available on the safety or efficacy of treating patients who are carriers of HBV with anti-viral therapy in conjunction with TNF blocker therapy to prevent HBV reactivation. In patients who develop HBV reactivation, stop HUMIRA and initiate effective anti-viral therapy with appropriate supportive treatment. The safety of resuming TNF blocker therapy after HBV reactivation is controlled is not known.

Neurologic Reactions

Use of TNF blocking agents, including HUMIRA, has been associated with rare cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of central nervous system demyelinating disease, including multiple sclerosis (MS) and optic neuritis, and peripheral demyelinating disease, including Guillain-Barré syndrome. Exercise caution in considering the use of HUMIRA in patients with preexisting or recent-onset central or peripheral nervous system demyelinating disorders.

Hematological Reactions

Rare reports of pancytopenia including aplastic anemia have been reported with TNF blocking agents. Adverse reactions of the hematologic system, including medically significant cytopenia (e.g., thrombocytopenia, leukopenia) have been infrequently reported with HUMIRA. The causal relationship of these reports to HUMIRA remains unclear. Advise all patients to seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g., persistent fever, bruising, bleeding, pallor) while on HUMIRA. Consider discontinuation of HUMIRA therapy in patients with confirmed significant hematologic abnormalities.

Use with Anakinra

Concurrent use of anakinra (an interleukin-1 antagonist) and another TNF-blocker, was associated with a greater proportion of serious infections and neutropenia and no added benefit compared with the

TNF-blocker alone in patients with RA. Therefore, the combination of HUMIRA and anakinra is not recommended *[see Drug Interactions]*.

Heart Failure

Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF blockers. Cases of worsening CHF have also been observed with HUMIRA. Exercise caution when using HUMIRA in patients who have heart failure and monitor them carefully.

Autoimmunity

Treatment with HUMIRA may result in the formation of autoantibodies and, rarely, in the development of a lupus-like syndrome. If a patient develops symptoms suggestive of a lupus-like syndrome following treatment with HUMIRA, discontinue treatment *[see Adverse Reactions]*.

Immunizations

In a placebo-controlled clinical trial of patients with RA, no difference was detected in anti-pneumococcal antibody response between HUMIRA and placebo treatment groups when the pneumococcal polysaccharide vaccine and influenza vaccine were administered concurrently with HUMIRA. Patients on HUMIRA may receive concurrent vaccinations, except for live vaccines. No data are available on the secondary transmission of infection by live vaccines in patients receiving HUMIRA.

It is recommended that JIA patients, if possible, be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating HUMIRA therapy. Patients on HUMIRA may receive concurrent vaccinations, except for live vaccines.

Use with Abatacept

In controlled trials, the concurrent administration of TNF-blockers and abatacept was associated with a greater proportion of serious infections than the use of a TNF-blocker alone; the combination therapy, compared to the use of a TNF-blocker alone, has not demonstrated improved clinical benefit in the treatment of RA. Therefore, the combination of abatacept with TNF-blockers including HUMIRA is not recommended *[see Drug Interactions]*.

ADVERSE REACTIONS

The most serious adverse reactions described elsewhere in the labeling include the following:

- Serious Infections *[see Warnings and Precautions]*
- Malignancies *[see Warnings and Precautions]*

Clinical Trials Experience

The most common adverse reaction with HUMIRA was injection site reactions. In placebo-controlled trials, 20% of patients treated with HUMIRA developed injection site reactions (erythema and/or itching, hemorrhage, pain or swelling), compared to 14% of patients receiving placebo. Most injection site reactions were described as mild and generally did not necessitate drug discontinuation.

The proportion of patients who discontinued treatment due to adverse reactions during the double-blind, placebo-controlled portion of studies in patients with RA (i.e., Studies RA-I, RA-II, RA-III and RA-IV) was 7% for patients taking HUMIRA and 4% for placebo-treated patients. The most common adverse reactions leading to discontinuation of HUMIRA in these RA studies were clinical flare reaction (0.7%), rash (0.3%) and pneumonia (0.3%).

Infections

In the controlled portions of the 34 global HUMIRA clinical trials in adult patients with RA, PsA, AS, CD, UC and Ps, the rate of serious infections was 4.6 per 100 patient-years in 7304 HUMIRA-treated patients versus a rate of 3.1 per 100 patient-years in 4232 control-treated patients. Serious infections observed included pneumonia, septic arthritis, prosthetic and post-surgical infections, erysipelas, cellulitis, diverticulitis, and pyelonephritis *[see Warnings and Precautions]*.

Tuberculosis and Opportunistic Infections

In 47 global controlled and uncontrolled clinical trials in RA, PsA, AS, CD, UC and Ps that included 23,036 HUMIRA-treated patients, the rate of reported active tuberculosis was 0.22 per 100 patient-years and the rate of positive PPD conversion was 0.08 per 100 patient-years. In a subgroup of 9396 U.S. and Canadian HUMIRA-treated patients, the rate of reported active TB was 0.07 per 100 patient-years and the rate of positive PPD conversion was 0.08 per 100 patient-years. These trials included reports of miliary, lymphatic, peritoneal, and pulmonary TB. Most of the TB cases occurred within the first eight months after initiation of therapy and may reflect recrudescence of latent disease. In these global clinical trials, cases of serious opportunistic infections have been reported at an overall rate of 0.08 per 100 patient-years. Some cases of serious opportunistic infections and TB have been fatal *[see Warnings and Precautions]*.

Autoantibodies

In the rheumatoid arthritis controlled trials, 12% of patients treated with HUMIRA and 7% of placebo-treated patients that had negative baseline ANA titers developed positive titers at week 24. Two patients out of 3046 treated with HUMIRA developed clinical signs suggestive of new-onset lupus-like syndrome. The patients improved following discontinuation of therapy. No patients developed lupus nephritis or central nervous system symptoms. The impact of long-term treatment with HUMIRA on the development of autoimmune diseases is unknown.

Liver Enzyme Elevations

There have been reports of severe hepatic reactions including acute liver failure in patients receiving TNF-blockers. In controlled Phase 3 trials of HUMIRA (40 mg SC every other week) in patients with RA, PsA, and AS with control period duration ranging from 4 to 104 weeks, ALT elevations ≥ 3 x ULN occurred in 3.5% of HUMIRA-treated patients and 1.5% of control-treated patients. Since many of these patients in these trials were also taking medications that cause liver enzyme elevations (e.g., NSAIDS, MTX), the relationship between HUMIRA and the liver enzyme elevations is not clear. In controlled Phase 3 trials of HUMIRA (initial doses of 160 mg and 80 mg, or 80 mg and 40 mg on Days 1 and 15, respectively, followed by 40 mg every other week) in patients with CD with control period duration ranging from 4 to 52 weeks, ALT elevations ≥ 3 x ULN occurred in 0.9% of HUMIRA-treated patients and 0.9% of control-treated patients. In controlled Phase 3 trials of HUMIRA (initial doses of 160 mg and 80 mg on Days 1 and 15 respectively, followed by 40 mg every other week) in patients with UC with control period duration ranging from 1 to 52 weeks, ALT elevations ≥3 x ULN occurred in 1.5% of HUMIRA-treated patients and 1.0% of control-treated patients. In controlled Phase 3 trials of HUMIRA (initial dose of 80 mg then 40 mg every other week) in patients with Ps with control period duration ranging from 12 to 24 weeks, ALT elevations ≥ 3 x ULN occurred in 1.8% of HUMIRA-treated patients and 1.8% of control-treated patients.

Immunogenicity

Patients in Studies RA-I, RA-II, and RA-III were tested at multiple time points for antibodies to adalimumab during the 6- to 12-month period. Approximately 5% (58 of 1062) of adult RA patients receiving HUMIRA developed low-titer antibodies to adalimumab at least once during treatment, which were neutralizing *in vitro*. Patients treated with concomitant methotrexate (MTX) had a lower rate of antibody development than patients on HUMIRA monotherapy (1% versus 12%). No apparent correlation of antibody development to adverse reactions was observed. With monotherapy, patients receiving every other week dosing may develop antibodies more frequently than those receiving weekly dosing. In patients receiving the recommended dosage of 40 mg every other week as monotherapy, the ACR 20 response was lower among antibody-positive patients than among antibody-negative patients. The long-term immunogenicity of HUMIRA is unknown.

In patients with JIA, adalimumab antibodies were identified in 16% of HUMIRA-treated patients. In patients receiving concomitant MTX, the incidence was 6% compared to 26% with HUMIRA monotherapy.

In patients with AS, the rate of development of antibodies to adalimumab in HUMIRA-treated patients was comparable to patients with RA.

In patients with PsA, the rate of antibody development in patients receiving HUMIRA monotherapy was comparable to patients with RA; however, in patients receiving concomitant MTX the rate was 7% compared to 1% in RA.

In patients with CD, the rate of antibody development was 3%.

In patients with moderately to severely active UC, the rate of antibody development in patients receiving HUMIRA was 5%. However, due to the limitation of the assay conditions, antibodies to adalimumab could be detected only when serum adalimumab levels were < 2 ug/ml. Among the patients whose serum adalimumab levels were < 2 ug/ml (approximately 25% of total patients studied), the immunogenicity rate was 20.7%.

In patients with Ps, the rate of antibody development with HUMIRA monotherapy was 8%. However, due to the limitation of the assay conditions, antibodies to adalimumab could be detected only when serum adalimumab levels were < 2 ug/ml. Among the patients whose serum adalimumab levels were < 2 ug/ml (approximately 40% of total patients studied), the immunogenicity rate was 20.7%. In Ps patients who were on HUMIRA monotherapy and subsequently withdrawn from the treatment, the rate of antibodies to adalimumab after retreatment was similar to the rate observed prior to withdrawal.

Other Adverse Reactions

Rheumatoid Arthritis Clinical Studies

The data described below reflect exposure to HUMIRA in 2468 patients, including 2073 exposed for 6 months, 1497 exposed for greater than one year and 1380 in adequate and well-controlled studies (Studies RA-I, RA-II, RA-III, and RA-IV). HUMIRA was studied primarily in placebo-controlled trials and in long-term follow up studies for up to 36 months duration. The population had a mean age of 54 years, 77% were female, 91% were Caucasian and had moderately to severely active rheumatoid arthritis. Most patients received 40 mg HUMIRA every other week.

Table 1 summarizes reactions reported at a rate of at least 5% in patients treated with HUMIRA 40 mg every other week compared to placebo and with an incidence higher than placebo. In Study RA-III, the types and frequencies of adverse reactions in the second year open-label extension were similar to those observed in the one-year double-blind portion.

Table 1. Adverse Reactions Reported by ≥5% of Patients Treated with HUMIRA During Placebo-Controlled Period of Pooled RA Studies (Studies RA-I, RA-II, RA-III, and RA-IV)

	HUMIRA 40 mg subcutaneous Every Other Week	Placebo
	(N=705)	(N=690)
Adverse Reaction (Preferred Term)		
Respiratory		
Upper respiratory infection	17%	13%
Sinusitis	11%	9%
Flu syndrome	7%	6%
Gastrointestinal		
Nausea	9%	8%
Abdominal pain	7%	4%
Laboratory Tests*		
Laboratory test abnormal	8%	7%
Hypercholesterolemia	6%	4%
Hyperlipidemia	7%	5%
Hematuria	5%	4%
Alkaline phosphatase increased	5%	3%
Other		
Headache	12%	8%
Rash	12%	6%
Accidental injury	10%	8%
Injection site reaction **	8%	1%
Back pain	6%	4%
Urinary tract infection	8%	5%
Hypertension	5%	3%

* Laboratory test abnormalities were reported as adverse reactions in European trials

** Does not include injection site erythema, itching, hemorrhage, pain or swelling

Juvenile Idiopathic Arthritis Clinical Studies

In general, the adverse reactions in the HUMIRA-treated pediatric patients in the juvenile idiopathic arthritis (JIA) trial were similar in frequency and type to those seen in adult patients *[see Warnings and Precautions and Adverse Reactions]*. Important findings and differences from adults are discussed in the following paragraphs.

HUMIRA was studied in 171 pediatric patients, 4 to 17 years of age, with polyarticular JIA. Severe adverse reactions reported in the study included neutropenia, streptococcal pharyngitis, increased aminotransferases, herpes zoster, myositis, metrorrhagia, appendicitis. Serious infections were observed in 4% of patients within approximately 2 years of initiation of treatment with HUMIRA and included cases of herpes simplex, pneumonia, urinary tract infection, pharyngitis, and herpes zoster.

A total of 45% of children experienced an infection while receiving HUMIRA with or without concomitant MTX in the first 16 weeks of treatment. The types of infections reported in HUMIRA-treated patients were generally similar to those commonly seen in JIA patients who are not treated with TNF blockers. Upon initiation of treatment, the most common adverse reactions occurring in the pediatric population treated with HUMIRA were injection site pain and injection site reaction (19% and 16%, respectively). A less commonly reported adverse event in children receiving HUMIRA was granuloma annulare which did not lead to discontinuation of HUMIRA treatment.

In the first 48 weeks of treatment, non-serious hypersensitivity reactions were seen in approximately 6% of children and included primarily localized allergic hypersensitivity reactions and allergic rash.

Isolated mild to moderate elevations of liver aminotransferases (ALT more common than AST) were observed in children with JIA exposed to HUMIRA alone; liver enzyme test elevations were more frequent among those treated with the combination of HUMIRA and MTX than those treated with HUMIRA alone. In general, these elevations did not lead to discontinuation of HUMIRA treatment.

In the JIA trial, 10% of patients treated with HUMIRA who had negative baseline anti-dsDNA antibodies developed positive titers after 48 weeks of treatment. No patient developed clinical signs of autoimmunity during the clinical trial.

Approximately 15% of children treated with HUMIRA developed mild-to-moderate elevations of creatine phosphokinase (CPK). Elevations exceeding 5 times the upper limit of normal were observed in several patients. CPK levels decreased or returned to normal in all patients. Most patients were able to continue HUMIRA without interruption.

Psoriatic Arthritis and Ankylosing Spondylitis Clinical Studies

HUMIRA has been studied in 395 patients with psoriatic arthritis (PsA) in two placebo-controlled trials and in an open label study and in 393 patients with ankylosing spondylitis (AS) in two placebo-controlled studies. The safety profile for patients with PsA and AS treated with HUMIRA 40 mg every other week was similar to the safety profile seen in patients with RA, HUMIRA Studies RA-I through IV.

Crohn's Disease Clinical Studies

HUMIRA has been studied in 1478 patients with Crohn's disease (CD) in four placebo-controlled and two open-label extension studies. The safety profile for patients with CD treated with HUMIRA was similar to the safety profile seen in patients with RA.

Ulcerative Colitis Clinical Studies

HUMIRA has been studied in 1010 patients with ulcerative colitis (UC) in two placebo-controlled studies and one open-label extension study. The safety profile for patients with UC treated with HUMIRA was similar to the safety profile seen in patients with RA.

Plaque Psoriasis Clinical Studies

HUMIRA has been studied in 1696 patients with plaque psoriasis (Ps) in placebo-controlled and open-label extension studies. The safety profile for patients with Ps treated with HUMIRA was similar to the safety profile seen in patients with RA with the following exceptions. In the placebo-controlled portions of the clinical trials in Ps patients, HUMIRA-treated patients had a higher incidence of arthralgia when compared to controls (3% *vs.* 1%).

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of HUMIRA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to HUMIRA exposure.

Gastrointestinal disorders: Diverticulitis, large bowel perforations including perforations associated with diverticulitis and appendiceal perforations associated with appendicitis, pancreatitis

Hepato-biliary disorders: Liver failure

Immune system disorders: Sarcoidosis

Nervous system disorders: Demyelinating disorders (e.g., optic neuritis, Guillain-Barré syndrome), cerebrovascular accident

Respiratory disorders: Interstitial lung disease, including pulmonary fibrosis, pulmonary embolism

Skin reactions: Stevens Johnson Syndrome, cutaneous vasculitis, erythema multiforme, new or worsening psoriasis (all sub-types including pustular and palmoplantar), alopecia

Vascular disorders: Systemic vasculitis, deep vein thrombosis

DRUG INTERACTIONS

Methotrexate

Although methotrexate (MTX) reduces the apparent adalimumab clearance, the data do not suggest the need for dose adjustment of either HUMIRA or MTX.

Biological Products

In clinical studies in patients with RA, an increased risk of serious infections has been seen with the combination of TNF blockers with anakinra or abatacept, with no added benefit; therefore, use of HUMIRA with abatacept or anakinra is not recommended in patients with RA *[see Warnings and Precautions]*. A higher rate of serious infections has also been observed in patients with RA treated with rituximab who received subsequent treatment with a TNF blocker. There is insufficient information to provide recommendations regarding the concomitant use of HUMIRA and other biologic products for the treatment of RA, PsA, AS, CD, UC, and Ps.

Live Vaccines

Avoid the use of live vaccines with HUMIRA *[see Warnings and Precautions]*.

