British Providers Compete In a Most Civilized Fashion ............ 4
New Cost Transparency Tools Don’t Seem to Excite Docs .......... 23
Medicaid Learns to Deal With The Down, Out, & Mentally Ill ..... 39

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Employer-Sponsored Insurance Stands Unsteadily After ACA

By John Marcille

One of our regular departments in decades gone by was called “Employer Update,” and it looked at what was on the mind of health plans’ most important customers: the businesses that buy coverage for employees.

We sort of stumbled into employer-sponsored health insurance, didn’t we? Wage and price controls during World War II forced worker-starved businesses to dangle fringe benefits as a way to compete. After the war, President Truman said, in effect, now let’s do something permanent, which raised such a political stink that all parties backed away with a “This will do, for now.”

That was nearly 70 years ago. Our cover story on page 19 is a timely “Employer Update” that reports on what may finally be (dipping, once again, into the World War II era for the phrase) “the end of the beginning” of employer-sponsored health care.

Contributing Editor John Carroll points out that the Affordable Care Act flashes like a neon exit sign for businesses wishing to turn their backs on a system that too few find satisfactory. Analysts at Standard & Poor’s pointed out that the ACA means companies can “radically redefine” their place in health care. The temptation to dump workers on state exchanges might be just too great.

Except, as many experts say, this is far from a sure thing. They can’t see how companies can “suddenly tear themselves out of a system that has been woven around the close bond they want to forge with their most highly valued — and paid — staffers.”

Fortune 500 companies are certainly standing pat. Brian Marcotte, MS, CEO of the National Business Group on Health, says that based on recent research, “most large employers are expected to continue coverage for the foreseeable future.”

Check back in 70 years? No.

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Managed Care (ISSN 1062-3388) is published monthly by MediMedia USA Inc. at 780 Township Line Road, Yardley, PA 19067. This is Volume 23, Issue 7. Phone: (267) 685-2786; fax (267) 685-2966. Send letters to the editor to Frank Diamond, Managed Care, 780 Township Line Road, Yardley, PA 19067. Letters may be edited for length and clarity.

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Postmaster: Send address changes to Managed Care, PO Box 2019, Morrisville, PA 19067. Periodicals postage paid at Morrisville, PA, and at additional mailing offices.
Cover Story

Employers Can Leave Insurance Behind
But do they want to? A recent report drew a lot of attention by pointing out that the Affordable Care Act makes it inviting for businesses to opt out and dump employees on exchanges. But some experts predict: Not likely.

Health Plans See Cost Transparency’s Worth
Many doctors don’t. Insurers are developing estimators because information is money. But remember physician buy-in? Mostly, we are still waiting.

Pharmacogenomic Testing for Mentally Ill?
Behavioral health plans like what they see: Tests that can predict how effective certain drugs will be in treating psychiatric patients. Many psychiatrists, however, think more research needs to be done.

Research Paper: Treatment of Diabetic Foot Ulcers
This is becoming a more prevalent problem as the rates of diabetes continue to climb. Researchers say that one drug heals the ulcers faster than other medications.

Down and Out – and Mentally Ill
The prevalence of serious behavioral and substance abuse problems among Medicaid beneficiaries is substantially higher than in the general population. Plans succeed when they address socioeconomic factors.
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I recently took a trip to the United States, and whilst flicking through the in-flight magazine I came across a major difference between U.S. health care and its British counterpart. Many of the advertisements in the magazine — we call them “adverts” — were from U.S. providers promoting themselves as the place to come to for health issues ranging from blocked arteries to crooked teeth. There were three pages on “best doctors in America” complete with smiling physicians (no crooked teeth on display). And on the way from the airport there were large billboards advertising various local providers.

This set me thinking: Would you see a United Kingdom hospital promoting its services anywhere, let alone in an in-flight magazine or on a roadside billboard? The answer: It would be most unlikely.

Why is this? Britain’s National Health Service (NHS) has supposedly been operating an internal market, with varying degrees of enthusiasm, since 1991. There is also the private health care market, which not only provides services to the nearly 11% of the U.K. population that has some form of private insurance, but also, according to Laing and Buisson’s Health Cover U.K. Market Report 2013, delivers 4.8% of the acute services for the NHS.

Privately owned elective treatment centers provide services to NHS patients in direct competition with NHS hospitals. In short, all these providers, both NHS and private, are supposed to be competing with each other for the attention and custom of the British public. If they are indeed genuinely competing, then they manage to do so whilst being particularly bashful about promoting their own virtues in contrast to those of their rivals.

Robert Royce, PhD, is European correspondent for Managed Care and an independent health care consultant.

The U.K. has a variety of national quality indicators covering such areas as waiting times, mortality rates, infection rates, patient satisfaction measures, and patient-reported outcome measures (PROMS), all of which lend themselves to reporting in a league table format.

The payment system is supposed to be based on the principle that the more patients you treat, the more income you receive. Empowering patients to make informed choices by providing accessible information and increasing one’s choice of provider are supposed to be forces for beneficial change and a key objective of governmental reform of health care. So why isn’t there more effort by providers to differentiate themselves and attract more customers/patients?

Web sites tell the tale

Evidence that they aren’t making this effort includes a survey I undertook in 2012 (Royce, R., “Trusts Lose Ground in Online Marketing Race,” Nov. 15, 2012, Health Service Journal, London). Trusts are the NHS organizations that run one or more hospitals in a particular region, and I evaluated the Web sites of the 27 NHS trusts in London. The idea was to establish the degree to which each organization was actively promoting its performance against national quality indicators, what attempt it made to explain those quality indicators, and how user-friendly its Web site was.

The results were singularly underwhelming. It turned out that a number of these multimillion-dollar organizations have poorly developed Web sites. In three cases, the sites repeatedly crashed. Furthermore:

- Only two trusts provided waiting times on their sites. No trust showed this information as part of its specialty/physician profiles.
- One trust Web site had no search field.
MMX® technology is designed to target delivery of budesonide throughout the full length of the colon.

3 times more patients taking UCERIS® achieved combined clinical and endoscopic remission compared with placebo.

The rates of overall glucocorticoid-related side effects were similar for UCERIS and placebo at 8 weeks—10.2% vs 10.5%, respectively.

Through the UCERIS savings program, 90% of eligible patients with commercial insurance will pay only $25.

INDICATION:
UCERIS® (budesonide) extended release tablets are indicated for the induction of remission in patients with active, mild to moderate ulcerative colitis.

IMPORTANT SAFETY INFORMATION:
UCERIS® (budesonide) extended release tablets are contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of UCERIS. When glucocorticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Since UCERIS extended release tablets are a glucocorticosteroid, general warnings concerning glucocorticoids should be followed. Care is needed in patients who are transferred from glucocorticosteroid treatment with higher systemic effects to glucocorticosteroids with lower systemic effects, such as UCERIS extended release tablets, since symptoms attributed to withdrawal of steroid therapy, including those of acute adrenal suppression or benign intracranial hypertension, may develop. Taper patients slowly from systemic corticosteroids if transferring to UCERIS extended release tablets.

Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Glucocorticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infection, untreated fungal, bacterial, systemic viral or parasitic infections, or ocular herpes simplex. More serious or even fatal course of chickenpox or measles can occur in susceptible patients. Patients with moderate to severe liver disease should be monitored for increased signs and/or symptoms of hypercorticism. Caution should be taken in patients with hypertension, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma or cataracts, or with a family history of diabetes or glaucoma, or with any other condition where glucocorticosteroids may have unwanted effects. Concomitant use of inhibitors of Cytochrome P450 3A4 (for example ketoconazole and erythromycin) should be avoided and patients should be closely monitored for increased signs and/or symptoms of hypercorticism. Avoid grapefruit juice, which is known to inhibit CYP3A4, when taking UCERIS.

In clinical studies, the most common adverse reactions (incidence ≥2%) were headache, nausea, decreased blood cortisol, upper abdominal pain, fatigue, flatulence, abdominal distension, acne, urinary tract infection, arthralgia, and constipation.

Please see Brief Summary for UCERIS extended release tablets on adjacent page and complete Prescribing Information at www.UCERIS.com.
BrieF Summary
UCERIS (budesonide) extended release tablets, for oral use
The following is a brieF summary only. See complete Prescribing Information at www.uceris.com or联系800-502-0024 for full prescribing Information by calling 1-800-502-0024.
INDICATIONS AND USES UCERIS (budesonide) extended release tablets are indicated for the induction of remission in patients with ulcerative colitis (UC).
CONTRAINdications UCERIS is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of the UCERIS tablets, including systemic adverse reactions having occurred with other budesonide formulations.
WARNINGs and PRECAUTIONS
Hypertension and Adrenal Axis Suppression When glucocorticosteroids are used chronically, systemic effects such as hypertension and adrenal suppression may occur. Glucocorticosteroids can reduce the response of the hypothalamic-pituitary-adrenal (HPA) axis to stress. In situations where patients are subjected to other stress situations, supplementation with a systemic glucocorticoid is recommended. Since UCERIS is a glucocorticoid, general warnings concerning glucocorticoids should be followed.
Toxicities from Systemic Glucocorticoid Therapy Care is needed in patients who are transferred from glucocorticoids, with or without a treatment with higher systemic effects to glucocorticoids with lower systemic effects, such as UCERIS, since such systems attributed to withdrawal of steroid therapy, including those of acute adrenal suppression or benign intracranial hypertension, may develop. Adrenocortical function monitoring may be required in these patients and the dose of glucocorticoid treatment with high systemic effects should be reduced cautiously.
Immunosuppression Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients who are immunosuppressed from glucocorticosteroid use. In patients who have not had these diseases, particular care should be taken to prevent exposure to these viruses. The effects of glucocorticosteroid administration affect the risk of developing a disease such as tuberculosis and the rate of progression of the underlying disease and/or prior glucocorticosteroid treatment to the disease of concern, as appropriate.
Intraocular Pressure For patients with ocular conditions, such as open angle glaucoma or cataracts, or with a family history of diabetes or glaucoma, caution should be exercised. Glucocorticosteroid therapy may unmask allergies (e.g., rhinitis and eczema), which were previously unrecognized.
The use of UCERIS tablets in patients with ocular conditions, such as open angle glaucoma, cataract, or with a family history of diabetes or glaucoma, caution should be exercised. Glucocorticosteroid therapy may unmask allergies, which were previously unrecognized.
No clinically significant differences were observed with respect to the overall percentages of patients with any glucocorticosteroid related effects between UCERIS and placebo. UCERIS for 8 weeks of induction therapy. Study 2 was an open-label study evaluating UCERIS 9 mg once daily for 4 weeks in 85 patients who had previously completed an 8-week induction study (Study 1). At the time of that trial, it had not been removed from the market. Patients who took UCERIS 8 mg or 16 mg were considered. Glucocorticosteroids should be used with caution, if at all, in patients with gastrointestinal disorders, untreated fungal, bacterial, systemic viral or parasitic infections. Repeated or prolonged use of glucocorticosteroid systemic effects may unmask allergies, which were previously unrecognized.
Increased Systemic Glucocorticoid Susceptibility Reduced liver function (e.g., liver failure with variceal bleeding) or systemic glucocorticoid susceptibility may have unwanted effects.
ADVERSE ReACTIONS
Systemic glucocorticosteroid use may result in the following:
• Immunosuppression
• Symptoms of adrenal suppression
• Hypertension and Adrenal Suppression
• Symptoms of steroid withdrawal in those transferring from other glucocorticosteroids
• Immunosuppression
• Immunosuppressant properties and uptake of the compound may be altered when UCERIS is used after treatment with gastric acid reducing agents (e.g., PPIs, H2 blockers and antacids).
• Increased systemic glucocorticoid susceptibility
• Acne
• Hirsutism
• Insomnia
• Moon face
• Nystagmus
• Rash
• Sleep changes
• Striae
• Telangiectasia
• Viral infections
• Weight gain
• Weight loss
• Moon face
• Nystagmus
• Rash
• Sleep changes
• Striae
• Telangiectasia
• Viral infections
• Weight gain
• Weight loss
• Hirsutism
• Insomnia
• Nasal dryness
• Nausea
• Nocturnal enuresis
• Osteoporosis
• Pruritus
• Pyrosis
• Rebound weight loss
• Rosacea
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Nineteen trusts had information on subspecialty interests by physician. One academic health science center had detailed profiles of consultants and their publications, while another did not even have subspecialty interests shown — just a list of consultants for the specialty concerned.

Three trusts did not have a specific part of the Web site for primary care physicians (known in the U.K., as in bygone days in the States, as general practitioners, or GPs). This is significant, as elective patients have to be referred via GPs in the U.K., where patients cannot directly access a specialist.

Searches for “PROMS” brought a zero return for 15 trusts.

Searches for “patient satisfaction” brought a zero return from four trusts, with a range for the others from 3 to 1,517 results.

Not one trust set out its PROMS score in relation to a specific service — for example, hip replacements. Moreover, trusts did not set out outcome measures, volumes, lengths of stay, or patient satisfaction results for any specific procedure, consultant or specialty, with the exception of a few specialist areas including pediatric cardiac surgery, infertility, and, in one case, hip replacements.

This kind of performance might serve to reinforce negative views about the public sector’s ability — and enthusiasm — when it comes to operating in a competitive manner, but interestingly, the private sector does not appear to be much more proactive. You are unlikely to find adverts promoting shorter waits and better patient satisfaction at private facilities, even though both are likely the case. Overall, there is a marked reluctance on the part of providers, both NHS and private, to contrast their performance with local competitors.

What might account for this reticence? Perhaps providers do not believe that the active promotion of quality measures really influences the public or GPs. Perhaps it is thought that any positive influence won’t be strong enough to make the investment in advertising worthwhile at the expense of something else. Perhaps there is nervousness about saying “We are performing well” when future league rankings might in fact show “us” slipping. Perhaps providers are not spending much time trying to differentiate their services in the public arena because they think influencing GP referral practices remains much more important than influencing would-be patients — although even if true, this wouldn’t explain why more isn’t done to market directly to GPs. Perhaps the answer lies in a view that the additional income that extra patients will bring in will not match the effort and expense of capturing and treating those patients.

Speak no ill of family

All of the above might serve as partial explanations — and to some degree may have a resonance in the U.S. marketplace. But even when taken together, they do not fully explain the lethargy in self-promotion. In the U.K., there is also a social dimension to consider. Until quite recently, restrictions by the General Medical Council (the body that regulates doctors’ conduct) effectively prohibited doctors from promoting their services, areas of expertise, or (for private services) prices. Culturally, that prohibition probably still holds considerable sway.

Clinicians also feel a need to be careful that any self-promotion is not seen as undermining fellow professionals. For hospitals, the notion that they are in competition with each other must itself compete with the much longer-established view that the NHS is a “family” and that a “duty of partnership” prevails.

Invisible but nevertheless real boundaries appear to exist in what is deemed unacceptable managerial action, and actively trying to increase market share at another party’s expense through the use of advertising appears to be one of them. This social dimension also applies to the private-sector enterprises, sensitive as they are to any accusation that they might be actively undermining the public’s faith in NHS services.

This may keep corporate feathers unruffled, but at what cost in terms of improved responsiveness to consumers? And what is its impact on the desire to improve quality and efficiency? It can be disputed whether advertising helps or hinders the aim of creating informed, empowered consumers. But in any case, you are unlikely to see a “Best Doctors or Hospitals in England” advert in your in-flight magazine any time soon.
Health Plans Step Up Management Of Drugs Under Medical Benefit

Report says half of all insurers are not taking advantage of rebates for drugs delivered through the medical benefit

By Thomas Reinke

There has been a lot of discussion about the potential benefits of moving specialty drugs from the medical benefit to the pharmacy benefit, which is supposed to give health plans more control over costs and make medical- and utilization-management more effective.

