Be member-centric
PAGE 37

Hepatitis C drugs
PAGE 40

Docs bemoan EHRs
PAGE 53

Managed Healthcare®
EXECUTIVE

The C-Suite Advisor ManagedHealthcareExecutive.com

ARE YOUR NETWORKS TOO NARROW?

Competition among providers
PAGE 25

Seattle hospital balks at exchange networks
PAGE 29

Pharmacies want preferred status
PAGE 35

March 2014 VOL. 24 NO. 3
ADVANSTAR MEDICAL COMMUNICATIONS GROUP

Managed Healthcare Executive
MARCH 2014
Narrow networks | Member-centric best practices | New hepatitis C drugs | EHR attitudes | ICD-10 deadline
VOLUME 24 | NUMBER 3

BECAUSE YOU'RE MORE THAN JUST A NAME PRINTED ON A PRESCRIPTION LABEL.

At LDI, we strive to find new ways to solve your specific health care needs, from effective and individualized cost management strategies to innovative pharmacy benefit advancements. Collaboration is a cornerstone of our company, and we pledge to always treat our relationship as just that – a relationship.

LDI

integrated pharmacy services

www.LDIRx.com

Health Solutions Made Personal.

the Advisors

MISSION STATEMENT: Managed Healthcare Executive provides senior-level decision makers the trends, analysis, strategies and applications they need to innovate value in a rapidly changing healthcare landscape.

EDITORIAL ADVISORY BOARD

DISEASE/CARE MANAGEMENT

Joel V. Brill, MD is chief medical officer of Predictive Health LLC, which performs predictive modeling analysis and implements care management solutions.

Paula M. Sauer is senior vice president of pharmacy care management at Medical Mutual of Ohio. She has made contributions in medical review, network management and health promotion.

Al Lewis is executive director of the Boston-based Disease Management Purchasing Consortium LLC, which assists health plans with their disease management outsourcing strategies, vendor selection/evaluation and contracting. He also is past president of the Disease Management Association of America.

HEALTH PLANS/PAYERS

Douglas L. Chaet, FACHE is senior vice president of contracting and provider networks at Independence Blue Cross in Philadelphia. He is also the founder and chairman emeritus of the American Association of Integrated Healthcare Delivery Systems.

Daniel J. Hilferty is president and chief executive officer of Independence Blue Cross, a leading health insurer in southeastern Pennsylvania with nearly 3.3 million members nationwide. Hilferty has more than 25 years of experience in healthcare, government affairs, communications and education.

Martin P. Hauser is the president and CEO of SummaCare, Inc., which he helped to create while serving as the president of the Akron City Health System. The plan has grown to more than 100,000 members. He also served as the first president of the Cleveland Health Network Managed Care Organization.

Margaret A. Murray is the founding CEO of the Association for Community Affiliated Plans (ACAP), which represents 54 nonprofit safety net health plans in 26 states. An expert on healthcare policy for low-income people, she is also the former New Jersey State Medicaid Director.

INDEPENDENT THOUGHT LEADERS

Don Hall, MPH is principal of DeltaSigma LLC, a consulting practice specializing in Medicaid and Medicare Special Needs Plans. He has more than 30 years of experience and most recently served as president and CEO of a non-profit, provider-sponsored health plan.

J.D. Kleinke is a medical economist, author and health information thought leader. He helped to create four healthcare informatics organizations and has served on various boards. J.D. is the CEO of Mount Tabor, a health IT development company, and is a resident Fellow at the American Enterprise Institute.

PHARMACY

Perry Cohen, PharmD is chief executive officer of The Pharmacy Group and the TPG family of companies, which offers services to associations, healthcare and information technology organizations, payers and pharmaceutical companies to grow revenue and improve the financial performance of their products and services.

Paul J. Setlak, PharmD is an associate director for Baxter Healthcare. He provides expertise related to health economics, market access and public policy. He teaches at Loyola University in Chicago.

PHARMACY BENEFIT MANAGERS

David Calabrese, RPh, MHP is vice president and chief pharmacy officer of Catamaran, a pharmacy benefits manager that manages more than 200 million prescriptions each year on behalf of 25 million members. Catamaran is headquartered in Lisle, Ill.

TECHNOLOGY

Mark Boxer is executive vice president and global chief information officer for CIGNA. He is an expert on public health as well as technology infrastructure and strategy.

Dennis Schmuland, MD health plan industry solutions director for Microsoft Corp., is responsible for the company's strategy and solutions for the managed care industry.

The board members and consultants contribute expertise and analysis that help shape the content of Managed Healthcare Executive

Managed Healthcare EXECUTIVE

EDITORIAL

DAN VERDON
Group content director
(440) 891-2614
dverdon@advanstar.com

JULIE MILLER
Content channel director
(440) 891-2723
julie.miller@advanstar.com

JULIA BROWN
Content specialist
(440) 891-2729
jbrown@advanstar.com

JILL WECHSLER
Washington bureau chief

ROBERT MCGARR
Group art director

Send editorial materials to:
Managed Healthcare Executive
24950 Country Club Blvd. #200
North Olmsted, OH 44070

PRODUCTION

KAREN LENZEN
Production director
klenzen@media.advanstar.com

AUDIENCE DEVELOPMENT

JOY PUZZO
Corporate director
(440) 319-9570
jpuzzo@advanstar.com

CHRISTINE SHAPPELL
Director
(201)-391-2359
cshappell@advanstar.com

JOE MARTIN
Manager
(218) 740-6375
jmartin@advanstar.com

SUBSCRIPTION SERVICES
888-527-7008

PUBLISHING & SALES

GEORGIANN DECENZO
Executive vice president
(440) 891-2778
gdecenzo@advanstar.com

KEN SYLVIA
Vice president, group publisher
(732) 346-3017
ksylvia@advanstar.com

MIKE WEISS
Group publisher
(732) 346-3071
mweiss@advanstar.com

PHIL MOLINARO
National account manager
(732) 346-3074
pmolinaro@advanstar.com

MARGIE JAXEL
Dir. of Business Develpment, Healthcare Technology Sales
(732) 346-3003
mjaxel@advanstar.com

PATRICK CARMODY
Account manager, classified/display advertising
(440) 891-2621
pcarmody@advanstar.com

KAREN GEROME
Account manager, classified/display advertising
(440)-891-2670
kgermone@advanstar.com

CHRISTINA ADKINS
Account manager, recruitment advertising
(440)-891-2762
cadkins@advanstar.com

JOANNA SHIPPOLI
Account manager, recruitment advertising
(440) 891-2615
jshippoli@advanstar.com

DON BERMAN
Business director, emedia
(212) 951-6745
dberman@advanstar.com

GAIL KAYE
Director, sales data
(732) 346-3042
gkaye@advanstar.com

HANNAH CURIS
Sales support
(732) 346-3055
hcuris@advanstar.com

REPRINTS

877-652-5295 ext. 121/
bkolb@wrightsmedia.com

Outside US, UK, direct dial:
(281) 419-5725. Ext. 121

TAMARA PHILLIPS
List Account Executive
(440) 891-2773
tphillips@advanstar.com

MAUREEN CANNON
Permissions
(440) 891-2742
mcannon@advanstar.com

ADVANSTAR

JOE LOGGIA
Chief executive officer

TOM FLORIO
Chief executive officer
fashion group,
executive vice president

TOM EHARDT
Executive vice president,
chief administrative officer
& chief financial officer

GEORGIANN DECENZO
Executive vice president

CHRIS DEMOULIN
Executive vice president

RON WALL
Executive vice president

REBECCA EVANGELOU
Executive vice president,
business systems

JULIE MOLLESTON
Executive vice president,
human resources

TRACY HARRIS
Senior vice president

FRANCIS HEID
Vice president,
media operations

MICHAEL BERNSTEIN
Vice president, legal

J VAUGHN
Vice-president, electronic
information technology

Managed Healthcare EXECUTIVE

Volume 24 Issue 3
MARCH 2014

COVER STORY

ARE YOUR NETWORKS TOO NARROW?

ESSENTIALS

SPECIAL REPORT

DEPARTMENTS

PIPELINE

COMMENTARY

Twitter.com/MHExecutive

Facebook.com/ManagedHealthcareExecutive

Microfilm or microfiche copies of annual issues available through Advanstar Marketing Services, (800) 346-0085 ext. 477.
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.*

Cover: Thinkstock/iStock (background); Thinkstock/Wavebreak Media/Wavebreak Media Ltd. (hand).

INDICATION

Velphoro® (sucroferric oxyhydroxide) is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

IMPORTANT SAFETY INFORMATION

- Velphoro must be administered with meals. Velphoro tablets must be chewed and not swallowed whole. To aid with chewing and swallowing, the tablets may be crushed.
- Patients with peritonitis during peritoneal dialysis, significant gastric or hepatic disorders, following major gastrointestinal (GI) surgery, or with a history of hemochromatosis or other diseases with iron accumulation have not been included in clinical studies with Velphoro. Monitor effect and iron homeostasis in such patients.
- In a parallel design, fixed-dose study of 6 weeks duration, the most common adverse drug reactions to Velphoro chewable tablets in hemodialysis patients included discolored feces (12%) and diarrhea (6%).
- Velphoro can be administered concomitantly with ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metformin, metoprolol, nifedipine, omeprazole, quinidine and warfarin. Take alendronate and doxycycline at least 1 hour before Velphoro. Velphoro should not be prescribed with oral levothyroxine and oral vitamin D analogs.

Introducing Velphoro® (sucroferric oxyhydroxide)

- Sustained phosphorus control and significantly lower pill burden over 52 weeks*[1,2]
  - Efficacy comparable to sevelamer carbonate[1]
  - 5.4 fewer tablets per day than sevelamer carbonate[2]
- Starting dose of 1 chewable tablet per meal[1]
- Non-calcium, iron-based formulation[1]
  - Minimal systemic iron absorption
- Well tolerated*[1]

* A 2-part, 52-week, open-label, active-controlled, parallel-group phase 3 clinical study evaluated the safety and efficacy of Velphoro in lowering serum phosphorus. Patients (N=1054) had chronic kidney disease, were on hemodialysis or peritoneal dialysis, and had serum phosphorus levels ≥6 mg/dL. In part 1 (Study 05A), patients were randomized to treatment with either Velphoro (starting dose: 2 tablets/day) or sevelamer carbonate (starting dose: 6 tablets/day) for 24 weeks. After 24 weeks, 93 hemodialysis patients on Velphoro were re-randomized to either a maintenance dose of Velphoro or low-dose control (Velphoro 250 mg/day) for 3 more weeks. Following completion of Study 05A, part 2 (Study 05B), a 28-week extension study, began. Patients continued treatment with either Velphoro (n=391) or sevelamer carbonate (n=267) according to their original randomization.[1,2]

Please see Brief Summary on the following page or visit www.Velphoro.com for full Prescribing Information

References: 1. Velphoro® [package insert]. Waltham, MA: Fresenius Medical Care North America; 2013. **2.** Data on file. Fresenius Medical Care North America, Waltham, MA.

Distributed by:
Fresenius Medical Care North America
Waltham, MA 02451

FRESENIUS MEDICAL CARE

VELPHORO®
(sucroferric oxyhydroxide)
chewable tablets

POTENCY MAKES IT POSSIBLE

Brief Summary:
Please see Full Prescribing Information for additional information

VELPHORO®
(sucroferric oxyhydroxide)
chewable tablets

INDICATIONS AND USAGE

Velphoro (sucroferric oxyhydroxide) is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

DOSAGE AND ADMINISTRATION

Velphoro tablets must be chewed and not swallowed whole. To aid with chewing and swallowing, tablets may be crushed.

The recommended starting dose of Velphoro is 3 tablets (1,500 mg) per day, administered as 1 tablet (500 mg) 3 times daily with meals.

Adjust by 1 tablet per day as needed until an acceptable serum phosphorus level (less than or equal to 5.5 mg/dL) is reached, with regular monitoring afterwards. Titrate as often as weekly.

DOSAGE FORMS AND STRENGTHS

Velphoro (sucroferric oxyhydroxide) chewable tablet 500 mg.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Patients with peritonitis during peritoneal dialysis, significant gastric or hepatic disorders, following major gastrointestinal surgery, or with a history of hemochromatosis or other diseases with iron accumulation have not been included in clinical studies with Velphoro. Monitor effect and iron homeostasis in such patients.

ADVERSE REACTIONS

In a parallel design, fixed-dose study of 6 weeks duration, the most common adverse drug reactions to Velphoro chewable tablets in hemodialysis patients included discolored feces (12%) and diarrhea (6%).

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Medical Care North America at 1-800-323-5188 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

Velphoro can be administered concomitantly with ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metformin, metoprolol, nifedipine, omeprazole, quinidine and warfarin.

Take alendronate and doxycycline at least 1 hour before Velphoro.

Velphoro should not be prescribed with oral levothyroxine and oral vitamin D analogs.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category B: Reproduction studies have been performed in rats and rabbits at doses up to 16 and 4 times, respectively, the human maximum recommended clinical dose on a body weight basis, and have not revealed evidence of impaired fertility or harm to the fetus due to Velphoro. However, Velphoro at a dose up to 16 times the maximum clinical dose was associated with an increase in post-implantation loss in pregnant rats. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

There are no adequate and well-controlled studies in pregnant women.

Labor and Delivery

No Velphoro treatment-related effects on labor and delivery were seen in animal studies with doses up to 16 times the maximum recommended clinical dose on a body weight basis. The effects of Velphoro on labor and delivery in humans are not known.

Nursing Mothers

Since the absorption of iron from Velphoro is minimal, excretion of Velphoro in breast milk is unlikely.

Pediatric Use

The safety and efficacy of Velphoro have not been established in pediatric patients.

Geriatric Use

Of the total number of subjects in two active-controlled clinical studies of Velphoro (N=835), 29.7% (n=248) were 65 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

OVERDOSAGE

There are no reports of overdosage with Velphoro in patients. Since the absorption of iron from Velphoro is low, the risk of systemic iron toxicity is negligible. Hypophosphatemia should be treated by standard clinical practice.

Velphoro has been studied in doses up to 3,000 mg per day.

HOW SUPPLIED/STORAGE AND HANDLING

Velphoro are chewable tablets supplied as brown, circular, bi-planar tablets, embossed with “PA 500” on 1 side. Each tablet of Velphoro contains 500 mg iron as sucroferric oxyhydroxide. Velphoro tablets are packaged as follows:

NDC 49230-645-51 Bottle of 90 chewable tablets

Storage

Store in the original package and keep the bottle tightly closed in order to protect from moisture.

Store at 25°C (77°F) with excursions permitted to 15 to 30°C (59 to 86°F).

PATIENT COUNSELING INFORMATION

Dosing Recommendations

Inform patients that Velphoro tablets must be chewed and not swallowed whole. To aid with chewing and swallowing, the tablets may be crushed *[see Dosage and Administration]*.

Velphoro should be taken with meals.

Some drugs need to be given at least one hour before Velphoro *[see Drug Interactions]*.

Adverse Reactions

Velphoro can cause discolored (black) stool. Discolored (black) stool may mask GI bleeding. Velphoro does not affect guaiac based (Hämocult) or immunological based (iColo Rectal, and Hexagon Opti) fecal occult blood tests.

Distributed by:

Fresenius Medical Care North America
920 Winter Street
Waltham, MA 02451

FRESENIUS
MEDICAL CARE

US Patent Nos. 6174442 and pending, comparable and/or related patents.

HEALTHCARE.GOV FULL OF HOLES

Target's breach is nothing compared to this

My local Target store still has a sign posted reminding customers that they can receive free credit monitoring and identity theft protection. It's a make-good after the retailer's massive data breach a few months ago.

Should Target hang its head in shame or should other businesses feel empathy because no system is 100% secure? It can happen to anyone? It's probably all of the above.

But at least Target—with 2,000 locations—can patch its system and help the 110 million affected customers recover. In fact, the store was bustling during my Saturday morning visit, as if nothing had happened.

Gateway to trouble

If there were a security breach to *healthcare.gov,* the fallout would be far worse than anything Target has experienced. A breach could spread well beyond the core marketplace platform and into much larger and far-reaching systems, such as IT interfaces for nearly all the nation's health insurers, state Medicaid agencies and the ubiquitous Internal Revenue Service, just to name a few.

According to Kevin Johnson, CEO of Secure Ideas, a security professional who testified before Congress recently about *healthcare.gov,* exposures on the site have been identified that leave the door open for cyber attacks. In the months since the 20 or more weaknesses were first documented, none of them have been fully remedied.

I called Johnson, and he told me there are generally two categories of vulnerabilities: hackers' access to sensitive personal data; and hackers' ability to launch malware through a site. *Healthcare.gov* has both of these problems, and federal officials were aware of them months ago.

A vulnerability report was presented by David Kennedy of TrustedSec, who is also known as the "white hat hacker" in IT circles. He engaged Johnson and five other experts to review his report in late 2013 and verify for lawmakers that he wasn't kidding about the faults.

"Their initial reaction was that security is fine," Johnson told me. "When more information was brought forward, the answer was that it wasn't as bad as it seems."

Healthcare.gov isn't a typical site, in that it's a gateway to so many other businesses and government entities. A breach could be disastrous.

"If you want to attack American citizens, this is the site to do it," according to Johnson.

In fact, when the Department of Health and Human Services changed tech vendors for *healthcare.gov* recently, it gave me the illusion that better security was forthcoming at last. Johnson, however, believes the new vendor has an even worse track record and anticipates the site will be just as weak as it ever was.

Best practice

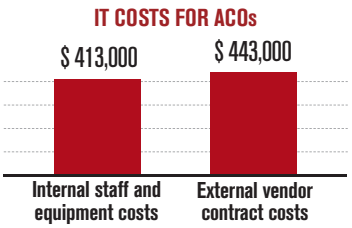
One of your best practices is to treat every interaction with *healthcare.gov*—or any state exchange site for that matter—as potentially dangerous to your security. Johnson says too many insurers will consider the exchanges to be trusted sources, with an assumption that what comes through a state or federal government channel must be secure.

"It's critical that organizations start to embed this type of process into their development and purchasing," he says. "Security is important, yet so many have treated it like something we can bolt on."

Read the blog by David Kennedy here:
http://bit.ly/1dkEkq8

Julie Miller

ABOUT THE AUTHOR
Julie Miller is the content channel director of Managed Healthcare Executive. She can be reached at julie.miller@advanstar.com.