Cytochrome P450 Substrates

The formation of CYP450 enzymes may be suppressed by increased levels of cytokines (e.g., TNFα, IL-6) during chronic inflammation. It is possible for a molecule that antagonizes cytokine activity, such as adalimumab, to influence the formation of CYP450 enzymes. Upon initiation or discontinuation of HUMIRA in patients being treated with

Exchange *from pg. 16*

"We conducted a lot of research into the uninsured populations in our four states and found a tremendous degree of confusion and lack of awareness of changes that are coming," says David Sandor, vice president of public affairs and corporate communications for Health Care Service Corporation (HCSC), which operates Blue Cross Blue Shield plans in Illinois, New Mexico, Oklahoma and Texas.

Sandor says the company will address the business opportunity through traditional marketing later and the educational opportunity now through Be Covered Texas and similar initiatives in the other three states.

The marketing tools include bilingual websites, printed materials that partners can co-brand, supplements in bilingual newspapers, and educational events with community organizations.

"Our program was designed to partner with anyone who might have an existing relationship with an uninsured individual to help them connect with easy to understand information about the upcoming change," he says. "We felt these would be credible partners but many lacked the sources in terms of content as well as the financial resources to scale communications in the way necessary."

Sandor says the goal is to help people prepare to make the right choices. As a not-for-profit, the organization's mission is to expand access to care for as many people as possible, he says.

The company felt it couldn't wait for insurance exchange materials from the federal government, or even approval of its proposed insurance plans. Sandor isn't even sure when HCSC will receive approval or when he can start marketing the actual products.

"I would argue that even we are a bit late to the party, considering October 1 is the enrollment date," he says.

California has already begun its campaign for Covered California and will hire 500 people for its call center. The federally operated exchanges will begin awareness campaigns this summer.

"You need to have large numbers of people in order to manage your risk effectively," Sandor says. "This is especially important in an exchange environment, where we have managed benefits and have to price those and can't underwrite as we have in the past." **MHE**

Health plans must respond to consumer feedback

Medicare Advantage could set a precedent for plan switching

JULIE MILLER
EDITOR-IN-CHIEF

NATIONAL REPORTS—Consumer ratings are no longer just "nice to have." Exchange marketplaces will begin to showcase health plan satisfaction scores in 2016, alongside price information and metal level to help shoppers choose a health plan. Higher satisfaction could translate into more business.

At the moment, however, consumers remain more confused by ratings than empowered by them, according to research conducted by PwC.

"If you look at the rating systems, there's a lot out there," says Vaughn Kauffman, a principal in PwC's Health Industries Payer Practice. "To some degree, there are too many choices from an ability to review quality scores for care, whether it's through a government program, through healthcare companies, a rating system or just Yelp or Google."

He says it's information overload and consumers are unsure of whom their trusted sources might be.

Data indicates that 48% of the 1,000 consumers surveyed have read a healthcare review online, while only 24% report they have written a review. After reading a review, 68% use them to make decisions. Only 11% of respondents indicate they have used a review of an insurance company to make a choice.

Low participation can be attributed to factors such as consumers' perception that they don't have choices, and the fact that personal influence such as word-of-mouth often trumps rating information.

"There is a notion in healthcare that decisions about health plans are made through the employer, and the primary care physician is making the choice on the specialists," says Kauffman. "Through consumer-directed healthcare and certainly the exchanges that are pushing more of a retail model, consumers are going to see that they get more choice."

He says price will be the primary vehicle for choosing a health plan but when given choices, consumers will figure in satisfaction scores. As plans adopt more narrow-network products, provider ratings will become more significant.

NOT JUST MARKETING

Kauffman says the next step is to use consumer ratings to drive better customer experiences and go to the next level by creating incentives around achievement of higher ratings.

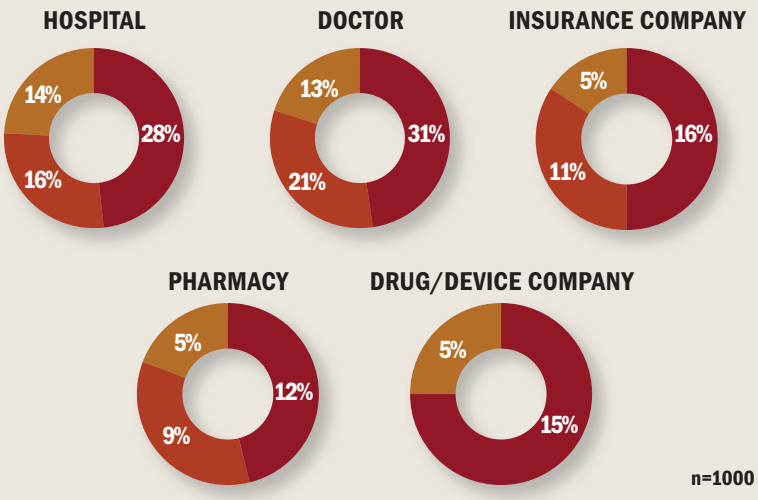
"It's not just a marketing thing," he says. "They're taking this information and combining it with other initiatives to become more consumer-centric. With health plans, that wasn't much of a priority. They are reorienting the organization around incentives all the way through the evolution."

PwC recommends:

- Ratings be sorted for relevancy among like-minded consumers;
- Health plans be aware of the Medicare Advantage precedent that allows enrollees to switch to high performing five-star plans at any time;
- Navigators be able to provide coordinated, ongoing decision support; and
- Insurers and providers combine data to create complete portraits of the consumer, especially when risk is shared.

"It's clear healthcare needs to simplify its language for consumers to better understand what their choices are," Kauffman says. "There's a long way to go to make that transition." **MHE**

CONSUMERS AND HEALTHCARE RATINGS



Source: PwC Health Research Institute Consumer Survey

Managed Medicaid plans now see more prescription claims

Significant variation seen in states and therapeutic areas

JULIA TALSMA
ADVANSTAR CONTRIBUTOR

NATIONAL REPORTS—The shift of Medicaid patients from fee-for-service to managed Medicaid during 2011 resulted in a massive shift of prescriptions nationally. Nearly half of all Medicaid prescriptions are now filled by managed Medicaid, according to a recent study released by the IMS Institute for Healthcare Informatics.

The number of monthly prescriptions dispensed through such managed care plans increased from 4.9 million in September 2011 to 12.5 million in June 2012. With many states playing a bigger role through Medicaid expansion, the trend will likely continue.

The IMS Institute studied prescription drug utilization in four states that have moved a substantial number of beneficiaries to managed care. The study analyzed the impact of care on managed Medicaid in Kentucky, New Jersey, New York and Ohio since 2011 in three therapeutic areas: antipsychotics, diabetes agents and respiratory medications.

"We compared prescription drug use for the cohort of patients for nine to 12 months before moving into a managed Medicaid plan and then nine to 12 months after the change to managed Medicaid. We also took a look at a cohort of patients who were in a fee-for-service model and remained there," says Murray Aitken, executive director, IMS Institute for Healthcare Informatics. "While it is still early days, our research reveals some important signs of impact."

All four states analyzed in the study demonstrated a greater use of antipsychotic generic drugs when available for managed Medicaid beneficiaries compared with fee-for-service Medicaid patients, Aitken says.

"The generic utilization rates for Managed Medicaid patients taking antipsychotics were between 3% and 14% higher than for fee-for-service patients in each state after the policy shifts," he says. "Patients in managed Medicaid plans in Kentucky and New Jersey were more likely to be using generic antipsychotic medicines compared to those in fee-for-service plans."

During the study period, both Zyprexa and Seroquel lost patent exclusivity. In the post-policy period, more than 55% of managed Medicaid beneficiaries in Kentucky were using antipsychotic generics. In Ohio, the percentage was about 47%, in New Jersey, it was about 48%, and in New York, it was 51%.

"There is still variation in terms of the extent to which generics are used. In addition, there is also a variation in terms of managed Medicaid plans versus fee-for-service plans," Aitken says.

DIABETES CARE

The IMS study also showed the impact upon care of diabetes patients moved to managed Medicaid plans.

In New York, more diabetes patients received diabetes drugs, with an increase in the average number of prescriptions in the post-policy shift period of 5%, and a change from an annualized average of 11.2 scripts per patient to 11.8 scripts per patient. In the fee-for-service cohort, the average number of diabetes medications remained stable.

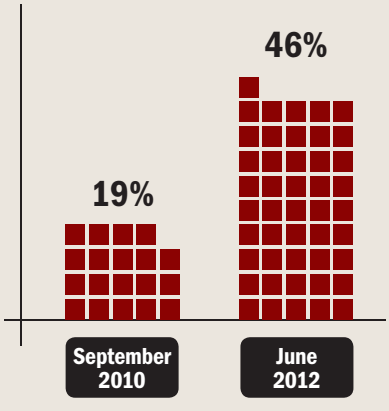
"Aggressive management of diabetes is understood by the managed Medicaid plans to be an important way to manage the overall costs. With the prescription drug benefits being carved in now, there is a greater incentive for the plans to be optimizing the treatment overall for the patient," Aitken says. "We also saw a greater use of metformin and the lower-cost drugs for the treatment of diabetes."

Edith A. Rosato, RPh, IOM, CEO of the Academy of Managed Care Pharmacy said in a press statement that the academy was encouraged by the positive results of the study on patients who received care through managed Medicaid programs.

"Given the variability in state programs, managed Medicaid plans will need to be continually evaluated," Rosato said. "Initial findings suggest that patients could be better managed in these programs, particularly when the drug benefit is carved into a state's managed care plan rather than maintained in a fee-for-service program." **MHE**

This article originally ran in Drug Topics.

GROWTH IN PRESCRIPTIONS HANDLED BY MANAGED MEDICAID



Source: IMS Institute for Healthcare Informatics, April 2013

Medicare Advantage plans escape new rate cuts

CMS revises rates for 2014 following heated protests from Congress, beneficiaries

BY JILL WECHSLER

Jill Wechsler, a veteran reporter, has been covering Capitol Hill since 1994.

April was positive for Medicare Advantage (MA) plans. The Centers for Medicare and Medicaid Services (CMS) pulled back on its proposal to reduce plan payments for 2014, a policy that caused a ruckus in the industry and on Capitol Hill.

Thousands of the 14 million MA plan members wrote to members of Congress in protest, prompting more than 160 legislators to press CMS to re-evaluate its rate-setting formula.

Health and Human Services (HHS) Secretary Kathleen Sebelius responded, evidently hoping that the move would help win Republican support for confirmation of Marilynn Tavenner as CMS administrator.

MA plans still face rate reductions steeper than cost trends, largely attributed to payment reforms enacted in the Patient Protection and Affordable Care Act. A new excise tax will raise costs and budget cuts will dampen revenues. Final rates, which will vary greatly by county, benefit design and other factors, will be shaped by changes in how CMS sets benchmarks for plan bids, adjusts for coding intensity, awards bonus pay to plans achieving higher star ratings, and implements other policy revisions. However, the final fee will be more attractive than what was proposed a few months ago.

In mid-February, CMS proposed a 2.2% reduction in cost trends, a number that reflected the actuaries' usual practice of basing rates on current law. That assumed a 25% reduction in doctors' fees under the sustainable growth rate (SGR) formula. HHS agreed with critics that policymakers will prop up Medicare provider fees and that MA plans will end up paying doctors prevailing rates. Instead of a sharp drop in trend, the April final call letter projected a 3.3% growth rate.

Consequently, MA plan rates are projected to decline 2% to 3% for 2014, as opposed to the 7% to 8% cut previously anticipated.

FUTURE REFORMS

The decision increases pressure on Congress and the White House to tackle the doc fix sooner, rather than later. While another short-term SGR patch is likely, there is greater support for a more permanent solution for the flawed payment formula.

A serious move to revise the SGR could encompass broader changes in the traditional Medicare program, which are surfacing in federal budget negotiations. One proposal is to combine Medicare Part A and Part B coverage to create a single deductible and cap on out-of-pocket costs for both programs. Beneficiary protection from catastrophic costs would reduce the need for Medigap plans with first dollar coverage, making seniors more sensitive to costs and likely to avoid unnecessary care.

Further MA reforms would be part of the package. The Medicare Payment Advisory Commission acknowledged in a March report that the gap is closing between MA plan payments and traditional Medicare, but there's still room to achieve parity. The Government Accountability Office similarly noted in a March report that MA plans received $5 billion in overpayments between 2010 and 2012 from upcoding risk scores that classified members as sicker than normal.

The promise of the MA program is that plans will reduce Medicare spending by better coordinating care for elderly patients with multiple chronic conditions and high costs. The challenge is to curb expenditures sufficiently to support the reduced plan payments. **MHE**

DIFICID® (fidaxomicin) tablets Granted New Technology Add-on Payment (NTAP) Status[1]

CMS* has granted a NTAP for DIFICID administered in the inpatient hospital setting to treat *Clostridium difficile*-associated diarrhea (CDAD)

- CMS will reimburse hospitals an additional amount up to $868 per case in fiscal year 2013, not for every case involving DIFICID, but only where the costs of the entire case exceed the MS-DRG† payment amount
- The CMS NTAP policy is designed to support timely access to innovative new therapies used to treat Medicare beneficiaries in the inpatient setting that provide a substantial clinical improvement over existing therapies
- DIFICID is the first oral medication ever approved for a NTAP

*Centers for Medicare & Medicaid Services.
†Medical severity diagnosis-related groups.

For more information about DIFICID, please visit **DIFICID.com**.

For a copy of the CMS final rule regarding FY2013 Add-On Payments, please visit **http://federalregister.gov/a/2012-19079**.

Indications and Usage

- DIFICID is a macrolide antibacterial drug indicated in adults ≥ 18 years of age for treatment of *Clostridium difficile*-associated diarrhea
- To reduce the development of drug-resistant bacteria and maintain the effectiveness of DIFICID and other antibacterial drugs, DIFICID should be used only to treat infections that are proven or strongly suspected to be caused by *Clostridium difficile*

Important Safety Information

- DIFICID is contraindicated in patients with hypersensitivity to fidaxomicin or to any of the excipients in the formulation
- DIFICID should not be used for systemic infections
- Only use DIFICID for infection proven or strongly suspected to be caused by *C. difficile*. Prescribing DIFICID in the absence of a proven or strongly suspected *C. difficile* infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria
- The most common adverse reactions are nausea (11%), vomiting (7%), abdominal pain (6%), gastrointestinal hemorrhage (4%), anemia (2%), and neutropenia (2%)

Please see brief summary of full prescribing information for DIFICID on following page.

Reference: 1. Department of Health and Human Services, *Centers for Medicare and Medicaid Services, Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Fiscal Year 2013 Rates*, 77 Fed. Reg. 53258-53750 (August 31, 2012).

OPTIMER PHARMACEUTICALS, INC.

DIFICID® (fidaxomicin) tablets 200 mg

DIFICID®

(fidaxomicin) tablets

Brief Summary of Prescribing Information

1 INDICATIONS AND USAGE

To reduce the development of drug-resistant bacteria and maintain the effectiveness of DIFICID and other antibacterial drugs, DIFICID should be used only to treat infections that are proven or strongly suspected to be caused by *Clostridium difficile*.

1.1 *Clostridium difficile*-Associated Diarrhea

DIFICID is a macrolide antibacterial drug indicated in adults (≥18 years of age) for treatment of *Clostridium difficile*-associated diarrhea (CDAD).

4 CONTRAINDICATIONS

Hypersensitivity to fidaxomicin or to any of the excipients in the formulation *[see Description (11) in the full prescribing information].*

5 WARNINGS AND PRECAUTIONS

5.1 Not for Systemic Infections

Since there is minimal systemic absorption of fidaxomicin, DIFICID is not effective for treatment of systemic infections.

5.2 Development of Drug Resistant Bacteria

Prescribing DIFICID in the absence of a proven or strongly suspected *C. difficile* infection is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse event rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of any other drug and may not reflect the rates observed in practice.

The safety of DIFICID 200 mg tablets taken twice a day for 10 days was evaluated in 564 patients with CDAD in two active-comparator controlled trials with 86.7% of patients receiving a full course of treatment.

Thirty-three patients receiving DIFICID (5.9%) withdrew from trials as a result of adverse reactions (AR). The types of AR resulting in withdrawal from the study varied considerably. Vomiting was the primary adverse reaction leading to discontinuation of dosing; this occurred at an incidence of 0.5% in both the fidaxomicin and vancomycin patients in Phase 3 studies.

Table 1. Selected Adverse Reactions with an Incidence of ≥2% Reported in DIFICID Patients in Controlled Trials

	DIFICID (N=564)	Vancomycin (N=583)
System Organ Class Preferred Term	**n (%)**	**n (%)**
Blood and Lymphatic System Disorders		
Anemia	14 (2%)	12 (2%)
Neutropenia	14 (2%)	6 (1%)
Gastrointestinal Disorders		
Nausea	62 (11%)	66 (11%)
Vomiting	41 (7%)	37 (6%)
Abdominal Pain	33 (6%)	23 (4%)
Gastrointestinal Hemorrhage	20 (4%)	12 (2%)

The following adverse reactions were reported in <2% of patients taking DIFICID tablets in controlled trials:

Gastrointestinal Disorders: abdominal distension, abdominal tenderness, dyspepsia, dysphagia, flatulence, intestinal obstruction, megacolon

Investigations: increased blood alkaline phosphatase, decreased blood bicarbonate, increased hepatic enzymes, decreased platelet count

Metabolism and Nutrition Disorders: hyperglycemia, metabolic acidosis

Skin and Subcutaneous Tissue Disorders: drug eruption, pruritus, rash

6.2 Post Marketing Experience

Adverse reactions reported in the post marketing setting arise from a population of unknown size and are voluntary in nature. As such, reliability in estimating their frequency or in establishing a causal relationship to drug exposure is not always possible.