For a variety of reasons, though, switching those drugs is more easily said than done. In addition, some health plans are developing in-house capabilities to manage medical drugs better, thus preserving coverage under the medical benefit. In this article, “medical drugs” refers to drugs covered though the medical benefit.

Magellan Rx Management’s Medical Pharmacy Trend Report for 2013 provides some insight into how health plans are managing medical drugs. The current report is based on responses from 48 large and small plans covering 166 million lives. The document is a good supplement to PBM trend reports, which generally are missing data on drugs administered under the medical benefit.

In addition to this report, recent activities at Blue Cross and Blue Shield of Minnesota (BCBSMN) provide insight as to what one plan is doing to retain and improve its in-house management of medical drugs. BCBSMN is working with Prime Therapeutics, which it owns with several other Blue Cross plans, to implement more sophisticated management techniques for medical drugs.

Benefit channel

BCBSMN does not see a pressing need to combine all drugs into a single benefit. There are important and valid reasons for it to continue to manage these drugs itself.

“The notion of moving drugs from the medical side to the pharmacy side gets more complex as you bring in additional voices,” says Paul Karazija, MD, a vice president at BCBSMN. “We have customer groups that work with other PBMs, so diffusing that type of a strategy across the board would be a real challenge.”

David Lassen, PharmD, chief clinical officer at Prime Therapeutics, says that “Moving drugs from the medical to the pharmacy benefit only makes sense when the discounts obtained through the pharmacy distribution channel exceed provider reimbursement rates on the medical side.”

In addition to keeping some drugs under the medical benefit, BCBSMN has not tampered with the acquisition channel. “We have not implemented aggressive strategies for infusion centers or white bagging. For the most part, we have maintained the buy-and-bill arrangement with our providers,” says Karazija.

“Conceptually, there may be an opportunity to change the distribution of these medications and require use of a specialty pharmacy, but there is value in maintaining the patient and provider relationship that is tied to the provision of

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rank</th>
<th>Indication</th>
<th>Allowed amount (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remicade</td>
<td>1</td>
<td>Inflammatory diseases</td>
<td>$21.2</td>
</tr>
<tr>
<td>Neulasta</td>
<td>2</td>
<td>Neutropenia</td>
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<td>Rituxan</td>
<td>3</td>
<td>Cancer</td>
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<td>Lucentis</td>
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<td>Macular degeneration</td>
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</tbody>
</table>

* If insurance allows $100 for a drug and it pays $80 with a $20 copayment, there is no way to know if the $20 was paid. So the $100 allowed is reported.

Source: Magellan Health

Top medical drugs by allowed amount* per 1 million lives in 2012

Managing medical drugs boils down to cancer and everything else,” says Paul Karazija, MD, at Blue Cross and Blue Shield of Minnesota.
these drugs by the provider,” Karazija continues. “So for the present, we prefer to manage through the unit cost and through evidence-based use.”

The Magellan report says that nationally, 75% of infused chemotherapy drugs and 70% of infused nonchemotherapy drugs were billed through the buy-and-bill arrangement.

While buy and bill is still dominant, the site-of-care shift away from physician’s offices and into the hospital outpatient setting continues to accelerate. In order to help combat this, health plans appear to be considering a move away from payment based on a percent of provider charges, which is currently the most common method of reimbursement to hospitals.

“In our survey, 56% of health plans indicated they have successfully implemented some form of fixed fee schedule,” says Mostafa Kamal, a senior vice president at Magellan Rx Management. “That demonstrates some progress in controlling cost; however, health plans continue to be wary of the implications of reducing reimbursement to hospitals for drugs. Their concern is that costs will balloon elsewhere — in rates for outpatient diagnostic services, or emergency room visits.”

A core objective of BCBSMN’s expanding efforts to manage medical drugs is to ensure that their use is based on evidence.

“Prior authorization is the primary lever that we use to manage medical drugs,” says Karazija. “Given the cost of these drugs, the goal of prior authorization is to ensure that drugs are used for FDA-approved indications.”

The insurer has implemented prior authorization for 80 medical drugs, with procedures for an additional 12 in the works.

Prime Therapeutics is working closely with the insurer to help it build operational procedures and information technology capabilities to bolster prior authorization. What's emerging from this collaboration are processes designed to reconcile prior authorization requests with the language of medical policies.

“Payment integrity is another lever for managing these drugs,” says Karazija. “When the claims come in for medical drugs, they are reviewed and synced up with the appropriate diagnoses, dosing, and appropriate charges.”

The data on diagnoses, dosing, and duration gleaned from claim reviews provide insight into the real-world use of medical drugs and, if necessary, serves as the basis for follow-up with providers or closer monitoring of utilization.

“Managing medical drugs boils down to cancer and everything else,” says Karazija. “Generally speaking, the cancer drugs are used appropriately as first-line therapy for newly diagnosed patients. In situations involving recurring or metastatic cancer, you see more variability. We are planning to implement a pathway strategy to reduce the variability of treatment from initial diagnosis through the progression of the disease.”

Karazija mentions two other challenges in cancer. “First, we have to stay abreast of the expansion of existing cancer drugs to new cancers where they haven’t been used before. The other challenge is in the use of support drugs like Neulasta, where that expense often exceeds the cost of the cancer drug itself.”

According to Magellan, pegfilgrastim (Neulasta) ranks second in total expenditures for medical drugs. Five cancer drugs are also in the top 10 (see box): rituximab (Rituxan), bevacizumab (Avastin), oxaliplatin (Eloxatin), trastuzumab (Herceptin), and pemetrexed (Alimta).

“On the noncancer side, it’s a matter of making sure the drugs are used for conditions for which there is evidence,” says Karazija.

Implementing formularies

“There are opportunities to move to preferred products among the medical drugs because multiple alternatives are becoming available,” says David Lassen, PharmD, chief clinical officer at Prime Therapeutics.

Using formularies and preferred products provides an opportunity to control costs, but only 22% of plans surveyed by Magellan said they had a formulary in place with tiered benefit structures.

A formulary, which includes the drugs managed through the medical benefit, may also serve as the basis for health plans to negotiate rebates from manufacturers. “Rebates are available on a number of medical drugs,” says Kamal.

However, “One of the important findings is that 50% of plans are not taking advantage of these rebates.”

“There are opportunities to move to preferred products among the medical drugs because multiple alternatives are becoming available,” says David Lassen, PharmD, chief clinical officer at Prime Therapeutics.
Clinically Nuanced Benefit Design Recommended for High-Cost Drugs

For patients using specialty pharmaceuticals, health plans and employers may need to adjust their benefit structure, according to a new report. Specialty pharmaceuticals have complex molecules or qualities that result in costly delivery, and can cost patients more than $600 per month, according to "Supporting Consumer Access to Specialty Medications Through Value-Based Insurance Design," a report from the Center for Value-Based Insurance Design at the University of Michigan.

Cost sharing for these medications should be related to clinical value and not simply tied to what the patient pays for the medication, the report says. Instead, insurers should use more nuanced approaches to financial incentives, says A. Mark Fendrick, MD, director of the center.

“We have to move the discussion away from how much we spend and toward how well we spend,” he adds.

The report suggests that for specialty medications, insurers should:

- Impose no more than modest cost-sharing
- Reduce cost-sharing in accordance with patient- or disease-specific characteristics
- Relieve patients of high cost-sharing after failure on a different medication
- Use cost-sharing to encourage patients to select high-performing providers and settings for their care

Specialty medications are commonly used to treat patients with cancer, multiple sclerosis, rheumatoid arthritis, and other serious health conditions like hepatitis C, new treatments which may be the fastest-growing class over the next two years. Specialty drugs constitute about 25% of all pharmaceutical spending, according to the Express Scripts Drug Trend Report, and by 2018 will make up half of all drug spending, according to another analysis by Artemetrx.

Last year, 23% of people with employer-sponsored prescription drug coverage were in plans with four or five tiers and the highest two were for specialty drugs. Coinsurance rates for these drugs average 30% and can be as high as 50%, the VBID report says. If a medication costs $1,000 per month and the patient has a high cost-sharing plan, the out-of-pocket cost could be $300 to $500 per month.

For years, health plans and employers have set high cost sharing levels for high-cost medications, but the report warns that indiscriminately high cost sharing may cause patients not to fill prescriptions.

For many patients and clinical indications, the cost of specialty medications is money well spent, the report adds.

But considering that the benefit any medication delivers can vary markedly depending on the patient’s response and other circumstances, health plans should implement condition-specific, clinically nuanced variation in benefit design.

Bundled Payment Programs Multiply

Hundreds of hospitals and thousands of physicians are participating in bundled payment programs, and most bundled payment contracts have
EXPERIENCE THE DIFFERENCE

Invokana®
canagliflozin tablets

Covered for more than 80% of commercially insured patients without prior authorization¹

The recommended starting dose of INVOKANA® (canagliflozin) is 100 mg once daily.²

INVOKANA® 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 m²), end stage renal disease, or patients on dialysis.

WARNINGS and PRECAUTIONS

> Hypotension: INVOKANA® causes intravascular volume contraction. Symptomatic hypotension can occur after initiating INVOKANA®, particularly in patients with impaired renal function (eGFR <60 mL/min/1.73 m²), elderly patients, and patients on either diuretics or medications that interfere with the renin-angiotensin-aldosterone system (eg, angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs]), or patients with low systolic blood pressure. Before initiating INVOKANA® in patients with one or more of these characteristics, volume status should be assessed and corrected. Monitor for signs and symptoms after initiating therapy.

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

The recommended starting dose of INVOKANA® (canagliflozin) is 100 mg once daily.²

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EXPERIENCE THE DIFFERENCE

INVOKANA® 300 mg vs Januvia® 100 mg
at 52 weeks, each in combination with metformin + a sulfonylurea (SU)²

Greater reductions in A1C²

Adjusted Mean Change in A1C From Baseline (%)

Mean baseline: 6.13% 8.12%

−0.66 −1.03

Januvia® 100 mg + metformin and an SU (n=378)
INVOKANA® 300 mg + metformin and an SU (n=377)

Difference from Januvia® (sitagliptin): −0.37% (95% CI: −0.50, −0.25); P<0.05

INVOKANA® (canagliflozin) starting dose: 100 mg once daily. In patients tolerating the starting dose who have an eGFR ≥60 mL/min/1.73 m² and require additional glycemic control, the dose can be increased to 300 mg once daily.²

IMPORTANT SAFETY INFORMATION (cont’d)

• 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 m².

• 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.

INDICATIONS INVOKANA® is indicated to improve glycemic control in adults with Type 2 diabetes mellitus in combination with metformin and/or a sulfonylurea (SU).

Indicated trademarks are registered trademarks of their respective owners.
**Greater reductions in body weight**

Difference from Januvia® 100 mg: 2.8%, P<0.001

**Greater reductions in systolic blood pressure**

Difference from Januvia® 100 mg: 5.9 mm Hg, P<0.001

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

*Prespecified secondary endpoint.

**Incidence of hypoglycemia**

INVOKANA® 300 mg: 43.2%; Januvia® 100 mg: 40.7%

The incidence of hypoglycemia increases when used in combination with insulin or an insulin secretagogue.

**Adverse reactions (ARs)**

Incidences of ARs were similar between groups except for:

- Male/female genital mycotic infection, INVOKANA® 300 mg: 9.2%/15.3%; Januvia® 100 mg: 0.5%/4.3%
- Increased urine frequency/volume, INVOKANA® 300 mg: 1.6%/0.8%; Januvia® 100 mg: 1.3%/0%

Learn more and register for updates at INVOKANAhcp.com

A randomized, double-blind, active-controlled, 52-week study of patients with type 2 diabetes inadequately controlled on maximum doses of metformin (2000 mg/day, or 2550 mg/day if higher dose not tolerated) and near-maximally or maximally effective doses of an SU.

**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.

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

- **UCGT Enzyme Inducers:** Rifampin: Co-administration of canagliflazin with rifampin, a nonselective inducer of several UGT enzymes, including UGT1A9, UGT2B4, decreased canagliflazin area under the curve (AUC) by 51%. This decrease in exposure to canagliflazin may decrease efficacy. If an inducer of these UGTs (e.g., rifampin, phenytoin, phenobarbital, rifabutin) must be co-administered with INVOKANA® (canagliflazin), 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 m², and require additional glycemic control. Consider other antihyperglycemic therapy in patients with an eGFR of 45 to less than 60 mL/min/1.73 m² 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 (Cmax) of digoxin (20% and 36%, respectively) when co-administered with INVOKANA® (canagliflazin), consider increasing the dose to 300 mg once daily. 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, canagliflazin 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 to 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 increases 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 <60 mL/min/1.73 m²). 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 m²); 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 m²), with end-stage renal disease (ESRD), or receiving dialysis. INVOKANA® is not expected to be effective in these patient populations.

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Canagliflazin is licensed from Mitsubishi Tanabe Pharma Corporation.
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Canagliflazin is licensed from Mitsubishi Tanabe Pharma Corporation.
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 (≥25%) 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, and nasopharyngitis.

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


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IVOKANA™

It is a trade name used for oral use.

Short 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 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 m²) and stage renal disease or patients on dialysis (see Warnings and Precautions and Use in Specific Populations).

WARNINGS AND PRECAUTIONS

Hyperglycemia and 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 an insulin or an insulin secretagogue (see Adverse Reactions). Therefore, a lower dose of insulin or insulin secretagogues 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 uncontrolled nausea are more likely to develop genital mycotic infections (see Adverse Reactions). Monitor treat appropriately.

Drug Interactions: Hypoglycemia reactions, eg, generalized weakness, some cases, were reported with INVOKANA® treatment; those reactions generally occurred within hours to days after initiating INVOKANA®. If hypoglycemia 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:

• Hypoglycemia (see Warnings and Precautions).
• Impairment in Renal Function (see Warnings and Precautions).
• Hypertension 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. Prolonged Plasma-Controlled Trial: The data in the Table 1 is derived from four 24-week, plasma-controlled trials. In one trial INVOKANA® was used as monotherapy and in three trials it 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™ (canagliflozin) tablets

INVOKANA™ was 26 weeks. Patients received INVOKANA 100 mg (N=833), INVOKANA 300 mg (N=834) or placebo (N=846) once daily. The mean age of the population was 58 years and 2% were older than 75 years of age.

The incidence of pancreatitis (acute or chronic) was 0.9, 2.7, and 0.9 per 1000 patient-years of exposure to placebo, INVOKANA 100/25 mg, and INVOKANA 300/25 mg, respectively.

In the pool of 8 placebo-controlled trials, the incidence rate of pancreatitis (acute or chronic) was 0.9, 2.7, and 0.9 per 1000 patient-years of exposure to placebo, INVOKANA 100/25 mg, and INVOKANA 300/25 mg, respectively.

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

Volume, Hypertension-Related Adverse Reactions: INVOKANA results in an antinatriuresis, which may lead to reductions in intravascular volume. In clinical studies, treatment with INVOKANA was associated with a decrease in the incidence in the volume depletion-related adverse reactions, which include hypotension, postural dizziness, orthostatic hypotension, syncope, and/or dehydration. An increased incidence was observed in patients on the 250 mg dose. The adverse reacti...
INVOKANA™ (canagliflozin) tablets

In a trial carried out in patients with moderate renal impairment with a baseline eGFR of 30 to less than 50 mL/min/1.73 m² (mean baseline eGFR 39.2 mL/min/1.73 m²) (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 less than 30 mL/min, was 8.3% with placebo, 18.1% 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 0.3% with INVOKANA 300 mg had a significant renal function decline.

