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CMS Star Ratings:

A Health System's Approach to Exceeding Expectations

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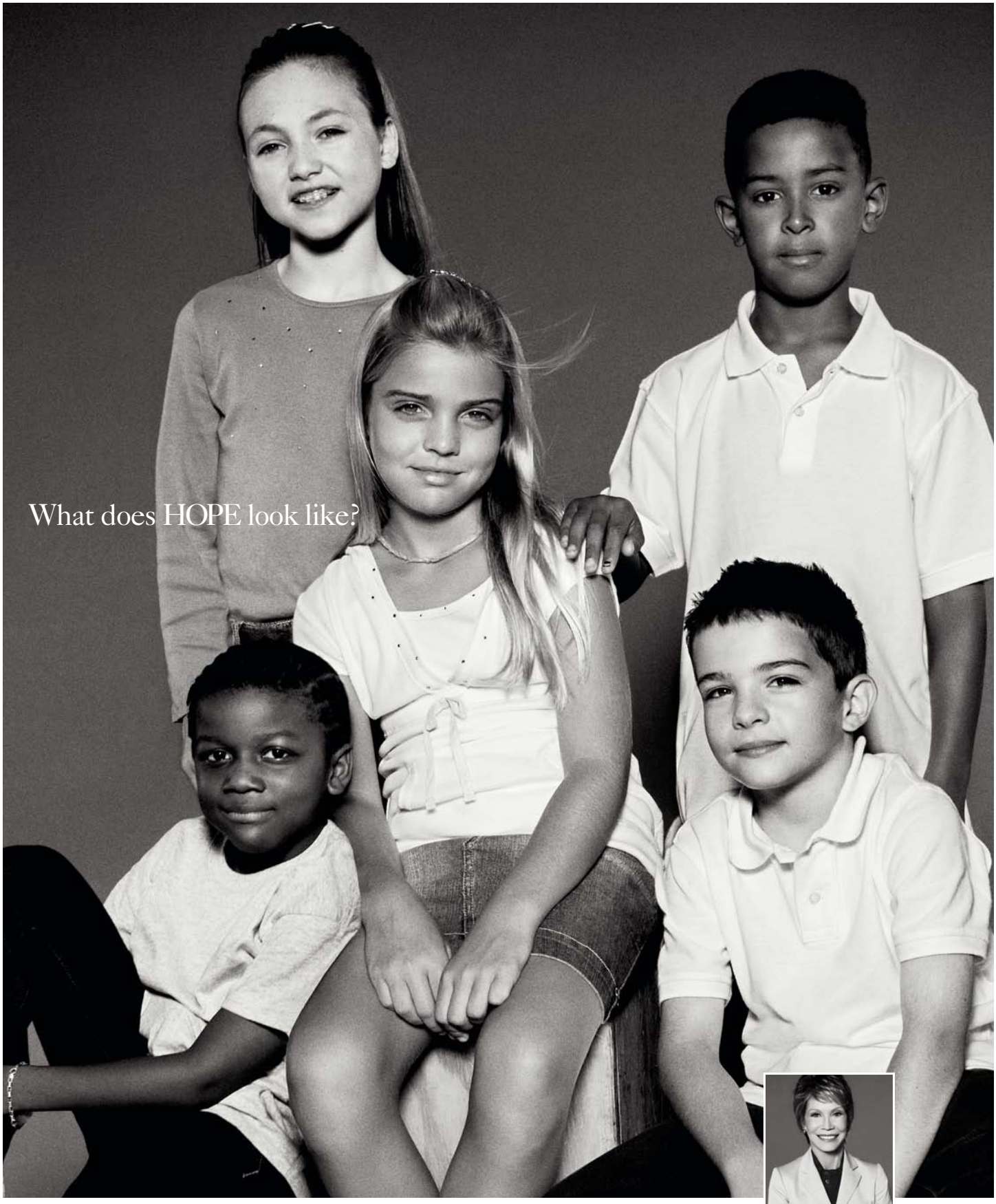

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CDMI REPORT

ISSN: 2159-5372

PUBLISHED BY:
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WELCOME

to this issue

features

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CDMI PEER REVIEW PROCEDURE

CDMI is committed to publishing high-quality, reliable, and honest manuscripts. For this reason, all of our publications are put through a meticulous peer-review process. Although the final decision to accept or reject the manuscript is made by the editors, the recommendations of our experienced reviewers and editorial committee are greatly considered. The reviewers act as consultants and do not receive additional benefits depending on the amount of manuscripts they accept or reject. They are asked to comment on scientific accuracy, composition, originality, and potential interest to readers. Our editors are constantly evaluating the reviews for thoroughness, persuasiveness, and fairness to ensure an unbiased approach.

The procedure is as follows:

- ☐ The manuscript is initially screened by the editor-in-chief and the executive editor. Works deemed unsuitable for our publication will be returned to the authors with a detailed letter explaining our reasons.
- ☐ If potentially acceptable, the manuscript will then be distributed to at least two outside reviewers of the executive editor's choosing. Our reviewers are extensively trained in medical literature analysis and their expertise has proven to be a valuable asset. The executive editor may also decide to submit the manuscript to an expert in the associated field.
- ☐ The comments from the reviewers will then be compared. Manuscripts that pass the peer-review process will undergo a final review by the editorial committee. If a manuscript passes this final stage, it will be added to the CDMI database and be a candidate for publication. Rejected manuscripts will then be returned to the author with a detailed letter explaining the reason for rejection. If there is still interest in the manuscript but editing is required, the reviewer's comments will be assessed by the executive editor. If the executive editor agrees with the comments and recommendations, the notes will be forwarded back to the author for appropriate modification of material.
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- ☐ CDMI retains the right to deny any work not deemed appropriate for our publication. This may include scientifically excellent manuscripts viewed as too specialized for our readers or not pertaining to the managed care industry.
- ☐ After approval of the manuscript and with the intent of CDMI to publish, the author will then be notified and compensated appropriately.