Acute hypersensitivity reactions have been reported during post marketing such as rash, pruritus, angioedema and dyspnea.

7 DRUG INTERACTIONS

Fidaxomicin and its main metabolite, OP-1118, are substrates of the efflux transporter, P-glycoprotein (P-gp), which is expressed in the gastrointestinal tract.

7.1 Cyclosporine

Cyclosporine is an inhibitor of multiple transporters, including P-gp. When cyclosporine was co-administered with DIFICID, plasma concentrations of fidaxomicin and OP-1118 were significantly increased but remained in the ng/mL range *[see Clinical Pharmacology (12.3) in the full prescribing information].*

Concentrations of fidaxomicin and OP-1118 may also be decreased at the site of action (i.e., gastrointestinal tract) via P-gp inhibition; however, concomitant P-gp inhibitor use had no attributable effect on safety or treatment outcome of fidaxomicin-treated patients in controlled clinical trials. Based on these results, fidaxomicin may be co-administered with P-gp inhibitors and no dose adjustment is recommended.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B. Reproduction studies have been performed in rats and rabbits by the intravenous route at doses up to 12.6 and 7 mg/kg, respectively. The plasma exposures (AUC_{0-t}) at these doses were approximately 200- and 66-fold that in humans, respectively, and have revealed no evidence of harm to the fetus due to fidaxomicin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

8.3 Nursing Mothers

It is not known whether fidaxomicin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when DIFICID is administered to a nursing woman.

8.4 Pediatric Use

The safety and effectiveness of DIFICID in patients <18 years of age have not been established.

8.5 Geriatric Use

Of the total number of patients in controlled trials of DIFICID, 50% were 65 years of age and over, while 31% were 75 and over. No overall differences in safety or effectiveness of fidaxomicin compared to vancomycin were observed between these subjects and younger subjects.

In controlled trials, elderly patients (≥65 years of age) had higher plasma concentrations of fidaxomicin and its main metabolite, OP-1118, versus non-elderly patients (<65 years of age) *[see Clinical Pharmacology (12.3) in the full prescribing information].* However, greater exposures in elderly patients were not considered to be clinically significant. No dose adjustment is recommended for elderly patients.

10 OVERDOSAGE

No cases of acute overdose have been reported in humans. No drug-related adverse effects were seen in dogs dosed with fidaxomicin tablets at 9600 mg/day (over 100 times the human dose, scaled by weight) for 3 months.

Manufactured for Optimer Pharmaceuticals, Inc., San Diego CA 92121 by Patheon, Inc.

DIFICID® is a registered trademark of Optimer Pharmaceuticals, Inc. in the United States and other countries.

Product protected by US Patent Nos. 7,378,508; 7,507,564; 7,863,249; and 7,906,489

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Supreme Court will define generic drugmakers' liability

Federal law does not allow generic pharma companies to deviate from brand formula

BY ALEXANDER B. REICH

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In late March, the U.S. Supreme Court heard arguments in a case being watched closely by pharmaceutical companies and federal regulators. The case will require the Court to clarify the legal remedies available to patients who are injured because they took generic drugs.

Karen Bartlett suffered horrific injuries following a reaction to the generic form of a relatively mild prescription anti-inflammatory medication that her physician prescribed in December 2004 for shoulder pain. Her injuries included blindness, lung and esophageal damage, and a skin condition known as toxic epidermal necrolysis, requiring two months in a hospital burn unit and months more in a medically induced coma. Bartlett sued the manufacturer of the drug, alleging the product was defective.

After 14 days of trial, a New Hampshire jury awarded her $21 million.

JUDICIAL PRECEDENT

The drug manufacturer, Mutual Pharmaceutical Company, appealed, arguing that it could not have changed the drug's design because federal law does not allow generic pharmaceutical companies to deviate from the brand-name drug being copied.

Bartlett's case will fit into a developing line of judicial precedent defining the limits of generic drugmakers' liability. In 2011, the Supreme Court held that generic drugmakers could not be sued for inadequate labels or warnings because such companies have no control over labeling, which is dictated by requirements imposed by the FDA on the generic drug's brand-name counterpart.

In the Bartlett case, Mutual claims that the same principle should apply to Bartlett's lawsuit because, similar to labeling, the recipe for a generic drug is dictated by its brand-name equivalent.

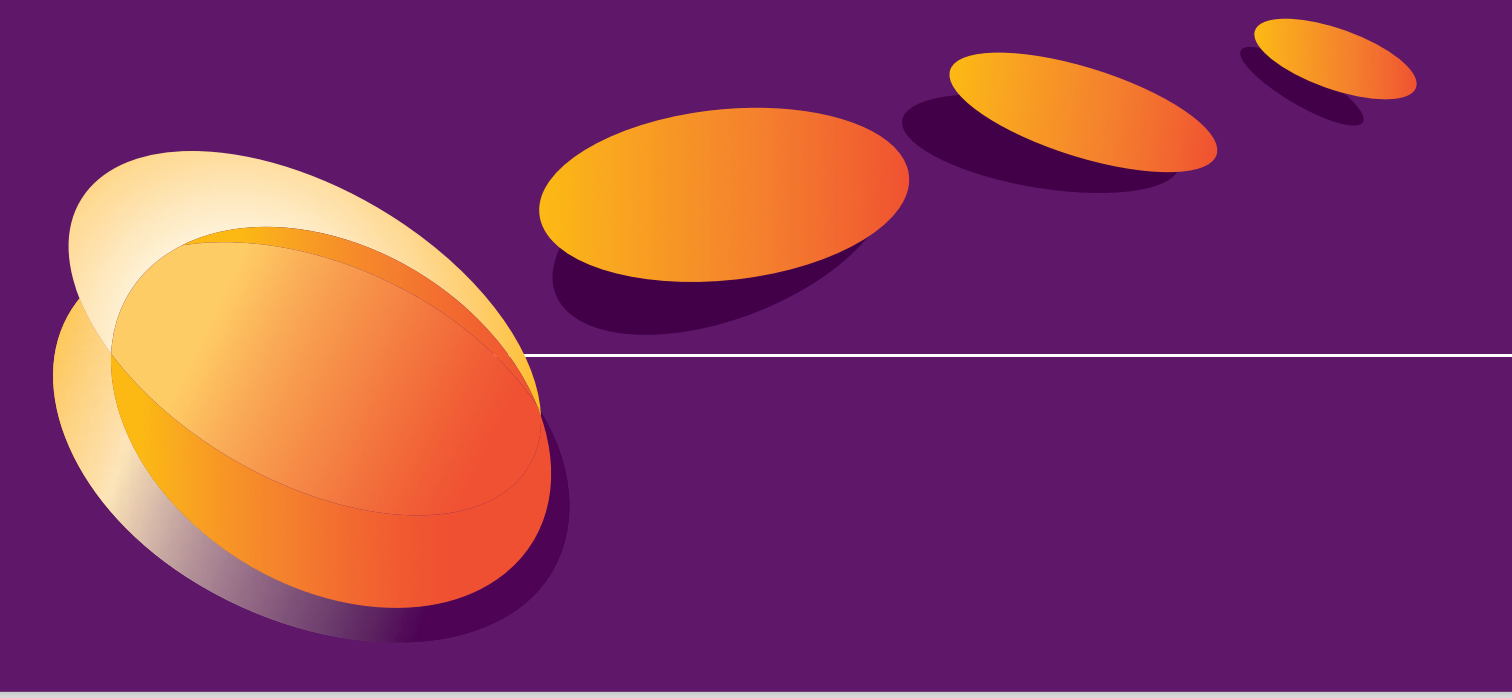
FAR-REACHING IMPLICATIONS

If the Supreme Court sides with Bartlett, generic drug manufacturers express concern that the decisions of individual juries would outweigh the authority of the federal agencies charged with regulating the manufacture of medications. Patient advocacy groups contend that Bartlett's case differs from the 2009 Supreme Court case limiting liability for the labeling of generic drugs because, although federal law may require a drug company to label its products a certain way, drug companies do not enjoy an absolute right to sell their products.

The outcome of Bartlett's case could affect millions of people: Generic drugs now account for 80% of all prescriptions in the United States, and most states permit pharmacists to dispense a generic in place of a brand-name drug.

Until the Supreme Court decides the latest case in this developing legal landscape sometime this summer, it remains uncertain whether injury-causing generic and brand-name drugs can give rise to the same liability in addition to the same potential side effects. **MHE**

This column is written for informational purposes only and should not be construed as legal advice.



BRILINTA plus aspirin significantly reduced the primary composite end point of CV death, myocardial infarction (MI),* or stroke by 16% RRR† (ARR‡ 1.9%) vs clopidogrel plus aspirin at 12 months§

At 12 months, for BRILINTA plus aspirin vs clopidogrel plus aspirin, there was no significant difference in Total Major Bleeding (11.6% vs 11.2%) and a somewhat greater risk of Non–CABG-related Major plus Minor Bleeding (8.7% vs 7.0%) and Non–CABG-related Major Bleeding (4.5% vs 3.8%), respectively

INDICATIONS

BRILINTA is indicated to reduce the rate of thrombotic cardiovascular (CV) events in patients with acute coronary syndrome (ACS) (unstable angina, non–ST-elevation myocardial infarction, or ST-elevation myocardial infarction). BRILINTA has been shown to reduce the rate of a combined end point of CV death, myocardial infarction (MI), or stroke compared to clopidogrel. The difference between treatments was driven by CV death and MI with no difference in stroke. In patients treated with PCI, it also reduces the rate of stent thrombosis.

BRILINTA has been studied in ACS in combination with aspirin. Maintenance doses of aspirin >100 mg decreased the effectiveness of BRILINTA. Avoid maintenance doses of aspirin >100 mg daily.

IMPORTANT SAFETY INFORMATION ABOUT BRILINTA

WARNING: BLEEDING RISK

- BRILINTA, like other antiplatelet agents, can cause significant, sometimes fatal, bleeding
- Do not use BRILINTA in patients with active pathological bleeding or a history of intracranial hemorrhage
- Do not start BRILINTA in patients planned to undergo urgent coronary artery bypass graft surgery (CABG). When possible, discontinue BRILINTA at least 5 days prior to any surgery
- Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), CABG, or other surgical procedures in the setting of BRILINTA
- If possible, manage bleeding without discontinuing BRILINTA. Stopping BRILINTA increases the risk of subsequent cardiovascular events

WARNING: ASPIRIN DOSE AND BRILINTA EFFECTIVENESS

- Maintenance doses of aspirin above 100 mg reduce the effectiveness of BRILINTA and should be avoided. After any initial dose, use with aspirin 75 mg - 100 mg per day

Please read additional Important Safety Information on next page and Brief Summary of Prescribing Information, including Boxed WARNINGS, on following pages.

In the treatment of acute coronary syndrome (ACS)

BRILINTA provided superior reductions versus clopidogrel in thrombotic CV events, including CV death

The difference between treatments was driven by CV death and MI with no difference in stroke

CONTRAINDICATIONS

- BRILINTA is contraindicated in patients with a history of intracranial hemorrhage and active pathological bleeding such as peptic ulcer or intracranial hemorrhage. BRILINTA is contraindicated in patients with severe hepatic impairment because of a probable increase in exposure; it has not been studied in these patients. Severe hepatic impairment increases the risk of bleeding because of reduced synthesis of coagulation proteins. BRILINTA is also contraindicated in patients with hypersensitivity (e.g. angioedema) to ticagrelor or any component of the product

WARNINGS AND PRECAUTIONS

- Moderate Hepatic Impairment: Consider the risks and benefits of treatment, noting the probable increase in exposure to ticagrelor
- Premature discontinuation increases the risk of MI, stent thrombosis, and death
- Dyspnea was reported in 14% of patients treated with BRILINTA and in 8% of patients taking clopidogrel. Dyspnea resulting from BRILINTA is self-limiting. Rule out other causes
- BRILINTA is metabolized by CYP3A4/5. Avoid use with strong CYP3A inhibitors and potent CYP3A inducers. Avoid simvastatin and lovastatin doses >40 mg
- Monitor digoxin levels with initiation of, or any change in, BRILINTA therapy

ADVERSE REACTIONS

- The most commonly observed adverse reactions associated with the use of BRILINTA vs clopidogrel were Total Major Bleeding (11.6% vs 11.2%) and dyspnea (14% vs 8%)
- In clinical studies, BRILINTA has been shown to increase the occurrence of Holter-detected bradyarrhythmias. PLATO excluded patients at increased risk of bradycardic events. Consider the risks and benefits of treatment

*Excluding silent MI.

†RRR=relative risk reduction.

‡ARR=absolute risk reduction.

§The PLATO (PLATelet Inhibition and Patient Outcomes) study was a randomized, double-blind, parallel-group trial comparing BRILINTA (180-mg loading dose, 90 mg twice daily thereafter) and clopidogrel (300-mg to 600-mg loading dose, 75 mg daily thereafter) for the prevention of CV events in 18,624 patients admitted to the hospital within 24 hours of symptom onset of ACS (UA [unstable angina], NSTEMI [non–ST-elevation MI], or STEMI [ST-elevation MI]). Patients were treated for at least 6 months and up to 12 months. BRILINTA and clopidogrel were studied with aspirin and other standard therapies.

For more information, go to BRILINTAtouchpoints.com

Reference: BRILINTA Prescribing Information, AstraZeneca.

BRILINTA® ticagrelor tablets

AstraZeneca

BRILINTA® *(ticagrelor)* Tablets

WARNING: BLEEDING RISK

- **BRILINTA, like other antiplatelet agents, can cause significant, sometimes fatal bleeding [see WARNINGS AND PRECAUTIONS and ADVERSE REACTIONS].**
- **Do not use BRILINTA in patients with active pathological bleeding or a history of intracranial hemorrhage [see CONTRAINDICATIONS].**
- **Do not start BRILINTA in patients planned to undergo urgent coronary artery bypass graft surgery (CABG). When possible, discontinue BRILINTA at least 5 days prior to any surgery [see WARNINGS AND PRECAUTIONS].**
- **Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), CABG, or other surgical procedures in the setting of BRILINTA [see WARNINGS AND PRECAUTIONS].**
- **If possible, manage bleeding without discontinuing BRILINTA. Stopping BRILINTA increases the risk of subsequent cardiovascular events [see WARNINGS AND PRECAUTIONS].**

WARNING: ASPIRIN DOSE AND BRILINTA EFFECTIVENESS

- **Maintenance doses of aspirin above 100 mg reduce the effectiveness of BRILINTA and should be avoided. After any initial dose, use with aspirin 75-100 mg per day [see WARNINGS AND PRECAUTIONS and CLINICAL STUDIES (14) in full Prescribing Information].**

BRIEF SUMMARY of PRESCRIBING INFORMATION:

For full Prescribing Information, see package insert.

INDICATIONS AND USAGE

Acute Coronary Syndromes

BRILINTA is a $P2Y_{12}$ platelet inhibitor indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS) (unstable angina, non-ST elevation myocardial infarction, or ST elevation myocardial infarction). BRILINTA has been shown to reduce the rate of a combined endpoint of cardiovascular death, myocardial infarction or stroke compared to clopidogrel. The difference between treatments was driven by CV death and MI with no difference in stroke. In patients treated with PCI, it also reduces the rate of stent thrombosis [*see Clinical Studies (14) in full Prescribing Information*]. BRILINTA has been studied in ACS in combination with aspirin. Maintenance doses of aspirin above 100 mg decreased the effectiveness of BRILINTA. Avoid maintenance doses of aspirin above 100 mg daily [*see Warnings and Precautions* and *Clinical Studies (14) in full Prescribing Information*].

DOSAGE AND ADMINISTRATION

Initiate BRILINTA treatment with a 180 mg (two 90 mg tablets) loading dose and continue treatment with 90 mg twice daily. After the initial loading dose of aspirin (usually 325 mg), use BRILINTA with a daily maintenance dose of aspirin of 75-100 mg. ACS patients who have received a loading dose of clopidogrel may be started on BRILINTA. BRILINTA can be administered with or without food. A patient who misses a dose of BRILINTA should take one 90 mg tablet (their next dose) at its scheduled time.

CONTRAINDICATIONS

History of Intracranial Hemorrhage BRILINTA is contraindicated in patients with a history of intracranial hemorrhage (ICH) because of a high risk of recurrent ICH in this population [*see Clinical Studies (14) in full Prescribing Information*].