In an assembled population of patients with moderate renal impairment (N=1089) with baseline eGFR of 30 to less than 60 mL/min/1.73 m² (mean baseline eGFR 46.6 mL/min/1.73 m²), 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 related adverse reactions was 3.7% with placebo, 8.9% with INVOKANA 100 mg, and 9.7% with INVOKANA 300 mg. Discontinuations due to renal-related adverse events occurred in 7.9% with placebo, 1.2% with INVOKANA 100 mg, and 1.8% with INVOKANA 300 mg, respectively. Patients with a history of renal mycotic infections were more likely to develop a new renal mycotic infection. Use of INVOKANA was more likely to experience recurrent episodes and require treatment with oral and 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%, 4.7%, and 3.5% of males treated with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively. Male genital mycotic infections occurred more commonly among patients in males with a prior history of acne, balanitis, or balanoposthitis. Male patients who developed genital mycotic infections were more likely to experience recurrent infections (22% on INVOKANA versus none on placebo), and require treatment with oral and topical agents and anti-microbial agents than patients on comparators. In the pooled analysis of 8 controlled trials, physicians were informed if an investigator identified 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 necessitating medical assistance or underlying clinical manifestation of serum glucose <36 mg/dL (2.0 mmol/L) and 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 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 11.4%, 12.4%, and 20.0% 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 2.2%, 2.3%, and 7.3% 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 serum creatinine 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 Phosphate: Dose-related increases in serum phosphate levels were observed early after initiation of INVOKANA (within 6 weeks) and remained elevated throughout treatment. In the pool of four placebo-controlled trials, mean changes (percent changes) from baseline in serum phosphate levels were 8.1% and 8.3% with INVOKANA 100 mg and INVOKANA 300 mg, respectively, compared to 2.1% 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 0.3%, 2.0%, 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 magnesium levels was 8.1% and 8.3% with INVOKANA 100 mg and INVOKANA 300 mg, respectively, compared to 2.1% 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 5.3% with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively.

In the pool of four placebo-controlled trials, mean changes (percent changes) from baseline in serum magnesium levels were 8.1%, 8.3%, and 8.0% with INVOKANA 100 mg and INVOKANA 300 mg, respectively. The mean baseline serum magnesium levels were 104 to 110 mg/dL across treatment groups.

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%, 11.8%, and 11.2% with INVOKANA 100 mg and INVOKANA 300 mg, respectively. The mean baseline LDL-C levels were 100 to 110 mg/dL across treatment groups (see Warnings and Precautions).

Increases in Serum Potassium: Dose-related increases in serum potassium levels were observed with INVOKANA. In the pool of four placebo-controlled trials, the mean change in serum potassium levels was 2.0%, 5.3%, and 5.4% with INVOKANA 100 mg and INVOKANA 300 mg, respectively, compared to 0.4% with placebo. In a trial of patients with moderate renal impairment (see Clinical Studies (14.3) in full Prescribing Information), the mean serum potassium levels increased by 1.2%, 5.0%, and 5.3% with placebo, INVOKANA 100 mg, and INVOKANA 300 mg, respectively.

DRUG INTERACTIONS

UGT Enzyme Inducers: Rifampin: Co-administration of canagliflozin with rifampin, a nonselective inducer of several UGT enzymes, including UGT2B7, was associated with an approximately 14.1 g/dL across treatment groups. At the end of treatment, 3.0%, 4.2%, and 2.7% of patients treated with placebo, INVOKANA 100 mg and INVOKANA 300 mg, respectively, had hemoglobin above the upper limit of normal.

This page contains complete prescribing information. Please refer to full prescribing information for the most current information.

Table 4: Incidence of Hypoglycemia* in Controlled Clinical Studies

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* 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.

2 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).

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2 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).
The efficacy and safety of INVOKANA have not been established in patients with renal impairment. Consider the risk of hypoglycemia in patients with an eGFR of 45 to less than 60 mL/min/1.73 m2 receiving concurrent therapy with a GLP-1 agonist and require additional glycemic control (see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)) in full Prescribing Information.

Dialysis: There was an increase in the AUC and mean peak drug concentration (Cmax) of drug (52% and 36%, respectively) when co-administered with INVOKANA (canagliflozin). Consider increasing the dose to 200 mg once daily to compensate for the decrease in exposure in dialysis patients (see Clinical Pharmacology (12.3)).

INTEGRAL CLINICAL TRIAL: Effect: The primary study was a randomized, blinded, placebo-controlled clinical trial that evaluated the efficacy and safety of INVOKANA in patients with type 2 diabetes. The study included 2661 patients who were randomly assigned to receive treatment with INVOKANA or placebo for a period of up to 24 weeks. The primary endpoint was change in HbA1c at 24 weeks. The study was conducted at sites in the United States, Canada, and other countries in Europe and Asia. The study was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki. The data from the study were analyzed using intent-to-treat and per-protocol populations. The results of the study showed that patients treated with INVOKANA had a significantly greater reduction in HbA1c compared to placebo. The results were consistent with other clinical studies of canagliflozin in patients with type 2 diabetes. The study was sponsored by Janssen Research & Development, LLC.

INTEGRAL PHARMACOLOGY: Canagliflozin is a sodium-glucose cotransporter 2 inhibitor (SGLT2) that inhibits the reabsorption of glucose in the proximal convoluted tubule of the kidney, leading to an increase in urinary glucose excretion. SGLT2 inhibitors increase the urinary excretion of sodium, potassium, and hydrogen ions, resulting in a decrease in blood pressure. Canagliflozin also has a renoprotective effect in patients with type 2 diabetes and kidney disease.

OVERDOSAGE

There were no reports of overdose during the clinical development program of INVOKANA. There is no specific antidote for INVOKANA overdosage.

MANAGEMENT

Instruct patients to discontinue INVOKANA and seek medical advice promptly if they experience signs or symptoms of ketoacidosis (e.g., nausea, vomiting, abdominal pain, rapid breathing, fruity breath odor). The patient should discontinue INVOKANA and seek medical advice promptly if they experience signs or symptoms of hypoglycemia (e.g., sweating, shakiness, confusion, palpitations, hunger) or hyperglycemia (e.g., increased thirst, frequent urination, blurred vision, fatigue).

INTEGRAL ADVERSE REACTIONS

The most common adverse reactions associated with INVOKANA were increased urination, genital mycotic infections (candidiasis and dermatophytosis), and increased uri- nary tract infections (UTIs). The incidence of these adverse reactions was generally comparable between patients treated with INVOKANA and placebo in clinical trials.

INTEGRAL CONTRAINdications

Patients with type 2 diabetes who are at risk for ketoacidosis due to volume depletion or who are receiving insulin or an insulin secretagogue should not receive INVOKANA. Patients with severe hepatic impairment should not receive INVOKANA.

INTEGRAL PRECAUTIONS

Patients with a history of kidney stones should be monitored for the development of new kidney stones during treatment with INVOKANA. The risk of kidney stones is increased in patients with decreased renal function.

INTEGRAL INTERACTIONS

The concomitant use of potent CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, clarithromycin, voriconazole, nefazodone) and CYP3A4 inducers (e.g., rifampin, phenytoin, phenobarbital, rifabutin) with INVOKANA may result in a significant decrease in canagliflozin exposure. Therefore, consider alternative medications in patients managed with these drugs. Avoid concomitant use of INVOKANA with medications that are highly dependent on CYP3A4 for metabolism (e.g., verapamil, diltiazem, felodipine, astemizole, terfenadine, cisaprid, ergot derivatives, theophylline, midazolam, triazolam).

INTEGRAL DOSAGE AND ADMINISTRATION

The recommended dose of INVOKANA is 100 mg once daily. The dose may be increased to 300 mg once daily in patients who experience an insufficient decrease in HbA1c or who require further reduction in blood sugar. The maximum recommended dose is 300 mg once daily. Do not exceed 300 mg once daily. The dose should be reduced in patients with renal impairment. The dose should be reduced to 50 mg once daily in patients with an eGFR of 30 to less than 60 mL/min/1.73 m2 receiving concurrent therapy with a GLP-1 agonist and require additional glycemic control (see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)).

INTEGRAL DOSAGE FORMS

INVOKANA is available as a film-coated, immediate-release tablet containing 100 mg or 300 mg of canagliflozin. The tablets are supplied in bottles of 100 and 1000 tablets.
continued from page 8

upside and downside risk, according to François de Brantes, executive director of the Health Care Incentives Improvement Institute (HCII3). “We’re now in the scaling phase of this payment model and no longer in pilot or early stage,” he added.

In a report that HCII3 commissioned, the consultant Bailit Health Purchasing showed that both public and private payers are starting to use bundles as a core strategy to reform both payment and the delivery of care.

Bailit interviewed executives from six insurers and one Medicaid program and found three strong trends. First, the insurers were significantly expanding their bundled payment programs by including more providers and more conditions and episodes.

Second, they were automating resource-intensive processes that had been done manually, usually with spreadsheets.

To automate cost and reconciliation calculations, insurers are investing significantly in information systems from MedAssets, Optum, and TriZetto.

Through these investments, insurers may be demonstrating that bundling is effective at controlling costs, limiting complications, and improving quality.

Third, the insurers were simplifying their methods to make them easier to administer.

The 16-page report is based on interviews with executives from Aetna, Arkansas Medicaid, Arkansas Blue Cross and Blue Shield, Blue Cross and Blue Shield of North Carolina, Geisinger Health Plans, HealthNow New York, and Horizon Blue Cross Blue Shield of New Jersey.

The most common bundled procedures were hip and knee replacements. Less common were bundles for attention deficit hyperactivity disorder, coronary artery bypass graft surgery, colonoscopy, congestive heart failure, developmental disabilities, perinatal care, tonsillectomy, and upper respiratory infection.

One payer reported doing bundles for bariatric surgery and cataract removal, and another is doing adjuvant breast cancer and pregnancy.

Hospitals Told: No Gouging

An appeals court in California ruled June 10 that a health plan does not need to pay the chargemaster bill from a hospital. The court ordered a new trial in the case between Children’s Hospital of Central California and Blue Cross of California.

At stake is whether Children’s Hospital, in the midst of a contract dispute with Blue Cross, could bill an insurer at its highest rates (those on the chargemaster) while the two sides did not have a contract.

The decision by the Fifth District Court of Appeals in Fresno, Calif., could have wide-ranging effects on hospitals and health plans in California, according to the Sacramento Business Journal.

The court said that hospitals cannot expect health plans to pay amounts that exceed the actual value of services provided. In 2007 and 2008, fewer than 5% of payers paid the hospital full charges listed on the chargemaster, the court found.

Quoting Dan Baxter, a lawyer who represented Blue Cross, the business journal reported, “This ruling will absolutely change the landscape between hospitals and health plans in litigation.... It’s a clear-cut California case we didn’t have until now — finally — that says in no uncertain terms you can consider a full body of information, not just billed charges.”

However, Glenn Solomon, a lawyer for Children’s Hospital, told the journal that the decision will be “bad for all patients in California and the health care system in general.”

Briefly Noted

Asthma rates are dropping, but don’t celebrate just yet warns a researcher at the Centers for Disease Control and Prevention. The percentage of Americans with asthma fell from roughly 8.6% in recent years to 7.4% in 2013. In addition, patients having an asthma attack or episode fell to a 15-year low of 3.8%, down from 4.4% in 2012. Jeannine Schiller, MPH, a lead researcher at the CDC, says that the downturn may just be a statistical anomaly, and wants to see 2014 statistics before pronouncing that asthma is in decline.... Yet more doubt has been thrown on the benefits of vitamin supplements. Antioxidants actually reduce the benefits of exercise, according to a study in the Journal of Physiology (http://tinyurl.com/vit-study). The study looks at 54 men and women, who are already in pretty good shape.

Most of them are runners or cyclists. One half got a placebo; the other got the vitamins. At the end of an intense 11-week training program, both groups showed improvements but the ones taking placebo had more energy and better health.... If perception is reality (placebo, anyone?), then the debate over the worthiness of wellness programs might be moot.

Workers who believe that their employers care about their health will give those companies a competitive advantage, according to a survey (http://tinyurl.com/survey-well) of 2,700 employees by the National Business Group on Health, Aon Hewitt, and the Futures Co. Such workers are also happier and less stressed.... When it comes to prescribing antibiotics, hospital doctors are all over the place, according to the Centers for Disease Control and Prevention (http://tinyurl.com/prescribe-hos). Physicians in some hospitals prescribe nearly 3 times as many antibiotics than physicians holding similar positions in other hospitals, according to a study of 300 hospitals. Some of the patients had not even been fully tested to see if they need an antibiotic.... Patients with type 2 diabetes that includes severe hypoglycemia have more incidence of cancer and higher mortality than those who do not have severe hypoglycemia, according to a study in the journal Diabetes Care. Among the predictors of severe hypoglycemia are older age, low body mass index, and high A1C levels.... Seventy-three percent of older patients would prefer getting care that’s coordinated, but only 27% describe the care they get that way, according to a survey by the John A. Hartford Foundation. Patients who get coordinated care like it: 83% say that their health improved.

— Joseph Burns
Employers’ health costs could increase as much as 9% this year, according to a study of 126 insurers and/or plan administrators by Buck Consultants. “The actual increase in rates will also depend upon the underlying claim experience,” says Harvey Sobel, a Buck principal and consulting actuary who co-wrote the study. And it will depend on whether that employer is self-insured and on other factors. Yes, it is complex.

The slight slowdown in the rate of increase is not much solace for cash-strapped employers and workers, according to Buck’s “National Health Care Trend Survey.” The study points to one of the conundrums of living at a time when the technology is constantly improving. “While technology may ultimately be the key to containing health care cost increases, research and development costs often result in higher initial costs for these services.”

But there are other factors.

“This may be a result of the economic slowdown and its impact on consumers’ willingness to seek medical treatment,” says Harvey Sobel, a Buck principal and consulting actuary, co-author of the survey. “Even though the decline is good news, most plan sponsors still find 8%–9% cost increases unsustainable.

“Health plans will need to continue to look for ways to help plan sponsors control costs, including through better utilization management, provider reimbursement rates, and selection of high quality providers.”

Another problem, the report tells us: “Providers — particularly hospitals — have consolidated into hospital systems, giving them greater bargaining leverage with managed care organizations. As a result, these providers have been able to negotiate higher fees.”

Sobel says, “Health plans will need to continue to look for ways to help plan sponsors control costs, including through better utilization management, provider reimbursement rates, and selection of high quality providers.”

Source: “National Health Care Trend Survey,” Buck Consultants, May 2014
Will the Affordable Care Act (ACA) sound a death knell for employer-sponsored health care? Analysts at Standard & Poor’s Capital IQ Global Markets Intelligence (GMI) stirred up a hornet’s nest recently with a prediction along those lines. The law gives U.S. companies an opportunity to “radically redefine” their role in health care, the report says, leaving purchasing responsibility in the hands of employees — backed by increased government health care funding — and leaving health plans to compete for these employees’ business on heavily regulated public state exchanges.

True, in crafting the ACA, legislators included provisions aimed at forcing companies with more than 50 employees to continue to provide coverage for employees. The big stick was a $2,000 per-employee penalty — or tax, depending on how you look at it — for failing to offer coverage, while many self-employed workers or low-income employees at small companies could qualify for the government subsidies available to finance a major migration of the uninsured into the marketplace.

Still, the GMI report suggests that legislators are likely to continue to tinker with the ACA, probably simplifying the switch from company plans to the exchanges. The law, it says, may well be the first step in a historic shift away from a world of employer-provided health care insurance.

GMI analysts liken the change they foresee to the transformation of retirement pensions that followed passage of the Employee Retirement Income Security Act of 1974. That law helped facilitate the transition from traditional company-funded pensions to the defined contributions fueling 401(k) plans that predominate today.

In the brave new world GMI envisions, individuals will be responsible for shopping for health coverage and — after some initial upward adjustments in salary — they’ll also shoulder a larger share of the rising cost of coverage, saving companies with more than 50 workers $3.3 trillion through the next decade. And the risk now being assumed by currently self-insured companies will be passed on to health plans.

GMI predicts that after a few big companies lead the way in the next few years, there will be a rapid sea change in the market, with relatively few holdouts.