Source: National Association of ACOs, January 2014

What consumers won't do 7 / Drug shortages affect care 8

ACA REVISION DELAYS MANDATE FOR SUBSET OF LARGE EMPLOYERS

House Republicans looking into the ultimate impact of Obama's latest alteration

ROBIN DEMATTIA
MHE CONTRIBUTOR

NATIONAL REPORTS — Undoubtedly, Affordable Care Act (ACA) guidelines will be modified in time to overcome implementation challenges, according to Timothy Jost, professor of law at the Washington and Lee University School of Law.

"This is probably far more ambitious than anything that's been tried in the private sector," Jost says. "You could say it's surprising it's gone as smoothly as it has."

However, Jost notes that the delay of the employer mandate is the most noteworthy rework of ACA.


TIMOTHY JOST

In July 2013, the administration moved the original 2014 mandate to 2015, requiring employers with 50 or more employees to offer healthcare coverage or pay a fine. However, last month, officials revised the date again, allowing employers with 50 to 99 workers until 2016 before they have to offer coverage. Still, larger employers (100 or more workers) must comply with the 2015 deadline.

Part of the reason behind the delay, according to federal officials, was to allow more time to simplify the reporting process for employers. Critics believe the mandate ultimately will drive employers to cut jobs. Republicans on the House Energy and Commerce Committee launched an investigation to estimate the impact resulting from the change.

A 2011 survey by McKinsey found that 30% of employers would consider dropping coverage. However, many also point to the fact that nearly all large employers already offered coverage prior to ACA.

Others are angling for the penalty related to the individual mandate to be forgiven for consumers in 2014.

Several other ACA provisions were adjusted during implementation—such as internal and external appeals of coverage determinations for insurers and the combining of out-of-pocket costs for medical and pharmacy when calculating caps on consumer outlays. Other adjustments were necessary because IRS regulations were not available to reflect the ACA.

Overall, Jost believes the administration is responding and trying to prioritize ACA implementation fixes.

"Since Congress is not functional, the administration is not able to go to Congress to ask for technical corrections," Jost says. "It has been prioritizing the provisions that are really important, like getting the exchanges up and running, and allowing more time for compliance."

Jost adds that ACA isn't taking place in a vacuum. The country is still recovering from "one of the great economic shocks in our lifetime."

Of course, many ACA challenges are politically driven. For example, Republican states are more likely to default toward not expanding Medicaid and not operating their own exchange marketplaces.

"This is all taking place in the context of an opposition party that has been almost entirely defined over the last four years in opposition to this program," Jost says.

He expects those who have been adamantly opposed to the law will come to terms with the reforms it has enacted. ■

EMPLOYER MANDATE

Original ACA rule (March 2010)	Beginning on January 1, 2014, employers with 50 or more full-time workers must offer health coverage or pay a fine.
First revision (July 2013)	Start date moved to January 1, 2015.
Second revision (February 2014)	Start date moved to January 1, 2016, but only for employers with 50 to 99 workers.

CONSUMERS UNWILLING TO CHANGE BEHAVIOR TO LOWER CARE COSTS

Accenture poll indicates only 23% would change primary care doctor

JEFF BENDIX
ADVANSTAR CONTRIBUTOR

NATIONAL REPORTS — While patients may complain about the rising cost of their healthcare, few of them appear willing to do much about it, according to a new survey.

The survey, by Accenture consulting group, finds that an overwhelming majority—72%—of retail consumers say affordability is their most important consideration when it comes to healthcare. That compares with 16% who cite the quality of care, and 9% who cite access.

When it comes to altering their own behavior to reduce healthcare costs, however, the picture looks very different:

- 23% of those surveyed say they would be willing to change the primary care physician they see for regular office visits;
- 29% would change the hospital they use for inpatient care;
- 43% would get routine care from a nurse practitioner rather than a physician; and
- 41% would change brand prescriptions for treating the same condition.

And while 60% say that low out-of-pocket costs for doctor visits is an important consideration, only 19% think it's important to know the cost of care in advance.

The survey defines a retail consumer as someone who is under age 65 and is either uninsured, has individual coverage, or coverage through an employer with fewer than 100 employees.

The findings are not surprising, given that the healthcare industry has long discouraged a sense of engagement among consumers, says Wayne Guerra, MD, MBA, a former emergency department physician and co-founder and chief medical officer of iTriage, an app that helps consumers identify medical problems and seek treatment for them.

"I think we're asking questions of people who have never really experienced true consumer choice in healthcare," Guerra says. "It's what they're used to and what we've created by not having those choices."

> "We're asking questions of people who have never really experienced true consumer choice in healthcare."
> —WAYNE GUERRA, MD

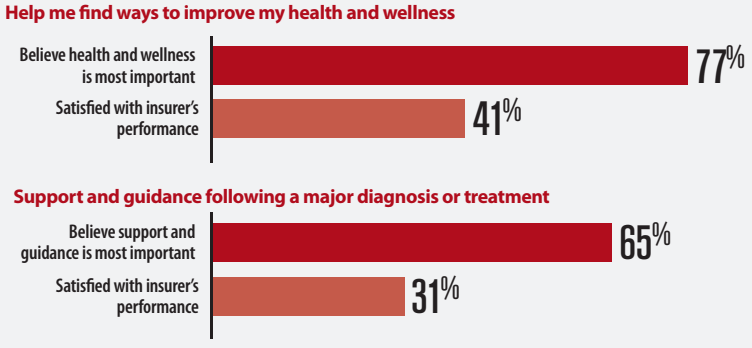
Other findings from the survey:

Among retail consumers eligible for subsidies to buy insurance, 81% say they want help in improving their health and wellness, but only 60% of subsidy-eligible consumers say getting regular checkups is a priority, and 26% say they don't do anything about their health until they actually become sick.

When it comes to what retail health customers want from a health insurance provider, 72% say the most important consideration is having a live person available to answer questions and resolve issues, 65% say it's support and guidance following a major diagnosis or treatment and 63% say it's help finding doctors, getting appointments and negotiating costs. ◘

WHAT CONSUMERS WANT

Retail health consumer needs when getting healthcare



Source: Accenture Healthcare Consumer Survey

@ More online

The survey, "Reconciling the Great Healthcare Consumer Paradox: Are Consumers Willing to Change to Get What They Want" can be viewed here: http://bit.ly/1fhMz6r

DRUG SHORTAGES IMPACT PATIENT CARE

Half of clinicians report errors, adverse events, higher costs

TRACEY WALKER
ADVANSTAR CONTRIBUTOR

NATIONAL REPORTS — Drug shortages remain a serious problem for patient safety, according to newly published results from a survey of pharmacy directors. Nearly half of the responding directors reported adverse events at their facilities due to drug shortages, including patient deaths.

The survey was conducted by Northwestern Medicine researchers in partnership with MedAssets, as part of the MedAssets Pharmacy Coalition to better understand how drug shortages affect patient outcomes. The survey asked pharmacy directors from a variety of healthcare settings to supply information on drug shortage-related patient complaints, adverse events, medication errors, patient outcomes, demographics and institutional costs. The survey's findings were detailed in "Effects on Patient Care Caused by Drug Shortages: A Survey," a research article published in the November/December issue of the *Journal of Managed Care Pharmacy* (JMCP).

"The basic findings of the study are that institutions are still reporting harms due to drug shortages. These harms include poor patient outcomes, medication errors and delayed or cancelled care. Participants also indicated that they are receiving patient complaints due to drug shortages," says Milena McLaughlin, PharmD, MSc, clinical pharmacist at Northwestern Memorial Hospital, assistant professor at the Midwestern University Chicago College of Pharmacy and lead author of the *JMCP* article.

This is the first study to date to address patient complaints, as well as the significance of adverse events relating to patient outcomes, according to Despina Kotis, PharmD, director of pharmacy at Northwestern Memorial HealthCare and co-author of the *JMCP* article.

> "Pharmacy directors still see significant shortages on a day-to-day basis."
> —DESPINA KOTIS

"The survey made it clear that patients were aware of drug shortages and that patient complaints were not uncommon as a result," Dr. Kotis says. "We also saw respondents report very troubling adverse outcomes associated with shortages, including patient deaths."

Of the respondents, two pharmacy directors reported patient deaths associated with drug shortages, three reported disabling adverse events and 34 reported adverse events that required intervention.

INCREASED READMISSIONS

In addition to the more well-known impacts, the study showed that nearly 10% of the reported adverse patient outcomes were increased readmissions due to drug shortage related treatment failures. Thirty-eight percent of the surveyed pharmacy directors also said their organization had received at least one patient complaint related to shortages, and of those respondents reporting the actual number of patient complaints about 20% reported a total of more than 10 complaints.

The article's authors suggest that documented occurrence of increased readmission rates and the impact of drug shortage-related patient complaints could affect healthcare reimbursements for providers in the future as part of the Affordable Care Act.

"Drug shortages are not going away," Dr. Kotis says. "The survey shows that pharmacy directors still see significant shortages on a day-to-day basis that put patients at risk. Outcomes due to shortages that were commonly reported include patient harm, canceled care, and delayed care. The results also showed increased resources were used to manage the shortage problem."

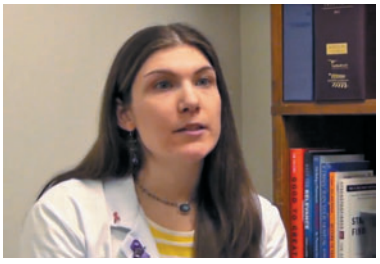
EXTRA STAFF NEEDED TO MANAGE THE EFFECTS

A majority of respondents estimated that the drug shortages cost their institutions close to $100,000 per quarter. In addition, about one-quarter reported adding one full-time equivalent staff to manage the drug shortages. ◘

@ More online

Read the February 5, 2014, FDA report that indicates the agency was able to prevent 140 drug shortages:
http://1.usa.gov/1j3kZdm

Watch the MHE video on drug shortages and patient care:



http://www.youtube.com/watch?v=nMff7NIc0EM

MANAGED HEALTHCARE
EXECUTIVE
For Decision Makers in Healthcare

ManagedHealthcareExecutive.com

RISKY BUSINESS WITH OBAMACARE

Insurers fight back as three Rs become the pawns of health reform politics

Painted as costly bailouts for insurers by "Obamacare" opponents, risk corridors and reinsurance have become hot political issues. In February, Republicans searched for ways to further discredit the Affordable Care Act (ACA) and trained their attention on provisions designed to make exchanges more efficient.

The main charge is that the federal government will end up paying millions to insurers under the risk corridor formula, because plans will run up huge costs to meet ACA mandates and requirements. While that's possible if all the plans end up suffering loses from pricing products too low, most actuaries and insurers believe the program will balance out. The Congressional Budget Office (CBO) recently calculated that risk corridors might actually save the government $8 billion because payments from profitable plans will greatly exceed outlays to plans that lose.

The three Rs will help create a stable and predictable environment for new markets.

Risk adjustment, reinsurance and risk corridors— dubbed the "three Rs"—were included in the ACA to attract private insurers to the exchanges by protecting them from major losses while they gain experience on enrollees and their costs. These provisions encourage plans to initially offer relatively lower premiums by requiring profitable plans and the government to share some of the losses if costs exceed initial expectations.

Risk adjustment is a permanent program designed to balance adverse selection. Insurers that enroll more high-cost individuals will collect funds from those with lower-risk enrollees, based on risk score calculations adjusted for demographics, geographic variation, plan cost-sharing and other factors.

Reinsurance is a temporary program that expires in 2016, funded by fees paid by insurers, based on enrollment, to stabilize premiums for individual exchange plans.

Risk corridors, also authorized for only three years, similarly provide a cushion for insurers against price uncertainties. Yet, calculating risk corridors will be tricky, based on complex formulas that align with medical loss ratio rules for calculating administrative expenses as well as quality improvements.

These provisions became more critical to insurers when exchanges experienced lower-than-expected enrollment. The Department of Health and Human Services also permitted insurers to reinstate cancelled policies, which increased uncertainty in the exchanges.

Debate heats up

Sen. Marco Rubio of Florida leads the anti-bailout campaign, warning that risk provisions could cost taxpayers millions and should be repealed, or at least required to be budget neutral. Rubio made his case at a hearing held by the House Committee on Oversight and Government Reform last month. While risk corridors are normally a valid means for protecting insurers from market anomalies, Rubio said the risk of a bailout is high under ACA because too many older and sicker individuals will sign up.

Reinsurance "is pure corporate welfare," stated health policy analyst Doug Badger, predicting that it will transfer $20 billion over three years from enrollees in commercial plans. But Washington & Lee University professor Timothy Jost noted that risk corridors stem from the Bush administration's Medicare Part D drug program, which encouraged private insurers to offer the untested drug-only plans.

Insurers are fighting the bailout charges, emphasizing the importance of risk protections in the wake of ACA implementation snafus. An issue brief from America's Health Insurance Plans explains how the three Rs will help create a stable and predictable environment for new markets and will promote competition based on quality and efficiencies, rather than risk selection. Read it here: *http://bit.ly/1mu49tC.*

ABOUT THE AUTHOR

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

MEDICAL REVIEW TIME FRAME EXTENDED

Documentation requirements and responsibilities under final rule must be learned

ON AUGUST 2, 2013, the Centers for Medicare & Medicaid Services (CMS) released its 2014 Inpatient Prospective Payment System (IPPS) Final Rule, which became effective on October 1, 2013.

The Final Rule revised CMS's reimbursement criteria for Part A inpatient hospital claims, creating new guidelines to establish the medical necessity of inpatient hospital admissions (establishing the "two-midnight rule") and clarifying CMS's documentation requirements related to physician inpatient admission orders and certifications.

Following implementation of the final rule, CMS created a program known as the "probe and educate" medical review program, designed to provide education to hospitals implementing the requirements of the final rule. The program was initially planned to cover Medicare Part A inpatient hospital claims with dates of service between October 1, 2013, and March 31, 2014.

During this time, recovery auditors and Supplemental Medical Review Contractors (SMRCs) would be prohibited from conducting post-payment reviews of Medicare Part A inpatient claims crossing zero to one "midnight" to determine whether inpatient status was appropriate.

On January 31, 2014, CMS announced an extension of its probe and educate medical review program for an additional six months. Despite misleading industry guidance to the contrary, CMS has not delayed the effective date of the final rule. For inpatient admissions with dates of service between October 1, 2013, and September 30, 2014, recovery auditors and SMRCs are prohibited from conducting medical reviews of hospital stays spanning zero to one midnight for the purposes of determining whether admission to inpatient status was medically necessary.

Significantly, medical review of Medicare Part A inpatient hospital claims will continue during the probe and educate time period, and the new requirements set forth in the final rule apply.

MACs provide education

During the probe and educate medical review program, Medicare Administrative Contractors (MACs)—rather than recovery auditors or SMRCs—will conduct prepayment reviews of a sampling of inpatient hospital claims crossing zero to one midnight for the purpose of determining whether the provisions of the final rule were satisfied: For example, were CMS's order and certification requirements satisfied? Did the documentation support a medically necessary hospital stay? Was the two-midnight benchmark satisfied? MACs also will hold educational sessions to provide further education regarding the requirements of the final rule.

The 'probe and educate' medical review program was initially planned to cover Medicare Part A between October 1, 2013, and March 31, 2014.

It is essential that physicians are educated regarding the documentation requirements for which they are responsible under the final rule. CMS guidelines are evolving. On January 30, 2014—one day prior to announcing the extension of the probe and educate program—CMS published additional sub-regulatory guidance related to physician orders and certifications for inpatient hospital admissions.

The guidance differs in certain respects from sub-regulatory guidance published previously. Hospitals must devote resources to closely monitor the CMS Inpatient Hospital Review website as CMS finalizes its guidance related to the final rule. ◘

Read the guidance here: ***http://go.cms.gov/1ebj6qE***

ABOUT THE AUTHORS

Jessica L. Gustafson, Esq. (right) and Abby Pendleton, Esq. (left) are founding partners of The Health Law Partners, P.C.

EXCHANGES MAKE PROGRESS FOR THE FUTURE

New features and support tools will drive consumer engagement

Though political banter has focused on website failures and lengthy customer service wait times, the new insurance marketplaces established by the Affordable Care Act (ACA) will prove their enduring worth.

Several anecdotes are already emerging of Americans who will no longer face bankruptcy when a family member falls ill, and personal tales are cropping up of individuals able to access life-saving procedures and medications previously out-of-reach. Despite the rocky operational launch of the marketplaces, these stories lay the groundwork for the future historian's perspective of ACA's effect on the nation.

For now, marketplaces will remain strictly focused on connecting the uninsured with coverage that meets their healthcare needs. As the marketplaces collectively assess the first six months of operation and review the numbers of newly insured patients, they will not only strive to increase interest among small businesses and continue to enroll individuals eligible for Medicaid, but begin to shift focus to longer-term goals: improving health and reducing costs.

Stakeholder opportunities

Healthcare consumers—Pent-up demand will keep physician offices and pharmacies busy as consumers possess greater "buying power" in the healthcare economy. Access to care should offer an unprecedented opportunity to empower individuals to follow their physicians' recommendations with lessened financial burden.

Hospitals, physicians and other care providers—Providers' revenue stream depends on paying customers. The marketplaces have introduced more than 3 million new paying customers into the healthcare economy through the end of January. Hospitals and physicians will undoubtedly find themselves explaining deductibles, coinsurance, networks and other coverage components. It is in healthcare providers' best financial interest to work with the new marketplaces to raise awareness among all patients, especially the newly insured, about how to use insurance to stay healthy, both physically and financially. Additionally, hospitals are now uniquely positioned to turn persistently uninsured low-income patients into paying customers with presumptive eligibility: If the patient provides information about their family and income indicating they're likely eligible for public coverage through Medicaid, the hospital can be paid for the services provided as though the patient were insured.

Marketplaces remain strictly focused on connecting the uninsured with coverage.

Insurance marketplaces—The health insurance marketplaces will develop new features and support tools to help customers navigate plan choices in a meaningful way, including quality data comparisons and provider directories. The federal and state websites can also be a useful tool for providing health information back to customers to help them better manage their own healthcare and also to provide people with public health information, prevention strategies and additional health information. Patterns that emerge from customer interactions with the marketplaces will drive innovation in insurance products—innovations vital to achieving the ACA's objectives of lowering costs and improving quality. ■

ABOUT THE AUTHOR ▮

Angela Sherwin is the Program Director of Brown University's Executive Master of Healthcare Leadership program and was integral in the health exchanges in Massachusetts and Rhode Island.

Cardiologists start more patients on XARELTO® than any other anticoagulant[1]

I like where this is heading...