Active Bleeding BRILINTA is contraindicated in patients with active pathological bleeding such as peptic ulcer or intracranial hemorrhage [*see Warnings and Precautions (5.1)* and *Adverse Reactions (6.1) in full Prescribing Information*].

Severe Hepatic Impairment BRILINTA is contraindicated in patients with severe hepatic impairment because of a probable increase in exposure, and it has not been studied in these patients. Severe hepatic impairment increases the risk of bleeding because of reduced synthesis of coagulation proteins [*see Clinical Pharmacology (12.3) in full Prescribing Information*].

Hypersensitivity BRILINTA is contraindicated in patients with hypersensitivity (e.g. angioedema) to ticagrelor or any component of the product [*see Adverse Reactions (6.1) in full Prescribing Information*].

WARNINGS AND PRECAUTIONS

General Risk of Bleeding

Drugs that inhibit platelet function including BRILINTA increase the risk of bleeding. BRILINTA increased the overall risk of bleeding (Major + Minor) to a somewhat greater extent than did clopidogrel. The increase was seen for non-CABG-related bleeding, but not for CABG-related bleeding. Fatal and life-threatening bleeding rates were not increased [*see Adverse Reactions (6.1) in full Prescribing Information*]. In general, risk factors for bleeding include older age, a history of bleeding disorders, performance of percutaneous invasive procedures and concomitant use of medications that increase the risk of bleeding (e.g., anticoagulant and fibrinolytic therapy, higher doses of aspirin, and chronic nonsteroidal anti-inflammatory drugs [NSAIDS]). When possible, discontinue BRILINTA five days prior to surgery. Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, PCI, CABG, or other surgical procedures, even if the patient does not have any signs of bleeding. If possible, manage bleeding without discontinuing BRILINTA. Stopping BRILINTA increases the risk of subsequent cardiovascular events [*see Warnings and Precautions (5.5)* and *Adverse Reactions (6.1) in full Prescribing Information*].

Concomitant Aspirin Maintenance Dose In PLATO, use of BRILINTA with maintenance doses of aspirin above 100 mg decreased the effectiveness of BRILINTA. Therefore, after the initial loading dose of aspirin (usually 325 mg), use BRILINTA with a maintenance dose of aspirin of 75-100 mg [*see Dosage and Administration* and *Clinical Studies (14) in full Prescribing Information*].

Moderate Hepatic Impairment BRILINTA has not been studied in patients with moderate hepatic impairment. Consider the risks and benefits of treatment, noting the probable increase in exposure to ticagrelor.

Dyspnea In PLATO, dyspnea was reported in 14% of patients treated with BRILINTA and in 8% of patients taking clopidogrel. Dyspnea was usually mild to moderate in intensity and often resolved during continued treatment, but occasionally required discontinuation (0.9% of patients taking BRILINTA versus 0.1% of patients taking clopidogrel). If a patient develops new, prolonged, or worsened dyspnea during treatment with BRILINTA, exclude underlying diseases that may require treatment. If dyspnea is determined to be related to BRILINTA, no specific treatment is required; continue BRILINTA without interruption. In the case of intolerable dyspnea requiring discontinuation of BRILINTA, consider prescribing another antiplatelet agent. In a substudy, 199 patients from PLATO underwent pulmonary function testing irrespective of whether they reported dyspnea. There was no significant difference between treatment groups for FEV_1. There was no indication of an adverse effect on pulmonary function assessed after one month or after at least 6 months of chronic treatment.

Discontinuation of BRILINTA Avoid interruption of BRILINTA treatment. If BRILINTA must be temporarily discontinued (e.g., to treat bleeding or for elective surgery), restart it as soon as possible. Discontinuation of BRILINTA will increase the risk of myocardial infarction, stent thrombosis, and death.

Strong Inhibitors of Cytochrome CYP3A Ticagrelor is metabolized by CYP3A4/5. Avoid use with strong CYP3A inhibitors, such as atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole [*see Drug Interactions (7.1)* and *Clinical Pharmacology (12.3) in full Prescribing Information*].

Cytochrome CYP3A Potent Inducers Avoid use with potent CYP3A inducers, such as rifampin, dexamethasone, phenytoin, carbamazepine, and phenobarbital [*see Drug Interactions (7.2)* and *Clinical Pharmacology (12.3) in full Prescribing Information*].

ADVERSE REACTIONS

Clinical Trials Experience

The following adverse reactions are also discussed elsewhere in the labeling:

- Dyspnea [*see Warnings and Precautions (5.4) in full Prescribing Information*]

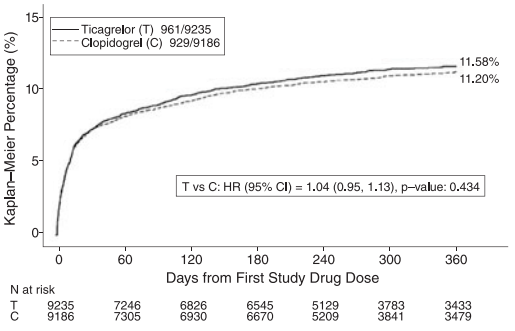
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. BRILINTA has been evaluated for safety in more than 10000 patients, including more than 3000 patients treated for more than 1 year.

Bleeding PLATO used the following bleeding severity categorization:

- Major bleed – fatal/life-threatening. Any one of the following: fatal; intracranial; intrapericardial bleed with cardiac tamponade; hypovolemic shock or severe hypotension due to bleeding and requiring pressors or surgery; clinically overt or apparent bleeding associated with a decrease in hemoglobin (Hb) of more than 5 g/dL; transfusion of 4 or more units (whole blood or packed red blood cells (PRBCs)) for bleeding.
- Major bleed – other. Any one of the following: significantly disabling (e.g., intraocular with permanent vision loss); clinically overt or apparent bleeding associated with a decrease in Hb of 3 g/dL; transfusion of 2-3 units (whole blood or PRBCs) for bleeding.
- Minor bleed. Requires medical intervention to stop or treat bleeding (e.g., epistaxis requiring visit to medical facility for packing).
- Minimal bleed. All others (e.g., bruising, bleeding gums, oozing from injection sites, etc.) not requiring intervention or treatment.

Figure 1 shows major bleeding events over time. Many events are early, at a time of coronary angiography, PCI, CABG, and other procedures, but the risk persists during later use of antiplatelet therapy.

Figure 1 Kaplan-Meier estimate of time to first PLATO-defined 'Total Major' bleeding event



Annualized rates of bleeding are summarized in Table 1 below. About half of the bleeding events were in the first 30 days.

Table 1 Non-CABG related bleeds (KM%)

	BRILINTA N=9235	Clopidogrel N=9186
Total (Major + Minor)	8.7	7.0
Major	4.5	3.8
Fatal/Life-threatening	2.1	1.9
Fatal	0.2	0.2
Intracranial (Fatal/Life-threatening)	0.3	0.2

As shown in Table 1, BRILINTA was associated with a somewhat greater risk of non-CABG bleeding than was clopidogrel. No baseline demographic factor altered the relative risk of bleeding with BRILINTA compared to clopidogrel. In PLATO, 1584 patients underwent CABG surgery. The percentages of those patients who bled are shown in Table 2. Rates were very high but similar for BRILINTA and clopidogrel.

Table 2 CABG bleeds (KM%)

	Patients with CABG	
	BRILINTA N=770	**Clopidogrel N=814**
Total Major	85.8	86.9
Fatal/Life-threatening	48.1	47.9
Fatal	0.9	1.1

Although the platelet inhibition effect of BRILINTA has a faster offset than clopidogrel in *in vitro* tests and BRILINTA is a reversibly binding $P2Y_{12}$ inhibitor, PLATO did not show an advantage of BRILINTA compared to clopidogrel for CABG-related bleeding. When antiplatelet therapy was stopped 5 days before CABG, major bleeding occurred in 75% of BRILINTA treated patients and 79% on clopidogrel. No data exist with BRILINTA regarding a hemostatic benefit of platelet transfusions.

Drug Discontinuation In PLATO, the rate of study drug discontinuation attributed to adverse reactions was 7.4% for BRILINTA and 5.4% for clopidogrel. Bleeding caused permanent discontinuation of study drug in 2.3% of BRILINTA patients and 1.0% of clopidogrel patients. Dyspnea led to study drug discontinuation in 0.9% of BRILINTA and 0.1% of clopidogrel patients.

Common Adverse Events A variety of non-hemorrhagic adverse events occurred in PLATO at rates of 3% or more. These are shown in Table 3. In the absence of a placebo control, whether these are drug related cannot be determined in most cases, except where they are more common on BRILINTA or clearly related to the drug's pharmacologic effect (dyspnea).

Table 3 Percentage of patients reporting non-hemorrhagic adverse events at least 3% or more in either group

	BRILINTA N=9235	**Clopidogrel N=9186**
Dyspnea[1]	13.8	7.8
Headache	6.5	5.8
Cough	4.9	4.6
Dizziness	4.5	3.9
Nausea	4.3	3.8
Atrial fibrillation	4.2	4.6
Hypertension	3.8	4.0
Non-cardiac chest pain	3.7	3.3
Diarrhea	3.7	3.3
Back pain	3.6	3.3
Hypotension	3.2	3.3
Fatigue	3.2	3.2
Chest pain	3.1	3.5

[1] Includes: dyspnea, dyspnea exertional, dyspnea at rest, nocturnal dyspnea, dyspnea paroxysmal nocturnal

Bradycardia In clinical studies BRILINTA has been shown to increase the occurrence of Holter-detected bradyarrhythmias (including ventricular pauses). PLATO excluded patients at increased risk of bradycardic events (e.g., patients who have sick sinus syndrome, 2nd or 3rd degree AV block, or bradycardic-related syncope and not protected with a pacemaker). In PLATO, syncope, pre-syncope and loss of consciousness were reported by 1.7% and 1.5% of BRILINTA and clopidogrel patients, respectively. In a Holter substudy of about 3000 patients in PLATO, more patients had ventricular pauses with BRILINTA (6.0%) than with clopidogrel (3.5%) in the acute phase; rates were 2.2% and 1.6% respectively after 1 month.

Gynecomastia In PLATO, gynecomastia was reported by 0.23% of men on BRILINTA and 0.05% on clopidogrel. Other sex-hormonal adverse reactions, including sex organ malignancies, did not differ between the two treatment groups in PLATO.

Lab abnormalities Serum Uric Acid: Serum uric acid levels increased approximately 0.6 mg/dL from baseline on BRILINTA and approximately 0.2 mg/dL on clopidogrel in PLATO. The difference disappeared within 30 days of discontinuing treatment. Reports of gout did not differ between treatment groups in PLATO (0.6% in each group). Serum Creatinine: In PLATO, a >50% increase in serum creatinine levels was observed in 7.4% of patients receiving BRILINTA compared to 5.9% of patients receiving clopidogrel. The increases typically did not progress with ongoing treatment and often decreased with continued therapy. Evidence of reversibility upon discontinuation was observed even in those with the greatest on treatment increases. Treatment groups in PLATO did not differ for renal-related serious adverse events such as acute renal failure, chronic renal failure, toxic nephropathy, or oliguria.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of BRILINTA. Because these reactions are reported voluntarily from a population of an unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune system disorders – Hypersensitivity reactions including angioedema [*see Contraindications (4.4) in full Prescribing Information*].

DRUG INTERACTIONS

Effects of other drugs Ticagrelor is predominantly metabolized by CYP3A4 and to a lesser extent by CYP3A5.

CYP3A inhibitors [*see Warnings and Precautions* and *Clinical Pharmacology (12.3) in full Prescribing Information*].

CYP3A inducers [*see Warnings and Precautions* and *Clinical Pharmacology (12.3) in full Prescribing Information*].

Aspirin Use of BRILINTA with aspirin maintenance doses above 100 mg reduced the effectiveness of BRILINTA [*see Warnings and Precautions* and *Clinical Studies (14) in full Prescribing Information*].

Effect of BRILINTA on other drugs Ticagrelor is an inhibitor of CYP3A4/5 and the P-glycoprotein transporter.

Simvastatin, lovastatin BRILINTA will result in higher serum concentrations of simvastatin and lovastatin because these drugs are metabolized by CYP3A4. Avoid simvastatin and lovastatin doses greater than 40 mg [*see Clinical Pharmacology (12.3) in full Prescribing Information*].

Digoxin *Digoxin:* Because of inhibition of the P-glycoprotein transporter, monitor digoxin levels with initiation of or any change in BRILINTA therapy [*see Clinical Pharmacology (12.3) in full Prescribing Information*].

Other Concomitant Therapy BRILINTA can be administered with unfractionated or low-molecular-weight heparin, GPIIb/IIIa inhibitors, proton pump inhibitors, beta-blockers, angiotensin converting enzyme inhibitors, and angiotensin receptor blockers.

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category C: There are no adequate and well-controlled studies of BRILINTA use in pregnant women. In animal studies, ticagrelor caused structural abnormalities at maternal doses about 5 to 7 times the maximum recommended human dose (MRHD) based on body surface area. BRILINTA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. In reproductive toxicology studies, pregnant rats received ticagrelor during organogenesis at doses from 20 to 300 mg/kg/day. The lowest dose was approximately the same as the MRHD of 90 mg twice daily for a 60 kg human on a mg/m^2 basis. Adverse outcomes in offspring occurred at doses of 300 mg/kg/day (16.5 times the MRHD on a mg/m^2 basis) and included supernumerary liver lobe and ribs, incomplete ossification of sternebrae, displaced articulation of pelvis, and misshapen/misaligned sternebrae. When pregnant rabbits received ticagrelor during organogenesis at doses from 21 to 63 mg/kg/day, fetuses exposed to the highest maternal dose of 63 mg/kg/day (6.8 times the MRHD on a mg/m^2 basis) had delayed gall bladder development and incomplete ossification of the hyoid, pubis and sternebrae occurred. In a prenatal/postnatal study, pregnant rats received ticagrelor at doses of 10 to 180 mg/kg/day during late gestation and lactation. Pup death and effects on pup growth were observed at 180 mg/kg/day (approximately 10 times the MRHD on a mg/m^2 basis). Relatively minor effects such as delays in pinna unfolding and eye opening occurred at doses of 10 and 60 mg/kg (approximately one-half and 3.2 times the MRHD on a mg/m^2 basis).

Nursing Mothers It is not known whether ticagrelor or its active metabolites are excreted in human milk. Ticagrelor is excreted in rat milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from BRILINTA, a decision should be made whether to discontinue nursing or to discontinue drug, taking into account the importance of the drug to the mother.

Pediatric Use The safety and effectiveness of BRILINTA in pediatric patients have not been established.

Geriatric Use In PLATO, 43% of patients were ≥65 years of age and 15% were ≥75 years of age. The relative risk of bleeding was similar in both treatment and age groups. No overall differences in safety or effectiveness were observed between these patients and younger patients. While this clinical experience has not identified differences in responses between the elderly and younger patients, greater sensitivity of some older individuals cannot be ruled out.

Hepatic Impairment BRILINTA has not been studied in the patients with moderate or severe hepatic impairment. Ticagrelor is metabolized by the liver and impaired hepatic function can increase risks for bleeding and other adverse events. Hence, BRILINTA is contraindicated for use in patients with severe hepatic impairment and its use should be considered carefully in patients with moderate hepatic impairment. No dosage adjustment is needed in patients with mild hepatic impairment [*see Contraindications, Warnings and Precautions,* and *Clinical Pharmacology (12.3) in full Prescribing Information*].

Renal Impairment No dosage adjustment is needed in patients with renal impairment. Patients receiving dialysis have not been studied [*see Clinical Pharmacology (12.3) in full Prescribing Information*].

OVERDOSAGE

There is currently no known treatment to reverse the effects of BRILINTA, and ticagrelor is not expected to be dialyzable. Treatment of overdose should follow local standard medical practice. Bleeding is the expected pharmacologic effect of overdosing. If bleeding occurs, appropriate supportive measures should be taken. Other effects of overdose may include gastrointestinal effects (nausea, vomiting, diarrhea) or ventricular pauses. Monitor the ECG.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

[*see section (13.1) in full Prescribing Information*]

PATIENT COUNSELING INFORMATION

[*see section (17) in full Prescribing Information*]

Issued: March 29, 2013

Distributed by: AstraZeneca LP, Wilmington, DE 19850

Rev. 3/13 2574902 4/13

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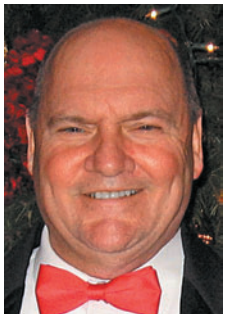
Health plan ownership matters to consumers

CMS has overlooked the importance of identifying not-for-profit status for consumers in the exchanges

BY BRUCE MCPHERSON



Bruce McPherson is president & CEO of the Alliance for Advancing Nonprofit Health Care.

Controversy abounds regarding many aspects of the federal, state and partnership health insurance exchanges to be established under the Patient Protection and Affordable Care Act (PPACA).