Senior analyst Gary Albanese, one of the authors of the report, cites as a similar phenomenon the airlines’ embrace of a no-frills approach. “Once a few started charging for luggage, others followed,” he says. After some major employers shed the responsibility of offering coverage to employees, he says, “other companies will quickly follow. In five years, it should be 90%.” The switch, he adds, will make these companies’ stock more attractive to investors — and that’s something those companies can’t ignore.

Albanese isn’t alone in his thinking. Ezekiel Emanuel, MD, PhD, one of the architects of the ACA as an adviser to the Obama administration (and a brother of Chicago Mayor Rahm Emanuel, former White House chief of staff), has been saying the same thing. If anything, Emanuel thinks we’re even closer to this new world of coverage. He makes the point in his new book, *Reinventing American Healthcare: How the Affordable Care Act Will Improve Our Terribly Complex, Blatantly Unjust, Outrageously Expensive, Grossly Inefficient, Error Prone System.*
“A few big blue-chip companies will announce their intention to stop providing health insurance,” Emanuel writes. “Instead, they will raise salaries substantially or offer large defined contributions to their workers. Then the floodgates will open.”

Helping pry open those floodgates will be the new “Cadillac” tax on high-cost health plans: a 40% tax on insurance that costs more than $10,200 per employee or $27,500 per family. It goes into effect in 2018.

Profits vs. benefits

On the other side of this discussion, though, is a whole galaxy of naysayers, from Harvard professors to business groups and market analysts, who just can’t see how companies can overlook the penalties involved or suddenly tear themselves out of a system that has been woven around the close bond they want to forge with their most highly valued — and paid — staffers.

But even defenders of the current system for big-company health care insurance see some of the same undercurrents that influenced GMI’s bold prediction as helping to reshape the market for America’s managed care companies.

In one sense, larger companies are already moving to exchanges. Private exchanges, in which health plans can compete for members at each company, have been rapidly capturing a growing amount of business for active workers. There is no federal penalty when employers use private exchanges.

Aon Hewitt, Buck Consultants, Mercer, and Towers Watson are among the benefit consultants now operating private exchanges. Walgreens, a retail employer with a large base of low-income workers, captured headlines last fall when it announced that the company was moving its 160,000 employees into a private exchange run by Aon Hewitt, where an initial 18 employers plan to participate and 20 insurers will offer plans.

“We see private exchanges moving closer to the way public exchanges are set up,” says Albanese. “It’s a stepping stone to a public-option kind of system, where private exchanges mirror the public exchanges.

“We think of this as an evolutionary process,” adds Albanese, whose GMI study highlights some recent business decisions that underscore the evolution of corporate thinking on health insurance. One prime example: UPS’s decision to stop providing coverage for the working spouses of nonunion employees, a move dictated by the bottom line. “This analysis uniquely highlights the basic premise that corporations will deliberately and strategically devolve their participation in providing health care benefits for Americans, shifting the obligation toward individuals and government,” GMI states in its study.

The intent behind the ACA is to get as many people into the system as possible, with wider participation helping to blunt the health care inflation rate that the Kaiser Family Foundation has tracked at 7.5%. Using certain assumptions about the success of the exchanges, annual inflation could dip to 6.5%, which would help make the cost of health care more affordable for everyone, GMI says.

“One way,” says Albanese, “is to get more people into the exchanges.”

With companies providing wage hikes to cover the initial added cost of coverage and health care inflation running at 6.5%, wages would then be likely to continue upward at a rate of 2%–3% a year, says the analyst. Employees would then absorb more and more of the cost over time, with companies leaving the field. And that would closely resemble what most employees are experiencing today.

“What we’ve seen,” says Albanese, “is that every year your [individual] rates and deductibles go up.” Companies with large ranks of low-skilled, low-paid workers who could benefit from government insurance subsidies will be the first to move.

“Low-skilled employees are most likely to be...
pushed off into the exchanges,” says the analyst. “They are also very thin-margin companies.” Any opportunity to thicken those margins, even by a small amount, would be a big deal. “Comparing the cost of doing it versus the cost of providing benefits, it’s very clear.”

Higher-paid employees, the ones most treasured by companies, would have to be given enough cash initially to make it possible for them to avoid the sting. “As long as you’re not seeing any out-of-pocket costs,” he adds, staffers won’t complain.

In return, companies that are already slashing costs associated with human resources could find even more ways to save. As more people come into the system, insurers will provide more and better options to compete for the growing business; costs will come down as inflation slows, and that will all make it more attractive for everyone.

Now that millions of people have signed up for the state-based exchanges, Albanese is operating on the assumption that the exchange system is here to stay. But that doesn’t mean the laws that govern them will remain unchanged. And there are uncertainties over just what changes could be ahead.

This isn’t the kind of discussion that inspires public stances among some prominent managed care organizations. A spokesperson for the Blue Cross & Blue Shield Association told Managed Care that the group hadn’t come down on either side of the argument. “Our view is that we’ll go where the members are,” said the spokesperson.

**Taxes vs. subsidies**

But some prominent observers are betting that GMI’s crystal ball isn’t working — with some important caveats. Like Albanese, Harvard economist David Cutler, PhD, believes that the exchanges have made it through the gauntlet of American politics and now have a permanent place in the system. But he’s not expecting large blue-chip companies to bow out of providing employer-sponsored insurance.

“Taxes vs. subsidies”

“Taxes vs. subsidies” economist David Cutler, PhD, is not expecting large blue-chip companies to bow out of providing employer-sponsored insurance.

Calling himself a “little skeptical,” economist David Cutler, PhD, is not expecting large blue-chip companies to bow out of providing employer-sponsored insurance.

income. The reason is that the employer that provided health insurance is excluded from taxation.” And if you compare, he says, the tax advantages are a bigger influence on companies than the low-income subsidies available.

Low-income workers may be happy with government subsidies, adds Cutler, but if you pay out your benefits in wages to high-income staffers, “that just compounds it. We’re going to go to your high-income workers and say, we’ll give you that $15,000 back. [After taxes] they’re left with $10,000 to buy insurance and no subsidies.”

Says Cutler: “Whom do companies want to make and keep happy? High-income, not low-income. The economics just don’t work out.”

The current trend in setting up private exchanges for active employees, though, “could be what they choose to go into.”

Many companies will think about where they want to go, says Cutler, and some are likely to go the private exchange route. “They could say, ‘We’re sick and tired of paying for benefits; we’re going to give you a fixed amount, either in an internal exchange or where we contract with a benefit firm to do a private exchange.’ That’s very different from dropping insurance coverage.”

Admittedly, there’s been little discernible shift in the attitudes shown publicly by Fortune 500 companies. “It’s obvious, based on our research and others’ research, that most large employers are expected to continue coverage for the foreseeable future,” says Brian Marcotte, MS, CEO of the National Business Group on Health. He doesn’t expect a sudden exodus.

“Employees in some industries would benefit from exchanges,” says Marcotte. Retirees and employees in low-margin, high-turnover businesses, who would qualify for subsidies, are likely to find it more attractive to move into the exchanges. “We expect to see some of that happen. But higher-paid workforces will have difficulty in exiting, as employees will not be eligible for subsidies.”

A lot of retirees among the large companies — such as IBM — are already being shifted into private exchanges, says Marcotte. That began even before the ACA and those private exchanges are likely to
attract a lot more interest in the near term than the public exchange market.

“It will be interesting to see how public and private exchanges evolve over the next five to six years,” he says. “Exchanges need to demonstrate how they will improve the delivery system and manage health care costs better than what large employers do today. This may take several years. Until exchanges can prove a better value proposition, most employers view a move to an exchange at this time as a leap of faith.

“Put another way, what is the difference if I access Blue Cross or any other health plan through my employer, a private exchange, or a public exchange? I still have the same insurance carrier and am receiving care through the same underlying delivery system generating costs at multiples of CPI.”

One of the challenges with the new GMI study, Marcotte adds, is that it appears to calculate how much a company can save by looking only at direct medical costs. “But other factors weigh in heavily when it comes to considering a big move like this,” he says. “The big one is the tax advantage associated with company-provided health care benefits. When projecting the company savings of moving to public exchanges, you have to net out the cost of grossing up employee salaries to keep them whole for losing the tax advantage of employer-sponsored health care.”

Then there are the unseen issues, says Marcotte. Given the country’s concern about heavy debt, the government isn’t likely to just sit idly by while companies abandon the traditional system of providing health care. Unlike GMI, he doesn’t expect the government to facilitate the transition because “someone’s savings will typically end up as somebody else’s cost. Who will pay for the billions in company savings estimated in the GMI study?”

Marcotte ticks off the big issues: Lower-than-anticipated enrollment in the early days of the health exchanges, the leap of faith needed in shifting staffers to exchanges, uncertainty about the future of the law. The way it stacks up now, he says, “companies will want direct control of their cost until they are confident there is a clear path to stabilizing cost and improving the delivery system. That path is still very unclear. Large companies are the market agitators in health care. They are the ones driving transparency, telehealth, centers of excellence, reference pricing and even private exchanges. We need them in the game to help reshape the delivery system before they exit or if they exit. That will take some time.”

**Going beyond coverage costs**

The argument over how the numbers will stack up also overlooks one of the biggest trends in company-provided health insurance. Many large companies have been gathering health-related data on their workforces for years, says Thomas Parry, PhD, executive director of the Integrated Benefits Institute, and they are using it to manage the health of their workers as part of a long-term effort to achieve strategic goals. If you end up dumping workers into the exchanges, that whole movement toward managing health goes out the window.

Those large companies with highly skilled employees aren’t just thinking about how many dollars they spend on health care, says Parry, whose group includes many Fortune 100 companies. They also devote considerable resources to managing care and tracking outcomes, he says.

Absenteeism and underperformance on the job because of poor health are big issues at all companies that employ skilled staffers, says Parry, “and CFOs in particular are very aware of that aspect of health. This is more than just financing and coverage; this is about managing health and quantifying outcomes so they can make better decisions.”

Parry also acknowledges that there will be pressure to exert better control of costs as the pioneers shift into exchanges. Ultimately, he says, you can expect to see some of the bigger companies with unskilled, low-wage workers lead the shift into the exchanges. On the other end of the spectrum, there will be the companies that still closely track health and measure outcomes with employer-provided coverage. And then a third group will develop, choosing private exchanges as the middle ground for managing costs as well as health.

One thing is certain, though: The market is changing and will continue to change. “This will play out in a very interesting way,” Parry predicts.
Doctors Aren’t Grasping For Cost Transparency Tools

Saving health care dollars requires information, and health plans are developing estimators to provide it. Now they have to make sure physicians are in the loop — and on board.

By Richard Mark Kirkner

In health care’s bad old days, doctors were often woefully ignorant of the costs to patients of the services they recommended. Today, with the industry striving to achieve cost transparency and physicians still the key influence on patient decision making, evidence suggests that in too many cases the bad old days are still here.

As health plans develop and refine tools to give members detailed information about how much they will pay for tests, procedures, and hospitalizations, members are taking that information to providers. Many of those providers, though well equipped to discuss the need for a test or procedure, are clueless about its cost — or where to get a more reasonably priced alternative.

That’s although physicians have a key role to play in helping payers and patients realize the savings the new cost transparency tools have been designed to yield. Despite their influence, doctors may be the last on board the cost-containment train as it prepares to leave the station.

Medical ethicist and lawyer Ben Rich, JD, PhD, who teaches at the University of California, Davis, sheds light on why. “Even in my field of medical ethics, the discussion of cost long seemed to be off the table,” he says. “It was somehow unethical to take cost into account. But there’s nothing so special about health care that cost is not a consideration, particularly when you talk about the state of our system, when patients’ copays continue to ratchet up.”

When providers do seek straight answers about costs for even routine tests, the task can be daunting, as Joseph Bernstein, MD, an internist at the University of Pennsylvania, found out. Bernstein and his daughter contacted 20 Philadelphia-area hospitals to get prices for electrocardiograms. Only three could provide them, although 19 furnished information about parking costs, according to an article in JAMA Internal Medicine.

Bernstein’s study was modeled on a 2013 study, also published in JAMA Internal Medicine, that surveyed 122 hospitals on the cost of hip replacement. That study found that only 19 hospitals gave a complete bundled price and 27 a partial price, while another 19 did not give any price. Despite a push toward greater cost transparency, study authors noted, getting up-front prices of common medical procedures is “very difficult,” which underscores why many providers cannot give patients reasonable answers about pricing.

Physician’s responsibility

Aiding the push toward greater cost transparency are tools that health plans started to develop before the Affordable Care Act was a twinkle in policymakers’ eyes. Aetna has its Member Payment Estimator, and private vendors such as Castlight have developed other tools for the likes of WellPoint and Anthem Blue Cross.

Now it’s up to providers to do their part, argues the medical ethicist Peter Ubel, MD, who recently wrote in the New England Journal of Medicine that medical costs are an “undisclosed toxicity” that can harm patients. “We can no longer afford to divorce costs from our discussion of patients’ treatment alternatives,” wrote Ubel, a professor of business administration and medicine at Duke University who blogs on bioethics and behavioral economics.

“Right now there’s a lot of pressure from...
policymakers on payers, and what’s missing largely is the focus on the responsibility of the physician,” says Neel Shah, MD, a Harvard obstetrician who is executive director of Costs of Care, a not-for-profit that advocates for full disclosure of health care costs. “The argument for it is that right now 90 cents of every dollar spent on health care is determined by the doctor,” Shah adds. “Even if you have really empowered patients, usually they’ll defer to the doctor.”

Out-of-pocket health care costs are becoming an increasing burden on American families. A 2009 American Journal of Medicine study reported that medical expenses accounted for almost two thirds of bankruptcies by 2007, and three quarters of those bankruptcy filers had health insurance. Between 2001 and 2007, the study said, the share of bankruptcies blamed on medical costs rose by 5%.

What’s more, much of that spending is unnecessary: The Institute of Medicine reported that about 30% of health spending in 2009, approximately $750 billion, was wasted on unnecessary services and other leaks in the system.

The issue becomes more acute as plan members pick up more of their costs. Enrollment in employer plans with deductibles of $1,000 or more quadrupled from 2006 to 2012, while enrollment in low-deductible plans declined 20%, according to the Survey of Employer-Sponsored Health Benefits 2012 produced by Kaiser and the Health Research & Educational Trust (HRET).

Plans provide estimating tools

Tools such as Aetna’s Member Payment Estimator have evolved to give plan members more detailed payment information on more services — 650 health care services at last count, says Christine Riedl, national accounts product director at Aetna. Through a secure online portal, members can get cost estimates of procedures tailored to their insurance plan design. Among the most common services members seek prices for are vaginal and cesarean birth, colonoscopy, MRI, upper gastrointestinal endoscopies, and office visits, Riedl says. Since it debuted in 2010, the Web site has had more than 4 million hits, and the Government Accountability Office noted it was the only private estimation tool that provides complete cost figures.

“After members used the Member Payment Estimator to obtain cost estimates on one of more than 30 commonly selected health care services, they chose a provider whose out-of-pocket cost estimate was on average $170 lower than the average of the estimates they received,” she says.

On the provider side, Aetna also has what it calls the Provider Estimator Tool, which works the same way as the member portal but with access limited to providers, Riedl says. This is how the doctor can discover how much it will cost the patient to have a test or procedure.

Anthem Care Comparison is another tool the GAO report cited. The agency noted that both Aetna and Anthem cited resistance by physicians as an obstacle to obtaining cost information on all network providers. One specific barrier some physicians cited: contractual obligations that prevented them from revealing prices.
Anthem Blue Cross developed its price estimator tool for employees of the California Public Employees’ Retirement System with Castlight, a San Francisco tech company that develops cloud-based price transparency tools for self-insured plans. Specifically, Anthem uses this price transparency tool for its reference-based pricing program, which sets a fixed fee for hip and knee replacements. Castlight has worked with WellPoint as well to provide members in reference-based plans with a tool to research costs. “Coupling transparency with benefit design heightens the shopping experience and encourages greater consumer interaction,” WellPoint Vice President Ken Goulet said in a written statement last June when the program was announced.