Xarelto®
rivaroxaban tablets

IMPORTANT SAFETY INFORMATION

WARNING: (A) PREMATURE DISCONTINUATION OF XARELTO® INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

A. PREMATURE DISCONTINUATION OF XARELTO® INCREASES THE RISK OF THROMBOTIC EVENTS

Premature discontinuation of any oral anticoagulant, including XARELTO®, increases the risk of thrombotic events. If anticoagulation with XARELTO® is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

B. SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas have occurred in patients treated with XARELTO® who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- Use of indwelling epidural catheters
- Concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants, *see* Drug Interactions
- A history of traumatic or repeated epidural or spinal punctures
- A history of spinal deformity or spinal surgery

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis.

Please see Important Safety Information on following pages.
Please see Brief Summary of full Prescribing Information, including Boxed WARNINGS, on following pages.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

- Active pathological bleeding
- Severe hypersensitivity reaction to XARELTO® (eg, anaphylactic reactions)

WARNINGS AND PRECAUTIONS

- **Increased Risk of Thrombotic Events After Premature Discontinuation:** Premature discontinuation of any oral anticoagulant, including XARELTO®, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from XARELTO® to warfarin in clinical trials in atrial fibrillation patients. If XARELTO® is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
- **Risk of Bleeding:** XARELTO® increases the risk of bleeding and can cause serious or fatal bleeding. Promptly evaluate any signs or symptoms of blood loss and consider the need for blood replacement. Discontinue XARELTO® in patients with active pathological hemorrhage.
  - A specific antidote for rivaroxaban is not available. Because of high plasma protein binding, rivaroxaban is not expected to be dialyzable.
  - Concomitant use of other drugs affecting hemostasis increases the risk of bleeding. These include aspirin, $P2Y_{12}$ platelet inhibitors, other antithrombotic agents, fibrinolytic therapy, and NSAIDs.
- **Spinal/Epidural Anesthesia or Puncture:** When neuraxial anesthesia (spinal/epidural anesthesia)

Please see Important Safety Information on following pages.
Please see Brief Summary of full Prescribing Information, including Boxed WARNINGS, on following pages.

Xarelto®
rivaroxaban tablets

XARELTO® is the first and only novel oral anticoagulant with:

- 6 indications approved by the FDA,
- >85% of commercial and Medicare patients covered at lowest branded co-pay,[2]
- >4 million US prescriptions,[3]
- >55K patients included in phase 3 trials,[4-12]
- Convenient oral dosing, and
- No routine coagulation monitoring[5-10,13]

The #1 prescribed novel oral anticoagulant in the US*[14]

Supported by Xarelto® CarePath™

A comprehensive support program focused on access, education, and adherence tools

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

or spinal puncture is employed, patients treated with anticoagulant agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma, which can result in long-term or permanent paralysis. An epidural catheter should not be removed earlier than 18 hours after the last administration of XARELTO®. The next XARELTO® dose is not to be administered earlier than 6 hours after the removal of the catheter. If traumatic puncture occurs, the administration of XARELTO® is to be delayed for 24 hours.

- **Use in Patients With Renal Impairment:**
  - **Nonvalvular Atrial Fibrillation:** Avoid the use of XARELTO® in patients with creatinine clearance (CrCl) <15 mL/min, since drug exposure is increased. Discontinue XARELTO® in patients who develop acute renal failure while on XARELTO®.

SIX INDICATIONS STRONG

- To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (AF). There are limited data on the relative effectiveness of XARELTO® and warfarin in reducing the risk of stroke and systemic embolism when warfarin therapy is well controlled
- For the treatment of deep vein thrombosis (DVT)
- For the treatment of pulmonary embolism (PE)
- For the reduction in the risk of recurrence of DVT and of PE following initial 6 months treatment for DVT and/or PE
- For the prophylaxis of DVT, which may lead to PE in patients undergoing knee replacement surgery
- For the prophylaxis of DVT, which may lead to PE in patients undergoing hip replacement surgery

*Among Factor Xa inhibitors and direct thrombin inhibitors.

Cardiologists start more patients on XARELTO® than any other anticoagulant[1]

LEARN MORE ABOUT

generationXARELTO®

visit **www.XARELTOhcp.com**

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

- **Treatment of Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), and Reduction in the Risk of Recurrence of DVT and of PE:** Avoid the use of XARELTO® in patients with CrCl <30 mL/min due to an expected increase in rivaroxaban exposure and pharmacodynamic effects in this patient population.
- **Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery:** Avoid the use of XARELTO® in patients with CrCl <30 mL/min due to an expected increase in rivaroxaban exposure and pharmacodynamic effects in this patient population. Observe closely and promptly evaluate any signs or symptoms of blood loss in patients with CrCl 30 to 50 mL/min. Patients who develop acute renal failure while on XARELTO® should discontinue the treatment.
- **Use in Patients With Hepatic Impairment:** No clinical data are available for patients with severe hepatic impairment. Avoid use of XARELTO® in patients with moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment or with any hepatic disease associated with coagulopathy, since drug exposure and bleeding risk may be increased.
- **Use With P-gp and Strong CYP3A4 Inhibitors or Inducers:** Avoid concomitant use of XARELTO® with combined P-gp and strong CYP3A4 inhibitors (eg, ketoconazole, itraconazole, lopinavir/ritonavir, ritonavir, indinavir/ritonavir, and conivaptan). Avoid concomitant use of XARELTO® with drugs that are P-gp and strong CYP3A4 inducers (eg, carbamazepine, phenytoin, rifampin, St. John's wort).
- **Risk of Pregnancy-Related Hemorrhage:** In pregnant women, XARELTO® should be used only if the potential benefit justifies the potential risk to the mother and fetus. XARELTO® dosing in pregnancy has not been studied. The anticoagulant effect of XARELTO® cannot be monitored with standard laboratory testing and is not readily reversed. Promptly evaluate any signs or symptoms suggesting blood loss (eg, a drop in hemoglobin and/or hematocrit, hypotension, or fetal distress).
- **Patients With Prosthetic Heart Valves:** The safety and efficacy of XARELTO® have not been studied in patients with prosthetic heart valves. Therefore, use of XARELTO® is not recommended in these patients.

DRUG INTERACTIONS

- Avoid concomitant use of XARELTO® with other anticoagulants due to increased bleeding risk, unless benefit outweighs risk. Promptly evaluate any signs or symptoms of blood loss if patients are treated concomitantly with aspirin, other platelet aggregation inhibitors, or NSAIDs.
- XARELTO® should be used in patients with CrCl 15 to 50 mL/min who are receiving concomitant combined P-gp and weak or moderate CYP3A4 inhibitors only if the potential benefit outweighs the potential risk.

USE IN SPECIFIC POPULATIONS

- **Pregnancy Category C:** XARELTO® should be used during pregnancy only if the potential benefit justifies the potential risk to mother and fetus.

References: 1. Data on file. Janssen Pharmaceuticals, Inc. Based on IMS Health, NPA Market Dynamics New to Brand, October 25, 2013. **2.** Data on file. Janssen Pharmaceuticals, Inc. Data as of 7/1/13. **3.** Data on file. Janssen Pharmaceuticals, Inc. Based on IMS Health, NPA Weekly, Total Prescriptions, July 2011–November 2013. **4.** Mega JL, Braunwald E, Wiviott SD, et al. *N Engl J Med*. 2012;366(1):9-19. **5.** The EINSTEIN–PE Investigators. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. *N Engl J Med*. 2012;366(14):1287-1297. **6.** The EINSTEIN Investigators. Oral rivaroxaban for symptomatic venous thromboembolism. *N Engl J Med*. 2010;363(26):2499-2510. **7.** Patel MR, Mahaffey KW, Garg J, et al; and the ROCKET AF Steering Committee, for the ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med*. 2011;365(10):883-891. **8.** Lassen MR, Ageno W, Borris LC, et al; for the RECORD3 Investigators. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. *N Engl J Med*. 2008;358(26):2776-2786. **9.** Kakkar AK, Brenner B, Dahl OE, et al; for the RECORD2 Investigators. Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial. *Lancet*. 2008;372(9632):31-39. **10.** Eriksson BI, Borris LC, Friedman RJ, et al; for the RECORD1 Study Group. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. *N Engl J Med*. 2008;358(26):2765-2775. **11.** Hori M, Matsumoto M, Tanahashi N, et al; on behalf of the J-ROCKET AF study investigators. Rivaroxaban vs. warfarin in Japanese patients with atrial fibrillation: the J-ROCKET AF study. *Circ J*. 2012;76(9):2104-2111. **12.** Cohen AT, Spiro TE, Büller HR, et al. *N Engl J Med*. 2013;368(6):513-523. **13.** Mueck W, Eriksson BI, Bauer KA, et al. Population pharmacokinetics and pharmacodynamics of rivaroxaban—an oral, direct Factor Xa inhibitor—in patients undergoing major orthopaedic surgery. *Clin Pharmacokinet*. 2008;47(3):203-216. **14.** Data on file. Janssen Pharmaceuticals, Inc. Based on IMS Health, NPA Weekly, October 2013.

IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS (cont'd)

There are no adequate or well-controlled studies of XARELTO® in pregnant women, and dosing for pregnant women has not been established. Use XARELTO® with caution in pregnant patients because of the potential for pregnancy-related hemorrhage and/or emergent delivery with an anticoagulant that is not readily reversible. The anticoagulant effect of XARELTO® cannot be reliably monitored with standard laboratory testing.

- **Labor and Delivery:** Safety and effectiveness of XARELTO® during labor and delivery have not been studied in clinical trials.
- **Nursing Mothers:** It is not known if rivaroxaban is excreted in human milk.
- **Pediatric Use:** Safety and effectiveness in pediatric patients have not been established.
- **Females of Reproductive Potential:** Females of reproductive potential requiring anticoagulation should discuss pregnancy planning with their physician.

OVERDOSAGE

- Discontinue XARELTO® and initiate appropriate therapy if bleeding complications associated with overdosage occur. A specific antidote for rivaroxaban is not available. The use of activated charcoal to reduce absorption in case of XARELTO® overdose may be considered. Due to the high plasma protein binding, rivaroxaban is not expected to be dialyzable.

ADVERSE REACTIONS IN CLINICAL STUDIES

- The most common adverse reactions with XARELTO® were bleeding complications.

K02X121084JR2

Please see Important Safety Information on preceding pages.
Please see Brief Summary of full Prescribing Information, including Boxed WARNINGS, on following pages.

Xarelto® rivaroxaban tablets

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Brief Summary of Prescribing Information for XARELTO® (rivaroxaban)

XARELTO® (rivaroxaban) tablets, for oral use
See package insert for full Prescribing Information

WARNING: (A) PREMATURE DISCONTINUATION OF XARELTO INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

A. PREMATURE DISCONTINUATION OF XARELTO INCREASES THE RISK OF THROMBOTIC EVENTS

Premature discontinuation of any oral anticoagulant, including XARELTO, increases the risk of thrombotic events. If anticoagulation with XARELTO is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant *[see Dosage and Administration (2.2, 2.6) in full Prescribing Information, Warnings and Precautions, and Clinical Studies (14.1) in full Prescribing Information]*.

B. SPINAL/EPIDURAL HEMATOMA

Epidural or spinal hematomas have occurred in patients treated with XARELTO who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:

- **use of indwelling epidural catheters**
- **concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants**
- **a history of traumatic or repeated epidural or spinal punctures**
- **a history of spinal deformity or spinal surgery**

***[see Warnings and Precautions and Adverse Reactions]*.**

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary *[see Warnings and Precautions]*.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis *[see Warnings and Precautions]*.

INDICATIONS AND USAGE

Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation: XARELTO is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

There are limited data on the relative effectiveness of XARELTO and warfarin in reducing the risk of stroke and systemic embolism when warfarin therapy is well-controlled *[see Clinical Studies (14.1) in full Prescribing Information]*.

Treatment of Deep Vein Thrombosis: XARELTO is indicated for the treatment of deep vein thrombosis (DVT).

Treatment of Pulmonary Embolism: XARELTO is indicated for the treatment of pulmonary embolism (PE).

Reduction in the Risk of Recurrence of Deep Vein Thrombosis and of Pulmonary Embolism: XARELTO is indicated for the reduction in the risk of recurrence of deep vein thrombosis and of pulmonary embolism following initial 6 months treatment for DVT and/or PE.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery: XARELTO is indicated for the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery.

CONTRAINDICATIONS

XARELTO is contraindicated in patients with:

- active pathological bleeding *[see Warnings and Precautions]*
- severe hypersensitivity reaction to XARELTO (e.g., anaphylactic reactions) *[see Adverse Reactions]*

WARNINGS AND PRECAUTIONS

Increased Risk of Thrombotic Events after Premature Discontinuation: Premature discontinuation of any oral anticoagulant, including XARELTO, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from XARELTO to warfarin in clinical trials in atrial fibrillation patients. If XARELTO is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant *[see Dosage and Administration (2.2, 2.6) and Clinical Studies (14.1) in full Prescribing Information]*.

Risk of Bleeding: XARELTO increases the risk of bleeding and can cause serious or fatal bleeding. In deciding whether to prescribe XARELTO to patients at increased risk of bleeding, the risk of thrombotic events should be weighed against the risk of bleeding.

Promptly evaluate any signs or symptoms of blood loss and consider the need for blood replacement. Discontinue XARELTO in patients with active pathological hemorrhage. The terminal elimination half-life of rivaroxaban is 5 to 9 hours in healthy subjects aged 20 to 45 years.

A specific antidote for rivaroxaban is not available. Because of high plasma protein binding, rivaroxaban is not expected to be dialyzable *[see Clinical Pharmacology (12.3) in full Prescribing Information]*. Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of rivaroxaban. There is no experience with antifibrinolytic agents (tranexamic acid, aminocaproic acid) in individuals receiving rivaroxaban. There is neither scientific rationale for benefit nor experience with systemic hemostatics (desmopressin and aprotinin) in individuals receiving rivaroxaban. Use of procoagulant reversal agents such as prothrombin complex concentrate (PCC),

activated prothrombin complex concentrate (APCC), or recombinant factor VIIa (rFVIIa) may be considered but has not been evaluated in clinical trials.

Concomitant use of other drugs affecting hemostasis increases the risk of bleeding. These include aspirin, $P2Y_{12}$ platelet inhibitors, other antithrombotic agents, fibrinolytic therapy, and non-steroidal anti-inflammatory drugs (NSAIDs) *[see Drug Interactions]*.

Concomitant use of drugs that are combined P-gp and CYP3A4 inhibitors (e.g., ketoconazole and ritonavir) increases rivaroxaban exposure and may increase bleeding risk *[see Drug Interactions]*.

Spinal/Epidural Anesthesia or Puncture: When neuraxial anesthesia (spinal/epidural anesthesia) or spinal puncture is employed, patients treated with anticoagulant agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma which can result in long-term or permanent paralysis *[see Boxed Warning]*.

An epidural catheter should not be removed earlier than 18 hours after the last administration of XARELTO. The next XARELTO dose is not to be administered earlier than 6 hours after the removal of the catheter. If traumatic puncture occurs, the administration of XARELTO is to be delayed for 24 hours.

Use in Patients with Renal Impairment: Nonvalvular Atrial Fibrillation: Avoid the use of XARELTO in patients with CrCl <15 mL/min since drug exposure is increased. Periodically assess renal function as clinically indicated (i.e., more frequently in situations in which renal function may decline) and adjust therapy accordingly. Discontinue XARELTO in patients who develop acute renal failure while on XARELTO *[see Use in Specific Populations]*

Treatment of Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), and Reduction in the Risk of Recurrence of DVT and of PE: Avoid the use of XARELTO in patients with CrCl <30 mL/min due to an expected increase in rivaroxaban exposure and pharmacodynamic effects in this patient population *[see Use in Specific Populations]*.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery: Avoid the use of XARELTO in patients with CrCl <30 mL/min due to an expected increase in rivaroxaban exposure and pharmacodynamic effects in this patient population. Observe closely and promptly evaluate any signs or symptoms of blood loss in patients with CrCl 30 to 50 mL/min. Patients who develop acute renal failure while on XARELTO should discontinue the treatment *[see Use in Specific Populations]*.

Use in Patients with Hepatic Impairment: No clinical data are available for patients with severe hepatic impairment.

Avoid use of XARELTO in patients with moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment or with any hepatic disease associated with coagulopathy since drug exposure and bleeding risk may be increased *[see Use in Specific Populations]*.

Use with P-gp and Strong CYP3A4 Inhibitors or Inducers: Avoid concomitant use of XARELTO with combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, lopinavir/ritonavir, ritonavir, indinavir/ritonavir, and conivaptan) *[see Drug Interactions]*.

Avoid concomitant use of XARELTO with drugs that are combined P-gp and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, St. John's wort) *[see Drug Interactions]*.

Risk of Pregnancy Related Hemorrhage: In pregnant women, XARELTO should be used only if the potential benefit justifies the potential risk to the mother and fetus. XARELTO dosing in pregnancy has not been studied. The anticoagulant effect of XARELTO cannot be monitored with standard laboratory testing nor readily reversed. Promptly evaluate any signs or symptoms suggesting blood loss (e.g., a drop in hemoglobin and/or hematocrit, hypotension, or fetal distress).

Patients with Prosthetic Heart Valves: The safety and efficacy of XARELTO have not been studied in patients with prosthetic heart valves. Therefore, use of XARELTO is not recommended in these patients.

ADVERSE REACTIONS

The following adverse reactions are also discussed in other sections of the labeling:

- Increased risk of stroke after discontinuation in nonvalvular atrial fibrillation *[see Boxed Warning* and *Warnings and Precautions]*
- Bleeding risk *[see Warnings and Precautions]*
- Spinal/epidural hematoma *[see Boxed Warning* and *Warnings and Precautions]*

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 clinical practice.

During clinical development for the approved indications, 16326 patients were exposed to XARELTO. These included 7111 patients who received XARELTO 15 mg or 20 mg orally once daily for a mean of 19 months (5558 for 12 months and 2512 for 24 months) to reduce the risk of stroke and systemic embolism in nonvalvular atrial fibrillation (ROCKET AF); 4728 patients who received either XARELTO 15 mg orally twice daily for three weeks followed by 20 mg orally once daily (EINSTEIN DVT, EINSTEIN PE) or 20 mg orally once daily (EINSTEIN Extension) to treat DVT, PE, and to reduce the risk of recurrence of DVT and of PE; and 4487 patients who received XARELTO 10 mg orally once daily for prophylaxis of DVT following hip or knee replacement surgery (RECORD 1-3).