A fundamental question has yet to be answered: Will the vast majority of consumers using these exchanges be able to make meaningful choices among the specific benefit plans being offered by the health plans participating in a particular exchange?

The Centers for Medicare and Medicaid Services (CMS) has designed a Summary of Benefits and Coverage (SBC) form for each health plan to complete to help consumers make meaningful choices. Unfortunately, at least for now, CMS has excluded one key piece of information that research has shown consumers want and for good reason.

The missing piece is a clear indication of whether a particular choice is being offered by a health plan that is not-for-profit or for-profit.

OWNERSHIP STATUS MATTERS

This needs to be corrected as quickly as possible, before the exchanges go live.

Why is that important? First, a nationwide Zogby International telephone survey conducted in August 2010 queried consumers about the ownership status of health plans.

The key findings were as follows:

- Most consumers surveyed think there is a difference between not-for-profit and for-profit plans (by a 4-to-1 margin);
- Most think the difference is important (by a 4-to-1 margin); and yet
- One-third do not know whether the plan they are participating in is not-for-profit or for-profit.

Of those surveyed who didn't know the ownership status of their plan, many were low-income individuals and families who will be purchasing individual or small group coverage through their health insurance exchanges (with or without federal premium subsidies) and whose coverage and care needs have always been a special concern and focus of not-for-profit health plans as well as not-for-profit healthcare providers.

Secondly, there is empirical evidence to back up consumer intuition that there are indeed important differences between the two types of health plans.

For all seven years that J.D. Power & Associates have issued member-satisfaction ratings of private health plans, most of the top-rated plans have been not-for-profit.

In the latest ratings, 82% of the Best, 86% of Among The Best, and 75% of Better Than Most plans are not-for-profit, even though they represented only 44% of all of the plans rated.

For all eight years that the National Committee for Quality Assurance has issued quality ratings, most top-quality plans have also been not-for-profit.

In the latest ratings, not-for-profits dominated the lists of the top 10 quality plans, (100% of Medicare, 100% Medicaid, 100% private), of the top 20 quality plans (100% Medicare, 75% Medicaid, 95% private) and of the top 25th percentile quality plans (50% Medicare, 64% Medicaid, 54% private), even though they represented relatively small portions of the all the plans rated (30% Medicare, 38% Medicaid, 24% private).

The evidence is clear. Consumers want the ownership status of health plans offering coverage options to be transparent, and they deserve it. Now it is up to the federal, state, and partnership health insurance exchanges to make that happen. **MHE**

THE STATE OF Mental Healthcare

Payers, providers, policymakers seek societal returns

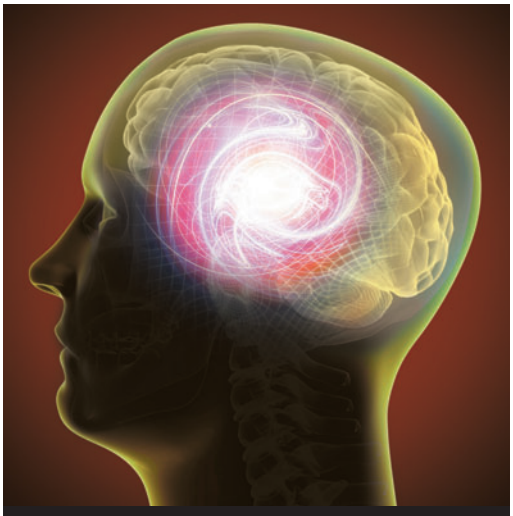
By **Marie Rosenthal, MS**

Between 2007 and 2011, spending on inpatient admissions for mental health and substance use treatment grew faster than spending on medical and surgical admissions, according to a recent report by the Health Care Cost Institute (HCCI). The escalation was driven by the Mental Health Parity and Addiction Equity Act of 2008.

In one of the first analyses of the law's impact, HCCI found that substance use admissions grew by 19.5% and mental health admissions grew 5.9% in 2011 for people younger than 65 and covered by employer-sponsored health insurance.

At first glance, this is an extraordinary increase in costs. However, the numbers do not reflect the savings that are seen when a person with a mental-health or substance-use issue seeks treatment, according to Wayne W. Lindstrom, PhD, president and CEO of Mental Health America, an advocacy organization that is working to enable access to quality care for those who have a mental-health or substance-use disorder.

There is a significant multiplier effect of total medical costs for untreated behavioral health problems, such as depression, bipolar disorder and substance use problems, adds William Wood, MD, PhD, chief medical officer of behavioral health for Amerigroup Tennessee, a public-program health plan. Many people with mental health conditions also suffer medical comorbidities, such as chronic pain, headaches, obesity and other physical ailments, increasing their costs of care. Many of those with mental health disorders also self-medicate and develop co-addiction disorders. These factors add costs and also have a negative impact on the person's quality of life. Patients can even have a shorter lifespan.



Children need access to care: The patient-centered medical home model provides an opportunity for primary care providers to address mental health among children and adolescents. **Read the statistics: http://bit.ly/ZL0Bmq**

ADDED SOCIETAL IMPACT

According to the Substance Abuse and Mental Health Services Administration (SAMHSA), which is part of the National Institutes of Health, treating behavioral disorders results in savings in medical healthcare costs, the criminal justice system and the workplace.

"SAMHSA cited evidence that when you treat these disorders with evidence-based practices, the yield is anywhere from $2 to $10 in savings for every dollar spent," Lindstrom says.

"We do believe that treatment results in cost savings," agrees Christina Severin, president of Network Health in Massachusetts, a Medicaid plan. "When we look at data for individuals engaged in treatment for issues around mental health or substance use, we see that their physical health costs are much lower."

Network Health's focus is on cost-reduction through prevention and engagement with treatment. For example, if someone is using drugs or alcohol and had an accident, they might arrive in an emergency department where the issue could be identified.

"If that emergency visit can translate into meaningful engagement with the healthcare system, we have the opportunity to learn about other medical issues the member might be facing, and to engage the member to address the full scope of their medical and behavioral health needs," Severin says. "If we can effectively help address all those needs in a holistic manner and help people meaningfully engage in their recovery, we might drive up costs in the short term, yet ultimately, costs will decrease over time."

The HCCI report, which also found that medical and surgical admissions declined by 2.3% for the mental healthcare population, reflects the potential savings of holistic care.

Likewise, as more people seek treatment, society could see significant savings in two unrelated areas: the criminal justice system and the workplace.

More people with mental illness are in jail than are in hospitals today, according to Dr. Wood. A national study in 2004 found that more than half of prisoners in state facilities suffered from a mental illness.

"It is not uncommon today for the criminal justice system to be referred to as the defacto mental health system in this country, and it costs more to incarcerate someone for a year than it would to send that person for the full ride to Harvard or Yale," Lindstrom says. "Between 60% and 85% of people who are incarcerated have an addiction and/or mental illness."

Another benefit of behavioral health treatment is the patient's improvement in the workplace. Workers with behavioral health issues that are left untreated are less productive and miss more work days than their peers, causing plan sponsors additional indirect costs. Many are not able to work at all and move to public assistance. According to a 2008 review in the *American Journal of Psychiatry*, major mental disorders cost $193 billion a year in lost earnings alone.

HIGH RISK OF POVERTY

The recent downturn in the economy has been a significant contributor to the prevalence of mental health conditions, says Dr. Wood.

"People are coming in with depression and anxiety disorders and other problems as a result of losing their homes and losing their jobs," he says.

There is a correlation between mental health and poverty.

"If you are living in poverty, you are more likely to suffer from a mental health issue, such as depression," Severin says. "Furthermore, if you originally came from a middle-class family and you suffer from a major mental health illness, such as bipolar disorder or schizophrenia, you are more likely to end up living in poverty."

Chronic, untreated mental illness might go unrecognized. The patient might resist treatment, continuing to decline in his or her ability to function. Because of this, Medicaid ends up being the disproportionate payer of mental health services. Dr. Wood says estimates from 2010 indicate that behavioral health treatment costs the United States about $135 billion, which is a large number, but a small portion of the country's total spending.

58%

PUBLIC PAYERS are responsible for 58% of the cost of mental health treatment

"The cost of behavioral health is only about 5% of the total cost of healthcare," Lindstrom says. "Public payers account for about 79% of substance use treatment and 58% of mental health treatment."

The Mental Health Parity Act was an important step in recognizing the chronicity of many mental health disorders, as well as their societal costs. The act prevents lifetime caps and mandates behavioral health coverage be on par with benefits offered for medical and surgical care. However, the parity act only applies to large-group, employer-funded, state-regulated plans and Medicaid managed care plans.

By making behavioral health an Essential Benefit, the Patient Protection and Affordable Care Act (PPACA) will reinforce care delivery and access.

"Under the Affordable Care Act, behavioral health is part of the Essential Health Benefits (EHBs). If an individual is going to purchase a plan—and not be subject to a tax penalty—the benefit plan that they are purchasing from a qualified carrier would include behavioral benefits," Severin says.

PPACA doesn't necessarily parallel the parity law, according to Dr. Wood.

"Under healthcare reform, the Mental Health Parity Acts' applicability is extended to smaller groups and individual market plans purchased through state health insurance exchanges and Medicaid non-managed-care benchmark and benchmark equivalent plans," Dr. Wood says. "But the smaller group coverage that is purchased outside an exchange will continue to be exempt from the Mental Health Parity Act."

CORRECTING THE PARADOX

Paying for care is only one aspect of parity, experts say. Before there can be true parity, the one in four Americans with a behavioral health issue must have access to treatment and a support system. Increasing access will be difficult because there are not enough mental-health professionals to handle the demand, especially as coverage becomes more robust.

"We cannot increase manpower overnight," says Dr. Wood. "But we need to increase manpower to improve access. There is a shortage of psychiatrists overall and an even greater shortage of child psychiatrists."

Accountable care organizations (ACOs) and patient-centered medical homes will help because they will treat the entire patient, ensuring both physical and emotional health.

As mental and physical health are integrated, primary care physicians will be relied on even more for recognizing when a patient is potentially experiencing a behavioral health condition and making sure that patient receives the proper assessment and care.

"In healthcare, there has been a paradox of excess and deprivation regarding the financing of the system," Severin says. "One of my hopes and aspirations

Continued on page 39

Continued from page 36

for ACOs is that they take on the quality and the financial risk for the individuals who are members of that ACO. The ACO has an incentive to say, 'Let's not underfund this and overfund that, rather let's fund everything the right way to get the optimum outcome at the end of the day.' I hope that this ACO movement will be one of the forces that corrects this paradox of excess and deprivation."

ADDITIONAL SOLUTIONS

Increasingly, technology will also come into play to improve access affordably. Patients and primary care physicians can benefit from online video interactions, according to Dr. Wood.

For example, physicians might have a telemedicine consult with a psychiatrist to help in the initial assessment of a patient and determine if a referral is needed. And patients, especially those in rural areas, can use telemedicine to access psychological and psychiatric services quickly.

Other ways to increase access as demand rises are to leverage open-access clinics that don't require appointments for assessments; increasing group therapy models of care—instead of typical one-on-one psychotherapy sessions; and offering peer-to-peer support services, according to Lindstrom.

In the wake of last month's Boston Marathon tragedy, for example, Cigna and Aetna opened hotlines offering provider referrals and free counseling for members and non-members.

Ultimately, reimbursements for mental health services must be restructured to increase telemedicine use and to encourage more clinicians to enter the specialty, experts say.

Millions of Americans, both adults and children, suffer from a behavioral health issue. Payers, providers and policymakers aim to improve care and access through innovation and reform. **MHE**

Marie Rosenthal is a freelance writer based in East Windsor, N.J.

Mental Health Models

Primary care providers must drive collaborative treatment

Much of the mental healthcare in this country is managed by the primary care physician (PCP).

As health insurers move to patient-centered medical homes and accountable care organizations, the PCP's role will become even more important because he or she will become the "quarterback" for that patient's physical and emotional care, according to William Wood, MD, PhD, chief medical officer of behavioral health for Amerigroup Tennessee.

A recent study, however, found that they might not recognize the early symptoms, such as depression, anxiety, sleep disturbance and paranoia of serious mental illness. Researchers from McGill University in Canada found that for almost 50% of patients between the ages of 14 to 25 received their first diagnosis of serious psychosis in the emergency room.

Wayne W. Lindstrom, PhD, says that this is also the case in the United States. "Most PCPs are not prepared to assess for a mental illness or an addiction disorder," he says.

Dr. Wood says it is difficult for a PCP to recognize a mental illness because he or she has such a limited time to spend with each patient and many of the symptoms could also point to a physical illness or temporary stress.

"Some physicians are really fantastic at recognizing behavioral health issues and some are not," says Christina Severin, president of Network Health in Massachusetts. "But when you talk about Medicaid patients, you will look at a group of PCPs who are very good at it because the majority of their patients have some type of behavioral health issue whether it is substance abuse, depression or post traumatic stress disorder from living in violent communities.

Even if the PCP recognizes that the patient has a behavioral health condition, he or she might not be able to access the behavioral healthcare system to get treatment. This is one reason why 70% to 75% of prescriptions for depression and anxiety disorders are written in the primary care arena.

"We've got a number of challenges on the primary care front. If the Affordable Care Act fills its promise, we will potentially overcome them with new integration and collaborative care models between mental health and primary care," says Lindstrom, who is president and CEO of Mental Health America.

These models include:

- **Hiring or contracting clinicians, case managers and peer specialists with expertise in behavioral health to practice in primary care settings to assist with crisis intervention, case consultations, assessments, appropriate interventions, collaborative care, and referrals when appropriate;**
- **Hiring or contracting with primary care physicians to offer integrated collaborative care in behavioral health treatment settings;**
- **Offering primary care consultations with behavioral health specialists through telephone or the internet, particularly in rural areas of the country;**
- **Merging community mental health centers (CMHCs) with Federally Qualified Health Centers (FQHCs); and**
- **Integrating behavioral healthcare treatment, planning and funding entities in the planning and implementation of healthcare homes, accountable care organizations and healthcare exchanges.**

"People have to be treated in a holistic way," Severin says. "We have members in our health plan who are all unique individuals, and they all have issues that deal with oral health, mental health and physical health. We must address these in the context of the patient, the family and the community."

—Marie Rosenthal

What we *don't know* about HEALTH REFORM

Last month, the Obama administration halted new enrollment in the Pre-existing Condition Insurance Plan because of financial concerns. Industry observers knew the program would run short of funding, so the announcement was hardly a surprise.

Other aspects of the Patient Protection and Affordable Care Act (PPACA) are much more difficult to forecast, for example whether Accountable Care Organizations (ACOs) will be successful or whether employers will abandon health benefits. MANAGED HEALTHCARE EXECUTIVE reached out to top industry thought leaders to find out what they believe we don't know about health reform.

Karen Ignagni

President and CEO
America's Health Insurance Plans

Will younger, healthier individuals under 40 purchase health insurance or will they choose to wait to buy coverage after they need medical services?

The Affordable Care Act will expand coverage to millions of Americans, but major provisions of the law, such as the $100 billion health insurance tax, minimum Essential Health Benefits requirement, and new restrictions on age rating, will result in significantly higher healthcare costs for individuals and families. While the law does provide premium and cost-sharing subsidies to help low- and moderate-income families afford healthcare coverage, millions of people are not eligible for subsidies, and many that are eligible will still pay more for their premium than they do today. When faced with higher healthcare costs, many younger, healthier people may choose to forgo purchasing coverage until they need it, especially when the penalty for not having insurance is as low as $95. If this happens, costs will go up for everyone, young and old.

Martin P. Hauser

President
SummaCare

MHE Editorial Advisor

Will the government be able to create a viable, long term solution to the Sustainable Growth Rate (SGR) payment model?

It will be interesting to see what type of solution is developed in both the short and long term for this ongoing problem, which has not been addressed for so many years. Any solution will have far reaching impact including, but not limited to: the impact on commercial rates as most insurers follow the same methodology; whether the 'fix' helps to alter the current mix and distribution of primary care and specialist physicians; whether the fix impacts the decisions of physicians to retire early or becomes a barrier to students pursuing a career in medicine.

Barbara Morales Burke

Vice President of Health Policy and Chief Compliance Officer
Blue Cross and Blue Shield of North Carolina

We don't really know what impact the introduction of premium and cost-sharing subsidies will have on the larger conversation about government entitlements.

Due to the 400% federal poverty level cap, subsidies will go to a larger percentage of Americans, many of whom are not accustomed to receiving support of any kind from government. Will these subsidies change public expectations about government assistance in general? Will these subsidies change the conversation about subsidies or will it change the conversation about the cost of healthcare?

When the cost of subsidies grows at a faster pace than the revenue sources identified to pay for it, there will need to be further discussion and debate on tradeoffs within or beyond the bounds of healthcare. What will be politically ac-

ceptable—or generally acceptable—to the American people as the debate continues about revenue needed to support the increasing cost of healthcare?

Finally, the subsidies under the Affordable Care Act are based on modified adjusted gross income rather than general wealth. A person living off substantial savings could qualify for a premium subsidy while a neighbor with higher annual income but no savings may not qualify. While perhaps not frequent, will these cases generate confusion and misunderstanding or generate controversy?