“You can imagine that if you’re going to implement referenced pricing for hundreds of lab tests and imaging tests and procedures, then you really need to provide patients and their families with the tools and services so that they can understand what those costs are,” says Dena Bravata, MD, chief medical officer for Castlight. “Our services are available via mobile tablets, so Castlight users can bring their cost and quality information right into discussions with their providers.”

Payers have high stakes in improved cost transparency, according to a recent report from the Gary and Mary West Health Policy Center in Washington, DC. Greater cost transparency could reduce health care spending by $100 billion over the next decade, the report states, but to achieve that, the focus must go beyond patients. “We’ve found that providing price information to three key stakeholders — physicians, employers, and policymakers — may have a far greater impact than giving it to patients alone, says Joseph Smith, MD, PhD, chief medical and science officer of the center.

To get providers on board, health plans must navigate some lingering, but powerful, resistance in the medical community. “In my clinical experience talking with patients, money is a bigger taboo than sex,” says Bernstein, the Philadelphia internist who tried to get prices on ECGs. “Patients would much sooner confess to all sorts of sexual escapades than admit they don’t have the 10 bucks to buy the antibiotics needed to deal with those adventures.”

For doctors treating the acutely ill, such as cancer patients, price is even more taboo. Says Deborah Schrag, MD, a Harvard professor and a gastrointestinal cancer specialist at Dana-Farber Cancer Institute in Boston, “I’ve been a cancer doctor for more than 20 years, and when people are sick it doesn’t matter whether they’re rich or poor, they want the best care and they want the life — and quality of life — of their loved one preserved. Cost is not at the forefront of the minds.”

“Right now 90 cents of every dollar spent on health care is determined by the doctor,” says Neel Shah, MD, executive director of Costs of Care, a not-for-profit that advocates full disclosure of health care costs.

A physician talking with a patient battling cancer involves a dynamic different from talking about cheaper antibiotics or different places to get an MRI, she says. “Context is everything,” Schrag says. “If it’s an early-stage cancer, then cost comes into play; if you feel your life is threatened, then cost trends not to come into play.”

Over the next decade, the national cost of cancer care has been projected to increase almost 40%, reaching $173 billion by 2020, and by 2030 the...
number of new cancer cases will increase by 25%, according to a report from the American Society of Clinical Oncologists. One driver of cost for the critically ill is unnecessary hospitalizations. Schrag and her colleagues identified types of patients most likely to encounter unnecessary hospitalizations: patients older than 70, those advised to enter hospice care, and those who have had three or more lines of chemotherapy. Most potentially avoidable hospitalizations occurred in patients near the end of life with difficult-to-treat advanced cancers.

Additionally, cost sensitivity gets little attention in medical education. Steven Weinberger, MD, executive vice president at the American College of Physicians, has gone so far as to propose that the governing bodies of medical education add cost-consciousness and stewardship of care resources as a seventh general competency.

**One goal, two paths at UnitedHealthcare**

UnitedHealthcare has worked with oncology groups to get oncologists to buy into cost-consciousness. Its episode payment program aims to reward quality and cost improvement using two payment strategies: the clinical pathways approach, in which oncologists use chemotherapy regimens predefined by a panel of physicians, and an episode-payment approach.

The clinical pathways approach uses higher fee schedules and bonuses to encourage physicians to use the least costly treatment when the panel has determined that a number of regimens are clinically equivalent, but oncologists may deviate from the pathway for medical reasons. A 2010 study in the *Journal of Oncology Practice* found that pathways developed by US Oncology, a national oncology management organization, resulted in a 37% reduction in drug costs for lung cancer patients. UnitedHealthcare Senior Vice President for Oncology Services Lee Newcomer, MD, noted in a *Health Affairs* article that three organizations — Cardinal Health, Via Oncology, and New Century Health — have also used the clinical pathways approach as an incentive to oncologists.

The episode-payment approach, which Newcomer also outlined in the *Health Affairs* article, is akin to bundled payment. In a pilot program, five large oncology groups each selected the treatment regimen for 19 discrete clinical episodes in breast, colon and lung cancer, and made a commitment to use those regimens at least 85% of the time for UnitedHealthcare patients, again allowing medically legitimate exceptions. UHC added a small case management fee to arrive at an episode payment for each clinical episode. “This approach is designed to reward oncologists at current levels for patient care while simultaneously severing the link between drug selection and practice income,” Newcomer wrote.

Shah of Costs of Care acknowledges that medical residencies can be a breeding ground for inefficient practices, such as ordering multiple or unnecessary tests for hospital patients. “The number one driver cited by residents about why this happens is that they’re trying to preempt future workload, so if you can get five tests at once and not think about it any more, that’s better for you than to get one test, wait for the result, then get the second,” he says.

Johns Hopkins used its electronic health records system to change physicians’ behaviors when ordering tests for hospital patients. After the IT department populated the information system that physicians use with test costs, the number of tests ordered per patient-day dropped from 3.72 to 3.40 — “about an 8.6% decrease, and that was statistically significant,” study leader Leonard Feldman, MD, says. That saved the hospital system approximately $500,000 over six months. “Not a huge amount,” Feldman says, “but we all need to do our part.”

To get doctors on board, health plans must keep refining their cost-containment tools. “The challenge is that because the people who pay are separated from the point of care, like the patient and the doctor, often it’s really hard to know what the true value of care is at the moment that it’s happening,” Shah says. “One role of physicians is to help patients better navigate those kinds of services. But the plans clearly have a role in taking all utilization and cost data that they’ve used in helping them design their benefits and reframing that information for both patients and physicians so it can be useful at the bedside.”

Rich at UC Davis thinks insurers can give physicians more incentives to get on board, particularly in addressing advance directives, which can play a pivotal role in helping the terminally ill, families and payers deal with the agony and costs of end-of-
life care. “I would think that, out of concern for costs, managed care organizations would be doing everything they possibly could to incentivize their provider network to engage in timely, thorough, well-documented advanced-care planning discussions with their patients, because the vast majority of patients who are doing an advanced directive are doing it to limit care, not to extend it,” he says.

That discussion should be part of the patient history that any physician obtains, but there is a strong perception among physicians that they have neither the time nor the support of insurers for doing this, Rich says. “To me, the litmus test is, What is the perception of the physicians in that network? As you know, perception becomes reality.”

Ubel, the medical ethicist, believes health plans have to do navigating of their own to better utilize these cost transparency tools. “I honestly don’t know why insurance companies haven’t had more success over the years in managing health care costs in general, other than that I think every time they try to do it, people say they’re micromanaging medical care,” he says.

Ubel notes that physicians “respond to financial incentives like any human being,” and that the financial incentives in health care need to align better with quality measures. “Physicians are always motivated mainly to help patients, and what the system has to do is figure out how to control cost, and how much of that comes out of the physician’s pocket, and how much comes out of someone else’s pocket,” he says.

Plans may be able to lure more physicians onto the cost-containment train by showing them that the price of a ticket will come out of someone else’s pocket.

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A new tool promises to make treatment of the mentally ill more cost-effective, but some experts wonder if it’s really ready for prime time. Pharmacogenomics — the burgeoning science of how individual genetic makeup affects a person’s response to medications — is being recruited to predict how effective certain drugs will be in treating mental health patients, with a goal of ensuring that drugs most likely to be effective are prescribed.

Genoa Healthcare, the nation’s largest behavioral health pharmacy provider, is collecting cheek swabs to identify patients who could benefit from certain medications aimed at treating mental illness. It takes the swabs from high-utilization patients and sends them to a laboratory for pharmacogenomic testing to determine how patients will respond to medications.

The testing is designed to improve the effectiveness of prescribing, says Julia Bartlow, RPh, the company’s regional operations manager. These tests also will allow Genoa to identify patients who might experience adverse effects from antidepressant or antipsychotic medications and thus may help to improve adherence, she adds.

Identifying biomarkers

Since 2013, Genoa has been working with SureGene, a Louisville, Ky.-based company that uses genetic testing to identify genes responsible for psychiatric illnesses and drug response. In collaboration with Louisville’s PGXL Laboratories, SureGene developed a test to identify biomarkers useful in predicting whether antipsychotic drugs are likely to be safe and effective for patients with mental health disorders such as severe depression and schizophrenia.

Predicting patient response

Other companies that specialize in treatment of patients with severe mental illness are developing similar tests. Last year, Mayo Clinic and AssureRx Health received a patent to identify genes to help physicians improve the selection of medications for patients with depression and other psychiatric disorders.

AssureRx Health has licensed the technology from Mayo and developed the GeneSight pharmacogenomic tests to identify genetic variants affecting patient response to psychiatric medications. GeneSight is intended to help clinicians make informed, evidence-based decisions about the most appropriate medications for patients, the companies said.

Earlier this year, ValueOptions, a managed behavioral health care company, began working with Genomind, a personalized medicine company, to study pharmacogenomic testing to treat patients diagnosed with such psychotic disorders as schizophrenia and bipolar disorder. The study began this spring at Zucker Hillside Hospital, in Glen Oaks, N.Y.

In the study, researchers will compare outcomes from treatment as usual with those of patients who receive pharmacogenomic-guided-treatment using Genomind’s Genecept Assay. The research will help to determine the efficacy of testing, its effects on treatment decisions, and its impact on costs and quality of care. Like the SureGene test, the Genecept Assay uses saliva and identifies genetic and biological markers that can inform clinicians’

Should Mental Health Patients Get Pharmacogenomic Testing?

Behavioral health companies are using cheek swabs to help choose the drugs that will work best for certain individuals. But psychiatrists say such testing still needs to prove itself.

By Joseph Burns
Contributing Editor

“Right now, it’s art as well as science,” says Julia Bartlow at Genoa Healthcare. “These tests would certainly add to the prescribers’ toolkit.”
treatment decisions for patients diagnosed with a variety of psychiatric conditions, ValueOptions and Genomind said.

Not ready for adoption
This level of activity is an indication that researchers believe these tests can help clinicians treat patients with mental illness more effectively. But even if this is the wave of the future, some observers don’t see it crashing on the shore quite yet.

The tests aren’t ready for widespread adoption in mental health clinics, says Shaili Jain, MD, a psychiatrist at Veterans Affairs Palo Alto Health Care System. A researcher affiliated with the National Center for Post-Traumatic Stress Disorder, Jain is a clinical assistant professor in the Department of Psychiatry and Behavioral Sciences at the Stanford University School of Medicine.

“Increasingly, psychiatry is combining pharmacogenomic findings with new therapeutic drug monitoring in the hope of improving the safety and efficacy of pharmacotherapy,” Jain says. “The problem is that much of the scientific data on pharmacogenomic testing might be statistically significant but is not necessarily clinically relevant because the number of patients tested is still very low.

“We don’t really yet know how to use pharmacogenomic data to improve medication options for people with psychiatric illness,” says Jain. “Right now we have identified a lot of biomarkers, which means that one day we should be able to improve medication options with these tests. But little of what we have so far is definitive.”

Clinical utility
To be fair, what we know today has some clinical utility, Jain adds. For patients of Asian ancestry who require the mood-stabilizing medication carbamazepine, for example, the FDA recommends a pharmacogenomic test, because such patients who take this medication are highly susceptible to Stevens-Johnson syndrome, which manifests as a severe skin rash.

“The FDA recommends that people appropriate for this medication who are of Asian ancestry be screened for the presence of a certain gene that makes them more susceptible to that side effect,” she says. “If the patient has that allele, she should not be treated with that medication unless there is a very strong clinical indication for it.”

Another example would be a test to identify patients who rapidly metabolize medications. “With data, we may know what kind of dose that person should be taking,” says Jain. “But we’re not ready to do that testing routinely.”

While some psychiatrists prescribe pharmacogenic testing for their patients, Jain questions whether such testing is worth the cost. “Many companies who provide the test kits are doing a lot of marketing for their use, but the jury is still out on what the test results mean clinically and whether the tests are necessary,” she says.

She adds that “We don’t have the data to support the use of these tests yet. To explore this avenue of care, we should definitely be doing testing, and that’s where we are right now: trying to figure out how to use these tests.”

A diagnostic odyssey
On that point, you’ll get agreement from Anil K. Malhotra, MD. Malhotra is a professor of molecular medicine and psychiatry at Hofstra University North Shore-LIJ School of Medicine and the director of psychiatry research at Zucker Hillside Hospital, where he is conducting the study for Genomind.

“The Genomind test has a number of genes on it that either help to identify the best medications or help to identify the best dose of the medications for these patients — or both,” says Malhotra. “Take risperidone, an antipsychotic, for example. There is a certain gene responsible for how that medication is metabolized. Knowing how it metabolizes will help with dosing in a particular individual.”

While these tests may have limited utility now, researchers hope they will be more useful in the future. Until then, Malhotra echoes Jain’s refrain. “Frankly,” he says, “there is more hope right now than reality.”

Currently, psychiatrists treat patients with a strategy that resembles flipping a coin, he adds. Often, a prescribing physician will begin with one medication and then try another and another until he...
or she finds one that produces the best response. This prescribing pattern is called a diagnostic odyssey, and that is what Malhotra’s research is designed to make unnecessary. “What we have for one patient might work for another patient, but we have very little data to suggest which way to go,” he says. “That’s why there is hope that with these pharmacogenomic strategies, we can identify better matches between patients and drugs.” Malhotra’s research for Genomind is one of several smaller studies that will lead to larger studies, all designed to assess the clinical utility of pharmacogenomic testing for patients with mental illness.

**Needed: a big study**

“No one has yet done a large-scale prospective study in which half of the patients get some kind of pharmacogenetic testing with a product and the other half do not,” Malhotra explains. “The clinician would treat all patients as usual. And the point would be to record some economic benefit such as reduced time in the hospital, reduced outpatient visits, reduced side effects, or whatever the results happen to show. We need a large-scale prospective study of 1,000 patients or more showing that kind of an outcome.”

But before anyone will do a large-scale trial, smaller studies are needed. “You have to power it with preliminary data, and that’s what we’re doing now,” says Malhotra. He has funding to do the research for one year and collect and report the results in a second year.

“But now, we are enrolling 100 patients, and 50 will get the pharmacogenomic intervention and 50 will not,” he says, adding that he expects to have results by about 2016.

Genomind has already conducted a study published earlier this year in the *American Journal of Managed Care* that assessed the cost of care for 300 patients with mental health disorders.

**700 patients**

Investigators found that the per-patient outpatient cost in those using the Genecept Assay was 9.5% lower — that’s $1,686 annually — than the per-patient cost in a matched control group, says Rachel Scott, PharmD, Genomind’s vice president of clinical research and operations.

“This study also looked at close to 700 patients to assess medication adherence and found that Genecept patients had 6% higher medication adherence than matched controls,” she adds.

“The savings largely reflected a reduction in outpatient visits,” Scott explains. “In a follow-up study that measures inpatient resource utilization, we will see an even more dramatic cost savings.”

Bartlow, of Genoa Healthcare, says that for many patients, such as those with treatment-resistant depression, this kind of testing could be beneficial. These people are high utilizers of the health care system, she says, so any medications that effectively control their depression may also help to cut expenses for inpatient stays or other high-cost services.

“Many psych drugs have markers that can be tested to aid in dosing, and there are a few proprietary tests that can aid in drug selection,” she adds. “Right now, it’s art as well as science, so these tests certainly would add to the prescribers’ toolkit.”

For this reason, Genoa says, such testing can aid pharmacists and mental health professionals in caring for behavioral health patients. Genoa Healthcare’s pharmacies are embedded in community mental health facilities in 27 states and the District of Columbia. Most of its patients are on Medicaid and Medicare.