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To inspire the reviews to be as critical and honest as possible, CDMI does not divulge the names of the reviewers of specific manuscripts. It is our impression that confidential reviewers are ideal for this procedure because they can feel free to be more candid and rigorous with their recommendations. Comments that may be hostile, belligerent, or unreasonable will not be transmitted back to the author. We will not withhold the author's identity from the reviewers unless otherwise requested by the author.

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Letter from the President

Susan Petrovas

Dear Managed Care Colleagues,

Susan Petrovas, RPh, President

Since the initial launch of *CDMI Report* in 2010, we have been striving to exceed industry standards in healthcare communications and provide an unbiased, reliable, and concise publication tailored to fit the needs of today's managed care executive. It is our goal to provide the most pertinent clinical and cost-saving strategies that the healthcare industry has to offer.

Thanks to all the great feedback from our friends and colleagues in managed care, *CDMI Report* has become a trusted resource for healthcare professionals across the country. We are pleased to announce that—because of your help—*CDMI Report* has been recognized as a leader in healthcare communications and has received several prestigious industry awards. Among the awards are:

We value your comments and feedback. Please feel free to contact me directly at **SPetrovas@CDMIhealth.com.**

2012 Hermes Creative Award—Platinum Award Winner

The Hermes Creative Awards program is an international competition for the content and design of traditional materials, as well as emerging technologies. The entries are judged on creative achievement and overall excellence.

2012 Aster Award—Gold Award Winner

The Aster Awards is a medical marketing awards program that recognizes outstanding excellence in healthcare advertising and other materials in the healthcare field. Winning entries, which are judged by a diverse panel of experts, are published in *Marketing Healthcare Today* magazine.

2012 Communicator Award—Award of Distinction

The Communicator Awards is an international awards program that recognizes creative excellence in the communications field. Entries are judged on quality, creativity, and resourcefulness, with an "award of distinction" signifying that the project exceeds industry standards.

We are proud to share all of these awards with our readers, and strive to continue providing valuable and relevant healthcare information. If you ever have any comments or suggestions as to how we can better meet your specific informational needs, please feel free to contact me directly at **SPetrovas@CDMIhealth.com.** As always, thanks for reading!

Sincerely,

Susan C. Petrovas, RPh
President, CDMI

CALL FOR SUBMISSIONS

The goal of *CDMI Report* is to empower managed care decision makers to appropriately and responsibly manage their chronically ill patient populations, while reducing overall healthcare costs. As healthcare is rapidly transitioning into a more accountable industry, a collective ambition to improve quality of care and patient well-being is fueling the expansion of clinical programs and healthcare reform throughout the managed care environment. *CDMI Report* strives to achieve excellence in communicating the most effective and pertinent healthcare strategies the industry has to offer. To continue on this path to excellence, the publishers of *CDMI Report* invite our readers to share their innovative solutions to chronic disease management by submitting articles for peer review.

CDMI Report invites article submissions pertaining to the following subjects:

- Accountable Care Organizations and Patient-Centered Medical Homes
- Chronic Disease Management and Education
- Clinical Effectiveness Research
- Clinical Guideline Updates/Reviews
- Compliance/Adherence Programs
- Cost-Benefit Research of Pharmaceuticals and Healthcare Strategies
- Cost-Containment Strategies for Managed Care
- Emerging Industry/Pharmacologic Trends
- Healthcare Reform Analysis
- Health Information Technology
- Innovations in the Managed Care Pipeline
- Literature Review
- Outcomes Data Analysis
- Pharmacoepidemiological Research
- Quality-Improvement Initiatives (HEDIS Measures and Star Ratings)

Disease States of Special Interest:

- Alzheimer's/Aging
- Asthma/COPD
- Cardiovascular Disease
- Diabetes
- Gastrointestinal Conditions
- Obesity
- Osteoarthritis
- Osteoporosis
- Overactive Bladder
- Mental Health
- Pain Management

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To learn more about CDMI and to view this publication online, visit us at **www.CDMIhealth.com.**

Please send articles for consideration to **TLord@CDMIhealth.com.**

MANAGED CARE NEWSSTAND

Reduced Lung Function Linked to Serious Cardiac Complication

Difficulty breathing may not be the only problem facing patients with poor lung function and obstructive airway disorders, such as chronic obstructive pulmonary disease (COPD). A recent study reported that these pulmonary conditions also increase the risk for heart failure.

Researchers drew data from the Atherosclerosis Risk in Communities (ARIC) Study. They analyzed the relationship between obstructed airways and heart failure in about 13,000 people ages 45 to 64 during a 15-year period. After adjusting for age, prior heart disease, smoking, and other cardiovascular risk factors, the authors found that the risk for heart failure increased as lung function decreased.

The researchers say that more studies are needed to determine if interventions to slow COPD progression and improve lung function reduce the risk for heart failure.

Source: Agarwal SK, et al. Airflow obstruction, lung function, and risk of incident heart failure: The Atherosclerosis Risk in Communities (ARIC) Study. *Eur J Heart Fail.* 2012;14(4): 414-422.

ARIC STUDY
Researchers found that the risk for heart failure increased as lung function decreased.

Stroke Risk Rises with Long-Term Diabetes

Patients' risks of ischemic stroke may increase the longer that they have diabetes. Researchers recently reported the results of a study of more than 3,000 participants involved in the Northern Manhattan Study. Data showed that stroke risk rose 3 percent each year that they had diabetes. The risk for patients who had diabetes 10 years or longer was triple the risk of those without diabetes.

3 PERCENT
Patient's stroke risk rose 3 percent each year that they had diabetes.

The researchers say that their findings could be a predictor of future public health problems. Although stroke rates have been declining among those with diabetes, the rise in diabetes could eventually lead to more strokes. The study emphasizes the importance of promoting healthy habits to help prevent or delay diabetes.