Daniel J. Hilferty

President and CEO
Independence Blue Cross

MHE Editorial Advisor

At Independence Blue Cross, we're prepared for healthcare reform. But we're not sure consumers are ready for reform—even people who are uninsured.

We've done consumer research in our region and many people had no idea about the big changes coming in 2014. In some focus groups, uninsured people had not heard of healthcare exchanges and had no idea that under the reform law they could be eligible for subsidies or tax credits. Some people think that the law provides free government healthcare. It's really awakened us to the serious responsibility we have to go where consumers are and help educate them about healthcare reform.

Margaret Murray

CEO
Association for Community Affiliated Health Plans

MHE Editorial Advisor

We don't know how much churning will go on between Medicaid and the exchanges.

A significant question is how smooth the transition will be for those who move from eligibility for Medicaid to subsidized coverage in the exchanges. Small, short-term changes in income may result in significant numbers of people moving between the two programs. Streamlining transitions between the two programs will be critical. California has introduced a 'bridge' plan, where managed care plans serving Medicaid populations may continue to do so once they become eligible for subsidized exchange coverage.

And come 2015, the Basic Health Program holds significant promise to provide a continuum of coverage for persons with incomes of up to 200% of the federal poverty level. Bringing quality coverage within reach for millions is the best feature of health reform. It's critical that policymakers take steps to make sure that people moving between Medicaid and the exchanges don't fall through the cracks. That's why ACAP has long championed making 12-month continuous eligibility upon enrollment in Medicaid and CHIP mandatory, and we hope to see such a bill introduced in this Congress.

Now that agreements for dual-eligible demonstration projects are in place, what's next?

We look forward to learning from the soon-to-be-implemented demonstrations how people enrolled in both Medicare and Medicaid respond to the opportunity of an integrated plan. It will be interesting to see which models of care improve quality and access while helping to contain costs; whether decline in function can be slowed by better care coordination; and if states with a dependence on institutional care achieve a rebalanced long-term care system. It bears noting that rates for health plans have not yet been set in the states where the demonstrations are set to launch. Properly balancing the need for savings with actuarially sound rates will be critical to the success of this initiative.

Vik Mangalmurti

Vice President, Office of Health Care Reform
Highmark Inc.

What kind of latitude do employers feel they have as far as altering their employee health benefits?

This question has been the source of a lot of discussion and study since the law was passed, with no definite or consistent conclusions. I sense a growing realization among employers that offering good benefits, particularly health coverage, makes for happier, more productive employees, and that happier, more productive employees are the number one most important and most strategic competitive advantage.

Don Hall

Principal
Delta Sigma LLC

MHE Editorial Advisor

One of the biggest unknowns in the upcoming implementation of the state healthcare exchanges is whether we will see the appearance of a paradigm changing, low-cost, great service, health plan that will change the health insurance game.

This Southwest Airlines-like plan could appear in the form of an ACO or new market entrant. If this happens, competition will truly reign.

Joel Brill, MD

Chief Medical Officer
Predictive Health LLC

MHE Editorial Advisor

We don't know whether there will be enough primary care providers to accommodate the 32 million-plus individuals who will now have health insurance on January 1, 2014.

While hospitals are buying up every PCP in sight, physician productivity drops with employment. Who will see these patients? Is this the opportunity for retail-based clinics and urgent care centers to become integrated into population health management and the care delivery system?

Jim Fox

Director and Senior CFO Consultant
Warbird Consulting Partners

> "Will the health exchanges actually be able to perform as they are envisioned?"

If they do not, what alternatives have we in the health industry done to prepare for the fallout? Have we analyzed or thought through the potential consequences of their failure or delay?

Bill Fera, MD

Principal, Health Care Advisory Services
Ernst & Young LLP

Can providers and payers align?

If accountable care constructs are really going to work, it will take payers and providers working together in a truly integrated fashion. This requires trust. Can payers and providers grow to trust each other quickly? Some payers are bypassing the trust question by buying their own providers and creating instant integrated delivery systems. It will be interesting to see how this trend of payers becoming providers fares compared with the trend in the 1980s and 1990s of providers trying to becoming payers—which did not go so well. On the face of it, the integrated delivery system, and the control of the healthcare premium dollar from start to finish that comes with it, makes sense. To the extent that transparent, evidence based protocols are deployed and adopted, quality metrics are collected and published, a skeptical public may yet buy into the concept of Managed Care 2.0.

Rebecca L. Ditmer

Principal, Health Care Advisory Services
Ernst & Young LLP

Another unknown is the impact of the higher-deductible metal plans on physicians' and hospitals' abilities to effectively identify patients' liabilities and manage that collection to minimize the impact on their accounts receivable and bad debt.

For members/patients covered through a metal tier under the exchange, physicians and hospitals may be used to more than 90% of the payment coming from a government subsidy or private payer. Tomorrow the members/patients may have large deductibles that must be collected before benefits are paid out. It's important for physicians, hospitals and payers to understand the shift of payment liability, work together to educate members/patients and set expectations for effective payment assurance.

Scott W. Van Valkenburg, MD

Senior Manager, Health Care Advisory Services
Ernst & Young LLP

We don't know the outlook for patient engagement and accountability.

PPACA will enable a significant number of more Americans—estimated at 30 million—to now have insurance. Patient engagement and motivation to be and stay healthy are critical components of population health. The unknown is how effectively the current healthcare model will encourage patient engagement for taking an active role in their health.

Bill Copeland

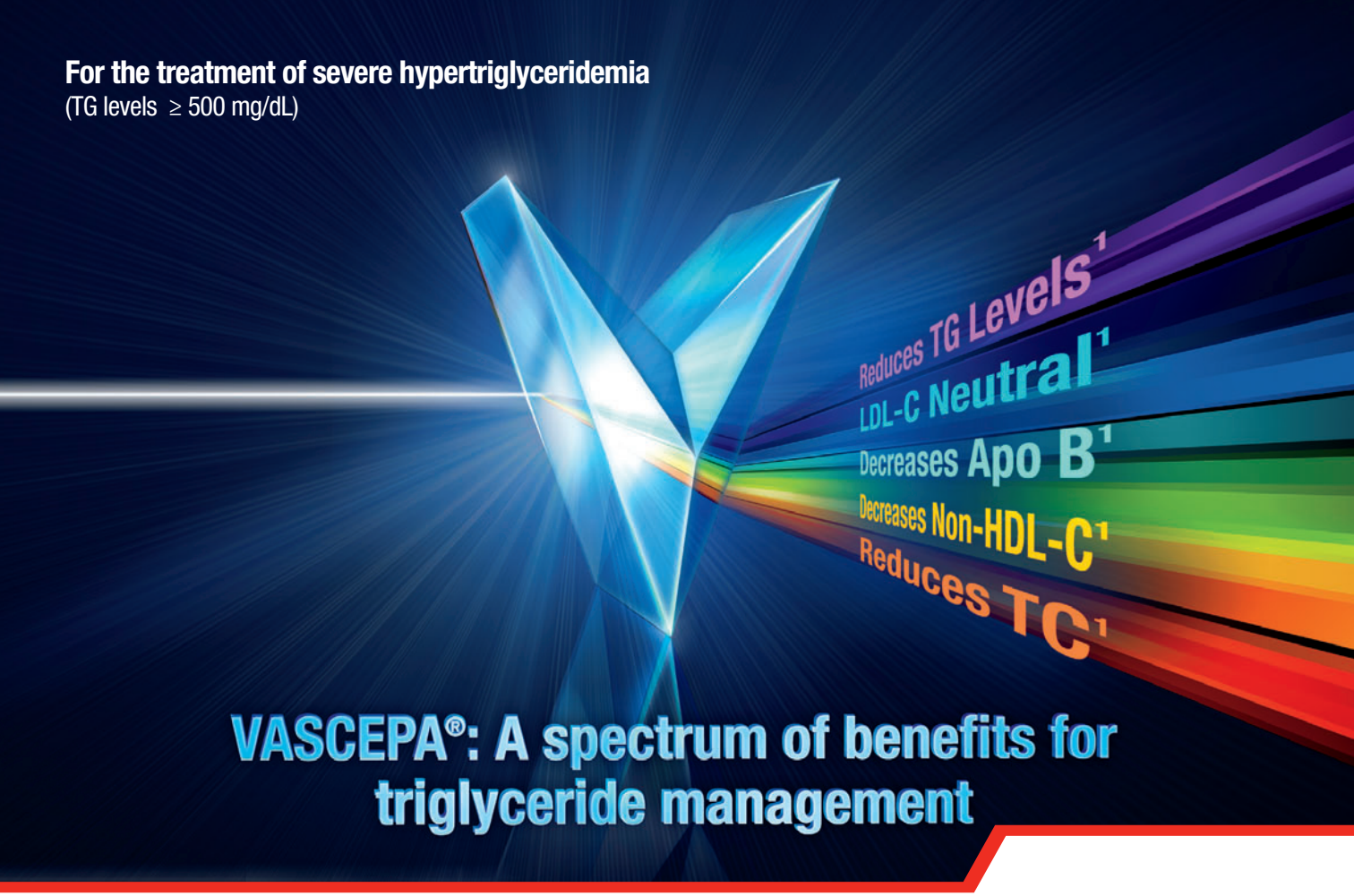
Vice Chairman, U.S. Life Sciences & Health Care Leader, U.S. Health Plans Leader
Deloitte LLP

Will health plans' market share get so watered down they can no longer negotiate with providers?

I don't think plans will see a drastic difference in their ability to negotiate, because they already operate in an environment in which physician reimbursement in most markets is comparable among the major competitors. There is a spread of about 5% to 10% advantage for the leading competitor when it comes to unit-cost pricing for inpatient and outpatient facility pricing. At the same time, the nationals have an advantage over the regional players in negotiations around drug pricing.

Continued on page 45

For the treatment of severe hypertriglyceridemia
(TG levels ≥ 500 mg/dL)



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Consider VASCEPA® an affordable option for your members with severe hypertriglyceridemia (TG levels ≥ 500 mg/dL).

Indications and Usage

VASCEPA® (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia.

- The effect of VASCEPA® on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined
- The effect of VASCEPA® on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined

Important Safety Information for VASCEPA®

- VASCEPA® is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to VASCEPA® or any of its components
- Use with caution in patients with known hypersensitivity to fish and/or shellfish
- The most common reported adverse reaction (incidence >2% and greater than placebo) was arthralgia
- Patients should be advised to swallow VASCEPA® capsules whole; not to break open, crush, dissolve, or chew VASCEPA®

Reference: 1. Bays HE, Ballantyne CM, Kastelein JJ, et al. Eicosapentaenoic acid ethyl ester (AMR101) therapy in patients with very high triglyceride levels (from the multi-center, placebo-controlled, randomized, double blind, 12-week study with an open-label extension [MARINE] trial). *Am J Cardiol*. 2011;108:682-690.

For more information on VASCEPA® see the brief summary or for the Full Prescribing Information please visit www.VASCEPA.com.

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VASCEPA® (icosapent ethyl) Capsules, for oral use
Brief summary of Prescribing Information

Please see Full Prescribing Information for additional information about Vascepa.

1 INDICATIONS AND USAGE

VASCEPA® (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet and exercise regimen before receiving VASCEPA and should continue this diet and exercise regimen with VASCEPA.

Attempts should be made to control any medical problems such as diabetes mellitus, hypothyroidism, and alcohol intake that may contribute to lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed, if possible, prior to consideration of TG-lowering drug therapy.

Limitations of Use:

The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

The effect of VASCEPA on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

2 DOSAGE AND ADMINISTRATION

Assess lipid levels before initiating therapy. Identify other causes (e.g., diabetes mellitus, hypothyroidism, or medications) of high triglyceride levels and manage as appropriate. *[see Indications and Usage (1)]*.

Patients should engage in appropriate nutritional intake and physical activity before receiving VASCEPA, which should continue during treatment with VASCEPA.

The daily dose of VASCEPA is 4 grams per day taken as 2 capsules twice daily with food.

Patients should be advised to swallow VASCEPA capsules whole. Do not break open, crush, dissolve, or chew VASCEPA.

4 CONTRAINDICATIONS

VASCEPA is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to VASCEPA or any of its components.

5 WARNINGS AND PRECAUTIONS

5.1 Monitoring: Laboratory Tests

In patients with hepatic impairment, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels should be monitored periodically during therapy with VASCEPA.

5.2 Fish Allergy

VASCEPA contains ethyl esters of the omega-3 fatty acid, eicosapentaenoic acid (EPA), obtained from the oil of fish. It is not known whether patients with allergies to fish and/or shellfish are at increased risk of an allergic reaction to VASCEPA. VASCEPA should be used with caution in patients with known hypersensitivity to fish and/or shellfish.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse reactions reported in at least 2% and at a greater rate than placebo for patients treated with VASCEPA based on pooled data across two clinical studies are listed in Table 1.

Table 1. Adverse Reactions Occurring at Incidence >2% and Greater than Placebo in Double-Blind, Placebo-Controlled Trials*

	Placebo (N=309)		VASCEPA (N=622)	
Adverse Reaction	**n**	**%**	**n**	**%**
Arthralgia	3	1.0	14	2.3

*Studies included patients with triglycerides values of 200 to 2000 mg/dL.

An additional adverse reaction from clinical studies was oropharyngeal pain.

7 DRUG INTERACTIONS

7.1 Anticoagulants

Some published studies with omega-3 fatty acids have demonstrated prolongation of bleeding time. The prolongation of bleeding time reported in those studies has not exceeded normal limits and did not produce clinically significant bleeding episodes. Patients receiving treatment with VASCEPA and other drugs affecting coagulation (e.g., anti-platelet agents) should be monitored periodically.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. It is unknown whether VASCEPA can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. VASCEPA should be used during pregnancy only if the potential benefit to the patient justifies the potential risk to the fetus.

In pregnant rats given oral gavage doses of 0.3, 1 and 2 g/kg/day icosapent ethyl from gestation through organogenesis all drug treated groups had visceral or skeletal abnormalities including: 13th reduced ribs, additional liver lobes, testes medially displaced and/or not descended at human systemic exposures following a maximum oral dose of 4 g/day based on body surface comparisons. Variations including incomplete or abnormal ossification of various skeletal bones were observed in the 2 g/kg/day group at 5 times human systemic exposure following an oral dose of 4 g/day based on body surface area comparison.

In a multigenerational developmental study in pregnant rats given oral gavage doses of 0.3, 1, 3 g/kg/day ethyl-EPA from gestation day 7-17, an increased incidence of absent optic nerves and unilateral testes atrophy were observed at ≥0.3 g/kg/day at human systemic exposure following an oral dose of 4 g/day based on body surface area comparisons across species. Additional variations consisting of early incisor eruption and increased percent cervical ribs were observed at the same exposures. Pups from high dose treated dams exhibited decreased copulation rates, delayed estrus, decreased implantations and decreased surviving fetuses (F2) suggesting multigenerational effects of ethyl-EPA at 7 times human systemic exposure following 4 g/day dose based on body surface area comparisons across species.

In pregnant rabbits given oral gavage doses of 0.1, 0.3, and 1 g/kg/day from gestation through organogenesis there were increased dead fetuses at 1 g/kg/day secondary to maternal toxicity (significantly decreased food consumption and body weight loss).

In pregnant rats given ethyl-EPA from gestation day 17 through lactation day 20 at 0.3, 1, 3 g/kg/day complete litter loss was observed in 2/23 litters at the low dose and 1/23 mid-dose dams by post-natal day 4 at human exposures based on a maximum dose of 4 g/day comparing body surface areas across species.

8.3 Nursing Mothers

Studies with omega-3-acid ethyl esters have demonstrated excretion in human milk. The effect of this excretion is unknown; caution should be exercised when VASCEPA is administered to a nursing mother. In lactating rats, given oral gavage ^{14}C-ethyl EPA, drug levels were 6 to 14 times higher in milk than in plasma.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Of the total number of subjects in clinical studies of VASCEPA, 33% were 65 years of age and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

9 DRUG ABUSE AND DEPENDENCE

VASCEPA does not have any known drug abuse or withdrawal effects.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 2-year rat carcinogenicity study with oral gavage doses of 0.09, 0.27, and 0.91 g/kg/day icosapent ethyl, respectively, males did not exhibit drug-related neoplasms. Hemangiomas and hemangiosarcomas of the mesenteric lymph node, the site of drug absorption, were observed in females at clinically relevant exposures based on body surface area comparisons across species relative to the maximum clinical dose of 4 g/day. Overall incidence of hemangiomas and hemangiosarcomas in all vascular tissues did not increase with treatment.

In a 6-month carcinogenicity study in Tg.rasH2 transgenic mice with oral gavage doses of 0.5, 1, 2, and 4.6 g/kg/day icosapent ethyl, drug-related incidences of benign squamous cell papilloma in the skin and subcutis of the tail was observed in high dose male mice. The papillomas were considered to develop secondary to chronic irritation of the proximal tail associated with fecal excretion of oil and therefore not clinically relevant. Drug-related neoplasms were not observed in female mice.