Hemorrhage: The most common adverse reactions with XARELTO were bleeding complications *[see Warnings and Precautions]*.

XARELTO® (rivaroxaban) tablets

Nonvalvular Atrial Fibrillation: In the ROCKET AF trial, the most frequent adverse reactions associated with permanent drug discontinuation were bleeding events, with incidence rates of 4.3% for XARELTO vs. 3.1% for warfarin. The incidence of discontinuations for non-bleeding adverse events was similar in both treatment groups.

Table 1 shows the number of patients experiencing various types of bleeding events in the ROCKET AF study.

Table 1: Bleeding Events in ROCKET AF*

Parameter	XARELTO N = 7111 n (%)	Event Rate (per 100 Pt-yrs)	Warfarin N = 7125 n (%)	Event Rate (per 100 Pt-yrs)
Major bleeding†	395 (5.6)	3.6	386 (5.4)	3.5
Bleeding into a critical organ‡	91 (1.3)	0.8	133 (1.9)	1.2
Fatal bleeding	27 (0.4)	0.2	55 (0.8)	0.5
Bleeding resulting in transfusion of ≥2 units of whole blood or packed red blood cells	183 (2.6)	1.7	149 (2.1)	1.3
Gastrointestinal bleeding	221 (3.1)	2.0	140 (2.0)	1.2

* For all sub-types of major bleeding, single events may be represented in more than one row, and individual patients may have more than one event.

† Defined as clinically overt bleeding associated with a decrease in hemoglobin of ≥2 g/dL, transfusion of ≥2 units of packed red blood cells or whole blood, bleeding at a critical site, or with a fatal outcome. Hemorrhagic strokes are counted as both bleeding and efficacy events. Major bleeding rates excluding strokes are 3.3 per 100 Pt-yrs for XARELTO vs. 2.9 per 100 Pt-yrs for warfarin.

‡ The majority of the events were intracranial, and also included intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, or retroperitoneal.

Treatment of Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), and to Reduce the Risk of Recurrence of DVT and of PE: EINSTEIN DVT and EINSTEIN PE Studies: In the pooled analysis of the EINSTEIN DVT and EINSTEIN PE clinical studies, the most frequent adverse reactions leading to permanent drug discontinuation were bleeding events, with XARELTO vs. enoxaparin/Vitamin K antagonist (VKA) incidence rates of 1.7% vs. 1.5%, respectively. The mean duration of treatment was 208 days for XARELTO-treated patients and 204 days for enoxaparin/VKA-treated patients.

Table 2 shows the number of patients experiencing major bleeding events in the pooled analysis of the EINSTEIN DVT and EINSTEIN PE studies.

Table 2: Bleeding Events* in the Pooled Analysis of EINSTEIN DVT and EINSTEIN PE Studies

Parameter	XARELTO† N = 4130 n (%)	Enoxaparin/VKA† N = 4116 n (%)
Major bleeding event	40 (1.0)	72 (1.7)
Fatal bleeding	3 (<0.1)	8 (0.2)
Intracranial	2 (<0.1)	4 (<0.1)
Non-fatal critical organ bleeding	10 (0.2)	29 (0.7)
Intracranial‡	3 (<0.1)	10 (0.2)
Retroperitoneal‡	1 (<0.1)	8 (0.2)
Intraocular‡	3 (<0.1)	2 (<0.1)
Intra-articular‡	0	4 (<0.1)
Non-fatal non-critical organ bleeding§	27 (0.7)	37 (0.9)
Decrease in Hb ≥ 2g/dL	28 (0.7)	42 (1.0)
Transfusion of ≥2 units of whole blood or packed red blood cells	18 (0.4)	25 (0.6)
Clinically relevant non-major bleeding	357 (8.6)	357 (8.7)
Any bleeding	1169 (28.3)	1153 (28.0)

* Bleeding event occurred after randomization and up to 2 days after the last dose of study drug. Although a patient may have had 2 or more events, the patient is counted only once in a category.

† Treatment schedule in EINSTEIN DVT and EINSTEIN PE studies: XARELTO 15 mg twice daily for 3 weeks followed by 20 mg once daily; enoxaparin/VKA [enoxaparin: 1 mg/kg twice daily, VKA: individually titrated doses to achieve a target INR of 2.5 (range: 2.0-3.0)]

‡ Treatment-emergent major bleeding events with at least >2 subjects in any pooled treatment group

§ Major bleeding which is not fatal or in a critical organ, but resulting in a decrease in Hb ≥2 g/dL and/or transfusion of ≥2 units of whole blood or packed red blood cells

EINSTEIN Extension Study: In the EINSTEIN Extension clinical study, the most frequent adverse reactions associated with permanent drug discontinuation were bleeding events, with incidence rates of 1.8% for XARELTO vs. 0.2% for placebo treatment groups. The mean duration of treatment was 190 days for both XARELTO and placebo treatment groups.

Table 3 shows the number of patients experiencing bleeding events in the EINSTEIN Extension study.

Table 3: Bleeding Events* in EINSTEIN Extension Study

Parameter	XARELTO† 20 mg N = 598 n (%)	Placebo† N = 590 n (%)
Major bleeding event‡	4 (0.7)	0
Decrease in Hb ≥2 g/dL	4 (0.7)	0
Transfusion of ≥2 units of whole blood or packed red blood cells	2 (0.3)	0
Gastrointestinal	3 (0.5)	0
Menorrhagia	1 (0.2)	0
Clinically relevant non-major bleeding	32 (5.4)	7 (1.2)
Any bleeding	104 (17.4)	63 (10.7)

* Bleeding event occurred after the first dose and up to 2 days after the last dose of study drug. Although a patient may have had 2 or more events, the patient is counted only once in a category.
† Treatment schedule: XARELTO 20 mg once daily; matched placebo once daily
‡ There were no fatal or critical organ bleeding events.

Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery: In the RECORD clinical trials, the overall incidence rate of adverse reactions leading to permanent treatment discontinuation was 3.7% with XARELTO.

The rates of major bleeding events and any bleeding events observed in patients in the RECORD clinical trials are shown in Table 4.

Table 4: Bleeding Events* in Patients Undergoing Hip or Knee Replacement Surgeries (RECORD 1-3)

	XARELTO 10 mg	Enoxaparin†
Total treated patients	**N = 4487 n (%)**	**N = 4524 n (%)**
Major bleeding event	14 (0.3)	9 (0.2)
Fatal bleeding	1 (<0.1)	0
Bleeding into a critical organ	2 (<0.1)	3 (0.1)
Bleeding that required re-operation	7 (0.2)	5 (0.1)
Extra-surgical site bleeding requiring transfusion of >2 units of whole blood or packed cells	4 (0.1)	1 (<0.1)
Any bleeding event‡	261 (5.8)	251 (5.6)
Hip Surgery Studies	**N = 3281 n (%)**	**N = 3298 n (%)**
Major bleeding event	7 (0.2)	3 (0.1)
Fatal bleeding	1 (<0.1)	0
Bleeding into a critical organ	1 (<0.1)	1 (<0.1)
Bleeding that required re-operation	2 (0.1)	1 (<0.1)
Extra-surgical site bleeding requiring transfusion of >2 units of whole blood or packed cells	3 (0.1)	1 (<0.1)
Any bleeding event‡	201 (6.1)	191 (5.8)
Knee Surgery Study	**N = 1206 n (%)**	**N = 1226 n (%)**
Major bleeding event	7 (0.6)	6 (0.5)
Fatal bleeding	0	0
Bleeding into a critical organ	1 (0.1)	2 (0.2)
Bleeding that required re-operation	5 (0.4)	4 (0.3)
Extra-surgical site bleeding requiring transfusion of >2 units of whole blood or packed cells	1 (0.1)	0
Any bleeding event‡	60 (5.0)	60 (4.9)

* Bleeding events occurring any time following the first dose of double-blind study medication (which may have been prior to administration of active drug) until two days after the last dose of double-blind study medication. Patients may have more than one event.
† Includes the placebo-controlled period for RECORD 2, enoxaparin dosing was 40 mg once daily (RECORD 1-3)
‡ Includes major bleeding events

XARELTO® (rivaroxaban) tablets

Following XARELTO treatment, the majority of major bleeding complications (≥60%) occurred during the first week after surgery.

Other Adverse Reactions: Non-hemorrhagic adverse reactions reported in ≥1% of XARELTO-treated patients in the EINSTEIN Extension study are shown in Table 5.

Table 5: Other Adverse Reactions* Reported by ≥1% of XARELTO-Treated Patients in EINSTEIN Extension Study

System Organ Class Preferred Term	XARELTO N = 598 n (%)	Placebo N = 590 n (%)
Gastrointestinal disorders		
Abdominal pain upper	10 (1.7)	1 (0.2)
Dyspepsia	8 (1.3)	4 (0.7)
Toothache	6 (1.0)	0
General disorders and administration site conditions		
Fatigue	6 (1.0)	3 (0.5)
Infections and infestations		
Sinusitis	7 (1.2)	3 (0.5)
Urinary tract infection	7 (1.2)	3 (0.5)
Musculoskeletal and connective tissue disorders		
Back pain	22 (3.7)	7 (1.2)
Osteoarthritis	10 (1.7)	5 (0.8)
Respiratory, thoracic and mediastinal disorders		
Oropharyngeal pain	6 (1.0)	2 (0.3)

* Adverse reaction (with Relative Risk >1.5 for XARELTO versus placebo) occurred after the first dose and up to 2 days after the last dose of study drug. Incidences are based on the number of patients, not the number of events. Although a patient may have had 2 or more clinical adverse reactions, the patient is counted only once in a category. The same patient may appear in different categories.

Non-hemorrhagic adverse reactions reported in ≥1% of XARELTO-treated patients in RECORD 1-3 studies are shown in Table 6.

Table 6: Other Adverse Drug Reactions* Reported by ≥1% of XARELTO-Treated Patients in RECORD 1-3 Studies

System/Organ Class Adverse Reaction	XARELTO 10 mg (N = 4487) n (%)	Enoxaparin† (N = 4524) n (%)
Injury, poisoning and procedural complications		
Wound secretion	125 (2.8)	89 (2.0)
Musculoskeletal and connective tissue disorders		
Pain in extremity	74 (1.7)	55 (1.2)
Muscle spasm	52 (1.2)	32 (0.7)
Nervous system disorders		
Syncope	55 (1.2)	32 (0.7)
Skin and subcutaneous tissue disorders		
Pruritus	96 (2.1)	79 (1.8)
Blister	63 (1.4)	40 (0.9)

* Adverse reaction occurring any time following the first dose of double-blind medication, which may have been prior to administration of active drug, until two days after the last dose of double-blind study medication.
† Includes the placebo-controlled period of RECORD 2, enoxaparin dosing was 40 mg once daily (RECORD 1-3)

Other clinical trial experience: In an investigational study of acute medically ill patients being treated with XARELTO 10 mg tablets, cases of pulmonary hemorrhage and pulmonary hemorrhage with bronchiectasis were observed.

Postmarketing Experience: The following adverse reactions have been identified during post-approval use of rivaroxaban. 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 drug exposure.

Blood and lymphatic system disorders: agranulocytosis

Gastrointestinal disorders: retroperitoneal hemorrhage

Hepatobiliary disorders: jaundice, cholestasis, cytolytic hepatitis

Immune system disorders: hypersensitivity, anaphylactic reaction, anaphylactic shock, angioedema

Nervous system disorders: cerebral hemorrhage, subdural hematoma, epidural hematoma, hemiparesis

Skin and subcutaneous tissue disorders: Stevens-Johnson syndrome

DRUG INTERACTIONS

Rivaroxaban is a substrate of CYP3A4/5, CYP2J2, and the P-gp and ATP-binding cassette G2 (ABCG2) transporters. Inhibitors and inducers of these CYP450 enzymes or transporters (e.g., P-gp) may result in changes in rivaroxaban exposure.

Drugs that Inhibit Cytochrome P450 3A4 Enzymes and Drug Transport Systems: In drug interaction studies evaluating the concomitant use with drugs that are combined P-gp and CYP3A4 inhibitors (ketoconazole, ritonavir, clarithromycin, erythromycin and fluconazole), increases in rivaroxaban exposure and pharmacodynamic effects (i.e., factor Xa inhibition and PT prolongation) were observed. The increases in exposure ranged from 30% to 160%. Significant increases in rivaroxaban exposure may increase bleeding risk *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

When data suggest a change in exposure is unlikely to affect bleeding risk (e.g., clarithromycin, erythromycin), no precautions are necessary during coadministration with drugs that are combined P-gp and CYP3A4 inhibitors.

Avoid concomitant administration of XARELTO with combined P-gp and strong CYP3A4 inhibitors *[see Warnings and Precautions]*.

Drugs that Induce Cytochrome P450 3A4 Enzymes and Drug Transport Systems: Results from drug interaction studies and population PK analyses from clinical studies indicate coadministration of XARELTO with a combined P-gp and strong CYP3A4 inducer (e.g., rifampicin, phenytoin) decreased rivaroxaban exposure by up to 50%. Similar decreases in pharmacodynamic effects were also observed. These decreases in exposure to rivaroxaban may decrease efficacy *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Avoid concomitant use of XARELTO with drugs that are combined P-gp and strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin, St. John's wort) *[see Warnings and Precautions]*.

Anticoagulants and NSAIDs/Aspirin: Single doses of enoxaparin and XARELTO given concomitantly resulted in an additive effect on anti-factor Xa activity. Single doses of warfarin and XARELTO resulted in an additive effect on factor Xa inhibition and PT. Concomitant aspirin use has been identified as an independent risk factor for major bleeding in efficacy trials. NSAIDs are known to increase bleeding, and bleeding risk may be increased when NSAIDs are used concomitantly with XARELTO. Coadministration of the platelet aggregation inhibitor clopidogrel and XARELTO resulted in an increase in bleeding time for some subjects *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Avoid concurrent use of XARELTO with other anticoagulants due to increased bleeding risk unless benefit outweighs risk. Promptly evaluate any signs or symptoms of blood loss if patients are treated concomitantly with aspirin, other platelet aggregation inhibitors, or NSAIDs *[see Warnings and Precautions]*.

Drug-Disease Interactions with Drugs that Inhibit Cytochrome P450 3A4 Enzymes and Drug Transport Systems: Patients with renal impairment receiving full dose XARELTO in combination with drugs classified as combined P-gp and weak or moderate CYP3A4 inhibitors (e.g., amiodarone, diltiazem, verapamil, quinidine, ranolazine, dronedarone, felodipine, erythromycin, and azithromycin) may have increases in exposure compared with patients with normal renal function and no inhibitor use, since both pathways of rivaroxaban elimination are affected.

XARELTO should be used in patients with CrCl 15 to 50 mL/min who are receiving concomitant combined P-gp and weak or moderate CYP3A4 inhibitors only if the potential benefit justifies the potential risk *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C: There are no adequate or well-controlled studies of XARELTO in pregnant women, and dosing for pregnant women has not been established. Use XARELTO with caution in pregnant patients because of the potential for pregnancy related hemorrhage and/or emergent delivery with an anticoagulant that is not readily reversible. The anticoagulant effect of XARELTO cannot be reliably monitored with standard laboratory testing. Animal reproduction studies showed no increased risk of structural malformations, but increased post-implantation pregnancy loss occurred in rabbits. XARELTO should be used during pregnancy only if the potential benefit justifies the potential risk to mother and fetus *[see Warnings and Precautions]*.

Rivaroxaban crosses the placenta in animals. Animal reproduction studies have shown pronounced maternal hemorrhagic complications in rats and an increased incidence of post-implantation pregnancy loss in rabbits. Rivaroxaban increased fetal toxicity (increased resorptions, decreased number of live fetuses, and decreased fetal body weight) when pregnant rabbits were given oral doses of ≥10 mg/kg rivaroxaban during the period of organogenesis. This dose corresponds to about 4 times the human exposure of unbound drug, based on AUC comparisons at the highest recommended human dose of 20 mg/day. Fetal body weights decreased when pregnant rats were given oral doses of 120 mg/kg. This dose corresponds to about 14 times the human exposure of unbound drug.

Labor and Delivery: Safety and effectiveness of XARELTO during labor and delivery have not been studied in clinical trials. However, in animal studies maternal bleeding and maternal and fetal death occurred at the rivaroxaban dose of 40 mg/kg (about 6 times maximum human exposure of the unbound drug at the human dose of 20 mg/day).

XARELTO® (rivaroxaban) tablets

Nursing Mothers: It is not known if rivaroxaban is excreted in human milk. Rivaroxaban and/or its metabolites were excreted into the milk of rats. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from rivaroxaban, a decision should be made whether to discontinue nursing or discontinue XARELTO, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

Geriatric Use: Of the total number of patients in the RECORD 1-3 clinical studies evaluating XARELTO, about 54% were 65 years and over, while about 15% were >75 years. In ROCKET AF, approximately 77% were 65 years and over and about 38% were >75 years. In the EINSTEIN DVT, PE and Extension clinical studies approximately 37% were 65 years and over and about 16% were >75 years. In clinical trials the efficacy of XARELTO in the elderly (65 years or older) was similar to that seen in patients younger than 65 years. Both thrombotic and bleeding event rates were higher in these older patients, but the risk-benefit profile was favorable in all age groups *[see Clinical Pharmacology (12.3) and Clinical Studies (14) in full Prescribing Information]*.

Females of Reproductive Potential: Females of reproductive potential requiring anticoagulation should discuss pregnancy planning with their physician.

Renal Impairment: In a pharmacokinetic study, compared to healthy subjects with normal creatinine clearance, rivaroxaban exposure increased by approximately 44 to 64% in subjects with renal impairment. Increases in pharmacodynamic effects were also observed *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Nonvalvular Atrial Fibrillation: In the ROCKET AF trial, patients with CrCl 30 to 50 mL/min were administered XARELTO 15 mg once daily resulting in serum concentrations of rivaroxaban and clinical outcomes similar to those in patients with better renal function administered XARELTO 20 mg once daily. Patients with CrCl 15 to 30 mL/min were not studied, but administration of XARELTO 15 mg once daily is also expected to result in serum concentrations of rivaroxaban similar to those in patients with normal renal function *[see Dosage and Administration (2.3) in full Prescribing Information]*.

Treatment of DVT and/or PE, and Reduction in the Risk of Recurrence of DVT and of PE: In the EINSTEIN trials, patients with CrCl values <30 mL/min at screening were excluded from the studies. Avoid the use of XARELTO in patients with CrCl <30 mL/min.