Source: Banerjee C, et al. Duration of diabetes and risk of ischemic stroke: The Northern Manhattan Study. *Stroke*. 2012;43(5):1212-1217.

Lifestyle Counseling Has Dramatic Impact on Diabetic Patient Outcomes

Persistent and frequent lifestyle counseling may help diabetic patients reach critical treatment goals faster. Researchers conducted a retrospective cohort study of more than 30,000 patients with diabetes. They looked at the impact of lifestyle counseling in the primary care setting on diabetic patients with high blood glucose, blood pressure, or cholesterol levels.

The study found that participants who received ongoing diet, exercise, and weight-loss counseling for at least two years lowered their glucose, blood pressure, or cholesterol levels faster than those who received less frequent counseling. For example, those who received personal counseling once or more a month achieved HbA_{1c} levels below 7 percent in three and a half months. Participants who had counseling less than once every six months took 22.7 months to meet their HbA_{1c} goals.

The researchers encourage physicians to explore efficient methods of providing this vital counseling. They suggest offering support in group settings and incorporating the use of physician assistants, nurse practitioners, and dietitians.

Source: Morrison F, et al. Lifestyle counseling in routine care and long-term glucose, blood pressure, and cholesterol control in patients with diabetes. *Diabetes Care.* 2012;35(2):334-341.

Multiple Brain Scans for Stroke Patients Redundant and Costly

Widespread—and sometimes redundant—brain scans are contributing to increasing costs for stroke care. A recent study looked at the utilization of neuroimaging scans in more than 600,000 stroke patients in 11 states between 1999 and 2008. Researchers found that the use of magnetic resonance imaging (MRI) rose in all states, but utilization varied widely from state to state. In addition, 95 percent of stroke patients who had MRIs also had computed tomography (CT) scans.

MRI scans are more accurate than CT scans in diagnosing strokes. They are also more expensive and time consuming. From 1999 to 2007, MRI costs increased by 413 percent. In 2007, 9 percent of total hospital costs were due to MRIs.

The researchers say that MRI scans are supplementing, rather than replacing, CT scans, and that reducing the use of duplicate scans could lower healthcare costs and improve efficiency.

Source: Burke JF, et al. Wide variation and rising utilization of stroke magnetic resonance imaging: Data from 11 states. *Ann Neurol.* 2012;71(2):179-185.

Giving Consumers Better Information Helps Them Choose High-Value Healthcare

A new study sheds light on how consumers make value-based healthcare choices and what can be done to encourage consumers to make more cost-effective selections. A team of researchers found that consumers who were provided with information on cost alone equated higher quality with higher prices and lower quality with lower prices. The authors noted that linking cost to quality is not a valid association because higher costs may not necessarily signal better care.

The researchers studied how more than 1,400 employees responded to different messages about the cost and quality of medical care. They found that consumers who were presented with cost information alone were more likely to choose the most expensive options. However, consumers who received strong and clear information on quality alongside cost data were more likely to choose high-value providers that offer high-quality care at lower costs.

These findings suggest that the presentation of healthcare costs and resources plays a large part in how consumers interpret that information. Cost data that is presented with easy-to-understand quality data can help consumers make high-value choices.

Source: Hibbard J, et al. An experiment shows that a well-designed report on costs and quality can help consumers choose high-value health care. *Health Affairs.* 2012;31(3): 560-568.

Integrating the Patient-Centered Medical Home and Health Information Technology

Focusing on technological improvements and patient-centered care are not incompatible goals, according to the authors of a recent report emphasizing the importance of integrating these two important components of healthcare practices.

The authors reviewed literature from medical journals and brought providers, researchers, and other key stakeholders together to share their experiences of transitioning from traditional primary care to a patient-centered medical home (PCMH) model of care. They found that health information technology (HIT) supports some PCMH principles, but not all technologies have functions that facilitate the PCMH.

The researchers say that the redesign and implementation of new HIT in primary care settings should facilitate patient-centered care and enhance provider-patient relationships, access, communication, and patient engagement.

Source: Leventhal T, et al. The patient-centered medical home and health information technology. *Telemed J E Health.* 2012;18(2): 145-149.

Aiming for the Stars: A Health System's Approach to Improving Quality of Care

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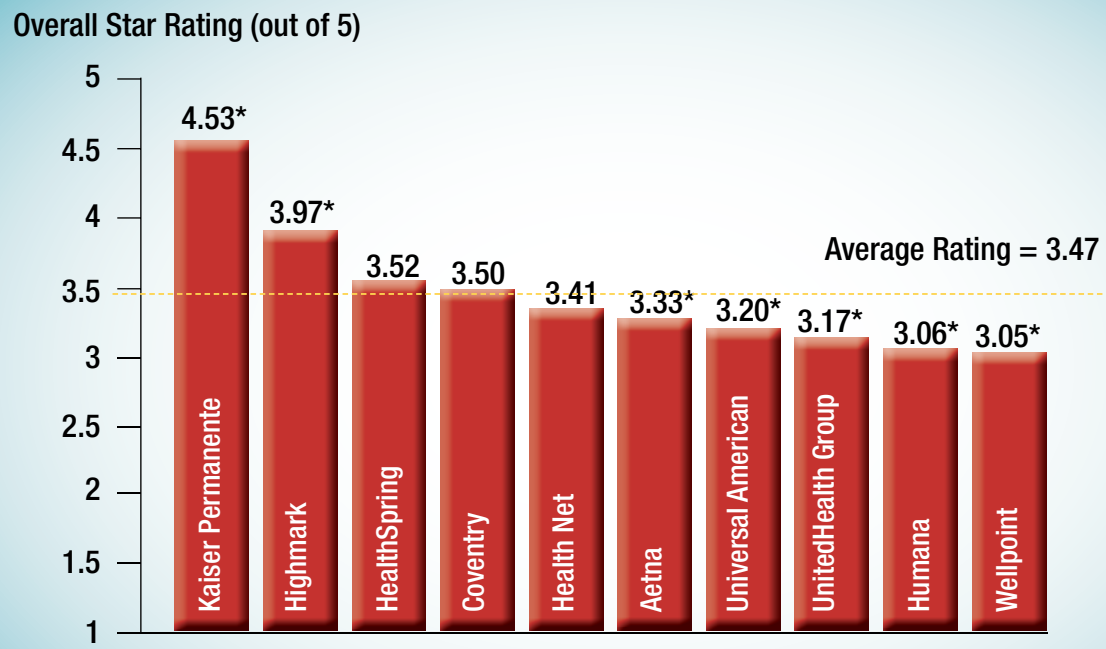
The Centers for Medicare & Medicaid Services (CMS) is expanding its value-based purchasing strategy to Medicare Part D. As part of this, reimbursement for Medicare Advantage Prescription Drug (MAPD) Plans will drop. With this transition, plans will be increasingly focused on achieving the safety and quality goals of the CMS Five-Star Quality Rating system. These quality ratings will be used to identify high- and low-performing MAPD plans, and will provide high-performing plans with adjusted bonus payments.[1]