Icosapent ethyl was not mutagenic with or without metabolic activation in the bacterial mutagenesis (Ames) assay or in the *in vivo* mouse micronucleus assay. A chromosomal aberration assay in Chinese Hamster Ovary (CHO) cells was positive for clastogenicity with and without metabolic activation.

In an oral gavage rat fertility study, ethyl-EPA, administered at doses of 0.3, 1, and 3 g/kg/day to male rats for 9 weeks before mating and to female rats for 14 days before mating through day 7 of gestation, increased anogenital distance in female pups and increased cervical ribs were observed at 3 g/kg/day (7 times human systemic exposure with 4 g/day clinical dose based on a body surface area comparison).

17 PATIENT COUNSELING INFORMATION

17.1 Information for Patients

See VASCEPA Full Package Insert for Patient Counseling Information.

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Continued from page 42

Liam Walsh

Principal, U.S. Healthcare and
Life Sciences Advisory Industry Leader
KPMG

[How will healthcare technology evolve as] PPACA dynamics and payment model transformations—which focus on population care and quality results, over per unit reimbursement—necessitate greater consumer engagement and unique approaches?

Healthcare technology has to enable more immediate consumer access to data, and more mobile tools will emerge to facilitate connectivity between consumers and providers. This more remote, but more persistent business-to-consumer connectivity will also help to bend the cost curve, increase access to care, and, if early results are an indicator, will improve quality of care through more continuous connectivity with providers.

John Meerschaert, FSA, MAAA

Principal and Consulting Actuary
Milliman

How many states will expand Medicaid eligibility up to 133% of the FPL?

Some states have already definitively accepted or rejected PPACA's enhanced federal funding for expanding Medicaid eligibility up to 133% of the federal poverty level. Other states are still analyzing the pros and cons of accepting the federal funding, or are looking for creative alternatives to use the funding for private insurance options. For example, Arkansas has received a conceptual go-ahead from the Centers for Medicare and Medicaid Services for its proposal to use Medicaid funding to enroll individuals eligible for the Medicaid expansion in exchange products.

David Calabrese

Chief Clinical Officer
Catamaran

MHE Editorial Advisor

What are the likely drug utilization patterns and financial impact for the millions of individuals soon to be accessing care through the health insurance exchanges?

Based upon learnings from the launch of healthcare reform in Massachusetts several years ago, one could expect that drug utilization within this population is likely to be significantly greater than that of the general commercial payer population. Remember that these are individuals that have historically had little to no prescription drug coverage, and now will have access to a fairly generous drug benefit based upon current Essential Health Benefit requirements. Many of these individuals are in and out of lower paying jobs, and a component of that dynamic may be health-driven. In my experience, we have seen high prevalence of mental illness, substance abuse, diabetes and other key chronic illnesses, several of which might require costly specialty therapies. Thus, one should not be surprised to see higher than average prescription volume per member, average costs per script, and overall drug expenditures.

Al Lewis

Executive Director
Disease Management Purchasing Consortium

MHE Editorial Advisor

We have absolutely no clue how many companies are going to move to the exchanges.

My suspicion is that there will be a major unintended consequence—which is the young and healthy companies sticking with self-insurance while the old economy companies move to the exchanges, if not right away then within 24 months. This will create all sorts of adverse selection issues.

Perry Cohen

Principal
TPG Family of Companies

MHE Editorial Advisor

We don't know the true costs for the U.S. healthcare system of expanding access to uninsured Americans.

We need to know if the people that will now access the healthcare delivery system (the working poor) will drive up the cost of the healthcare system (physician visits, hospitalizations and drug costs). If we get these people into integrated care systems (Kaiser Permanente, Geisinger) with the right financial incentives (health plans and accountable care organizations) the costs can be managed.

Kathy Prosser

Senior Partner
Mercer

> "Will PPACA have an adverse effect on the productivity of U.S. employees?"

While some companies—particularly retailers and employers with high part-time workforces—are solving for one problem, they may unknowingly be creating another, bigger problem. **MHE**

Co-ops focus on the uninsured to secure their niche as a payer

Early response bodes well for new plans

BY JILL SEDERSTROM

CO-OP LEADERS across the country know they don't have the manpower or brand recognition of large commercial insurers, but they believe they will be able to carve out a niche in the evolving healthcare landscape. They'll begin by targeting the uninsured, focusing on creating member-centered systems and policies, and adopting care management practices that don't rely on fee-for-service payment structures.

"We do not think that we're going to slip a lot of insured people into our plan," says Peter Beilenson, MD, chief executive officer of Evergreen Health Cooperative in Maryland. "We would love if that was the case. We are trying not to be naïve."

Dr. Beilenson says the Consumer Operated and Oriented Plan (CO-OP) will target the approximately 420,000 in the state who are uninsured and not eligible for Medicaid and says it will need approximately 15,000 to 20,000 covered lives in the first year to be sustainable.

"The uninsured folks—who hopefully we will have reached with our marketing strategy—they are much less likely to have brand loyalty. Many of them have been uninsured for a long period of time. They don't trust the healthcare system as much, so they don't tend to necessarily go with the big insurers," he says.

CO-OP ON TARGET

Evergreen Health Cooperative is one of 24 CO-OPs that were able to secure federal loans before the fiscal cliff deal abruptly shut down the loan program earlier this year. CO-OP executives who managed to secure the loans before the funding halted say they are poised and ready to open enrollment on the insurance exchanges.

"We have filed our rates and forms and expect to be on the exchange on October 1 when enrollment starts and start services January 1," says Dr. Beilenson. "We're right on target."

Executives are uncertain how their premiums will compare to other commercial plans since the deadlines in many states for submitting proposed plans have not occurred and rates are unknown, but they say they believe their premium rates will likely be on the lower end of plans offered on the exchanges.

Dr. Beilenson also says the organization believes it will be cost competitive in its preferred provider organization (PPO) because of a leaner staff and lower administrative costs.

Evergreen Health Cooperative will also offer an exclusive provider organization (EPO), which he says will be a closed panel system based on the primary care medical home model, payment reform and evidence-based practices that are tied together with technology. With the EPO, he says the most significant cost savings will likely be derived from reductions to hospitalizations and emergency room visits.

PRICE DRIVES CHOICE

Martin Hickey, MD, chief executive officer of New Mexico Health Connections, says price will ultimately drive consumer choice.

"A lot of us are getting pretty good rates, particularly when compared to usual commercial rates. The problem facing the other carriers is cannibalizing their own commercial business," he says.

While Dr. Hickey says the cooperative will need to create some margin to repay loans, he says the plan will pass a portion of savings onto providers, particularly for good health outcomes.

"Our goal is to do shared savings programs in particular with primary care, high quality specialists and highly functional hospitals who not only have a track record of safety but also are outstanding in transitions of care and so

Jill Sederstrom is a freelance writer based in Kansas City.

forth," he says. "Since we have no external stakeholder, we don't have to pay a share holder, we don't have to meet the requirements of the mutual company and we are the only not-for-profit plan, so that gives us some leeway."

NURSE COORDINATORS

Bobbette Bond, project officer for the Nevada Health CO-OP, says members of the cooperative's formation board plan to draw from their previous success with the Culinary Health Fund, a self-funded plan for hospitality workers that has operated for decades in Las Vegas and covers about 120,000 lives. While the Culinary Health Fund continues to run, many of the members on the cooperative's formation board have held leadership roles in the health fund and plan to adopt similar methods and approaches to care.

For instance, the Culinary Health Fund runs a health advocate program where nurses go directly into hospitals to visit members to improve discharge planning, nurse engagement and member navigation.

"We've found that that really saves money," Bond says. "When you take really good care of members, you save money by trying to anticipate their healthcare needs and preventing them from getting worse. That has actually worked a lot for us in terms of our healthcare trend, so that's our version of managed care."

The Nevada Health CO-OP also hopes to benefit from the Culinary Health Fund's established relationship in the Latino community. Since about 40% of the health fund's members are bilingual, they have experience engaging and navigating for the Spanish speaking community.

"We were the first plan that I know of in the country to create a bilingual explanation of benefits," Bond says of the Culinary Health Fund, adding that the cooperative hopes to attract members who are already familiar with the Culinary Health Fund and either no longer have access to the plan serving hospitality workers or have heard about the plan through friends and family.

In addition to adopting similar programs and outreach efforts, the cooperative will also use the Culinary Health Fund's provider network to provide care in the southern region of the state and is working to create a new provider network in the northern area of the state.

As CO-OPs establish provider networks, they say provider interest has been positive.

MHE EXECUTIVE VIEW

- **Just 24 CO-OPs secured federal loans before the program stopped earlier this year.**
- **Nurse engagement has saved money for one CO-OP.**
- **Establishing a brand will be a CO-OP's biggest challenge.**

"The bottom line is we come with payment for patients that previously were not paid for," Dr. Beilenson says.

CO-OPs won't know the community's true interest or investment in the community-run healthcare option until October when enrollment opens, but Bond says early indications are promising. The Nevada Health CO-OP has created a reservation system that allows potential members to reserve a spot in the plan early.

"When they come back in the fall we can work with them directly in a more expedited way to get them enrolled, and we are really excited about the early response we're having to that," she says.

Leaders are in the process of constructing custom claims and enrollment systems, but New Mexico Health Connections and Evergreen Health Cooperative say they will turn to third parties for claims processing.

"Our goal is if we are successful as a co-op—which we think we will be—we would certainly eventually bring it in house—probably in the near future, but not in the first year," Dr. Beilenson says.

The Evergreen Health Cooperative, which is being led by a formation board consisting of insurance executives and former public health officials, is also using a third-party administrator to handle enrollment.

While the cooperative's primary demographic target is working class individuals who may have struggled in the past to afford healthcare, Dr. Beilenson says, the EPO's smaller patient panels, care coordinator and personal health coaches in every primary care center could attract a larger demographic as well.

"We think we'll actually be of interest to people, professionals and others, who believe in a co-op," he says.

The plan's PPO will be a robust network throughout Maryland, but the EPO will begin with a smaller footprint. Initially, the EPO will begin with four primary care centers along the corridor between Baltimore and Washington D.C., with the intent to expand over time.

RATIONAL HEALTHCARE

Dr. Hickey says the most significant hurdles for CO-OPs will be the lack of an established brand and initially generating and sustaining enrollment. Despite these challenges, he believes CO-OPs will secure their place in the industry.

"Our orientation toward care and toward the market will give us an excellent chance to grow and be a strong factor in getting healthcare delivered and be rational instead of this volume-based fee-for-service craziness that we totally wrapped ourselves into," Dr. Hickey says. **MHE**

Pioneer ACOs build infrastructure to collect patient data

The 32 Pioneers underscore ACO optimism

BY MATT BOLCH

THE FIRST OFFICIAL results from Pioneer ACOs aren't due until this summer, but early data from at least one ACO is encouraging.

Banner Health Network, which serves 57,000 patients primarily in Maricopa County (Phoenix), Ariz., shows a 7% reduction in readmission rates, a 10% drop in inpatient admissions and a 7% decrease in high-tech imaging, according to Matt Horn, operations director for Banner Health Network.

Pioneer ACOs are considered the cutting edge of the accountable care organization movement. The nearly three dozen organizations selected represent many of the most well-respected provider organizations in the country.

In February, the 32 Pioneers asked the Center for Medicare and Medicaid Innovation to delay the move from reporting-only status to pay for performance. Reasons cited include lack of benchmarking methodology for a majority of measures, and benchmarks that are set higher than current best-of-class performance. In the same letter, the ACOs reiterated their support for the program.

"The Pioneers are providing high quality care but are struggling in their ability to send that information to Centers for Medicare and Medicaid Services (CMS)," says Michael Gleeson, senior vice president of product strategy at Arcadia Solutions. The company works with five Pioneers to improve the performance of electronic health records.

Believing instinctively that outcomes are improving is not the same as reporting it. A strong EHR creates a consistent data repository that ACOs can use to study populations, disseminate data to providers and track progress. But getting at that data can be a challenge, especially among certain patients. Unlike true managed care, patients are free to seek treatment outside an ACO network, which can stymie efforts to track comprehensive patient data and manage the health of the population.

"We believe that engagement of providers and beneficiaries is a key issue," Horn says. "The model allows patients active roles in their health and wellness."

Banner Health's 23 hospitals are connected to a robust electronic health record, allowing physicians, nurses and other providers to view a common medical record that reduces test duplications and medical errors. The system incentivized physicians to adopt a common EHR platform.

"It's not just about the patient record," Horn says. "It's about having a common EHR strategy and bringing in tools to predict population trends, as well as the data registry to serve [patients] best."

Banner uses employed and contracted physicians in its network and offers EHR incentives to get providers on a common platform.

COMMITMENT TO PRACTICE

Bringing on the right providers and engaging patients are among the overarching goals of Heritage Medical Systems, an affiliate of the Heritage Provider Network, the organization that runs the Heritage California ACO and—through its affiliated medical groups and independent physician associations—provides care to nearly 1 million lives in three states. Other goals focus on data and how to parse it correctly, says President Mark L. Wagar.

"It's very important that physicians understand that participating is a commitment to a different way to practice medicine that's not present in fee-for-service," says Wagar. "They must be much more involved with patients—those with complex illnesses and emerging conditions."

Social interventions are just as important as medical ones, says Wagar, who believes the primary care physician office is the pivot point around which patient

Matt Bolch is an Atlanta-based freelance writer.

health revolves. But engagement should involve every medical and nonmedical provider who interacts with the patient. Like other ACOs, Heritage emphasizes engaging patients following discharge from the hospital. The handoff from acute to post-acute care is critical to ensure patients continue progress made in rehab, such as having the correct medications, a follow-up physician visit and the proper societal or family resources needed for recuperation at home.

CONTROLLING COSTS

For Banner, teams also focus on case management, using mainly RNs with social work backgrounds, "with the added skill of being able to connect with someone and make a difference," Horn says. "They manage prescriptions, go over the discharge schedule and go into patient homes, when necessary, to proactively manage their patients."

As a result, Horn says the ACO has been able to reduce readmissions and length of stays.

Another key element of success is Banner Health's decision to partner with insurance providers that work with Banner to provide a highly coordinated patient care experience, one that Horn says emphasizes wellness, prevention and the close monitoring of chronic illnesses. The Pioneer ACO is actively looking to deploy patient-centered medical homes and an intensive ambulatory care program that would harness the power of telehealth to give high-risk patients the tools to monitor their health at home.

Despite quality efforts, ACOs may have difficulty hitting targets. CMS provides data on patient populations, but panels change regularly and updates often lag, giving ACOs an inaccurate view of the population, Gleeson says. Not only can patient turnover affect how an ACO reacts, provider turnover also can be a stumbling block. Many ACOs need to shore up adequate clinician resources to provide comprehensive services.

Horn agrees that finding the right talent can be a challenge in patient-centered care models. The organization must not only find talent with the right skill sets, those clinical employees must also thrive in a culture of change.

"Especially in a large organization, it's hard to flip the switch and focus on value," Horn says. "And in moving from volume to value, you have to have the right leadership to carry out the mission."

And in this environment, every patient counts. ACOs can't just focus on the high risk populations, they have to focus on the entire patient panels and all the associated providers, Gleeson says.

"I'm optimistic for ACOs to work," he says. "Through the enhanced concepts of accountable care and shared savings, I think all of these organizations will get through these reporting challenges in some shape or form."

A successful ACO will have both the right programs to manage risk and help patients care for themselves as well as the right technology platform to measure results and help providers proactively deliver care, says Horn.

"ACOs will need both to coordinate care on a real-time basis, with the right technology for caregivers, case managers and physicians," he says.

Looking longer term, Heritage Medical Systems plans to compile a baseline measure of every patient from medical and social standpoints, such as whether patients have adequate transportation to make medical visits or if they have children or other relatives close by who can step into a caregiver role.

"Ultimately, we want to engage those in a good state of health and help them do the right things to keep them healthy," Wagar says. "If we manage the population in this way, they will be better off overall, healthier and cost less in the long run. It's a worthwhile goal, and we have to be patient." **MHE**

Pioneer ACOs

- Allina Health
- Atrius Health
- Banner Health Network
- Beacon Health
- Bellin-Thedacare Healthcare Partners
- Beth Israel Deaconess Physician Organization
- Brown & Toland Physicians
- Dartmouth-Hitchcock ACO
- Fairview Health Systems
- Franciscan Alliance
- Genesys PHO
- Healthcare Partners Medical Group
- Healthcare Partners of Nevada
- Heritage California ACO
- JSA Medical Group, a division of HealthCare Partners
- Michigan Pioneer ACO
- Monarch Healthcare
- Montefiore ACO
- Mount Auburn Cambridge Independent Practice Assn.
- OSF Healthcare System
- Park Nicollet Health Services
- Partners Healthcare
- Physician Health Partners
- Plus (formerly North Texas ACO)
- Presbyterian Healthcare Services
- Primecare Medical Network
- Renaissance Health Network
- Seton Health Alliance
- Sharp Healthcare System
- Steward Health Care System
- Trinity Pioneer ACO, LC
- University of Michigan

Source: Centers for Medicare and Medicaid Services

Multidrug therapy for hepatitis C can reduce treatment timelines

Interferon-free solutions expected soon

BY MARI EDLIN

THE STANDARD OF CARE for hepatitis C (HCV) was uprooted in 2011. Prevailing treatment involved a combination of two drugs—pegylated-interferon and anti-viral ribavirin—taken for one year. Two new protease inhibitors, boceprevir and telaprevir, joined the regimen.