“Because our pharmacies are in community mental health centers, we deal with a specific segment of the population that includes those with serious and persistent mental illness,” Bartlow says. “Some of our mental health center clients are for-profit, but most are not for profit.”

**Prescribing guided by testing**

“For specific prescribers who have identified the way they want to incorporate this testing into their practices for certain patients, pharmacogenomic testing could be useful,” says Bartlow. “Some prescribers have already picked the group of patients they believe will be more apt to see value in this testing. They plan to consistently test patients with the same diagnosis and then use that information to guide their prescribing.”

Jain is more cautious. “Pharmacogenomics will be useful one day because it will add one more piece to a complex puzzle,” she says. “But it won’t provide all the answers. It will be nice to have a few more clues, and we might be close, but we are not at the point of using pharmacogenomics on patients in everyday practice.”

30  MANAGED CARE / JULY 2014
An Evaluation of Healing Metrics Associated With Commonly Used Advanced Wound Care Products For the Treatment of Chronic Diabetic Foot Ulcers

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ABSTRACT

Purpose: As rates of diabetes escalate worldwide, diabetic foot ulcers are an increasingly significant public health problem. Advanced wound therapies that promote rapid and complete healing, thus reducing the risk for infection and amputation, can substantially improve quality of life while decreasing financial burdens to the individual and health care system. Our purpose is to compare standardized healing metrics in patients with diabetic foot ulcers treated with three widely used advanced wound-healing products.

Design: Retrospective analysis of data collected and reported in published randomized controlled trials, physician product prescribing information, and premarket approval summary documents from the U.S. Food and Drug Administration.

Methodology: Rates of complete wound closure within 12 weeks, time to healing, number of graft applications to wound closure, durability of healed wounds, and safety were examined for patients with diabetic ulcers treated with Apligraf, Dermagraft, or EpiFix.

Results: Complete wound closure within 12 weeks of treatment initiation occurred in 56%, 30%, and 92% of Apligraf-, Dermagraft-, and EpiFix-treated ulcers, respectively. EpiFix-treated ulcers had the shortest time to healing (median 14 days) and least amount of graft material used (14 cm²) versus comparative products. Rate of ulcer recurrence was 5.9% for Apligraf (after 6 months), 18.8% for Dermagraft (after 8 months), and 5.6% for EpiFix (after 9–12 months).

Conclusion: Although prospective comparative effectiveness trials are needed, the differences recorded suggest EpiFix results in the most rapid improvement and resolution of diabetic foot ulcers.

Key words: advanced wound care; chronic wounds; diabetic foot ulcers

INTRODUCTION

Chronic wounds are defined as those that fail to proceed through an orderly and timely reparative process, which results in anatomic and functional integrity of an injured site (Lazarus 1994). Chronic wounds create a challenging cellular environment characterized by excessive proteases, increased cellular senescence, and increased bacterial infiltration resulting in a disordered and uncoordinated process of healing. Diabetic foot ulcers, venous leg ulcers, and pressure ulcers are the most common types of chronic wounds, but any time there is a breakdown in the protective function of the skin, by whatever cause, there is a risk for chronicity. Almost 6.5 million people the United States are affected by chronic wounds (Crovetti 2004, Sen 2009). The economic impact is substantial, as more than $25 billion is spent annually on the treatment of these chronic wounds (Brem 2007, Sen 2009). The cost of treatment for chronic diabetic foot ulcers accounts for one third to one half of this amount, at $9 billion to $13 billion annually (Rice 2014). In addition to financial burdens, ulcer-associated personal and societal quality-of-life issues also affect patients with diabetic ulcers (Evans 2005). With an aging population and the sharp rise in the incidence of diabetes and obesity in the United States, the number of chronic wounds and corresponding costs will continue to escalate rapidly.

Approximately one quarter of people with diabetes will develop a foot ulcer over their lifetime (Boulton 2008). Even if a foot ulcer heals, the rate of recurrence is greater than 50% after 3 years (Boulton 2005). Underlying conditions such as peripheral vascular disease, neuropathy, and poor blood glucose control contribute to slow healing rates and recurrence of diabetic ulcers, which in turn increase the risk for wound chronicity, infection, and amputation. Increased
comorbidity and mortality associated with these wounds are associated with infection, cellulitis, and osteomyelitis. In addition, their presence often suggests important contributing comorbidities, such as peripheral vascular disease, cerebrovascular disease, and renal disease (Rice 2014). More than half of patients have ulcers that become infected, often with osteomyelitis, and up to 20% require some form of amputation (Wu 2005). After new-onset diabetic ulceration, 5-year mortality rates between 43% and 55% have been reported, approaching 74% in patients with lower-extremity amputation (Robbins 2008). These rates are higher than those for several types of cancer, including prostate, breast, colon, and Hodgkin's disease (Robbins 2008). Diabetic foot ulcers precede 85% of lower-extremity amputations, and it is estimated that 49% to 85% of these amputations are preventable (Driver 2008). Diabetes-related amputations cost the health care system approximately $3 billion per year ($38,077 per amputation procedure) (Shearer 2003, Gordois 2003). Underscoring the need for rapid healing, it is reported that ulcer duration of more than 30 days is independently associated with a 4.7-fold increase in infection, and that an infected foot ulcer increases the risk of hospitalization by nearly 56 times and risk for amputation by nearly 155 times (Lavery 2006).

Many diabetic foot ulcers will not heal with conventional therapy. The Wound Healing Society guidelines recommend consideration of advanced wound therapies if a diabetic ulcer does not reduce in size by 40% or more after 4 weeks of standard therapy (Steed 2006). Clinical trial results have shown that bioengineered skin substitutes, such as Apligraf (human neonatal fibroblasts cultured in polyglyactin mesh; Organogenesis, Canton, Mass.), and EpiFix (dehydrated human amnion/chorion membrane; MiMedx Group Inc., Marietta, Ga.) promote wound closure, resulting in more frequent and rapid healing of chronic diabetic foot ulcers when compared with standard therapy with moist to dry dressings (Veves 2001, Marston 2003, Zelen 2013a). Determining the cost-effectiveness of any advanced wound care treatment or product in achieving wound closure is a complex calculation and must consider a number of variables. The rate of wound healing, time to healing, complications, and wound reoccurrence are primary cost drivers. Additional factors influencing the cost-effectiveness of any advanced wound product include the amount and cost of product used and the amount of product discarded at each application due to wastage of unused dispensed product.

The purpose of this evaluation is to compare the clinical effectiveness and product attributes of Apligraf, Dermagraft, and EpiFix advanced wound products for the treatment of chronic diabetic foot ulcers.

METHODS

A retrospective evaluation of randomized controlled trial data was performed. Rates of complete wound closure, time to healing, number of graft applications to wound closure, durability of healed wounds, and safety data were examined for three commonly available skin substitutes: Apligraf, Dermagraft, and EpiFix.

Included for analysis were data only from patients receiving the active intervention (Apligraf, Dermagraft, or EpiFix). The Apligraf and Dermagraft study groups were identified from peer-reviewed publications of pivotal clinical study data (Veves 2001, Marston 2003). The pivotal study of Apligraf included 112 Apligraf-treated patients. The pivotal study of Dermagraft included 163 treated patients overall who were included in the safety analysis; 130 treated patients with ulcer duration of more than 6 weeks were used to determine efficacy. The EpiFix group (n=64) consisted of pooled data from patients enrolled in three separate randomized controlled trials of EpiFix for the management of lower-extremity ulcers (Zelen 2013a, Zelen 2013b, Zelen 2014a). Additional source documents included product prescribing information and premarket approval summary documents (FDA 2000, FDA 2001). All included studies were industry-sponsored and funded.

Product description: Apligraf, Dermagraft, and EpiFix

Apligraf is supplied as a living, allogeneic bilayered cultured skin substitute: the epidermal layer is formed by human keratinocytes and has a well-differentiated stratum corneum; the dermal layer is composed of human fibroblasts in a bovine Type I collagen lattice. While matrix proteins, cytokines, and growth factors found in human skin are present in Apligraf, it does not contain Langerhans cells, melanocytes, macrophages, lymphocytes, blood vessels, or hair follicles. The cells are originally derived from donated human neonatal male foreskin tissue (FDA 2001). Apligraf is supplied in a sealed, heavy-gauge polyethylene bag with a 10% CO2/air atmosphere and agarose nutrient medium. Each Apligraf is supplied ready for use and intended for application on a single patient. To maintain cell viability, Apligraf should be kept in the sealed bag at 68–73°F (20–23°C) until use (FDA 2000).

Dermagraft is a cryopreserved human fibroblast-derived dermal substitute; it is composed of fibroblasts, extracellular matrix, and a bioabsorbable scaffold. Dermagraft is manufactured from human fibroblast
cells derived from donated newborn foreskin tissue. During the manufacturing process, the human fibroblasts are seeded onto a bioabsorbable polyglactin mesh scaffold. The fibroblasts proliferate to fill the interstices of this scaffold and secrete human dermal collagen, matrix proteins, growth factors and cytokines, to create a three-dimensional human dermal substitute containing metabolically active living cells. Dermagraft does not contain macrophages, lymphocytes, blood vessels, or hair follicles (FDA 2001). Dermagraft is supplied frozen in a clear bag and instructions for use include a 20-step process of thawing and rinsing the product prior to application to the wound (FDA 2001).

EpiFix is a dehydrated human amnion/chorion membrane allograft. Human amniotic membrane comprises the innermost layer of the placenta and lines the amniotic cavity. The allograft consists of layers of the amniotic sac, including an epithelial lining, amnion, and chorion, which contain important biological molecules such as collagen, connective tissue, cytokines, and growth factors. Although it contains no living cells, EpiFix provides a biologically active matrix and growth factors for cellular ingrowth. Processed through a proprietary Purion method that combines cleaning, dehydration, and sterilization, EpiFix has been shown to contain growth factors that help in wound healing, as well as such cytokines including anti-inflammatory interleukins and tissue inhibitors of metalloproteinase (TIMPs), which help regulate the matrix metalloproteinase (MMP) activity, the key to extracellular matrix remodeling (Koob 2013). In vitro and in vivo experiments established that EpiFix contains one or more soluble factors capable of stimulating mesenchymal stem cell migration and recruitment (Koob 2013). EpiFix is supplied in a sterile package and is stored under ambient conditions. It is clearly embossed to aid in identification of proper orientation for placement on the wound. EpiFix can be applied dry into the moistened wound bed, or moistened with sterile saline (Zelen 2013a, Zelen 2013b, Zelen 2014a).

**Description of patient population used in analysis**

The population of this analysis consisted of patients with type 1 or type 2 diabetes enrolled in randomized controlled trials who received one of the advanced wound therapies, Apligraf, Dermagraft, or EpiFix, for the treatment of a chronic foot ulcer (Veves 2001, Marston 2003, Zelen 2013a, Zelen 2013b, Zelen 2014a). Prior to study enrollment and receiving advanced wound therapy, all patients were required to have a noninfected foot ulcer that had not responded to standard wound care, and all had adequate circulation to the affected extremity. In all studies, infection was assessed by clinical evaluation of the enrolling physician. In both the Apligraf and Dermagraft studies, wound duration of at least 2 weeks was required for study inclusion (Veves 2001, Marston 2003), while in the EpiFix studies wound duration of at least 4 weeks was required (Zelen 2013a, Zelen 2013b, Zelen 2014a). Treatments consisted of Apligraf (up to 5 weekly applications), Dermagraft (up to 8 weekly applications), or EpiFix (weekly applications, n=20, or every-2-week applications, n=44) applied until wound closure or up to 12 weeks, whichever came first. In all studies, standard principles of diabetic foot care were adhered to. Products were applied after sharp debridement followed by moist-to-dry dressings. In each study, various methods were used to relieve areas of elevated plantar pressure (offloading), which has been shown to help prevent or heal plantar ulceration (Cavanagh 2010). Apligraf-treated patients were required to use crutches or a wheelchair for the first 6 weeks of the study and were fitted for customized tridensity sandals to be worn throughout the study (Veves 2001). Dermagraft-treated patients were allowed to be ambulatory using extra-depth diabetic footwear with custom inserts or healing sandals (Marston 2003). EpiFix-treated patients' wounds were offloaded using a removable cast walker (Active Offloading Walker; Darco, Huntington, W.V.). All studies followed patients with weekly visits until complete healing was verified or up to 12 weeks.

**Data analysis**

Statistical analysis was limited in that patient-level data were not available for the Apligraf or Dermagraft groups. Patient-level data were available for EpiFix-treated patients enrolled prospectively in three published studies, N=13, N=11, and N=40 (Zelen 2013b, Zelen 2013a, Zelen 2014a). These data were aggregated into one dataset and a pooled analysis was performed. Rates of wound closure after 6 and 12 weeks of treatment were compared with a Fisher’s exact test. Adjusted P values of <.017 were considered significant, as the risk of making erroneous false-positive conclusions is increased when testing multiple hypotheses on a single set of data, and the Bonferroni correction was applied. GraphPad InStat v3 was used to perform statistical testing.

**RESULTS**

Product attributes are compared in Table 1. Both Apligraf and Dermagraft were determined by the FDA to be Class III medical devices and were required to undergo a premarket approval (PMA) process before being available for clinical care. EpiFix, regulated by the FDA as a Human Cells, Tissues, and Cellular and Tissue-Based Product (HCT/P, 21
## TABLE 1
Product comparisons

<table>
<thead>
<tr>
<th>Product description</th>
<th>Apligraf</th>
<th>Dermagraft</th>
<th>EpiFix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product description</td>
<td>Neonatal fibroblasts cultured in bovine collagen matrix overlaid with neonatal keratinocytes</td>
<td>Neonatal fibroblasts cultured in polyglactin mesh</td>
<td>Dehydrated human amnion/chorion membrane allograft</td>
</tr>
<tr>
<td>Regulatory pathway</td>
<td>Premarket approval</td>
<td>Premarket approval</td>
<td>HCT/P; PHS Act Section 361</td>
</tr>
<tr>
<td>Graft sizes available</td>
<td>One 44 cm² disc</td>
<td>One 37.5 cm² sheet</td>
<td>Multiple sizes: 14 mm diameter disc (1.54 cm²) to 9 cm x 20 cm (180 cm²) sheet</td>
</tr>
<tr>
<td>Cost per graft</td>
<td>$1,806.14</td>
<td>$1,688.34</td>
<td>Various costs depending on graft size, starting at $329.70 for 14 mm disc</td>
</tr>
<tr>
<td>Storage considerations</td>
<td>Consists of living cells that must be kept sealed in nutrient medium and 10% CO₂/air atmosphere under controlled temperature 68–73°F (20–23°C). Shelf life 15 days.</td>
<td>Must be stored continuously at minus 75°C ± 10°C. For continuous storage, transfer of Dermagraft from shipping container into freezer must take ≤60 seconds to ensure cell viability. Frozen 6-month shelf life.</td>
<td>Sterilized tissue that may be stored at ambient conditions for up to 5 years.</td>
</tr>
<tr>
<td>Wound application instructions</td>
<td>Remove from liquid-filled pouch. Use within 15 minutes.</td>
<td>20-step application process including thawing.</td>
<td>Remove from dry pouch.</td>
</tr>
</tbody>
</table>

HCT/P=Human Cells, Tissue, and Cellular and Tissue-Based Product, PHS=Public Health Service.