Starting in 2017, plans that have a five-star rating will receive a 5 percent bonus, while those with a three-star rating or higher will receive a bonus commensurate with their ranking (for example, a plan that receives three and one-half stars will get a 3.5 percent bonus).[1] It is estimated that the per-member per-month payment difference between a three- and a five-star plan will be $16. Extrapolated to a plan with 1 million MAPD enrollees, this figure represents up to $200 million in new revenue annually.[1]

This is a wake-up call for MAPD plans in the United States. As shown in Figure 1, in 2011 the quality ratings achieved by the country's highest-enrolled plans varied substantially.[2] Although average summary scores have increased over time, in 2011 only 15 percent of 523 plans nationwide had ratings meeting or exceeding four stars.[2]

CMS Star Ratings assess patient outcomes, patient-reported experience and customer service, adherence to regulatory requirements, and specific clinical prevention and improvement measures.[3] Because CMS Star Ratings data is calculated on a two-year delay (i.e., 2013 rankings will be based on

Fig. 1 **2011 Star Quality Ratings Across Medicare Advantage Plans with the Highest Enrollment[2]**



Note: No statistical comparisons were made between organizations. Asterisks (*) denote differences that are significantly different from the mean p<0.05 level. Includes HMOs, local PPOs, regional PPOs, and PFFS plans.
Source: Kaiser Family Foundation analysis of the 2011 Medicare Health Plan Quality and Performance Rating

2011 data), it is important for MAPD plans to act now to make the changes necessary to improve their scores and impact future reimbursement.[3]

2013 and 2014 Proposed CMS Star Score Measures and Weighting

Each CMS Star metric is assigned a weighted value, ranging from one to three, with outcomes- and intermediate outcomes-related measures having the highest value. Patient experience and/or complaint measures, as well as measures of patient access, have a value of 1.5, while process measures have a one-point weighting.[4,5]

Table 1 (page 12) summarizes proposed 2013 Star Rating metrics, stratified by weighting categories. Of note, two new measures (the outcome measure "Improvement" and the patient experience and complaint measure "Consumer Assessment of Healthcare Providers and Systems [CAHPS] survey measure of care coordination") have been assigned a value of one for the first year they are measured. In 2014, these items' ratings will be updated to match their weighting category. Table 2 (page 13) provides summary details of these new measures.[4]

CMS is also considering adding the following to its 2014 plan ratings: measures from the Hospital Inpatient Quality Reporting Program; use of highly rated hospitals by plan members (Part C); medication therapy management (MTM) program (Part D); grievance rate per 1,000 enrollees (Part C and D); serious reportable adverse events (SRAEs) and hospital-acquired conditions; and a Special Needs Plans (SNP) care management measure (Part C).[4] For 2013, these metrics will be calculated and published as display measures.

Research indicates that a number of plan characteristics are associated with higher CMS Star scores, including more experience, nonprofit status, urban location, relatively high Medicare Advantage penetration, and plans

CMS STAR RATINGS *continued*

Table 1 — **CMS 2013 Star Ratings: Summary of Proposed Measures[4]**

Outcome Measures (3.0 points)	• Improving or maintaining: a) physical health; b) mental health* • Plan all-cause readmissions • Improvement**
Intermediate Outcome Measures (3.0 points)	• Diabetes care: a) blood glucose controlled; b) cholesterol controlled* • Controlling blood pressure • High-risk medication • Diabetes treatment*** • Part D medication adherence: a) oral diabetes medications; b) hypertension (ACEI or ARB); c) cholesterol (statins)*
Measures Capturing Access (1.5 points)	• Beneficiary access and performance problems • Plan makes timely decisions about appeals • Reviewing appeals decisions • Call center: a) foreign language interpreter and TTY/TDD availability; b) pharmacy hold time* • Appeals: a) auto-forward; b) upheld*
Patient Experience and Complaint Measures (1.5 points)	• Getting needed care • Getting appointments and care quickly • Customer service • Overall rating of healthcare quality • Overall plan rating • Complaints: a) about the plan; b) about the drug plan* • Members choosing to leave the plan • Getting information from drug plan • Rating of drug plan • Getting needed prescription drugs • CAHPS survey measures of care coordination**
Process Measures (1.0 points)	• Breast cancer screening • Colorectal cancer screening • Cardiovascular care—cholesterol screening • Diabetes care—cholesterol screening • Glaucoma testing • Annual flu vaccine • Monitoring physical activity • Adult BMI assessment • Care for older adults: a) medication review; b) functional status assessment; c) pain screening* • Osteoporosis management in women with fracture history • Diabetes care: a) eye exam; b) kidney disease monitoring* • Rheumatoid arthritis management • Improving bladder control • Reducing the risk of falling • Enrollment timeliness • MPF price accuracy