Prophylaxis of DVT Following Hip or Knee Replacement Surgery: The combined analysis of the RECORD 1-3 clinical efficacy studies did not show an increase in bleeding risk for patients with CrCl 30 to 50 mL/min and reported a possible increase in total venous thromboemboli in this population. Observe closely and promptly evaluate any signs or symptoms of blood loss in patients with CrCl 30 to 50 mL/min. Avoid the use of XARELTO in patients with CrCl <30 mL/min.

Hepatic Impairment: In a pharmacokinetic study, compared to healthy subjects with normal liver function, AUC increases of 127% were observed in subjects with moderate hepatic impairment (Child-Pugh B).

The safety or PK of XARELTO in patients with severe hepatic impairment (Child-Pugh C) has not been evaluated *[see Clinical Pharmacology (12.3) in full Prescribing Information]*.

Avoid the use of XARELTO in patients with moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment or with any hepatic disease associated with coagulopathy.

OVERDOSAGE:

Overdose of XARELTO may lead to hemorrhage. Discontinue XARELTO and initiate appropriate therapy if bleeding complications associated with overdosage occur. A specific antidote for rivaroxaban is not available. Rivaroxaban systemic exposure is not further increased at single doses >50 mg due to limited absorption. The use of activated charcoal to reduce absorption in case of XARELTO overdose may be considered. Due to the high plasma protein binding, rivaroxaban is not expected to be dialyzable *[see Warnings and Precautions and Clinical Pharmacology (12.3) in full Prescribing Information]*.

Active Ingredient Made in Germany

Finished Product Manufactured by:
Janssen Ortho, LLC
Gurabo, PR 00778

Manufactured for:
Janssen Pharmaceuticals, Inc.
Titusville, NJ 08560

Licensed from:
Bayer HealthCare AG
51368 Leverkusen, Germany

Revised: August 2013

10185207

K02X13244B

janssen

ARE YOUR NETWORKS TOO NARROW?

Slimming down the list of preferred providers is one of the primary tools plans have left to keep premiums low and quality high. Changes under the Affordable Care Act—specifically guaranteed issue and adjusted community rating—have left plans with a renewed interest in contracting with only the highest value hospitals and physician practices.

Narrow networks aren't new, of course. The trend started about a decade ago but has accelerated under health reform.

However, pushback from members—who believe their plans don't have enough providers or the right providers for their needs—has caused regulators to take notice. Mississippi and Pennsylvania are considering bills that would more tightly regulate the number of doctors and hospitals in a network, while the federal government has released a new proposal that would have insurers submit their network lists for review before being approved to participate on the federally operated exchange.

Unlike the HMO networks of the past that plans eventually backed away from in favor of PPOs, today's narrow networks will likely have longer tenures. What remains to be seen is how just "narrow" a narrow network can be.

The use of narrow networks by health insurance plans is a complicated balancing act, simultaneously seeking to lower premiums while still offering a selection of quality providers to consumers. The success of such networks hinges on consumers accepting the tradeoff of limited provider access for lower rates.

"Nobody wants to pay premiums, much less higher premiums, but everybody wants access to every doctor they want to see," says Lee Harrell of the Jackson, Miss., offices of Baker Donelson. "So, it's a Catch-22 from the regulatory perspective. Each commissioner is charged with keeping the health insurance markets affordable, as well as keeping the health insurance industry solvent and available."

While the Affordable Care Act (ACA) and the advent of exchanges may be escalating the

EXECUTIVE VIEW

- Finicky network selection is one of the few tools plans have left to control premium costs
- Legislators propose to regulate networks in the exchanges in 2015

Thinkstock/iStock

> Leveraging the respective strengths of providers and insurers will lead to better affordability and quality of care for consumers."
>
> —WENDY SHERRY

narrow network trend, the concept of limiting networks is reminiscent of HMOs of the 1980s and 1990s. Although the latest iteration of narrow networks may be an improved version, Harrell says they will still present many of the same challenges.

"The access to providers versus keeping the premium affordable is a challenge that all state regulators are faced with on a daily basis when they are looking at rate increases," he says. "These challenges will only increase with the implementation of the ACA."

HEALTHY COMPETITION

Harrell, who previously worked as Deputy Commissioner and General Counsel for the Mississippi Insurance Department, says the situation is further complicated by the fact that regulators have jurisdiction over the insurer, but not over the providers.

"The commissioners regulate the price that a health insurance company charges its policyholders; they control that part of the equation, but who controls what the providers charge?" Harrell says. "That part is not regulated. That's the free market system."

Therefore, he says, broadening networks to allow all qualified providers could conceivably nullify the main leverage insurance companies have over providers, especially considering ACA rules demand guaranteed issue and adjusted community rating.

"Would it be easier if insurance companies allowed anybody and everybody who was qualified into the network? Well, on the one hand, they wouldn't have to deal with the issues involved in offering narrow networks," Harrell says, "But then what incentive is there for the provider to discount what they charge? That incentive is then somewhat diluted or diminished, or even done away with, without the network issue."

It is the promise of inclusion in a narrow network, and the patient volume and reimbursement it brings, that prompts providers to offer competitive prices.

"If the out-of-network doctor gets the same reimbursement as the in-network doctor, what incentive is there for the in-network provider to discount, say 20%? If they lose that incentive, are they going to continue to discount? Historically, the answer has been no," he says.

Also, this dilution of competition has been an obstacle to the passage of "any willing provider" legislation.

"What's going to happen if the providers stop offering competitive discounts? Ultimately, the way it's borne out in my regulatory experience is, the carrier's going to pay," he says. "And if the carrier pays more, then ultimately, the consumer's going to pay more."

According to Wendy Sherry, vice president of development at Cigna, the provider competition fostered by narrow networks not only lowers prices, but raises the bar for performance.

"Because there are fewer providers in a narrow network, this should lead to price and quality competition among them," she says. "There will not be room for everyone. As the use of narrow networks continues to increase, this leverage will also increase."

Sherry says in striving to compete on the highest level, providers will be able to promote their "brand" while offering quality patient care. While patients largely association higher cost with better care, they also need to hear the message that affordability can equal quality care, she says.

Provider competition for customers could also include providers seeking to market their own networks, Sherry says.

"Provider systems are certainly exploring entering the health insurance business," she says. "Leveraging the respective strengths of providers and insurers will lead to better affordability and quality of care for consumers."

GEOGRAPHIC CHALLENGES

Harrell says for the insured who live in rural areas of the country, it is a significant challenge to find any in-network providers nearby, much less the patient's preferred provider.

"You might have patients driving 60, 70, 80 miles to get to a hospital for childbirth, for example."

Sherry says Cigna's narrow networks aim to provide the same level of geographic accessibility as the plan would through a provider network of any size.

"Cigna approaches narrow networks with the same guidelines for network adequacy as for our larger networks," she says. "We seek to ensure that there is good access to care to treat all covered services within a reasonable distance from a customer's home."

Harrell says although the issue of adequate network options in rural areas continues to be a challenge, there are several valid approaches to mitigating this problem. One, he says is the use of telemedicine where appropriate.

"We have companion deals pending in our Mississippi state legislature as we speak. They've both passed out of their respective committees, promoting the benefits of telemedicine," he says.

@ More online

Read the proposed federal guidance here:
http://go.cms.gov/1byeKg7

See what Kathleen Sebelius says about narrow networks:
http://bit.ly/1alx6mj

"That is expected to help, especially in these rural areas where patients would otherwise have to drive 70 or 80 miles in one direction."

He says telemedicine would enable a patient to be seen by a local doctor, who could then conference with a remote provider. In today's connected world, the consultation can occur in real time. Telehealth has the potential to save costs from the consumer perspective and the payer perspective. Increasingly, insurers are reimbursing physicians for telehealth.

THE TIERED NETWORK APPROACH

In an effort to control costs while still maintaining some degree of consumer choice, some payers have instead opted for tiered networks. By varying out-of-pocket costs, plans can funnel members to high performers.

"The way we structured our game plan was to not limit access, but rather enhance what is being offered to members from an out-of-pocket and cost-share standpoint when they access our tier-one providers," says Mike Munoz, senior vice president of sales and marketing for AmeriHealth, New Jersey. "For example, they might have a $30 coinsurance advantage on certain services, or a $30 copay for certain services, for using a tier-one provider."

Munoz says AmeriHealth has partnered with Cooper University Health in Camden, N.J., to offer a branded network. The tier-one benefits would be offered to those who use the Cooper Advantage Network, which includes the hospital and more than 100 outpatient offices. According to AmeriHealth, a visit to a Cooper primary care physician might result in a $15 copay, for example, while a visit to a physician within the broader Local Value network might be $50.

"Patients always have access to tier-two providers; they just get an enhanced out-of-pocket experience when accessing the tier-one providers," Munoz says.

He says most of the relationships that have been structured in narrow networks are driven by volume. But AmeriHealth needed to look at it differently, not being the largest player in the marketplace. Rather, the payer and provider work together toward sustainable, long-term cost savings, and lower premiums over time. Cooper has a 20% interest in AmeriHealth New Jersey with the option to buy more equity in the future—a deal the two struck in May 2013.

Munoz says consumer education is essential in a tiered network, adding that AmeriHealth is working with providers to offer consumer outreach.

"It's also very important to make sure we provide enough variation in our product offerings so that people can make these decisions based on what is right for them," he says.

AmeriHealth's portal has implemented various technologies for a more consumer-focused approach, Munoz says. The portal asks consumers a series of questions designed to direct them toward the best coverage.

"If, for example, you need more of an expansive, low out-of-pocket program because you are high utilizer, these tiered networks might not be the best, unless your provider participates with them," he says.

For the average consumer without an ongoing need for specialized medical care, narrow or tiered networks might represent lower premiums or copays without reduced quality of care. However, for patients with specific medical needs, such as cancer treatment, narrow or tiered networks may make care delivery cumbersome for the member and ultimately affect outcomes.

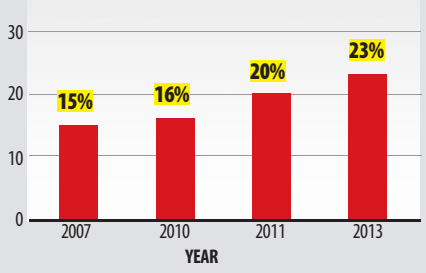
According to a report recently commissioned by the Leukemia and Lymphoma Society, many of the health plans available through the ACA exchanges have limited access to National Cancer Institute (NCI) designated cancer or transplant centers. These insurers also charge what the group considers high out-of-pocket expenses—often at least $2,000 and $4,000 respectively—for patients purchasing silver or bronze plans. The report, "2014 Individual Exchange Policies in Four States: An Early Look for Patients with Blood Cancers," evaluated coverage benefits and premiums for plans offered by four state exchanges: California, New York, Florida and Texas, specifically for blood cancer care.

In terms of network adequacy, the study, which was conducted by Millman, found that

"It's also very important to make sure we provide enough variation in our product offerings so that people can make these decisions based on what is right for them."

—MIKE MUNOZ

Use of narrow networks in employer plans



Source: Kaiser Family Foundation/HRET Survey of Employer-Sponsored Health Benefits, 2013

many of the providers and hospitals that cancer patients depend on are largely excluded from the new exchange plans. According to Brian Rosen, senior vice president of public policy for the Leukemia and Lymphoma Society, the current exchanges also limit access to tertiary care centers for specialized cancer care.

"At a comprehensive cancer center, the patient has access to the skill and expertise of a team of clinicians—a highly specialized medical team that can provide an integrated approach in caring for a patient," Rosen says. "We also don't know to what extent the networks are excluding community medical oncologists."

Rosen says the society is currently working with Congress and the Centers for Medicare and Medicaid Services to ensure better network adequacy for patients with blood cancer.

"The insurance companies need to ensure the availability of tertiary cancer centers. If they are not in the network, they should at least be recognized as a contracted facility," he says.

TERRIBLE SITUATION

Harrell says although the narrow network situation is currently a source of concern for consumers, it will be examined at the federal level.

"Network adequacy provisions in the Affordable Care Act have not all been formulated, but sooner or later, I'm sure there will be further regulations and guidance on this from the federal government," he says. "But right now, it's a terrible situation from a regulatory perspective. It's not just about 'evil' insurance companies or 'evil' commissioners. It's a very difficult balancing act."

For employers, too, Harrell says the choice between a larger network and a lower premium for workers is a difficult decision. With the typical employer shouldering the larger portion of the premium, most want to find any means necessary to reduce their health benefit outlays.

"They want to ensure adequate care for their employees, but they don't want to pay $100 when they could pay $70," he says.

Harrell says, if consumers are forced to make the choice between lower costs or more choices, they will choose the lower costs.

"I have never had a consumer thank me for a rate increase," he says. "We get calls from consumers about the costs, and we get calls from consumers about wanting to see Dr. X. And in my experience, at the end of the day, consumers would rather be limited and have affordable premiums."

Jennifer Byrne is a freelance writer based in Glassboro, N.J.

PROVIDER LISTS MUST INCLUDE QUALITY RATINGS

Differentiation needed among behavioral health providers

BY JULIA BROWN

Providing a list of in-network providers online is a start, but experts say service and quality information should also be highlighted for members. The issue is especially concerning to mental-health advocates who say patients have a difficult time navigating the system and finding adequate providers.

A 2014 report to Congress says that about 55% of the country's 3,100 counties have no practicing psychiatrists, psychologists or social workers and clinicians are leaving the profession. Maintain an adequate network of behavioral health providers can be especially difficult in rural areas and for Medicaid populations that tend to have higher needs for mental and behavioral services.

"As a society, we need to start looking at funding for the education and training of more mental health professionals," says Carolyn Wolf, executive partner, Abrams, Fensterman, Fensterman, Eisman, Formato, Ferrara & Wolf, LLP and director of the firm's mental health law practice. "Even in-house providers who are full-time faculty and staff need to have the resources to be able to keep patients longer and to offer better discharge planning and better services in the community so we can to move patients through the system more effectively and more efficiently."

FIND A FACILITY

Jamison Monroe, CEO of Newport Academy, with adolescent treatment centers located in Southern California and Connecticut, says that there are still barriers to mental health treatment, including a lack of providers and information about the providers.

"We get over 1,000 calls a month, yet we can only really treat about 5% of those ourselves and refer the rest based on health needs, financial and economic needs and insurance coverage," he says.

Wolf says that the industry would benefit from the creation of a centralized database to allow consumers to vet the quality and capacity of mental health providers on managed care provider lists.

"Through the managed care websites, mental healthcare providers are supposedly 'easy' to find, but there's really no way of differentiating how good or effective they are," she says.

When patients try to seek specialized care, more detailed information should be provided, including where provider's credentials and any disciplinary actions can be checked, she says.

Some insurer sites are better than others at listing in-network providers online. However the issue can also be complicated by carve-out behavioral health services. When plans use carve-outs, the site should have a seamless connection to the network listings.

Monroe says more specific information should be listed for facilities' services provided as well.

"Some sites give you a name of a facility that has a similar licensure, but it may be a three-to-five-day psychiatric stabilization center, when in fact someone's looking for a long-term partial hospitalization treatment program," he says.

Health plans should consider turning to their members to ask for quality feedback, Wolf says. Surveying those who have used in-network providers would prove useful in determining whether the mental healthcare services received were adequate.

COMMUNITIES BALANCE ACCESS ISSUES

Top payer and provider at odds over cost and care in Seattle

Clearly the worst effect of change under the Affordable Care Act (ACA) is the initial disruption it can cause for patients. Payers and providers are acutely aware of the issue, even if they don't always agree about how to solve it.

In Washington, Seattle Children's Hospital has been publicly at odds with insurers over the trend toward narrow networks.

The disagreements have been going on since October 2013. Seattle Children's balked when it noticed that half of the insurance carriers on the state's exchange did not include the hospital in their networks.

"We were concerned that families did not know the plans they were buying did not include care for their children at Seattle Children's," says Sandy Melzer, MD, senior vice president and chief strategy officer for the hospital.

Children's filed a suit against the state Office of the Insurance Commissioner (OIC), citing failure to ensure adequate network coverage in the exchange plans. Separately, Seattle Children's also filed an administrative appeal asking OIC to kick three insurers out of the exchange—Coordinated Care Corporation, Bridgespan Health Company and Premera Blue Cross—that had been previously approved as Qualified Health Plans. The complaints are still pending.

The insurers have remained on the exchange, and consumers have enrolled in their plans.

CARE CONTINUITY

In January, Dr. Melzer says, the specialty hospital treated 125 patients who didn't have in-network coverage and vowed to forgive the families' additional costs. He says the reason why the hospital went ahead with treatment was for the sake of care continuity and because Seattle Children's offers unique services that he believes the patients' in-network providers don't offer.

Children's also filed paperwork with the plans asking for exceptions. It was certainly a reasonable request since even President Obama had asked health insurers to be flexible and allow patients to continue treatment at in-network levels during the ACA transition. Dr. Melzer says only 21 out of some 200 coverage requests had been answered by the end of January—and eight were denials.

"Plans have been very uncommunicative with us regarding how they were going to handle patients who were referred to us or what the process would be for a patient request to be seen by us, not in-network," Dr. Melzer says.

Some patients were in the process of treatment on January 1 when their new coverage began, and some had been specifically referred to Seattle Children's after January 1 for specialized care.

For certain specialty services, such as transplant and pediatric rheumatology, for example, the hospital is the sole provider not just in the state but in the region, according to Dr. Melzer.

"We're the only full-service children's hospital in a four-state area," he says. "There are very unique services at the hospital that are simply not available at any of the hospitals that the plans have said are in-network."

PAYER PRIORITY

Premera Blue Cross was particularly singled out by the hospital. It's the largest individual insurer in the state—claiming 60% of the exchange enrollments so far—and covers 1.8 million people. But the plan says the hospital is only telling one side of the story.

"One of our priorities is making sure our members have access to unique services like the ones at Children's," says Eric Earling, direc-

Continued on page 35

MANAGED HEALTHCARE
EXECUTIVE
For Decision Makers in Healthcare

ManagedHealthcareExecutive.com

Continued from page 29

tor of corporate communications for Premera. "Unfortunately the information that Children's recently released gives a really incorrect impression about how our members are able to access those services."

While Children's is not in the exchange-plan network for Premera, access is still available, Earling says.

For unique services at the hospital, Premera offers its exchange-plan members the in-network benefit levels, paying 80% of the costs. For all other services, members pay out-of-network rates, at 50% of the costs. Either way, patients still have access, and Children's still receives reimbursement, Earling says.

But there's also the issue of the appeals. According to Dr. Melzer, only 21 appeals for in-network coverage had been answered by Premera—a statement Earling disputes.