## TABLE 2
Wound area and healing metrics

<table>
<thead>
<tr>
<th></th>
<th>Apligraf (n=112)</th>
<th>Dermagraft (n=130)</th>
<th>EpiFix (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound area (cm²)</td>
<td>2.97 ± 3.10</td>
<td>2.31</td>
<td>2.72 ± 2.6</td>
</tr>
<tr>
<td>Mean grafts received</td>
<td>3.9</td>
<td>5.7</td>
<td>2.4</td>
</tr>
<tr>
<td>Complete wound closure within 12 weeks</td>
<td>56% / 63/112</td>
<td>30% / 39/130</td>
<td>92% / 59/64</td>
</tr>
<tr>
<td>Median days to closure</td>
<td>65 (7, 88) / (n=63)</td>
<td>NR</td>
<td>14 (7, 77) / (n=59)</td>
</tr>
<tr>
<td>Ulcer recurrence</td>
<td>5.9%b</td>
<td>18.8%c</td>
<td>5.6%d</td>
</tr>
<tr>
<td>Adverse events* (infection, cellulitis, osteomyelitis)</td>
<td>22.3%</td>
<td>19%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

Data reported as mean ± SD, percentage, or median (min, max) as indicated.

*To healing or to maximum allowed during 12-week study period.

aAt 6 months.
bAt 8 months (32 weeks).
cAt 9–12 months.
dOf study wound.
CFR 1271) and by Section 361 of the Public Health Service Act, does not require premarket approval but does come under other FDA and regulatory pathways as described above. In each study, mean wound size at treatment initiation was between 2 and 3 cm². Mean wound size was 2.97 cm², 2.31 cm², and 2.72 cm², for Apligraf, Dermagraft, and EpiFix groups, respectively. Healing metrics reported in the studies evaluated are shown in Table 2.

Complete wound closure
For each product evaluated, the definition of complete wound healing was defined as full epithelialization of the wound with the absence of drainage. Healing rates at 6, 9, and 12 weeks are presented in Figure 1. Of the products evaluated, wounds treated with EpiFix had the highest rate of complete closure (92%) at the end of the 12-week study period, compared with a 56% closure rate with Apligraf and a 30% closure rate with Dermagraft (all pairwise comparisons $P \leq .003$).

Time to closure
For those wounds that closed in the study period, median days to closure were 14 days in the EpiFix group and 65 days in the Apligraf group. Days to closure was not reported for the Dermagraft study patients. Overall, within 2 weeks of the first application of EpiFix, median percent wound closure was 94%. A similar reduction in size (91%) was not achieved in the Dermagraft group until study completion at 12 weeks. This metric was not reported for the Apligraf group.

Number of graft applications and estimated costs
During the 12-week study period, Apligraf was applied at weekly intervals for a maximum of 5 applications. Total number of grafts used in the study was 440, and the mean number of Apligraf discs used per patient was 3.9 (minimum 1, maximum 5). Each Apligraf 44 cm² disk was trimmed to fit the ulcer and remaining material was discarded (Veves 2001). We calculated the cost of Apligraf and the other 2 products using allowable charges for each product from the Centers for Medicare & Medicaid Services (CMS) product reimbursement schedule found at http://www.cms.gov/apps/ama/license.asp?file=/hospitaloutpatientps/downloads/October-2013-Web-Addendum-B.zip. Overall cost for Apligraf product used in the study is estimated at $794,922 or $7,097 per patient.

EpiFix allografts were applied weekly or every 2 weeks, according to study protocol. Twenty patients received weekly application and 44 received EpiFix every 2 weeks. Patients received a minimum of 1 application to a maximum of 8. Overall, 154 EpiFix allografts were applied and a mean of 2.4 grafts were used per study patient. Total cost for EpiFix allograft material used in the study is estimated to be $197,819 or $3,091 per patient. Although grafts were trimmed to approximate wound size, the size of the packaged graft used depended on wound measurements at time of application, minimizing wastage. The number of product applications per healed wound is not able to be compared between treatment regimens, as this information is available only for the EpiFix pooled data (2.2 ± 1.5 grafts per healed wound). Based on available data, the average amount of graft material used per treated patient is presented in Figure 2.

Durability of healed wounds
An important consideration of advanced wound care product effective...
ness is ulcer recurrence after primary healing. In patients treated with Apligraf, ulcers healed by 12 weeks were reassessed at 4, 5, and 6 months. Within the 6-month follow-up period, the reported incidence of recurrence was 12.5%, 2%, and 5.9% at 4, 5, and 6 months, respectively (Veves 2001). In the Dermagraft FDA PMA summary, ulcer recurrence is reported for 2 separate studies of Dermagraft-treated patients. In a dataset of 139 patients treated with Dermagraft, all patients were followed to Week 32. Ulcer recurrence (defined as ulcers that healed by Week 12 and reopened on or before Week 32) was 26% (11/42). A retrospective analysis was also performed on the subset of patients enrolled in the published study (Marston 2003) who had ulcer duration of more than 6 weeks and who received Dermagraft that met the final metabolic release criterion used to determine consistency of the product; in this population, ulcer recurrence was 19% (3/16) at Week 32 (FDA 2001). In a long-term follow-up report of patients with ulcers treated with EpiFix, 94% (17/18) of wounds remained fully healed 9 to 12 months following primary healing (Zelen 2014b).

Safety

Although all patient clinical events during treatment were recorded in the three studies, for this investigation we chose to examine only those adverse events that were reported to be associated with ulcer complications. The incidence of serious wound complications (infection, cellulitis, osteomyelitis) was reported individually or in aggregate form for all studies. Percent of patients with serious wound complications during the study periods ranged from 1.6% (EpiFix) to 22% (Apligraf) (Table 2). Infection was the most common adverse event in all studies.

DISCUSSION

The pathogenesis of foot ulcers is often complex and their management is difficult. Knowledge of new techniques, technology, and products can allow clinicians to excel in their effort to provide optimal care and promote positive outcomes for these challenging patients. With standard wound care, healing can be slow and many ulcers remain unhealed over a long period. Prolonged care and associated morbidity often generate a burden to the health care system and to patients. Advanced therapies have been shown to accelerate the healing process in many patients, yet there is no perfect treatment for all patients in all situations (Shores 2007). Therapies that promote rapid and complete healing of foot ulcers can reduce the risk for infection and amputation and may substantially improve quality of life while decreasing financial burdens to the individual and to society overall (Albert 2002).

Advanced wound care products have been demonstrated to be ben-
Healing Metrics Associated With Advanced Wound Care Products

efficial in the treatment of diabetic foot ulcers. Indeed, statistically significant differences in rates of wound healing were observed versus controls for Apligraf (56% vs. 38%, P=.004), Dermagraft (30% vs. 18%, P=.02), and EpiFix (92% vs. 8%, P<.001). A meta-analysis provided additional support that 12-week treatment of diabetic ulcers with either Apligraf or Dermagraft increases the chance of healing over standard care alone (Ho 2005). Both products are widely used in the clinical setting. The purpose of the present analysis was to compare healing metrics between Apligraf, Dermagraft, and the more newly available allograft EpiFix for the treatment of diabetic foot ulcers. These comparisons suggest that diabetic foot ulcers treated with EpiFix have higher closure rates and heal more rapidly than ulcers treated with Apligraf or Dermagraft.

Skin substitutes may follow multiple regulatory pathways to reach market, and all of them are regulated by the FDA. One route is to qualify for regulation solely under Section 361 of the Public Health Service Act and 21 CFR 1271 in the Code of Federal Regulations, which is the regulation governing many human tissue products on the market today. If tissue qualifies for regulation solely under Section 361, it is not required to be licensed by the FDA and, in fact, no license is available. This is true not just of placental tissue, but also of many cornea, dermis, tendon, and bone products, which may also qualify as Section 361 tissues that do not require FDA clearance, approval, or licenses.

Both clinical effectiveness and cost-effectiveness are important considerations when choosing an advanced wound care product. Rates of healing, time to healing, number of grafts applied, costs per treatment, and ease of use must all be evaluated when determining if a treatment is cost-effective. For example, the utilization of a larger-than-necessary sheet of graft material for the wound size will produce both product and dollar wastage, as product is dispensed on a per-patient, per-application basis and any unused product must be discarded. This wastage must be factored in when determining the true cost-effectiveness of a wound-healing product. Indeed, when a graft of 44 cm² or 37.5 cm² must be used to treat wounds averaging less than 3 cm² over 90% of material is discarded. The availability of various-sized EpiFix grafts resulted in less waste of graft material when compared with Apligraf and Dermagraft. Although actual cost of materials may vary greatly due to contractual prices, we estimated differences in costs of treatment based on allowable charges for each product from the CMS product reimbursement schedule. The per-square centimeter price allowed for EpiFix is higher than for Apligraf and Dermagraft, but the ultimate product expense per patient was reduced by 55.2% (EpiFix versus Apligraf) and 73.6% (EpiFix versus Dermagraft) due to the reduction of product wastage with the EpiFix various sized grafts and more rapid healing times.

There are limitations to our analysis. Data were identified from source documents in the public domain and we did not have patient-level data from the Apligraf and Dermagraft studies, so we were limited in the amount of statistical analysis that could be conducted, including comparison of demographic factors that may or may not influence healing. As raw data were unavailable for the Apligraf and Dermagraft studies, we were unable to control for differences in study design and degree of off-loading. As both studies (Veves 2001, Marston 2003) were published more than 10 years ago, changes in clinical practice may have influenced outcomes compared with data collected more recently (Zelen 2013a, Zelen 2013b, Zelen 2014a). Our cost comparisons were estimated from data collected in separate studies and based on mean number of grafts used per study patient and may not reflect product costs outside a study setting. Product cost data were obtained from a recent CMS reimbursement schedule and do not reflect the cost of material when studies were performed. Although inclusion and exclusion criteria among all protocols were similar, the Veves and Marston studies were larger and multicenter, whereas the Zelen studies were smaller and conducted at one site. Although the differences we observed in this analysis show the superiority of EpiFix in achieving complete wound closure when compared with Apligraf and Dermagraft, prospective comparative effectiveness trials are needed to elucidate these results. This analysis was conducted to assist in sample size calculations for proposed trials.

Advanced wound care products have been shown to increase healing rates of diabetic foot ulcers compared to standard wound care. Although prospective comparative studies are needed to confirm our findings, this retrospective analysis of published data appears to favor the use of EpiFix as a clinically effective and a cost-effective treatment for diabetic foot ulcers over Apligraf and Dermagraft, with high rates of rapid wound healing, low number of grafts per healed wound, availability of multiple sized grafts, and simplicity of application.

REFERENCES
Boulton AL, Armstrong DG, Albert SF; et al; American Diabetes Association; American Association of Clinical Endocrinologists. Comprehensive foot examination and risk assessment: a report of the task force of the foot care
HEALING METRICS ASSOCIATED WITH ADVANCED WOUND CARE PRODUCTS

interest group of the ADA, with endorsement by the AACE. Diabetes Care. 2008;8:1679-1685.


Medicaid Fosters Innovations In Treatment of Mental Illness

The ‘health home’ is just one of the strategies helping to meet the needs of this vulnerable and costly population

By Thomas Reinke
Contributing Editor

The Medicaid program is proving to be an incubator of innovative services and delivery system reforms for people with complex behavioral health conditions. And in a way, it stands to reason.

The prevalence of serious mental illness and substance use disorder within the Medicaid population is substantially higher than in the general population. Data compiled from federal sources indicate that serious mental illness — defined to include schizophrenia, obsessive-compulsive disorder, bipolar illness, and delusional disorders — is found in just 4.1% of the general population, but in 11% of the Medicaid population. It’s a similar story with drug dependency — it shows up in 6.6% of the populace at large, but in 12.4% of Medicaid recipients.

“Behavioral health acts as a multiplier of health care costs,” says Al White, MD, chief medical officer of Aetna’s Medicaid plans. “When a behavioral disorder is added to an existing physical condition, the intensity of services increases exponentially. We now realize you cannot effectively treat either physical or behavioral problems without addressing the other.”

Besides recognizing the need to tackle behavior disorders, state Medicaid agencies and health plans have learned that out-of-the-box approaches that are both collaborative and coordinated are needed to have a meaningful effect on Medicaid beneficiaries with behavioral disorders — that the silo approach often doesn’t work.

After all, Medicaid patients face a wide variety of obstacles stemming from poverty, lack of food and housing, and often a lifetime of inconsistent access to health and education services. The social safety net has too often been fragmented.

These days, behavioral health is receiving more attention from state Medicaid agencies. Some states are taking advantage of an innovative Medicaid service delivery model established by the Affordable Care Act to create programs that target serious mental illness. But important, longstanding hurdles remain.

“The ACA created a new opportunity called health homes, for states to pay for care management for people with chronic conditions,” says Allison Hamblin, MSPH, vice president for strategic planning at the Center for Health Care Strategies, a Medicaid policy and implementation resource company. Health homes target individuals with two or more chronic conditions, or individuals with one chronic condition who are at risk for a second condition.

Behavioral health is at the top of CMS’s list of chronic conditions targeted for health homes:
1. Mental health condition
2. Substance use disorder
3. Asthma
4. Diabetes
5. Body mass index over 25

“CMS allows states to broadly define mental health conditions and to add many additional chronic medical conditions,” says Hamblin.

Coordinates general medical care

Iowa, Missouri, Rhode Island, and other states have created health homes specifically for behavioral health services. Medicaid beneficiaries with certain diagnoses are assigned to a behavioral health provider network that also coordinates their general medical care.

Health homes go beyond physician visits to
health home plan in Iowa. “Our integrated health home plan covers adults with serious mental illness and kids with serious emotional disturbances,” says Henschen. Out of a population of 411,000 Medicaid members, this program is available to approximately 30,000 adults with serious mental illness and 16,000 children with serious emotional disturbance.

Supportive services have been widely talked about for several years, and finally they appear to be arriving.

To qualify as having a serious childhood emotional disturbance, a child must have a diagnosable emotional or mental condition with a minimum duration that results in a functional impairment and substantially limits his or her role or function in family, school, or community activities.

Magellan’s Iowa plan was set up in 2011 with five comprehensive mental health centers serving as health homes. It has since been expanded to 11 providers in the five counties with additional plans to add more counties. “We expect to enroll about 50% of target populations into integrated health homes,” says Henschen.

Medicaid has a track record of innovations in delivering services, and now Medicaid managed care plans and Medicaid providers have recognized the need to expand beyond traditional medical services delivered in clinics or physician offices.

“Medicaid has always dealt with a challenging population with high support needs that have not been issues in the general population,” says Kathleen Nolan, director of state policy and programs at the National Association of Medicaid Directors. “So a lot of Medicaid efforts have focused on a holistic approach to patients rather than narrow medical needs. That’s where Medicaid works.”

Social needs

“Where Medicaid plans excel is in having an understanding of patients’ social needs and how to communicate effectively,” says Tricia Barrett of the
National Committee for Quality Assurance. “And that positions them to be attuned to the complex nature of treating people with serious mental illness because of the need to coordinate care across services that are not just medical services.”

Key to success

Building on past innovations is the key to success in these health homes. Serious medical illness plans are placing increased emphasis on supportive services that improve individuals’ ability to function in their daily lives. Supportive services have been widely talked about for several years, and finally they appear to be arriving.

Community mental health centers have been leaders in expanding care teams with new people in new roles, says Henschen. “These expanded care teams often include crisis intervention teams or individuals providing peer support, supportive housing, and supportive employment,” he adds.

Supportive housing may involve a small group of consumers living together with a staff person, and supportive employment may include a job coach. The idea is to make clients more viable participants in their community by providing employment training and job advice.

Peer support is increasingly viewed as a game changer that goes beyond traditional medical services. “We hire the right people who have been successful in recovery themselves, train them, and use them in the community, where they are matched up with members who are in the early stages of recovery,” says Henschen.

Such peer support is one of the truly innovative services. “People who have been able to overcome their behavioral or mental health conditions and who are now leading more normal lives are helping those who have active conditions or problems,” says Don Fowls, MD, who is CMO of a not-for-profit joint venture in Arizona of Mercy Care Plan (Medicare Advantage) and Maricopa Integrated Health System. “We involve these individuals in our case management activities because they are able to engage members.”