* Each item listed is a separate measure.
** These measures have been assigned a score of 1.0 point for 2013.
*** In 2013, CMS will test adding direct renin inhibitors to this specification.
ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMI = body mass index; CAHPS = Consumer Assessment of Healthcare Providers and Systems; MPF = Medicare Plan Finder

Table 2

Summary of Two New 2013 Star Rating Measures[4]

1. Measures of care coordination from the Consumer Assessment of Healthcare Providers and Systems (CAHPS) survey administered in 2012 (Part C), including questions related to the following areas:

- Whether doctor had medical records and other information about the enrollee's care
- Whether there was follow-up with the patient to provide test results
- How quickly the enrollee received test results
- Whether the doctor spoke with the enrollee about prescription medicines
- Whether the enrollee received help managing care
- Whether the personal doctor is informed and up to date about specialist care

2. A measure of quality care improvement (Part C and D)

Prior to creating a measure of net improvement at the contract level, the proposed methodology will calculate improvement at the individual level and use statistical tests to determine whether there has been significant improvement or decline. The steps are:

- For each measure that has been collected for two years using the same specifications, calculate a contract-level improvement score. This will be a simple change from year one to two.
- Perform a t-test for the year-to-year change at the measure level. Score the change as significant decline, no change, or significant improvement.
- Multiply the number of significant improvements/declines by the respective measure weights and net the improvements (e.g., number of significant improvements minus number of significant declines).
- Score the net improvement/decline count into a five-star classification by examining the distribution and setting cut points.

All contracts with at least two years of data would receive an improvement score. CMS has not determined how to account for contracts already achieving high scores; however, the final methodology will not penalize high-performing plans and will not reward improvement over attainment.

that are health maintenance organizations (HMOs) and/or that provide patient-centered care or a medical home.[2] Since one of the biggest factors stifling efficient healthcare delivery in the U.S. is a fragmented system and lack of coordinated care,[6] it is expected that integrated approaches to patient management will be an essential component of any successful plan.[5]

An Integrated Approach to CMS Star Success

Since successful CMS Star Ratings remain the exception and not the rule, it is important to share information on strategies to improve overall ratings for MAPD plans.

Denver Health and Hospital Authority (DHHA) is an academic, public health system, and is Colorado's largest safety net institution. It serves 30 percent of Denver's adults and 40 percent of its children; three-quarters of its patients are below 185 percent of the federal poverty level, and nearly 50 percent are uninsured. Denver Health encompasses an acute care hospital, nine federally qualified health centers, 14 school-based clinics, nurse-staffed patient help lines, centralized patient appointment and translation services, and has a salaried medical staff. Because its physicians are employees, they do not have financial incentives to overuse procedures, which can increase costs and reduce efficiency. Also included under the DHHA umbrella is Denver Health Medical Plan Inc. (DHMP).[7,8] DHMP offers Commercial, Child Health Plan Plus, Medicaid Choice, Medicare Choice, and Medicare Select plans.

DHHA's pharmacy department comprises eight outpatient pharmacies that work collaboratively with DHMP Pharmacy Services. The DHMP Pharmacy Services team helps to ensure that patients receive integrated, timely, and coordinated care—steps that consequently lead to improved CMS Star outcomes. DHMP Pharmacy Services works to provide value-added benefits to members to improve the quality of care already provided by DHHA.

Being part of an integrated system allows DHMP to enjoy certain advantages that facilitate quality

Expanding staff

DHMP created several new, targeted staff positions to address reporting requirements. A new Clinical Project Manager is responsible for tracking CMS Stars and other key metrics. In pharmacy, a Clinical Pharmacist position has been created to focus on MTM management, medication adherence, as well as comprehensive medication reviews (CMRs). Also new is a Pharmacy Intervention Manager, who is both a licensed practical nurse and a pharmacy technician.

improvement efforts, including access to the DHHA electronic medical record system, which is shared by all providers and pharmacies.[7,8] Additionally, DHMP provides multiple services under one roof. These services include:

- Pharmacy Services
- Case Management
- Complex Case Management
- Health and Wellness
- Care Support
- Quality
- Member Services
- Finance
- Compliance
- Government Programs
- Information Services
- Marketing
- Provider Relations

Close contact among these various departments enhances DHMP's ability to work collaboratively and enables rather than discourages innovation and the system-wide incorporation of best practices. For example, the DHMP Pharmacy Services team has access to comprehensive patient records; this, in addition to daily provider and pharmacy correspondence, facilitates greater staff engagement and cross-consultation in patient management.

All of DHMP's improvement initiatives emerge from an overarching goal of facilitating improved patient care. If patients are not engaged with their healthcare, they will not engage with their treatment. To this end, managed care staff members across DHMP are trained in motivational interviewing and patients are referred to complex case managers, health coaches, psychologists, nurse case managers, and/or pharmacists to stimulate behavior change and improve interventions. Most recently, DHMP has introduced a care support team. This team provides patient navigation services—for example, helping to make appointments and arrange transportation as needed. If patients attend their visits, they will receive appropriate care and, as a result, better outcomes are anticipated. In addition to laser-like strategies aimed at specific disease states or other specific quality measures, this coordination of care encourages improved overall access.