"As of January 29, we received approximately 190 requests for members on metallic plans looking to access unique services at Children's—or what they believe to be unique services," he says. "We approved 70% of those requests, so the members have access at the in-network rate."

And he says, the requests are processed in five days with members receiving notification of denials and lists of alternate in-network providers that Premera has proactively confirmed can manage the patient.

"We looked at our options, understanding the upward pressure ACA puts on rates for coverage," Earling says. "If you look at the affordability for Children's non-unique services—services that can be provided at other facilities in the area—they are simply not affordable."

Premera ran a data analysis of distinctive services offered by Children's against its claims experience and found only 12% of the member visits to the hospital were for unique services, and the other 88% were not. And utilization wasn't the only factor.

"Children's costs 60% more than the statewide network for non-unique services," Earling says. "If you drill down even further to inpatient costs for non-unique services, Children's costs 100% more."

He says Premera's data analysis was normalized for the complexity and severity of the cases.

"Our data points acknowledge and call that out many times: They are seeing a different kind of patient," he says.

But Dr. Melzer doesn't see it that way. He says the pediatric patients at Seattle Children's have underlying medical conditions that aren't figured in.

"These comparisons from what we can tell are not apples-to-oranges but apples-to-orangutans," Dr. Melzer says.

Earling says some providers have tried to portray the network selection as an access issue, but it isn't because Premera members have access to unique services at an in-network level.

"The issue is the cost at Children's for non-unique services and the impact that would have on the affordability of health plans."

***Julie Miller** is MHE's Content Channel Director*

PHARMACIES RELY ON PREFERRED STATUS

Savings opportunity drives selection

Narrow pharmacy networks are booming. On the Medicare side, 75% of Medicare Part D beneficiaries have signed up for a prescription drug plan that uses a preferred pharmacy network this year. That's up from 43% of seniors who opted for narrow network coverage in 2013.

On the commercial side, 70% of those who signed up for prescription drug coverage under the Affordable Care Act selected a plan that uses narrow provider networks.

"Plan-sponsor savings drive narrow networks," says Adam Fein, PhD, president of Pembroke Consulting in Philadelphia. "Pharmacy savings drive plan savings, which is why pharmacies don't like narrow networks."

That's not strictly true. Some pharmacies love narrow networks—if they happen to be the ones that made the cut.

CVS, Walmart, Walgreens, RiteAid and other chains compete aggressively to gain preferred provider status. So do pharmacy services administrative organizations such as McKesson's Health Mart and AmerisourceBergen's Good Neighbor Pharmacy franchise brands.

"The narrower preferred network offers an opportunity for a deeper discount to provide more value for members."

—TERRI SWANSON

Independent pharmacy is less enamored of preferred provider networks. One reason: Independent pharmacies and small chains are at an economic disadvantage when it comes to reduced copays and network prices.

They are also at an administrative disadvantage. Plan sponsors and managed care organizations obviously would rather negotiate a single contract that covers thousands of pharmacies than keep track of thousands of contracts that each cover a single provider.

NETWORK MODELS

Provider networks under both public and commercial plans come in three basic models, says Charles Cote, vice president, strategic communications, for the Pharmaceutical Care Management Assn. (PCMA): open, narrow and closed. As a general rule, the more restricted the network, the lower the costs.

The Aetna CVS/pharmacy Prescription Drug Plan narrow network, for example, uses $2 copays for 800 generics and $1 copays on generics for hypertension, hypercholesterolemia and diabetes to entice beneficiaries into preferred CVS, Walmart and Sam's Club pharmacies. Plan members can use other, non-preferred pharmacies, but copays are higher.

"The narrower preferred network offers an opportunity for a deeper discount to provide more value for members," says Terri Swanson, vice president and head of Medicare Part D for Aetna. "We use benefit design to reinforce the use of preferred providers."

The alternative is a closed network, and the best-known is Kaiser Permanente, which requires its 9 million members to use its own pharmacies. There are exceptions for emergency care, however.

HOW WIDE IS NARROW?

Creating a narrow network is as much art as science. Payers must balance the financial savings that stem from restricted provider networks with beneficiaries' need for pharmacy access.

There are more than 60,000 pharmacies in the United States. That is more than the total of the top eight fast-food franchises combined, according to PCMA. There are also geographic areas with just one or no pharmacies within a reasonable distance of where patients live and work—generally in rural areas.

Patient access rules also play a role. Medicare Part D pharmacy access is governed by rules set by the Centers for Medicare and Medicaid Services (CMS). For 2015, CMS is considering changes that might limit the use of narrow networks.

According to the National Community Pharmacists Assn. (NCPA), currently, in an urban area, at least 90% of Medicare members in a Part D service area, on average, must live within two miles of an in-network retail pharmacy. In suburban areas, at least 90% must live within five miles of an in-network retail pharmacy. And, in rural areas, at least 70% of Medicare beneficiaries, on average, must live within 15 miles of an in-network retail pharmacy. However, the standards only apply to the plan's primary pharmacy network. Plans are not required to meet these same standards when establishing preferred pharmacy networks, according to NCPA.

And, CMS does not apply the "any willing provider" provision to pharmacy networks.

Medicaid pharmacy programs are governed by other rules, including state requirements, while commercial plan access is influenced by the plan sponsor.

"There is no magic rule," Swanson says. "We need to drive enough volume to entice pharmacies to participate without impeding members' access. Pharmacy benefit plans in the commercial space have been around for a long time, so there is quite a bit of experience to rely on."

The typical preferred pharmacy network for Aetna includes 10,000 to 20,000 pharmacies nationally, Swanson says. Fein offers an alternate definition: any network that includes less than 50% of providers, which would benchmark at 30,000 pharmacies nationally.

Consumer resistance is generally not an impediment to narrow networks, Fein says. Kaiser Permanente, for example, gets high marks for quality and patient satisfaction despite having a closed network. Most consumers are willing to use a specific pharmacy as long as they see concrete benefits such as lower copays.

Last year, CMS found that negotiated pricing for the top 25 brands and 25 generics in the Part D program at preferred retail pharmacies is lower than at non-preferred pharmacies. However, when mail-order costs were included, some preferred network pharmacies were offering "somewhat higher negotiated prices," according to CMS.

"Preferred provider networks are a very common part of healthcare that pharmacy has successfully avoided for decades," Fein says. "Narrow networks already dominate Part D and are starting to penetrate commercial networks."

Fred Gephardt is a freelance writer based in Gold Hill, Ore.

@ More online

CMS preferred pharmacy price analysis:

http://go.cms.gov/1ekCqY5

The Drug Channels Institute chart of retail pharmacy participation 2014:

http://bit.ly/1cNe9Iv

KEEP MEMBERS IN MIND

5 ways to be member-centric

by **TRACEY WALKER**

In response to increasingly more educated and knowledgeable consumers, health plans have looked for ways to better engage and connect with members. They strive to provide not just services, but also an overall experience that can become a more integral part of members' daily decisions that will ultimately affect outcomes.

Cigna, for example, created a comprehensive healthcare experience several years ago, according to Matt Manders, president of regional and operations.

"We've banished the term 'member' from our vocabulary," Manders says. "Our thinking is that people don't consider themselves to be members of a health plan—they think of themselves as individuals, customers, consumers of health services. The sooner we begin to refer to people in those terms, the more our mindset is to treat people as they want to be treated."

Aetna has taken a similar approach, according to spokesperson Ethan Slavin.

"Over the past few years, Aetna has had a focus on reaching out directly to consumers to help them become more engaged in their healthcare and empower them to live healthier lives," he says.

Refreshing its brand with a new logo back in January 2012 helped Aetna highlight its evolution from an insurance carrier to a health solutions company conveying "much more of a lighter feel and consumer focus," according to Slavin. In the summer of 2013, it also launched the "what's your healthy?" campaign and interactive website.

These approaches exemplify the path health plans need to take for effective consumer centricity, says John E. Schneider, PhD, CEO, Avalon Health Economics, a Morristown, N.J.-based healthcare consultancy.

"First and foremost, plans need to convey to enrollees that they are on the side of the consumer—on their team," he says. "This sentiment must be expressed consistently through all of the main points of contact between plans and enrollees."

These approaches exemplify the path health plans need to take for effective consumer centricity.

The health plan should also play a role in helping members manage logistics, Schneider adds. "This approach has two advantages: It increases enrollee satisfaction and it increases the opportunities for the plan to improve the outcome of a case," he says.

Members with increasing access to data from multiple sources have demanded a new experience "focused on ease of ac-

VIDEO

Watch our video on being member-centric: managedhealthcareexecutive.com/consumercentricity

cess to the healthcare system; billing and payment transparency; effectiveness; and actionable information from their health plans and providers to improve their health," according to Joseph Mack, MPA, president of Joseph Mack & Associates, a business healthcare advisory in Dana Point, Calif.

How can the industry change from provider- or payer-centered processes to member-centered processes?

More than likely, the member-centered processes would have to be in addition to the provider and payer processes, according to L. William Katz of Katz & Associates, a healthcare consultancy in Gilbert, Ariz.

"It is difficult to imagine how this would be possible given the limitations on administrative costs in the Affordable Care Act," he says.

Consumer-centric health plans strive to meet the following benchmarks:

1/ Define quality in terms of convenience

In the digital world in which we now live, consumers are defining quality in terms of convenience, according to Aetna's Slavin.

"It's important to meet members where they are with resources and information that help simplify and improve their healthcare experience," he says. "We strive to have essential information available at someone's fingertips at the point where it matters most."

In addition to providing valuable information at the right time, Aetna hopes that the tools it offers are convenient and help consumers become more fully engaged in their own healthcare. For example, the plan provides tools such as the Member Payment Estimator, a transparent cost estimator that can help people compare the varying range of prices for health services, technologies such as the iTriage app, a symptom checker that helps consumers make better healthcare decisions, and its CarePass platform, which offers access to health and wellness mobile apps, Slavin says.

These tools help consumers and providers make better decisions, which can lead to improvements in outcomes and costs, he adds.

2/ Resolve logistical nightmares

It is only natural that members will complain if there is a "drop" in the perceived service level.

"As we are seeing with the public exchanges, health plan members need easy access to the plan and their provider network. Those who have trouble finding doctors, getting their ID cards, or who need help with claims, referrals, or determination, need these services and will complain if they are not available," says James Smith, senior vice president of The Camden Group, a healthcare consulting firm headquartered in Los Angeles, Calif.

The good news is with feedback, health plans can and are improving these utility functions to provide better services over time. Schneider urges health plans to consider the small things.

"By paying closer attention to the small services—finding a doctor, finding a radiology center, figuring out how to get a colonoscopy—plans may very well be preventing more costly outlays down the road. Moreover, this approach has the potential to make enrollees feel like the plan is indeed on their side—their partner in helping navigate the often confusing and daunting healthcare syste m."

3/ Optimize communications

The healthcare system is viewed by most as a confusing and intimidating patchwork of providers and payers, with the consumer often caught in the middle of disputes between payers and providers, according to Schneider.

The use of jargon generally exacerbates the feelings of alienation that enrollees can sometimes feel. "Plans should look for 'softer' ways to communicate with enrollees," he says. "Describe the concept before tagging it with its official name, and do so repeatedly in all forms of communications—telephone, mail and web. Too often there is a lack of consistency in the content plans deliver to enrollees."

Aetna, for example, has had a wide range of initiatives over the past few years to use more plain language when interacting with members. Aetna's work in this area has been recognized several times over the past three years by the Center for Plain Language. Aetna's efforts to help people better understand their health benefits include writing materials at a fifth-grade reading level and sharing self-help tools.

The classic example of a confusing, jar-

gon-laced document is the Explanation of Benefits (EOB).

"We found that most people think that coinsurance is 'insurance for me and my spouse,' that the provider is the insurance company, and EOB is the 'This is not a bill' letter," Cigna's Manders says. "We've taken these learnings and socialized them throughout the enterprise so that we can better connect with our customers by using simple, clear and common-sense language."

Now, its EOB resembles a supermarket receipt: Treatment price, plan discount, how much the plan paid, applied health savings account dollars and how much, if anything, the consumer owes.

"In doing so, service call questions about the EOBs have dropped by one-third," Manders says.

4/ Be a facilitator of care

Cigna has transitioned from "gatekeeper" to facilitator for the individual.

"For example, we all know about the potential health risks and costs associated with excessive radiology imaging, and so our contracted physicians will direct their patients to our consulting services to help them find the best local option for those services," Manders says.

In most cases, if a physician recommends a particular test or treatment, the patient will believe that the test or treatment is critical to their well-being, according to Schneider.

"This is less of a problem when dealing with patients who have done their homework—a well-prepared patient may very well challenge a physician as to whether a test or procedure is necessary," he says. "However, most patients lack this level of preparation, or simply lack the nerve to challenge the authority of a doctor."

Schneider says plans should explain when the test or procedure the physician ordered is inconsistent with guidelines. The statement could be generated using the same database query used to determine prior authorization, he says.

It is important that health plans respond quickly with treatment recommendations based upon the latest medical scientific knowledge. There still can be a disagreement and in those cases a progressive review by care managers or committees of physicians become part of the process. But the ultimate goal would be real-time response at the point of care.

This is where health plans can perhaps learn from the provider community.

"Most clinical areas of medicine have developed clinical practice guidelines [CPGs] in their respective disease areas," Schneider says. "CPGs also have spread to acute care settings, offering real-time guidance on diagnosis and treatment. Plans can do the same. Leveraging the wealth of data that plans now have on their enrollees, it should be possible to quickly 'score' each request for authorization against the backdrop of the patient profile and clinically recommended diagnoses and treatments based on CPGs."

Outright denials for treatment are rare—occurring less than one-half of 1% of the time, according to Manders.

In general, Slavin says that Aetna has prompt turnaround times for preauthorizations and uses a peer-to-peer review when needed. The plan posts all of its clinical policy bulletins on its public website.

"We want members and doctors to know what to expect," Slavin says.

As performance-based and narrow networks begin to dominate the public and private exchange markets, authorization and referral mechanisms must become even more member responsive.

5/ Enhance provider relationships

Plans have a goldmine of claims data and should empower providers to produce quantifiably better outcomes.

"The information must provide physicians with a better understanding of their patients' diseases and how their treatments positively or negatively affect results; how it can mitigate their malpractice risks; and, how it will increase practice profitability, through efficiencies that are qualitative and which are the most cost-effective," Mack says.

At the same time, it's important to be proactive in counseling members about choice of providers as well as treatments, according to Katz. Narrow networks might scale down choices to only the best or most efficient, but he believes network optimization should reach beyond just the physician and hospital participants.

Members have demanded a new experience "focused on ease of access to the healthcare system; billing and payment transparency; effectiveness; and actionable information from their health plans and providers to improve their health."

—JOSEPH MACK, MPA

NEW HEPATITIS C DRUGS BETTER AND FASTER

Experts outline the advantages

by **MARI EDLIN**

Less than three years ago, the FDA approved two new breakthrough drugs for treating chronic hepatitis C (HCV)—Victrelis (boceprevir) and Incivek (telaprevir)—the first protease inhibitors approved for HCV. Although their introductions caught the attention of the marketplace, their successors are arriving quickly.

Late last year, the FDA approved two new HCV drugs, Solvadi (sofosbuvir), a polymerase inhibitor to treat genotypes 1 through 4, manufactured by Gilead Sciences, and Olysio (simeprevir), a protease inhibitor from Janssen Therapeutics targeting genotype 1.

Costing $1,000 a day, 400 mg of sofosbuvir is taken with either ribavirin alone, or with ribavirin and interferon, orally, once a day for 12 to 24 weeks, depending on the genotype. Simeprevir at 150 mg, also an oral, once-a-day drug, is recommended for 12 weeks in combination with ribavirin and interferon, followed by another 24 weeks of ribavirin and interferon. Its cost is $790 a day.

The Centers for Disease Control and Prevention (CDC) estimates that 3.2 million persons are chronically infected with HCV. Approximately 75% to 85% of people infected with the HCV virus will develop chronic infection.

Successful treatment is measured by a sustained virologic response (SVR), which signifies an undetectable viral load/serum HCV RNA (ribonucleic acid—the virus' genetic material) after the designated period of treatment.

As with any new specialty drugs, insurers, pharmacy benefit managers and physicians must weigh the value of the new products, balancing cost, efficacy, effectiveness and ease of use.

MANAGED HEALTHCARE EXECUTIVE recently convened

Continued on page 49

THE PANEL

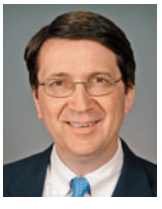
Mary Dorholt PharmD

leads Express Script's specialty clinical strategy and protocol development, creating clinical guidelines for patient care and physician interaction. She is also responsible for driving organizational research around specialty medications and Express Scripts' experience. Prior to her current role, she was responsible for specialty strategic guidance to employer, government and labor organizations. She holds a doctor of pharmacy degree from the University of Minnesota College of Pharmacy in Minneapolis and B.S. degrees in mathematics and biology.

Karla Thornton, MD, MPH,

is a professor in the Division of Infectious Diseases at the University of New Mexico School of Medicine in Albuquerque. She also serves as the associate director of Project ECHO (Extension for Community Healthcare Outcomes). Using her clinical expertise in the treatment of hepatitis C and HIV, she facilitates teleECHO clinics through which she trains other clinicians on comprehensive care. In 2009, Dr. Thornton started an education project that trains New Mexico state prisoners to be peer educators in hepatitis C, other infectious diseases and addiction.

John Poniatowski MS



joined CIGNA in 1994, and currently serves as clinical program director, specialty pharmacy for CIGNA Pharmacy Management. He is responsible for establishing and executing utilization management and health management strategies related to the use of specialty pharmaceuticals. Programs focus on the integration of medication therapy with CIGNA's medical, health and wellness programs to improve health outcomes and lower overall healthcare costs. Poniatowski received his bachelor of pharmacy degree from Northeastern University and his M.S. degree from Saint John's University. He completed an American Society of Health-System Pharmacists' hospital pharmacy residency at Mercy Hospital in Rockville Centre, N.Y.

INVOKANA™ is the #1 branded therapy prescribed by endocrinologists when adding or switching non-insulin type 2 diabetes medications*

ENVISION NEW **POSSIBILITIES**

Invokana™
canagliflozin tablets

*Data on file. Based on NBRx data sourced from IMS NPA Market Dynamics Database, weekly data through 9/20/13.