A new position, health resilience specialist, is an example of the nontraditional roles being added to Medicaid health care teams. This position was created by CareOregon, a not-for-profit organization providing health care services to coordinated care organizations, serving Medicaid recipients.

CareOregon’s health resilience specialists are embedded in many of its partner clinics for Medicaid members. They help consumers address the social issues that contribute to poor health. The patients tend to be characterized by any combination of Medicaid behavioral plans understand the social needs of beneficiaries, says Tricia Barrett of the National Committee for Quality Assurance. “And that positions them to be attuned to the complex nature of treating people with serious mental illness.”

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medical comorbidities, poverty, unstable housing, mental health and addiction challenges, trauma, and cognitive impairment.

In June, the Association for Community Affiliated Plans (ACAP), a group of Medicaid plans, named a CareOregon health resilience specialist as a recipient of its “Making a Difference” award for going beyond normal job expectations to help patients improve their health status.

The employee, Amy Vance, is an experienced social worker serving members of the community with mental health and addiction issues. ACAP recognized her for her efforts to find affordable alternatives to narcotic management for patients who suffer from chronic pain. For example, she established a relationship with Working Class Acupuncture, an organization dedicated to providing acupuncture therapy on a sliding scale. Vance secured an agreement for the group to provide acupuncture services to patients at no cost — and in an effort to build their trust in a therapy they otherwise might not try, she agreed to be treated alongside them.

More work lies ahead

Health homes may be a model for improving behavioral health services, but this alternative has its own challenges. One is predicting and controlling costs. Capitation is common in health homes. In 2012 and 2013, Ohio attempted to develop a capitated health home for serious mental illness and it encountered deal-breaking resistance that forced it to go back to the drawing board.

The state’s Department of Mental Health and Addiction Services proposed to have a two-level capitation rate based on acuity that was determined by a combination of diagnosis and service utilization history. The proposed monthly rates were $215 and $315 for low- and high-acuity enrollees. Those rates met with resistance from providers, who questioned the enrollment criteria and the tiered rates. In August 2013, the state delayed implementation of the health home program. Work is continuing on implementation.

One of the greatest challenges facing behavioral health homes is implementing care coordination and integrating physical health and behavioral health services. Behavioral health homes commonly reassign members away from medical providers to behavioral health organizations, but they are required to coordinate all care and to avoid duplication of payments. The mechanisms for meeting these requirements are not firmly established, but a recent development in Arizona may be the proving ground.

Billion-dollar contract

On April 1, Mercy Maricopa Integrated Care took on a $1 billion state contract to administer mental health and substance abuse services for adults and children in the greater Phoenix area. Aetna Medicaid Administrators provides management services for the contract, which includes integrating physical health services for people diagnosed with a serious mental illness.

“The model for the Maricopa County mentally ill population integrates physical health, behavioral health, and pharmacy benefits,” says Fowls. “Our efforts to integrate care have involved coordination meetings with 115 organizations — including medical providers, mental health centers, and employment and housing organizations.”

Care managers will play a key role in integrating care, and Mercy Maricopa also plans to rely on information technology and data sharing systems. “This program is an important attempt to better integrate administrative and financial arrangements for physical and behavioral health services, and it will be watched closely in the Medicaid world,” says Hamblin.

FEEDBACK Please!

Any thoughts about this article? Is there a pertinent angle that we haven’t touched upon? Let us know. We strive to present must-read material for busy clinician executives and other officials at health insurance plans. So, talk to us. If you want to remain anonymous, send responses to Managing Editor Frank Diamond at fdiamond@medimedia.com. If you want to write a letter to the editor, send it to:

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Conflict data on testosterone replacement therapy

Trimel’s Natesto, a nasal treatment indicated as testosterone replacement therapy (TRT), is entering the market at a time when many are questioning the safety of TRTs.

On May 28, Natesto joined Fortesta, Testim, AndroGel, Axiron, Androderm, and Striant as noninvasive formulations for hypogonadism. Although the hypogonadism market has been expanding in recent years, emerging evidence questions TRT’s long-term safety, as there is mixed data suggesting increased risk of cardiovascular (CV) events and prostate cancer.

Two recently published studies by Vigen, et al., and Finkle, et al., suggest that TRT leads to increased risk of cardiovascular events. Yet another recently published study, by Tan, et al., suggests that TRT may actually have a protective effect when it comes to CV disease.

Furthermore, a recent study published by Cui, et al., suggests that TRT may not lead to increased risk of prostate cancer.

Why all of this contradiction? Aren’t studies supposed to objectively provide an answer that formulary decision makers can use? The studies providing conflicting conclusions regarding risk of CV events are observational studies, not large-scale long-term randomized control trials.

Finkle, et al’s study regarding risk of prostate cancer is a meta-analysis of randomized controlled trials, although a single large-scale randomized controlled trial is needed to resolve the conflicts in data for risk of prostate cancer as well. —Krishna Rutvij Patel, Pharm D

References
Aetna Includes Medications In Weight-Loss Strategies

The insurer hopes two recently approved drugs — Belviq and Qsymia — will help people who do not get results from diet and exercise

By Frank Diamond

Let’s go out on a limb and say that it’s tough to lose weight. Let’s go even further out and explain that a great deal of people who do lose weight regain it. The 95% figure is often bandied about, but that might not be accurate for a lot of reasons (http://tinyurl.com/Times-weight), including the fact that people who tend to participate in weight loss clinical trials probably have tried everything else.

The harsh truth is that the one method of weight reduction that’s been proven effective is bariatric surgery. Surgery, though, is painful, costly, and can be problematic. “Like any surgery, there can be complications,” says Ed Pezalla, MD, MPH, the national medical director in charge of Aetna’s pharmacy policy and strategy. “There are failures. There are patients who have to get the surgery reversed. Bariatric surgery certainly has less morbidity and mortality now than it did several years ago, but it still has more morbidity and mortality than many other common surgical procedures.”

Aetna, like practically every other insurer in the country, operates wellness programs that aim to change lifestyles. When you “go on a diet,” after all, the implication is that you’ll go off it. But are surgery and wellness the only options? “Very little middle ground has been available that would help people if they’re trying hard with diet and exercise but are just not making it with those things alone,” says Pezalla.

Pezalla thinks there may now be that middle ground. Aetna is collaborating with the pharmaceutical companies Eisai and Vivus in a pilot program offering two recently approved weight-loss medications — Belviq and Qsymia. The drugs will be offered along with lifestyle support through Aetna’s healthy lifestyle programs and its CarePass Web site, https://www.carepass.com.

“The drugs provide a tool for people beyond diet and exercise — which is not easy — and surgery,” says Pezalla.

The medications are part of a three-prong approach. “The first is to tell employers and their employees about what’s already available,” says Pezalla. “Many of our larger clients are already purchasing wellness programs, metabolic screening programs, and health advisory programs from us. And all these things can help patients be healthier even if they don’t lose a lot of weight. If they eat healthier and exercise, this improves their outcomes as well.”

Members who qualify and begin treatment with Belviq or Qsymia receive free premium membership to the mobile app “Lose It!” by signing up through Aetna Navigator and CarePass.

And for employers that offer coverage for prescription weight-loss drugs, those medications are covered through the pharmacy benefit on the preferred tier 2, less expensive than the nonpreferred medications but more expensive than generics.

“Members must meet the criteria for the medication, which is consistent with the National Heart, Lung and Blood Institute guidelines, and also the package labeling from the FDA,” says Pezalla.

The move comes in the wake of the American Medical Association last June declaring obesity a disease, a step the AMA took against the recommendation of its Committee on Science and Health. The committee worries that the metric used to gauge obesity — the Body Mass Index — is imperfect and that unnecessary prescribing may follow. But a growing number of physicians say they wanted to improve coverage so that treatment could be extended to more patients.

Where it makes the most sense

Aetna’s program is geared toward self-insured companies.

“It’s easier to introduce something mid-year or mid-stream like this to a self-insured client
than it is to try and put it into an already formulated, fully insured benefit package that also would require a benefit change to be filed,” says Pezalla. “We placed the program where it makes the most sense. Also, we’re not charging for this pilot. The cost is entirely just in the drugs and in the physician’s office visits to monitor the members. We think this is a great opportunity for us to supplement and augment the wellness programs that we already offer to those clients.”

Pezalla says enrollees are expected by this month. “We intend to evaluate as many members as we can in the program for at least a year so that we can get a good read on what’s happening. By the end of the year, we might have some preliminary data.”

He hopes to have the pilot available to approximately 200,000 members. “That will give us a large enough number to understand the percentage of utilization,” says Pezalla. “We will also understand the impact on medical costs. We want to be able to get that kind of data so that we can guide our clients in the future because more of these medications are expected to be approved over the next couple of years. Some of them are going before the FDA fairly soon. There are going to be questions for us and we want to have valid answers for our clients.”

No specific launch date

Pazalla expects to have four or five companies enrolled by the end of the summer, though there is no cap on number of participants. “Companies are going to come in as they’re willing to. There’s no specific launch date, and there’s also no specific end date.”

The program does not target individuals. “This is a population-level approach,” says Pezalla. “We make the drugs and all the other tools available and accessible as covered benefits for people. The members have the choice and are encouraged to talk to their doctors. We’re not telling people they should be using the medicines.”

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The coagulation system is an amazing cascade consisting of more than a dozen reactions mediated by a number of compounds with names such as “factors,” “regulators,” and “cofactors.” Defects in this system result in bleeding, a condition called hemophilia.

Biblical era references describe a bleeding tendency among male children born into the same family. In the early 1800s, scientists found how the X and Y chromosomes determined the sex of offspring as well as how hemophilia is transmitted. Two factors, VIII and X, are on the X chromosome.

Since males only have one X chromosome, a defect of a critical gene on this chromosome will primarily affect males. Females would need to inherit two defective X chromosomes to express this disease, clearly rare if the incidence of the disease is rare.

No cure

There are two main types of hemophilia. The most common is hemophilia A, caused by a deficiency in the function of factor VIII, with an incidence of 1 in 5,000 births. Hemophilia B, a deficiency in the function of factor IX, is much more rare, with an incidence of 1 in 25,000 births. About 18,000 people in the United States have various forms of hemophilia, with approximately 400 babies born each year with one of the diseases.

If insufficient factor is not available or if the factor is defective, the clotting function can be partially or totally inadequate to prevent spontaneous or traumatically induced bleeding. There is no cure for hemophilia. The first effective treatments (late 1950s) consisted of fresh frozen plasma (FFP) for both A and B. FFP contained many of the proteins in the blood, including factors VIII and IX.

Advances in treatment

But because there is only a very small quantity of factor VIII and factor IX in FFP, large quantities were required to treat a bleed; this necessitated admission to the hospital for therapy. Later it was discovered that by freezing and slowly thawing plasma, a more concentrated “cryoprecipitated plasma” form of factor could be obtained. The next significant advance was when, in the 1980s, scientists discovered ways to separate factor VIII from factor IX. These discoveries paved the way for patients to treat their disease at home.

Because treatment required the use of a human product, many patients were exposed to HIV and hepatitis viruses until the advent of screening laws and techniques. In the late 1980s, the discovery of the way to transfer human genes into other organisms ushered in the biologic age and shortly afterward, the first clinical trials utilizing factor VIII derived with recombinant DNA were started. By 1992, two manufactured factor A products were approved by the Food and Drug Administration.

The original protocols for treatment of hemophilia were reactive: Treatment was started after a significant bleed, typically into a joint. Boys with hemophilia were cautioned to avoid virtually any physical activity and especially sports. But later studies revealed that prophylactic treatment could significantly reduce the amount of joint destruction and allow young men to participate in more physical activities.

Some need daily infusions

Hemophilia treatment intervals are based on the severity of the hemophilia. People suffering from milder forms may require treatment only...
occasionally, prior to surgery or after trauma. Those with very low hemophilia factor levels may need infusions as often as daily, but typically about every two days, which creates a significant burden to those suffering from hemophilia. Patients have longed for a less-frequent infusion interval, but factors degrade rapidly and must be replenished often. Recently, the FDA approval of Eloctate, manufactured by Biogen Idec, has given hope to many hemophilia A patients for a much less laborious schedule.

**Significant treatment**

Eloctate, a recombinant, Fc fusion protein, is indicated for the control and prevention of bleeding episodes, perioperative management, and routine prophylaxis to prevent or reduce the frequency of bleeding episodes for hemophilia A (factor VIII deficiency). The manufacturer calls it the first significant hemophilia A treatment advancement in more than 20 years.

The novel approach used for the creation of this new drug is to start with factor VIII and delete the B-domain. The resulting active portion of factor VIII is fused to the Fc portion of immunoglobulin G subclass 1 (IgG1). The body is rather stingy with IgG molecules and basically has a natural process to avoid the rapid metabolism of these proteins.

By fusing the active portion of factor VIII to the IgG1, the body treats it like other immunoglobulins and allows it to recirculate for a much longer period than natural or recombinant factor VIII.

**Frame of reference**

The weight-dependent starting dose of Eloctate for an acute bleed is based on the desired rise of factor VIII, calculated from a formula in the prescribing information. For routine prophylaxis, the dose is 50 IU/kg every four days and can be adjusted based on the patient’s response. Just as a frame of reference, an empirical finding discovered that 1 IU of factor VIII per kg body weight raises the plasma factor VIII level by 2 IU/dL.

Eloctate was studied in two phase 3 trials: a pharmacokinetics study and a clinical study. The clinical study to determine safety and efficacy consisted of a multicenter, prospective, open-label trial including 165 previously treated male patients with severe hemophilia A, defined as less than 1% endogenous factor VIII activity or a genetic mutation consistent with severe hemophilia A. The study endpoints were efficacy of each of two prophylactic treatment regimens (individualized interval and fixed weekly) compared to episodic, on-demand treatments.

A total of 757 bleeding episodes, mostly spontaneous bleeds into joints, in 106 subjects were treated with Eloctate. There were also nine patients who had scheduled major surgical procedures included in the trial.

The results of the trial demonstrated that prophylactic treatment resulted in only about one tenth the number of bleeds overall, compared to on-demand treatment. Also of note is that an individualized approach is better than a fixed-interval dose. The projected annualized bleeding rates were 1.6 in the individualized prophylaxis arm, 3.6 in the weekly prophylaxis arm, and 33.6 in the on-demand arm.

The actual number of infusions per year was also much more infrequent. The National Hemophilia Foundation guidelines suggest about 150 to 180 infusions per year. Eloctate will significantly reduce this burden. In the individualized treatment arm, 99% of subjects were able to infuse every three days or longer, 35% achieved a dosing schedule of four days or longer, and 29% achieved a dosing schedule of five days or longer. Some could be controlled by weekly infusions.

**Hopeful change**

Given that most children afflicted with severe hemophilia A receive an infusion every other day, the opportunity to move to twice per week or even less often is certainly welcome. With significantly fewer bleeds, the clinical trial for Eloctate reinforced the prophylactic approach over the on-demand approach. Eloctate fulfills the promise of Tomorrow’s Medicine.
Within five years, more than two thirds of all payments are expected to be based on measures of value, as payers and providers move away from fee-for-service payment, according to research commissioned by McKesson Health Solutions.

For the report *The State of Value-Based Reimbursement and the Transition from Volume to Value in 2014*, ORC International, a consultant specializing in research and business intelligence, interviewed executives from 114 payers and 350 providers.

From the interviews, ORC estimated the percentage of payments in fee for service, capitation, pay for performance, episodes of care/bundled payment, global payment, and other methods, such as shared savings.

ORC also used the interview results to estimate how the percentages would change in two years and in five years. Note that both payers and providers predict FFS will decline from 56% and 52% to 32% and 34%, respectively. Below are payers’ and providers’ estimates.

**Research shows transition from volume to value**

**PAYERS**
Mix of payment models

**PROVIDERS**
Mix of payment models

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Source: *The State of Value-Based Reimbursement and the Transition from Volume to Value in 2014*, ORC International