Initially, DHMP's greatest challenge to addressing CMS Star measures was a lack of institutional knowledge regarding the program. Historically, the quality department understood the CMS Star Ratings system, but the importance of the information was not effectively understood by the majority of the medical management team. Staff trainings were conducted to address gaps in knowledge. This was critical for the pharmacy department, as Medicare Part D CMS Star requirements have increased substantially over the past several years. By incorporating a knowledge-sharing approach, DHMP was able to initiate an organization-wide discussion regarding quality goals; this has encouraged employees to take a proactive stance in anticipating forthcoming CMS measures. Simultaneously, DHMP developed an internal tracking mechanism to follow its weighted performance on all CMS Star measures, both historically and in a more real-time fashion. The health system also uses Toyota-developed lean management strategies, which heightened its ability to work in teams, rapidly identify problems, and implement solutions.

Alongside improving overall internal expertise, DHMP created several new, targeted staff positions to address reporting requirements. Within the quality department, a new Clinical Project Manager is responsible for tracking CMS Stars and other key metrics. In pharmacy, a Clinical Pharmacist position has been created to focus on MTM management, medication adherence, as well as comprehensive medication reviews (CMRs). Also new is a Pharmacy Intervention Manager, who is both a licensed practical nurse and a pharmacy technician and was previously a DHMP Medicare broker. In his role as a Medicare broker, he was responsible for enrolling new patients and initiating DHMP's relationship with them.

These staff roles will help DHMP reach its CMS Star goals, but even more importantly, they will ensure that patients receive appropriate, coordinated care—something that a high completion rate of MTM assessments will not accomplish in and of itself.

It is also crucial for health systems to consider the expertise that external vendors can bring. For example, DHMP contracts with a pharmacy benefit manager who is well-versed in CMS policies and procedures. This saves staff time and ensures that all essential memos and deliverables are appropriately monitored.

All of this work complements internal efforts to enhance efficient, patient-centric care. The majority of DHMP's Medicare patients have barriers to effective care, most notably financial concerns and limited health literacy. Although DHMP has historically performed well on measures related to appropriate prescribing (it has a five-star rating for the Part D "Diabetes Treatment" metric, which measures appropriate use of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers in patients with both diabetes and hypertension),[9] ensuring treatment adherence presents a challenge. When the health system evaluated its patient population, drug copayments were a substantial barrier, particularly for patients on multiple medications. Several teams worked together to tackle this problem, and one response has been to encourage patients to fill 90-day prescriptions. This approach saves out-of-pocket costs and travel time. Also, the initiative's outreach and marketing strategies were developed in consultation with patients. The response has been universally positive, with patients themselves now providing substantial word-of-mouth referrals.

Currently, DHMP is exploring ways to address the CAHPS care coordination measure being incorporated into the Star Ratings. Patients with limited health literacy can find it problematic to successfully complete this survey. CAHPS language also tends to be primary provider-centric, which can confuse patients who receive coordinated care from multiple providers. DHMP has implemented an internal health literacy committee to ensure that all internally generated patient communications match its population's literacy levels. However, it is not possible to adjust the language in official CMS documents. To improve its CAHPS outcomes, DHMP has focused on two areas: First, it strives to ensure that every communication or outreach activity with patients is positive, provides benefit, and leads to better overall care coordination. Second, since CAHPS allows for oversampling, the medical plan has progressively increased its sample size. The health system hopes that a more representative patient data set will lead to improved mean results.

At DHMP, the integrative focus is not limited to systems management; quality goal achievement is also part of the focus. By identifying areas where goals overlap, DHMP can focus its efforts on broad intervention themes—in addition to discretely measured items. For example, if medication management is improved, better HbA_{1C} and low-density lipoprotein scores will follow. In addition, when making decisions, it is important to have all the players in the room, including physicians, nurses, pharmacy, quality, case management, and finance.

Integration has turned out to be the key to DHMP's quality improvement efforts. The health system strives to achieve excellent CMS Star Ratings, but its primary goal is to provide patients with excellent care. The more successfully integrated the system becomes, the better it can achieve both of these goals.

Editorial assistance for this article was provided by Caitlin Rothermel.

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Enhancing Adherence through the Patient-Provider Relationship

Bruce A. Berger, PhD, President, Berger Consulting, LLC, Professor Emeritus, Auburn University; and Debra Gordon, MS

For managed care plans, physician offices, hospitals, and pharmaceutical companies, the issue of patient nonadherence to treatment regimens is one of the most costly and frustrating components of patient care—one that can no longer be ignored.

The New England Healthcare Institute, a nonprofit health policy organization, conservatively estimates that nonadherence to medication regimens costs the U.S. healthcare system $290 billion a year.[1] However, there can be an even greater cost for health plans and physician practices given the growing number of pay-for-performance programs and quality initiatives that rely on outcomes. These outcomes, including medication adherence, blood glucose levels, and readmission rates, all rely on patient adherence for success.

While there are numerous reasons for nonadherence, including psychosocial, economic, and treatment-related barriers, one of the most important barriers has to do with patients' understanding and acceptance of their illnesses and their willingness to change health behaviors, including their lifestyles. Unfortunately, the directive communication style that most clinicians use, in which patients are told what to do, when to do it, and what will happen if they do not do it, does not work effectively to change behavior, and often alienates the patient.

Promoting adherence, whether to medication regimens, a weight-loss plan, a healthier diet, smoking cessation, or physical activity—the underpinnings of nearly every chronic disease—requires behavior change.

Motivational Interviewing to Improve Behavioral Change

One set of skills that can promote behavior change is motivational interviewing (MI). First developed for use in the addiction treatment field, it is now in the forefront of healthcare as an important component in helping patients manage chronic health conditions.

MI is a patient-centered method of identifying and enhancing the patients' internal commitment to change by exploring and resolving any ambivalence and/or resistance they may have while focusing on the three key components of motivation: importance, confidence, and readiness.[2] These key components are described in more detail in the box on page 19.

As an approach to patient care, MI changes the way healthcare

Bruce A. Berger, PhD

professionals communicate with their patients. Numerous managed care organizations, pharmacies, and even the military are training their healthcare staffs to use MI skills, due to the growing body of evidence demonstrating its effectiveness.