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

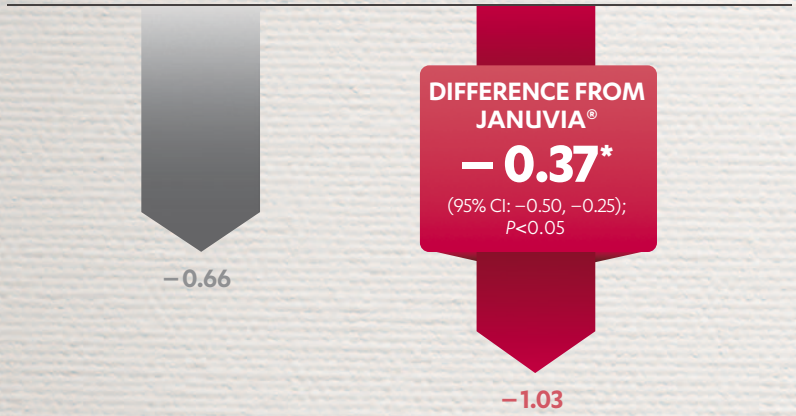
CONTRAINDICATIONS

- 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.

Please see additional Important Safety Information and brief summary of full Prescribing Information on the following pages.

INVOKANA™ 300 mg demonstrated greater reductions in A1C vs Januvia® 100 mg at 52 weeks...

Adjusted Mean Change in A1C From Baseline (%): INVOKANA™ 300 mg vs Januvia® 100 mg, Each in Combination With Metformin + a Sulfonylurea[1]



Incidence of Hypoglycemia

With metformin + a sulfonylurea over 52 weeks: INVOKANA™ (canagliflozin) 300 mg: **43.2%**; Januvia® 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[1]

Convenient Once-Daily Oral Dosing[1]

- Recommended starting dose: INVOKANA™ 100 mg
- Dose can be increased to 300 mg in patients tolerating 100 mg who have an eGFR ≥60 mL/min/1.73 m^2 and require additional glycemic control

*INVOKANA™ + metformin is considered noninferior to Januvia® + metformin because the upper limit of the 95% confidence interval is less than the prespecified noninferiority margin of 0.3%.

IMPORTANT SAFETY INFORMATION (cont'd)

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.
- **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™. 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.

COVERED FOR >**75%** OF COMMERCIALLY INSURED PATIENTS WITHOUT PRIOR AUTHORIZATION[3]

...as well as greater reductions in body weight† and systolic blood pressure (SBP)†

Change in Body Weight†

Significant reductions in body weight at 52 weeks, each in combination with metformin + a sulfonylurea (*P*<0.001)[1]

»Difference from Januvia®‡:
300 mg: **–2.8%**

Change in SBP†

Significant lowering of SBP at 52 weeks, each in combination with metformin + a sulfonylurea (*P*<0.001)[2]

»Difference from Januvia®‡:
300 mg: **–5.9 mm Hg**

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

†Prespecified secondary endpoint.

‡Adjusted mean.

INVOKANA™ provides SGLT2 inhibition, reducing renal glucose reabsorption and increasing urinary glucose excretion.[1]

Adverse Reactions

In 4 pooled placebo-controlled trials, the most common (≥5%) adverse reactions were female genital mycotic infection, urinary tract infection, and increased urination.[1§]

References: 1. INVOKANA™ [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2013. **2.** Schernthaner G, Gross JL, Rosenstock J, et al. Canagliflozin compared with sitagliptin for patients with type 2 diabetes who do not have adequate glycemic control with metformin plus sulfonylurea: a 52-week randomized trial. *Diabetes Care*. 2013;36(9):2508-2515. **3.** Data on file. Janssen Pharmaceuticals, Inc., Titusville, NJ. Data as of 9/17/13.

SGLT2 = sodium glucose co-transporter-2.

§Included 1 monotherapy and 3 add-on combination trials with metformin, metformin + a sulfonylurea, or metformin + pioglitazone.

Learn more at **INVOKANAhcp.com/journal**

»**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.

Please see additional Important Safety Information and brief summary of full Prescribing Information on the following pages.

ENVISION NEW
POSSIBILITIES

Invokana™
canagliflozin tablets

IMPORTANT SAFETY INFORMATION (cont'd)

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, 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 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.

Janssen Pharmaceuticals, Inc.

Canagliflozin is licensed from Mitsubishi Tanabe Pharma Corporation.

November 2013 004991-131021

» **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 pruritus, thirst, nausea, and constipation.

K02CAN13149

Please see brief summary of full Prescribing Information on the following pages.

Invokana™
canagliflozin tablets

janssen
PHARMACEUTICAL COMPANIES OF Johnson&Johnson

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.

INVOKANA™ (canagliflozin) tablets

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.

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

INVOKANA™ (canagliflozin) tablets

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]*.

INVOKANA™ (canagliflozin) tablets

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, e.g., 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.

PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Medication Guide).

Instructions: Instruct patients to read the Medication Guide before starting INVOKANA (canagliflozin) therapy and to reread it each time the prescription is renewed.

Inform patients of the potential risks and benefits of INVOKANA and of alternative modes of therapy. Also inform patients about the importance of adherence to dietary instructions, regular physical activity, periodic blood glucose monitoring and HbA1C testing, recognition and management of hypoglycemia and hyperglycemia, and assessment for diabetes complications. Advise patients to seek medical advice promptly during periods of stress such as fever, trauma, infection, or surgery, as medication requirements may change.

Instruct patients to take INVOKANA only as prescribed. If a dose is missed, advise patients to take it as soon as it is remembered unless it is almost time for the next dose, in which case patients should skip the missed dose and take the medicine at the next regularly scheduled time. Advise patients not to take two doses of INVOKANA at the same time.

Inform patients that the most common adverse reactions associated with INVOKANA are genital mycotic infection, urinary tract infection, and increased urination.

Inform female patients of child bearing age that the use of INVOKANA during pregnancy has not been studied in humans, and that INVOKANA should only be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Instruct patients to report pregnancies to their physicians as soon as possible.

Inform nursing mothers to discontinue INVOKANA or nursing, taking into account the importance of drug to the mother.

Laboratory Tests: Due to its mechanism of action, patients taking INVOKANA will test positive for glucose in their urine.

Hypotension: Inform patients that symptomatic hypotension may occur with INVOKANA and advise them to contact their doctor if they experience such symptoms *[see Warnings and Precautions]*. Inform patients that dehydration may increase the risk for hypotension, and to have adequate fluid intake.

Genital Mycotic Infections in Females (e.g., Vulvovaginitis): Inform female patients that vaginal yeast infection may occur and provide them with information on the signs and symptoms of vaginal yeast infection. Advise them of treatment options and when to seek medical advice *[see Warnings and Precautions]*.

Genital Mycotic Infections in Males (e.g., Balanitis or Balanoposthitis): Inform male patients that yeast infection of penis (e.g., balanitis or balanoposthitis) may occur, especially in uncircumcised males and patients with prior history. Provide them with information on the signs and symptoms of balanitis and balanoposthitis (rash or redness of the glans or foreskin of the penis). Advise them of treatment options and when to seek medical advice *[see Warnings and Precautions]*.

Hypersensitivity Reactions: Inform patients that serious hypersensitivity reactions such as urticaria and rash have been reported with INVOKANA. Advise patients to report immediately any signs or symptoms suggesting allergic reaction or angioedema, and to take no more drug until they have consulted prescribing physicians.

Urinary Tract Infections: Inform patients of the potential for urinary tract infections. Provide them with information on the symptoms of urinary tract infections. Advise them to seek medical advice if such symptoms occur.

Active ingredient made in Belgium

Finished product manufactured by:
Janssen Ortho, LLC
Gurabo, PR 00778

Manufactured for:
Janssen Pharmaceuticals, Inc.
Titusville, NJ 08560

Licensed from Mitsubishi Tanabe Pharma Corporation

10282400

K02CAN13080B

janssen

Continued from page 40
three key thought leaders to discuss the impact of simeprevir and sofosbuvir and whether they will stand the test of time. The transcript has been edited for length.

MHE: Why has there been an increase in cases of hepatitis C?

Thornton: There actually is not an increase in the incidence of new infections, but what's happening is that we're identifying more people who are chronically infected with hepatitis C. The actual incidence of hepatitis C has decreased dramatically over the last 20-plus years. In the 1980s, incidence was about 200,000 cases per year compared to an estimated 17,000 cases in 2010.

About a year ago, the CDC and the U.S. Preventive Services Task Force came out with guidelines to actually screen more people. They recommend that anyone born between 1945 and 1965 get a blood test for hepatitis C. The recommendation is important because we haven't been very good at screening in the past.

Dorholt: Sometimes there's a perception of increasing new infections because there's been this warehousing phenomenon going on where patients who don't necessarily need to be treated—those who are not showing overt signs of disease or are not deteriorating—are being held back [from treatment] while physicians wait for the newer, more efficacious and perhaps easier-to-use medications to treat those patients that they know are infected.

MHE: As for warehousing patients to wait for a newer treatment, is that a problem?

Thornton: I don't think I would characterize it as a problem. These folks that have the virus are not always becoming sicker, so there is time to wait for perhaps a more successful opportunity for treatment.

Poniatowski: When Incivek and Victrelis came to market in mid-2011, they were obviously seen as improvements over the prior two drug combinations, so we saw an increase of people coming in to be treated. That continued through 2011 into late 2012, and then started tapering off by 2013 for the reason that Mary stated: It's not always urgent to treat these folks, and clinicians knew

HEPATITIS C PIPELINE PHASE III

Generic Name	Investigational Name	Company	Product Type
telaprevir	N/A	Vertex	New Indication
N/A	BMS-791325	Bristol Myers Squibb	New Molecular Entity
daclatasvir / asunaprevir / BMS-791325	BMS-790052 / BMS-650032 / BMS-791325	Bristol Myers Squibb	New Combination
deleobuvir	BI-207127	Boehringer Ingelheim	New Molecular Entity
N/A	ABT-450	AbbVie	New Molecular Entity
sofosbuvir / ledipasvir	GS-7977 + GS-5885	Gilead Sciences	New Molecular Entity; New Combination
ledipasvir	GS-5885	Gilead Sciences	New Molecular Entity
dasabuvir	ABT-333	AbbVie	New Molecular Entity
ombitasvir	ABT-267	AbbVie	New Molecular Entity
N/A	ABT-450 + ritonavir + ombitasvir (ABT-267)	AbbVie	New Molecular Entity; New Combination
taribavirin HCl	ICN-3142; KD-024	Valeant	New Molecular Entity
faldaprevir	BI-201335	Boehringer Ingelheim	New Molecular Entity
ABT-450/ritonavir + ombitasvir + dasabuvir	ABT-450/ritonavir + ABT-267 + ABT-333; M11-646	Enanta; AbbVie	New Molecular Entity; New Combination
alisporivir	DEB-025; Debio-025, UNIL-025	Novartis	New Molecular Entity
peginterferon lambda-1a	BMS-914143	Bristol Myers Squibb	New Formulation
thymalfasin	thymosin alpha 1	SciClone; Sigma Tau	New Molecular Entity
daclatasvir	BMS-790052	Bristol Myers Squibb	New Molecular Entity

Source: Data provided exclusively for Managed Healthcare Executive by Catamaran LLC

that there were better drugs coming around the corner.

MHE: Before the introduction of Incivek and Victrelis, what was the situation for HCV drugs? And what can sofosbuvir and simeprevir do that their predecessors cannot?

Thornton: The prior treatment before May of 2011 was injected pegolated interferon and oral ribavirin for all genotypes.

The success rate with that particular regimen was about 50% in genotype 1 patients, which is the predominant genotype in the United States, and higher in genotype 2 and 3 patients—up to 70%. All genotypes required interferon—that is a very difficult drug to take. It has a lot of toxicity; people can't tolerate it. And the duration of therapy at that time for genotype 1 patients was a minimum of 48 weeks.

Telaprevir and boceprevir increased the cure rate in genotype 1 to about 70%, compared to about 50% with interferon and ribavirin alone. They also introduced what was called response-guided therapy, meaning the duration of therapy will depend on a patient's actual response to the medication. If someone had a good initial response to therapy, they might just need six months of therapy versus 48 weeks. The new therapies had the potential to increase the cure rate and shorten the duration.

Simeprevir is an improvement over its immediate predecessors because it's one pill, once a day. It has fewer side effects and drug interactions and has a very similar cure rate to that of telaprevir and boceprevir. Unfortunately, you still have to take interferon and ribavirin, and it's a response-guided therapy just like the other ones are. Therefore, people would also have to continue on interferon with simeprevir.

HCV PREVALENCE IN 2013 BY HEALTH INSURANCE TYPE

Health Insurance Type	Total U.S. Population (Thousands)	Estimated Prevalence of HCV-RNA+	Estimated Number of HCV-RNA+ (Thousands)
Uninsured	48,600	2.08%	1,012
Veteran Affairs	5,600	5.40%	302
Commercial	164,200	0.47%	779
Dual Medicare and Medicaid	6,900	2.91%	201
Medicare (non-dual)	37,600	0.31%	117
Medicaid	43,300	0.87%	377
Other Military	2,200	0.47%	10
Prison	1,500	30.0%	450
Total	310,000	1.05%	3,249
Total without Prison	308,500	0.91%	2,799

Sources: Milliman analysis of NHANES. Variable:LBXHCR - Hepatitis C RNA (HCV-RNA) in NHANES. Chien N, Dundoo G, Horani M et al. Seroprevalence of viral hepatitis in an older nursing home population. *J Am Geriatr Soc.* 1999;47:1110-3. Dominitz JA, Boyko EJ, Koepsell TD et al. Elevated prevalence of hepatitis C infection in users of the United States veterans medical centers. *Hepatology.* 2005;41:88-96. Chak E, Talal A, Sherman K et al. Hepatitis C virus infection in USA: an estimate of true prevalence. *Liver International.* 2011;10:1090-1101.

Sofosbuvir is a brand new class of drugs called a polymerase inhibitor. For genotype 1, it's given in combination with pegolated interferon and ribavirin, but it's only for 12 weeks. It shortens the duration for using interferon, and the cure rate for 12 weeks is about 90% in patients who have not previously been treated. For the other genotypes, that particular drug is given just in combination with ribavirin. And again, there is a much higher cure rate than what we were seeing in the past with interferon-based regimens.

Dorholt: I think it also is fair to say that the direction of new drug development in this area continues to move toward the shorter, all-oral regimen that can be used in the majority of hepatitis C patients in the United States. That really eliminates the historically used pegolated interferons and ribavirin. We're not necessarily there for genotype 1, which is the most predominant type of hepatitis C in the United States, but these drugs are getting us much, much closer, and there is a lot in the pipeline that will help us move the needle as well.

Poniatowski: As each generation of HCV medications comes to market, they bring different advances, hopefully all driving towards the fact that the patient

will be more likely to take the drug as intended, and for the full duration. The result is not just achieving better effectiveness, but fewer side effects with less likelihood of stopping the drug.

MHE: Are sofosbuvir and simeprevir considered to be cures?

Thornton: Yes. Any drug that gets rid of the hepatitis C virus, and there's no virus six months after therapy, is considered a cure.

Dorholt: All of the approved agents, even the interferons and ribavirins have been cures; they just differ in the number of patients that are successfully cured. For patients who achieve SVR, the incidence of them actually relapsing is very low at 1% to 2%. For the older two drugs, the SVR is around 40%, while it is in the range of 80% to even 90% with the new medications.

MHE: Since simeprevir requires interferon, won't the problem with side effects and longer treatment times with that drug still exist?

Thornton: That's true, because with simeprevir as a response-guided therapy, somebody could still end up getting an entire year of interferon therapy. Recently, guidelines for treatment of chronic hepatitis C from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) came out, and they do not recommend simeprevir as first line therapy for genotype 1 because of the risk of having to prescribe that much interferon. However, when simpeprevir is used in combination with sofosbuvir, it's only 12 weeks of interferon, and there is a very high cure rate.

Poniatowski: There is at least one interferon-free regimen in genotype 1 that is FDA-approved for the population that's considered interferon-ineligible.

Thornton: FDA labeling says that for interferon intolerant, or unwilling individuals, the second-line therapy would be a combination of sofosbuvir and ribavirin for 24 weeks. You don't get as good of a cure rate, but it is an option for people who really need therapy and can't wait for newer therapies, nor can they take interferon.

MHE: Let's discuss the new guidelines and their implications.

Thornton: The guidelines are the result of a joint effort by the two associations (AASLD and IDSA), and this is the first time this has ever happened. It is exciting for us in the field to have guidelines that are going to be kept up-to-date and are user-friendly. In the past, they were always behind if a new drug came out. At least in my practice, they reflect exactly what we're doing.

Poniatowski: I was impressed and surprised by the timing because practice-based guidelines don't typically react that quickly to changes in the marketplace. I was struck by the fact that the earlier two new, improved drugs are not recommended. The other thing that's interesting is that the guidelines recommend a combination of simeprevir and sofosbuvir, which is not yet approved by the FDA. It's precedent setting so that when the next drugs arrive, we can expect guidelines to be just as timely.

Thornton: The combination has been shown—at least in Phase II clinical trials—to be extremely effective for even people who are the most difficult to treat, who have cirrhosis and have previously failed therapy. In the clinical practice, we are desperately trying to get that combination for the patients who are interferon-ineligible.

Dorholt: This is kind of groundbreaking in terms of how quickly they have encompassed the new drugs into the guidelines and even incorporated some things that are not necessarily FDA approved, that are a little bit off-label but have evidence.

MHE: Is the FDA working on approval of the combination of simeprevir and sofosbuvir?

Poniatowski: It's a tough question about which to speculate because it comes down to the manufacturers' strategies—two different companies deciding whether or not they want to actually pursue that type of label and indication. Not only has the combination been incorporated into the guidelines, but there also are ongoing studies, so you know the requirement for FDA approval is certainly not a necessity for practitioners to use the drugs in such a way. The lack of approval is not the only consideration for payers in determining whether it would be appropriate to cover that combination.

The coverage question at Cigna is based on the evidence in terms of published studies, and we really consider the specific characteristics of each patient case and hold periodic conversations between our medical director and the physician.

Thornton: The many different permutations and combinations of drugs and durations of therapy for hepatitis C must come into play when decisions are being made about what types of therapy to

recommend and which courses of therapy are most appropriate.

MHE: How are patients going to be able to afford these new drugs?

Dorholt: At Accredo, we never want to see cost be a barrier to patients who need a medication. If patients express any level of concern about costs or payment while we're working with them, we connect them to our reimbursement specialists, who can find appropriate financial assistance, including a patient assistance program or resources available from a foundation.