While the multidrug combination reduces treatment timelines to 24 to 48 weeks, its complexity also hampers adherence.

Patients only take telaprevir for the first 12 weeks of treatment on a specific dosing schedule. An additional 12 or 36 weeks of peginterferon alfa and ribavirin is also required.

A clinical study from Weill Cornell Medical College known as ADVANCE compared patients on a standard two-drug therapy to those on a 12-week course with the triple combination therapy of protease inhibitors followed by standard care. Results showed a sustained response of 44% versus 79%, respectively. In other words, telaprevir with peginterferon-ribavirin, compared to peginterferon-ribavirin alone, had a better response.

HCV patients typically have adherence issues with the prevailing therapy because of side effects, and the added complexity of self-management of multiple drugs exacerbates the problem. Patient lack of adherence with interferon is often attributed to depression, pain, fatigue, chronic pain and flu-like side effects.

The inherent complexity of managing hepatitis C patients has rallied specialty pharmacies, many of which have developed care management programs targeting HCV.

Andrew Muir, MD, director of gastroenterology and hepatology research at Duke University School of Medicine, says one of the biggest challenges for HCV is the large number of people who do not know they are infected.

"Since liver damage is not always related to how long someone has had HCV," he says, "there is an opportunity to develop a liver wellness strategy, not just related to drugs but also to care coordination and affordability."

Paul Turner, MD, therapeutic strategy lead for Quintiles, a biopharmaceutical services company, anticipates that the advent of new therapies and recommended testing by the Centers for Disease Control and Prevention (CDC) will raise awareness.

Last year, the CDC recommended that everyone born during the years 1945 through 1965 receive a one-time blood test for HCV to potentially uncover an estimated 800,000 undiagnosed cases of the disease. The CDC says that baby boomers are five times more likely than other adults to be infected.

Approximately 3.2 million Americans have a chronic HCV infection, with an estimated 40,000 new infections per year, according to the World Health Organization. By 2029, total annual medical costs in the United States for people with the condition are expected to more than double, from $30 billion in 2009 to approximately $85 billion.

TRIPLE THERAPY

Express Scripts, a pharmacy benefits manager (PBM), has adopted adherence initiatives for HCV. Mary Dorholt, vice president, clinical practice lead for specialty pharmacy, says the programs fit into a consumer-based, behavioral sciences approach to healthcare.

Patients might be prescribed telaprevir three times a day, seven to nine hours apart, always taken with food. A meal or snack containing about 20 grams of fat within 30 minutes before each dose is recommended. Treatment would include ribavirin twice a day and a weekly injection of interferon.

"We are helping patients to better understand how to manage side ef-

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fects from therapy, such as scheduling doses so they won't interfere with a work schedule; partnering patients with someone who can support their therapy; anticipating when patients need drug refills; and solving member cost issues," Dorholt says.

Express Scripts' care management program targeting HCV provides specialty pharmacist support to patients, including a log to schedule blood tests that help regulate drug dosage and length of therapy. The results dictate how the PBM can facilitate ongoing treatment education and follow-up. Patients also receive a treatment diary.

In addition, a new video-based virtual coaching tool provides patients with information on how a protease inhibitor works to prevent the virus from reproducing, along with instructions on how to take medications.

The Express Scripts Drug Trend Report 2012 indicates that the total drug trend for HCV therapy at the end of 2011 was 194.8%, more than 10 times the total trend for any other specialty therapy class, with the average cost per prescription rising to $3,370.99 (up from $1,389.04 in 2010).

"The triple therapy and its significant side effects make self-management difficult," says Sumit Dutta, MD, senior vice president and chief medical officer of Catamaran, a PBM based in Lisle, Ill.

Dr. Dutta says that specialty pharmacy is an ideal model for not only managing the disease itself, but also associated conditions such as depression.

Catamaran pharmacists contact patients prior to shipment of medication to offer counseling. Patients also receive calls from nurses at least two times during the first month of therapy to discuss side effects and barriers to adherence and continue during the next three months as needed.

The PBM's systems document laboratory information, such as viral load levels and hemoglobin, to gauge treatment response and anemia.

Over a six-month period, a comparison of two groups—program enrollees and those not enrolled—showed a 5% increase in the medication possession rate using the model.

FDA Approved Combination Therapy

Boceprevir + Pegylated Interferon + Ribavirin
Telaprevir+ Pegylated Interferon + Ribavirin
Pegasys + Copegus (peginterferon alfa-2a + ribavirin)
PegIntron + Rebetol (peginterferon alfa-2b + ribavirin)
Roferon A + Ribavirin (standard interferon alfa-2a + ribavirin)
Intron A + Rebetol (standard interferon alfa-2b + ribavirin)
Infergen + Ribavirin (consensus interferon + ribavirin)

Source: http://www.hivandhepatitis.com

Walgreens Specialty Pharmacy maintained medication adherence rates of 93% to 95% when moving patients from double therapy to the more complicated triple therapy regimen, says Rick Miller, director, clinical services for the pharmacy.

"Our ConnectedCare high-touch, clinical program for diseases requiring specialty pharmaceuticals, such as hepatitis C, focuses on ensuring that patients understand how and when to take their medications, assesses barriers to adherence, manages issues related to side effects and educates patients about therapy expectations," he says.

Walgreens also collects and reviews lab data to determine if a patient's response to therapy could lead to recommendations for discontinuing medications, Miller says.

Walgreens' program utilizes care management services via a call center but has supplemented triage by identifying 77 health system and retail locations closely associated with physicians to provide face-to-face intervention.

The industry is moving quickly toward transforming therapy once again by bringing interferon-free options to market for patients with genotypes 1, 2 and 3 hepatitis C. The therapy for type 1 is expected by 2015, the latter two for 2014. According to GBI Research, the market for interferon-free treatments could increase to $15 billion by 2015.

Gilead Sciences is one of the organizations developing an option to treat patients with genotypes 2 and 3 HCV. In early April, the company applied for FDA approval for its oral pill sofosbuvir taken in combination with ribavirin. Gilead said a late-stage trial testing of the drug showed no detectable virus level in 73% of study patients after 16 weeks of therapy.

Santaris Pharma A/S conducted a phase 2a trial for miravirsen, the first microRNA-targeted drug for genotype 1 to enter clinical trials. The results, reported in the online edition of the *New England Journal of Medicine* on March 27, 2013, indicate that four out of nine patients treated at the highest dose of miravirsen became HCV RNA-undetectable with just five weekly doses and without any discontinuation related to adverse effects.

New therapies are expected to cause fewer side effects and can be taken for a shorter duration. Because HCV may take years to show liver damage, it might be safe for some patients to wait for interferon-free solutions. **MHE**

Evaluate your ability to safeguard personal health information

Stage a dry run to test your response

BY KIMBERLY B. HOLMES

WHILE IT MAY BE nearly impossible to prevent a data breach from occurring, healthcare organizations should anticipate vulnerabilities and implement fixes.

The statistics are staggering. A December 2012 study by the Ponemon Institute notes 94% of health care organizations have suffered at least one data breach over the past two years, and 45% have suffered more than five incidents in the same time period.

The healthcare industry is one of the most vulnerable industries to data breaches. Security gaps and weak or non-existent IT security and internal training protocols can make organizations easy targets for hackers or become accidents waiting to happen. According to a 2011 study by Kaufman, Rossin & Co., 4.9 million individuals had their protected health information (PHI) compromised during 2009, and lost or stolen laptops were the cause of more than 25% of the reported breaches during that year—affecting more than 1.5 million individuals.

The Health Information Technology for Economic and Clinical Health (HITECH) Act was enacted in 2009 in part to promote and expand the adoption of health information technology. The HITECH Act has made significant changes to the 1996 Health Information Portability and Accountability Act (HIPAA), previously the federal standard with respect to the privacy and security requirements of PHI. The HITECH Act Final Rule, released in January 2013, provided additional clarification and guidance to the Act including an expanded definition of "business associate."

The Final Rule also includes additional burdens and liabilities on both covered entities and business associates with respect to the handling and sharing of PHI. In addition, breaches are now presumed reportable unless there is a low probability that the PHI has been compromised as determined after a risk assessment.

With the HITECH Act Final Rule just released and compliance required on or before September 23, 2013, managed care organizations and all other healthcare organizations (as well as their business associates) should consider putting pre-breach risk management and risk assessment policies into place now, before a data breach occurs and the HITECH Act's new requirements come into play.

The Office of Civil Rights currently does not offer definitive guidance on what "full compliance" with HIPAA and the HITECH Act means. However, recent government settlements and court cases involving civil monetary penalties as a result of a healthcare data breach demonstrate there are several steps healthcare organizations could be taking to build the best pre-breach defenses possible.

The following list of eight protocols can help mitigate the risk of a data breach and the potential liabilities if a breach should occur.

1

Conduct an internal security risk analysis and document ongoing risk assessment activities. Identifying and shoring up known and discovered security gaps as a result of these efforts may go a long way to positioning your organization as deliberate, thoughtful and committed to data security in the wake of a breach and a possible government audit.

2

Routinely test your organization's incident response plan, so key people are not only aware of their duties and responsibilities when a breach is discovered, but can act quickly and effectively. Document these internal "dry runs" to dem-

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onstrate, if needed post breach, that your organization's response plan was not collecting dust on a shelf but was routinely tested.

3

Conduct an internal self-audit, using the Office for Civil Rights' (OCR's) audit standards.

The OCR's pilot protocol (used to complete 115 audits last year), is the basis for the permanent protocol scheduled to begin late 2013 or early 2014. The OCR also offers examples that show how covered entities can effectively comply with the requirements of the HIPAA Privacy and Security Rules.

4

Strengthen security protocols for all mobile electronic devices, and consider creating a security policy dedicated to mobile devices. According to the Ponemon Institute's Third Annual Benchmark Study on Patient Privacy & Data Security, 81% of respondent healthcare organizations allow their employees and medical staff to use personal mobile devices to connect to the organization's network, and 46% do not require any security safeguards for these devices.

Since it's common for a lost or stolen laptop or smart phone to result in a breach of PHI, managed care organizations should take steps to shore up security with respect to these devices. Consider encrypting data, restricting access or use, developing policies and procedures prohibiting the downloading of PHI, and employing data loss prevention technology.

5

Re-evaluate your business associate agreements and their security practices. The HITECH Act final rule provides that, in some cases, business associate compliance failures may become your organization's problem. Liability for customer/patient notification under the HITECH Act always remains with the managed care organization as the "covered entity"—even if the notification obligations are delegated to a business associate. In addition, healthcare organizations with operations in multiple states may be subject to an evolving series of state privacy laws, which may impose stricter requirements than those under the HITECH Act.

MHE EXECUTIVE VIEW

The Ponemon Institute's 3rd Annual Benchmark Study on Patient Privacy & Data Security finds that:

- **Employee mistakes continue to be a significant cause of data breach incidents.**
- **Costs for data breaches can reach $1 million.**
- **Ninety-four percent of the 80 organizations studied had a breach in the past two years.**

6

Consider your organization's use of cloud computing, as well as that of your business associates. According to Ponemon Institute, more than 60% of healthcare organizations use the cloud both for storage of and sharing access to PHI. Your organization should have policies in place regarding the use of cloud-based services. Review your business associates' use of cloud-based services and their policies to ensure that any inconsistencies in usage protocols can be addressed by both organizations to help better safeguard stored PHI.

7

Train your employees. Apart from the fact that it's required under the HITECH Act, data privacy training for all employees and other individuals under your organization's control is essential. The training should be frequent, pertinent to an individual's job function and—to be most effective—it should be delivered in person by your organization's data security officers or other IT security personnel. In the wake of a data breach, training offered as an annual online program may not strongly demonstrate your commitment to fully educating all employees about their roles with respect to maintaining the security of the organization's PHI.

8

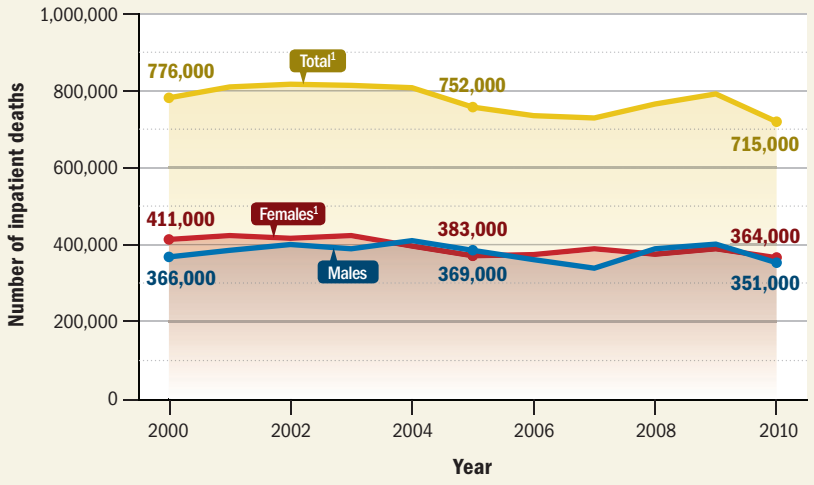
Maintain rigor and discipline around the simple basics, such as: locking cabinets and doors to rooms where PHI is stored; limiting access to PHI to only those individuals with a need to know; paying particular attention to keeping paper records locked up and closely monitored for access; and ensuring employees have the ability to easily lock and freeze their computer screens to prevent the errant viewing of PHI by others.

Our fast-evolving, technology-dependent world has made it more difficult to protect and secure PHI. While it may be nearly impossible to prevent a data breach from occurring, healthcare organizations should anticipate vulnerabilities and implement fixes to shore up their organization's risk profile in advance of a breach. Taking these steps will also help increase the possibility of having an unremarkable outcome if the OCR either audits or post-breach evaluates your organization's commitment to preparedness and security with respect to safeguarding PHI. **MHE**

MHE Resource

Inpatient hospital deaths on the decline

INPATIENT HOSPITAL DEATHS: UNITED STATES, 2000–2010



[1]Significant decrease from 2000 to 2010.
NOTE: Statistical significance was measured using a weighted least-squares regression method, including data from all years, to measure linear trends over time.

Source: CDC/NCHS, National Hospital Discharge Survey, 2000–2010.

AS HOSPITALIZATIONS rise, hospital deaths are on the decline.

According to the Department of Health and Human Services, the number of inpatients who died while hospitalized decreased while the rate of hospitalizations increased. The report looked at data from the National Hospital Discharge Survey.

During the 11-year period of 2000 to 2010, hospital deaths decreased by 8%, while the rate of all hospitalizations increased by 11%. In 2000, out of every 100 patients, 2.5 would die in the hospital. This number fell to 2.0 out of 100 in 2010.

Despite most Americans hoping to die peacefully in their own home, roughly one-third of the deaths between 2000 and 2010 occurred during an inpatient stay in a general hospital. However, the number of deaths decreased from 776,000 in 2000 to 715,000 in 2010, but hospitalizations went from 31.7 million to 35.1 million. Male inpatient hospital deaths did not decrease in a significant way over the 11-year period, but female hospital deaths went from 411,000 to 364,000.

The average age of hospitalized patients remained relatively constant over the studied period: age 72, during 2000 and 2005, and age 73, during 2010.

While patients under the age of 65 have a lower rate of death, the percentage of deaths increased from 24% in 2000 to 27% in 2010. At the other end of the spectrum, patients over the age of 85 accounted for roughly a quarter of all hospital deaths, seeing a slight increase over the reported period. Patients over the age of 75 years made up the majority of patients at 56% in 2000 and 54% in 2010.

Kidney disease and cancer saw the greatest decreases, at 65% and 46%. Other diagnoses that saw the hospital deaths decrease include respiratory failure, pneumonitis, stroke, pneumonia, and heart disease.

However, the first-listed diagnosis of septicemia did see an increase in the rate of death, 17% from 2000 to 2010. The number of patients who died in the hospital while being treated for the condition tripled from 45,000 in 2000 to 132,000 in 2010. These first-listed diagnoses accounted for 66% of all hospital deaths in 2000 and 70% in 2010.

As a group, patients who died in the hospital were more likely to have longer hospitalizations than the typical patient with an average length of stay being 7.9 days. The average length of stay for all inpatients was 4.8 days. And 45% of patient deaths did occur during stays lasting 3 days and under, but hospital stays of this length make up the bulk of all inpatient stays. Far more important is the fact that 27% of hospital deaths occurred during hospitalizations lasting 10 or more days, despite the fact that hospitalizations of this length only account for 10% of all inpatients. **MHE**

—Miranda Hester

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