Studies find that MI generally works better than traditional treatment in eliciting change and improving outcomes, particularly if providers undergo a sufficient amount of training to refine their communication skills. It can be used in brief five-to-15 minute encounters and can be effective in just one to three sessions.[3] After more than 20 years of research, MI has demonstrated improved clinical and behavioral outcomes in nearly all aspects of chronic disease management—including weight loss, physical activity, nutrition, and medication adherence—and in the most common chronic medical conditions: hypertension, hypercholesterolemia, diabetes, and obesity.[4]

One multidimensional meta-analysis of 30 randomized clinical trials in which MI was used to change behavior in the addiction, diet, or exercise realms found a significant benefit compared to no-treatment/placebo-controlled trials ($P<0.05$). The effects were long lasting, with similar benefits at 20 weeks and 67 weeks post-intervention, and demonstrated significant clinical benefits compared to usual care. For instance, MI, in addition to or instead of typical treatment for alcohol/drug addiction, doubled abstinence rates.[5]

Another meta-analysis of 72 randomized controlled trials found that 75 percent of studies demonstrated a significant effect of MI on numerous conditions, including depression and several chronic diseases.[3] Other disease-specific outcomes include:

- Greater weight loss in 217 overweight women with Type 2 Diabetes Mellitus (T2DM) on oral medication who received group-based behavioral obesity treatment plus five sessions of individual MI compared to a control group (3.5 kg vs. 1.7 kg [$P=0.04$]).[6]
- A nearly threefold increase in the number of overweight individuals (n=141 total) who received up to 11 individual MI sessions (median of eight in person and one and a half by telephone) and met their weight-loss goals compared to those who received usual care (informational literature) (24 percent vs. 7 percent, odds ratio = 3.96; 95 percent confidence interval, 1.4 to 11.4).[7]
- A reduction in nonadherence for a multiple sclerosis drug from 13 percent to 1.2 percent with the use of telephone-based motivational interviewing vs. an 8.7 percent reduction in the standard care group.[8]

Origins of MI

First developed for use in the addiction treatment field, motivational interviewing is now in the forefront of healthcare as an important component in helping patients manage chronic health conditions. As an approach to patient care, MI changes the way healthcare professionals communicate with their patients. Numerous managed care organizations, pharmacies, and even the military are training their healthcare staffs to use MI skills.

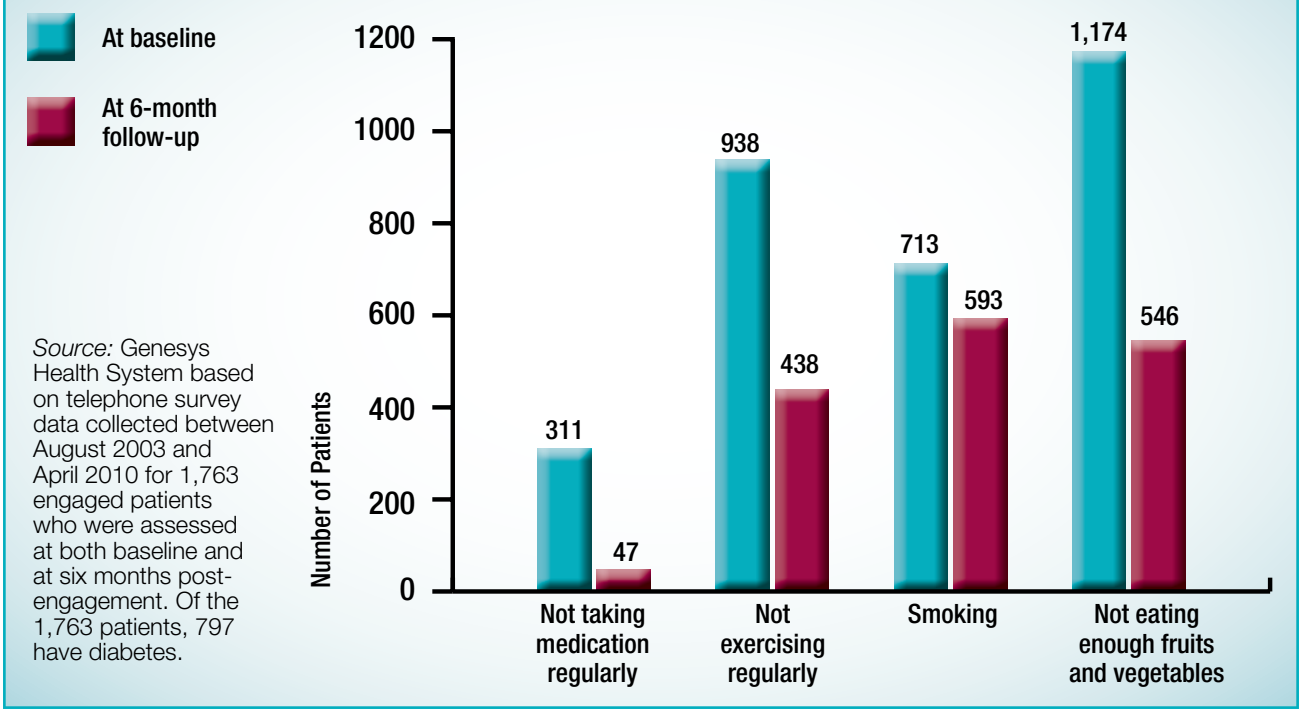
Using Motivational Interviewing in Managed Care

Managed care is embracing MI as an essential tool to help manage chronic medical conditions in its growing patient population.