We also work with our payer clients to help them make cost share choices to manage costs, while also not deterring patient access because costs are so excessive. From our research and understanding of patient behavior, we know that there's a tipping point where that can occur, and so benefits also have to be created using that perspective.

Poniatowski: Due to our holistic approach to patients, Cigna Specialty Pharmacy Services also informs customers about programs and resources available to them, including financial assistance programs for the costly specialty medications.

MHE: Is there a way for physicians to determine who is going to benefit most from these new drugs?

Dorholt: Because of the complexity of the drugs and the nuances of patients, I think there are many elements that play into the individual selection process. Efficacy, for example, is a major factor. You also have to think about the viral genotypes and their subsets because that will influence which drug you pick and which is more successful.

Other things that need to be considered are: previous treatment history and the response to that treatment, because there is some cross resistance between some of these products; the severity of the disease and whether the patient already has cirrhosis; a patient's other diseases that might influence drug choices; whether medications for those other conditions have an effect; and if a patient has HIV.

In addition, you have to look at patient dynamics: What is that patient's ability to handle a really complicated regimen with complicated side effects?

Poniatowski: A combination of what a person's disease looks like, what drugs are on the market and their pros and cons, and what is on the horizon is necessary in making that decision about treating now or waiting.

MHE: What kinds of disease management programs prove to be most effective in targeting non-adherence and eliminating the virus?

Poniatowski: At Cigna, we approach disease management programs by looking at patients holistically, not just paying attention to their hep C because they may have comorbid conditions. Instead, we consider their care across the whole spectrum of their disease.

Cigna Specialty Pharmacy Services creates teams of pharmacists, certified pharmacist technicians, registered nurses and call center personnel whose training focuses on a particular chronic condition such as hepatitis C. They continually monitor adherence, side effects and drug interactions and reach out to the treating doctor when adjustments are needed.

Dorholt: Any effective program in our portfolio has to include a multifaceted approach to support the patient, including direct education, clinical outreach, ongoing adherence messaging and reminders, and technology-based tools to create a sense of community or patient connection.

Express Script's specialty unit, Accredo, offers patients with hepatitis C one-on-one counseling by pharmacists with expertise specifically in managing hepatitis C. Nurses and pharmacists make follow up calls to these patients depending on their specific situations.

Thornton: Our most important offering is Project ECHO, providing 24 service centers of excellence around the state of New Mexico that treat hepatitis C.

Hepatitis C treatment is actually embedded in patients' primary care settings, which offer a team-based approach. Along with a clinician, there is always a community health worker, a medical assistant or someone with similar capabilities. The key is having very close follow-up with providers and the hepatitis C team in clinics where patients are treated. When we studied the effectiveness of treatment through the project, we had really phenomenal responses and adherence rates because people were being treated within their own home base and in their own primary care setting.

Mari Edlin is a freelance writer based in Sonoma, Calif.

@ More online

How will payers determine the value proposition of HCV drugs? Watch our video of Steven Flamm, MD, medical director of the liver transplant program for Northwestern Medicine:

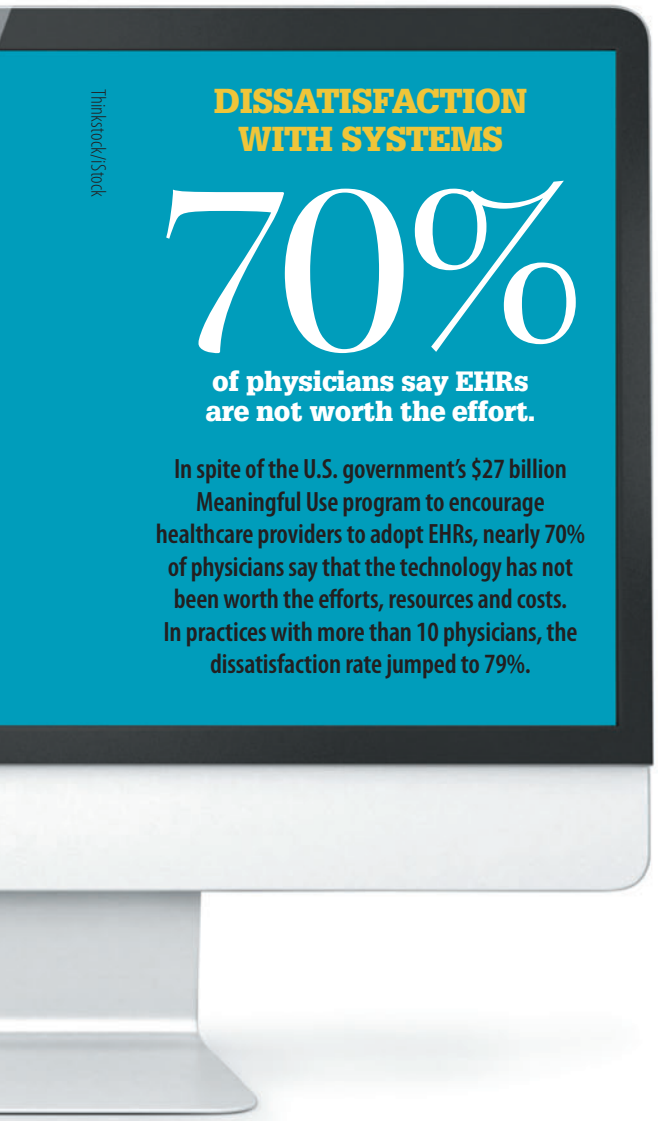
http://managedhealthcareexecutive.com/hep C

5 UNSETTLING STATISTICS ABOUT EHR USE IN MEDICAL PRACTICES

PHYSICIANS SAY EHRs NOT WORTH IT

by **DONNA MARBURY**

Sobering statistics about electronic health records (EHRs) and their inability to better coordinate care and improve costs and workflow are at the center of a recent survey of nearly 1,000 physicians administered by MPI Group for *Medical Economics* magazine. The majority of physicians report frustration with their EHR systems in more ways than one, but will the healthcare information technology industry take note of the time, money and efforts that these systems are costing?



Thinkstock/iStock

BUYER'S REMORSE

63%

EHR dissatisfaction scores increase by practice size. About 63% of physicians would not purchase the same EHR system if given a choice. Practices with 10 or more physicians say they would not purchase the same EHR system again. Sixty percent of family medicine physicians wouldn't repurchase their same EHR system, while 66% of internal medicine physicians agree.

SWITCHING EHRs

67%

Physicians gave multiple reasons why they plan on switching EHRs. The majority of doctors (67%) cited system functionality as a top reason for wanting to switch. Cost (48%) and poor customer service (33%) are also big factors in physicians wanting to switch EHR vendors.

CARE IS WORSE

45%

Almost half (45%) of physicians surveyed thought that EHRs are making patient care worse. In larger practices with more than 10 physicians, 52% of them thought EHRs provided worse quality of care, while in practices with six to 10 physicians, 54% of physicians agreed.

LACK OF CARE COORDINATION

69%

Among the promises of EHR technology is to create efficiencies in doctor-to-hospital and doctor-to-doctor communication. However, 69% of physicians surveyed say that care coordination has not been improved. Specialists and subspecialists outside of primary care seem to be most dissatisfied with EHR care coordination, as 72% say that coordination with hospitals has not improved.

MINIMIZE THE TROUBLE OF ICD-10 TRANSITION

Test your systems early and often

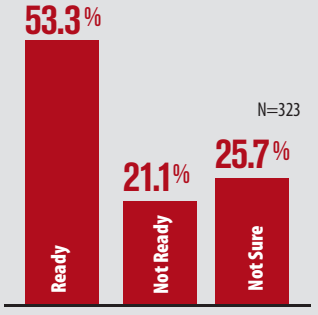
by **JAMIE GOOCH**

The results are in, and they don't all look good for the transition to ICD-10. Everyone covered by the Health Insurance Portability Accountability Act (HIPAA) is required to use the updated code set for diagnosis and inpatient coding on October 1. According to the Centers for Medicare & Medicaid Services (CMS), payers should have completed planning, budgeting and impact assessment by now, have revised provider contracts and policies, and have integrated ICD-10 systems. They should have completed internal testing and be well into testing with their partners. All that should be left to do is finish up testing and training.

But not everyone is on time.

- **Twenty-one percent of Managed Healthcare Executive readers last year said they are not ready for the change.**
- **Half of the healthcare organizations that responded to a separate poll conducted by KPMG LLP had not yet estimated the new coding system's impact on their cash flow.**
- **An October 2013 ICD-10 readiness survey from the Workgroup for Electronic Data Interchange (WEDI) showed about 40% of health plan respondents had not fully completed their impact assessment.**

ICD-10 UPGRADE READY BY OCTOBER 1



Source: Managed Healthcare Executive State of the Industry, 2013

"If you don't know what you have to do, how can you figure out how long it will take to do it?" asks Jim Daley, chairman of the board for WEDI and director, IT risk and compliance at BlueCross BlueShield of South Carolina. "No one should not know the impact ICD-10 will have on their organization by now. That's being like an ostrich with your head in the sand."

KPMG says those who have completed assessments are estimating upgrades to cost anywhere from $1 million to more than $15 million. And they still have a long way to go before being fully prepared for ICD-10.

"One thing that I see is that the testing of the systems hasn't started or are just beginning," says Wayne Cafran, a partner at KPMG who has been in the industry for more than 20 years. "That could be a big process to make sure you're upgraded and can accommodate the data. I think that's critical."

WEDI survey payer respondents indicate that competing internal priorities and other regulatory mandates continue to be the top obstacles for planning and implementation. However, provider readiness concerns surpassed staffing concerns as the third highest obstacle.

Additionally, WEDI reports over two-thirds of health plans indicate that direct ICD-10 code processing will be their primary strategy, up slightly from the group's February 2013 results. The number that planned to use a combination of direct processing and crosswalking dropped slightly, while a few payer respondents plan to use crosswalking as their primary ICD-10 transition. For providers, a small percentage plan to use crosswalking alone, but more than half say they will do direct ICD-10 coding.

A study by the American Association of Professional Coders indicates that only 24% of the old codes can actually be crosswalked to ICD-10. For example, the new codes often require documentation of the left side or right side of the body—an entirely new data piece.

More procrastination

Why the lack of readiness? ICD-10 was developed in 1992. The Department of Health and Human Services (HHS) first proposed using it in 2008. The deadline for

implementation was previously extended, but October 2014 seems like the final date. The code switchover was not something that was suddenly sprung upon the industry, experts say.

"There was a hope for another extension," admits Cafran. "As it is not being delayed, people are starting to wake up."

Part of the reason another extension was expected by many in the healthcare industry is because they already face a number of other huge transitions brought about by healthcare reform.

"The dialog we've been having from the health plan side of the equation has largely centered around other challenges they faced: getting ready for exchanges, shifting their business models to be more group oriented," says Mark Jamilkowski, managing director of KPMG's Health Actuarial Services Practice. "When you think of medical loss ratio requirements and shifts in accountability and reporting—these changes have shifted the business requirements of the data they use. So they're looking more holistically at data architecture and that has pushed ICD-10 to the back burner."

WEDI's Daley agrees.

"Providers are dealing with electronic health records and Meaningful Use requirements," he says. "So many changes have to be accomplished in the same timeframe that ICD-10 is being pushed to the side or fighting for resources with other requirements."

But representatives from CMS have clearly and publicly stated ICD-10 and its 68,000 codes would not be delayed again. So, what now?

Locate the risk

For healthcare organizations that are just starting to take the deadline seriously, it's time to minimize the damage non-compliance will cause.

> "You shouldn't fall into the trap of thinking your vendor will do it for you."
> —JIM DALEY

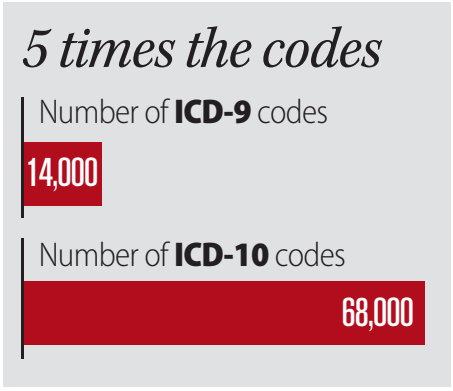
"For those just trying to get through, there are software tools that can run claims data in ICD-9 versus 10 and let you see where you're vulnerable by service line," says Cafran. "You could see those service lines that may be more directly impacted versus those that may stay the same or are a low risk."

That type of information could allow organizations to pinpoint where they should focus their efforts to make the biggest impact. It's a shortsighted plan, says Cafran, compared to those who have time to investigate all the processes that are affected by ICD-10 and get everyone prepared. For smaller organizations, especially, it could allow them to survive the transition and move forward.

For large healthcare organizations, especially payers, ICD-10 will touch almost every corner of their systems, from business processes to individual employees' spreadsheets.

Last month, Florida Blue announced that it was doing Level 2 end-to-end testing for external use, which is on schedule with the CMS recommendations.

"If you haven't done anything, and you're a big organization, you better look at retirement," says Daley. "If you're big and you haven't done anything yet, it's too late. If you're small, you may be okay, but you shouldn't fall into the trap of thinking your vendor will do it for you. If you don't even know what's required, how can you verify your vendor is going to perform that function?" ■



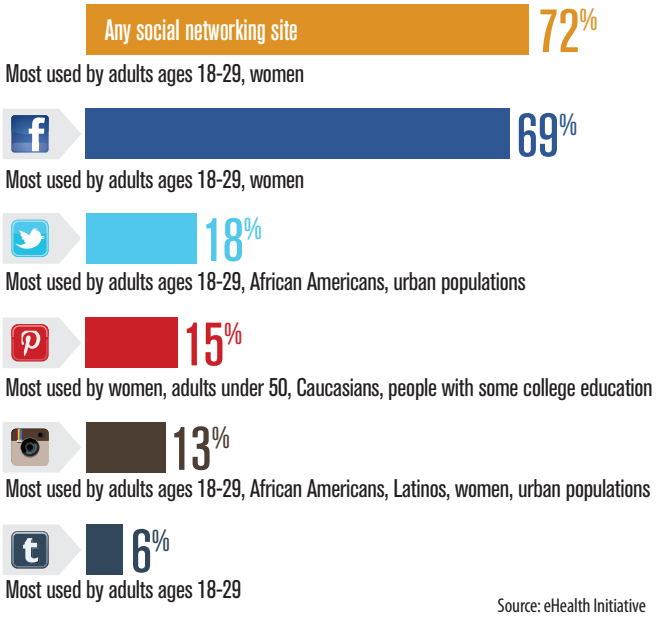
Jamie Gooch is a freelance writer based in northeastern Ohio.

ADVERTISER INDEX

The following is a list of the advertisers in this issue. Although every effort is made to ensure accuracy, this publication assumes no liability for errors or omissions.

LANDSCAPE OF SOCIAL MEDIA USE

Percentage of internet users by social media platform



Source: eHealth Initiative

HEALTH MANAGEMENT

Adverse events for patients treated for heart attack and heart failure have declined, according to a study in the *New England Journal of Medicine*. However, the analysis funded by the Agency for Healthcare Research and Quality (AHRQ), found that there hasn't been a significant decrease in adverse events for patients being treated for pneumonia and those recovering from surgery. Researchers found that 81,000 adverse events among heart attack and heart failure patients were averted annually in 2010 and 2011 compared with 2005 and 2006. However, some common adverse events in pneumonia and surgical patients (like pressure ulcers and urinary tract infections) did not show improvement. *http://1.usa.gov/1n8V7gX*

HEALTH MANAGEMENT

Horizon Blue Cross Blue Shield of New Jersey and 190 network OB/GYNs have created the state's first Patient-Centered Pregnancy and Delivery Program for better coordination of care for pregnant women. Participating OB/GYNs lead and organize the full-spectrum of care related to a patient's pregnancy, delivery and post-delivery recovery.

HEALTH MANAGEMENT

Cigna and Commonwealth Primary Care ACO in Phoenix launched a collaborative accountable care initiative—Cigna's model to improve health, affordability and patient experience. The program, which benefits over 7,000 Cigna members, has the same goals as industry ACO models (*http://bit.ly/1bLIOHZ*). Commonwealth care coordinators will work with Cigna to help individuals navigate the healthcare system. Cigna will compensate Commonwealth physicians for their services and they also may be rewarded through a "pay-for-value" structure if they meet targets for improved quality and lower costs.

BUSINESS

Blue Cross and Blue Shield of North Carolina (BCBSNC) will now offer family coverage to same-sex married couples. BCBSNC made the change March 1. The announcement came after a report that BCBSNC cancelled family coverage sold to 20 gay and lesbian couples on the exchange. Although North Carolina does not recognize same-sex marriages, the plan recognizes marriages as defined by the federal government for plans on and off the exchanges.

BUSINESS

Priority Health is the only health plan in Michigan to receive wellness accreditation from the National Committee for Quality Assurance (NCQA). Priority Health offers customized wellness plans and solutions, such as health assessments and biometric screenings. NCQA measured the number of wellness performance guidelines that Priority Health submitted against a minimum scoring threshold.

BUSINESS

WellPoint's fourth quarter 2013 net income was $148.2 million. Medical enrollment totaled approximately 35.7 million members as of Dec. 31, 2013, a decrease of 477,000 members, or 1.3%, from 36.1 million at Dec. 31, 2012. Commercial enrollment decreased by 234,000, as attrition in the national and individual markets was partially offset by growth in local group business. Membership in the Medicaid and Medicare businesses declined by 142,000 and 108,000, respectively. Operating revenue exceeded $17.6 billion in fourth quarter 2013, an increase of about $2.5 billion, compared with about $15.2 billion in the prior year quarter. The increase was driven by the inclusion of Amerigroup business for the entire fourth quarter of 2013. The benefit expense ratio was 87.8% in fourth quarter 2013.

Getty Images/E+/franckreporter

Helping you win in regulated markets is our healthy obsession

Attract and retain lives with expertise from the pharmacy benefits leader.

With the complexities of the ACA, growing your business takes more than ordinary support. It demands a deep commitment to compliance, care and cost-control that only Express Scripts can provide. We've been serving millions of Medicare and Medicaid members for years, and are partnering with health plans in states representing more than 90% of expected public exchange lives.

» Take a few minutes to see what our experts can do for you at Express-Scripts.com/GovernmentSolutions

EXPRESS SCRIPTS®

Compliance Counts.
Experience Matters.

sovaldi.com/hcp

NOW AVAILABLE

His moment has arrived

GILEAD

SOVALDI™
SOFOSBUVIR
400 mg TABLETS