In 2009, Aetna began training disease management professionals in MI. Since the program was fully implemented in 2010, Aetna reports that participation in its Care Management Disease Management program increased from 53.1 percent to 76 percent, while the number of members who quit the program fell by 55 percent during the third quarter of 2011, compared to pre-2009. The company used a "train-the-trainer" approach to teach 50 healthcare professionals MI skills. Today, it reports more than 1,800 clinicians and clinical support staff use MI to encourage behavioral change.[9]

Pittsburgh-based Highmark Blue Cross Blue Shield embraced MI about five years ago, said Dolores Fuhrman, a learning delivery consultant in the company's Corporate Learning division. At the time, the entire company was shifting from a disease focus to an emphasis on developing positive health behavior changes. "We found that we needed to make a bigger difference in having our

Fig. 1 **Impact of Health Navigator Program on Selected Health Risks among Engaged Patients Enrolled in Genesee Health Plan[10]**



Source: Genesys Health System based on telephone survey data collected between August 2003 and April 2010 for 1,763 engaged patients who were assessed at both baseline and at six months post-engagement. Of the 1,763 patients, 797 have diabetes.

members take charge of their own health and make positive changes to help impact their chronic illness and the cost," Fuhrman said. "Studies show that the old way of getting people to do things by beating them over the head doesn't work; we need to engage them in a way that makes them aware of the risks if they continue their current behavior, and that talks to them in a respectful, nonjudgmental way that shows you care about them."

Highmark placed its disease and case management nurses through a one-week training course in MI with regular follow-up training. Although Highmark has yet to identify metrics or outcomes for MI, Fuhrman said the anecdotal feedback from the nurses "has been great." For instance, she has received emails from nurses excited about changes they see in members when they use MI.

Michigan-based Genesee Health Plan uses MI as part of a triple-component program designed to improve chronic health conditions in primary care settings. An analysis of its Health Navigator program by the Commonwealth Fund found that MI significantly improved health behaviors among 1,763 patients, including 797 patients with diabetes, between its implementation in 2003 and 2010 (Figure 1).[10]

Given the beneficial effects of MI on patient adherence, the pharmaceutical company Amylin offers its managed care and pharmacy accounts an eight-hour training seminar in MI to improve adherence in patients with diabetes. "If you want to provide a true service and partner with your health plan—in terms of helping—MI will significantly impact adherence and bring a greater understanding among members about the importance of their medications. You need to train your providers how to talk *with* their patients, and not *at* them," said Lori Bunton, Director of Payor Marketing at the San Diego-based company.

The problem of inappropriate medication adherence is one reason North Carolina-based specialty pharmacy Kerr Health began training pharmacists in MI last summer. "We know that adherence isn't what it should be," said Executive Vice President Rebecca Chater. "Papers have been written about adherence for four decades, and no one has found a solution." Motivational interviewing, she said, "is another tool in the kit."

One advantage of MI, she said, is that it is appropriate for all disease states and medications. "It basically is a way to communicate with a patient, to empower the patient, and to enable better outcomes." Kerr Health pharmacists have completely embraced the program and relish being able to change outcomes and see patients improve their health-related behaviors.

At ConnectiCare, a managed care plan based in Farmington, Conn., 13 nurses and two tobacco cessation treatment specialists have integrated the technique into their daily jobs. Health Management Programs Manager Bonnie Bauer continually hears success stories; as one nurse told her: "For me, during our weekly conversations, asking open-ended questions, listening, identifying, and addressing her core concerns were the key to helping her become successful . . . before MI, my conversations would have been mostly one-sided, and never getting to the root of what was happening with the individual to really be able to help them."

A qualitative study evaluating the perceptions of 19 adults with diabetes to a MI approach by trained nurses vs. standard care with physicians found that participants were much more positive about MI.[11] Participants perceived that the nurses had more time with them, did not lecture them, were more positive and reassuring about their conditions, and listened to what the patients had to say. In contrast to traditional care, in which negative feedback and guilt were used to try to persuade them to change, participants felt they received more encouragement with the MI intervention and developed a greater sense of responsibility for their own care.

An important component of any successful MI program, said Bauer and others, is to continually reinforce the skills. This can be done with maintenance training once or twice a year, regular exercises, and monthly MI "pearls" sent via email, which include various MI skills used in a case-based approach. In addition, MI is a standing agenda item during monthly staff meetings at ConnectiCare. Each month, one employee presents a case summarizing the MI techniques used and asks for feedback from other staff members.

The difficulty in directly tracing patient behavior change back to MI comes from the fact that these organizations are simultaneously making other changes to improve quality in today's dynamic healthcare environment. "In this environment, it is impossible to isolate MI from all of the other initiatives we have implemented in our

Motivational Interviewing Defined

Motivational interviewing is a person-centered, guided method of communication for enhancing intrinsic motivation to change by exploring and resolving ambivalence and resistance.[2,8] It is designed to form a therapeutic alliance between the healthcare professional and the patient. The goal is to use this alliance to elicit behavior change in patients by understanding their resistance and exploring options together to overcome that resistance. It involves:

Using open-ended questions.

- **Instead of saying:** "Are you taking your blood pressure medication?"
- **Ask:** "How are you taking your medication?" and "Why do you think you need this medication?"

Exploring and resolving ambivalence and resistance.
When people are resistant to change, the worst strategy is to try to persuade or argue with them about why they should change. Instead of relying on facts to change a patient's mind, clinicians need to explore the reasons for the patient's resistance or ambivalence. For example:

- **Instead of saying:** "You need to take this medicine or you're going to have a stroke."
- **Ask:** "Why do you think you're having trouble taking the medicine? What would make taking this medication more important to you? What is getting in the way of you taking this medication?"

Being patient-centered.
This means that the clinician operates in the patient's world and gives up his or her own agenda, serving instead as a resource to assist patients in reaching their health goals.

Expressing empathy.

- **Patient:** "Everyone makes it sound so easy . . . take your medicine, quit smoking, change your diet, exercise more."
- **Healthcare professional:** "You sound frustrated. You've been asked to make a lot of changes to control your diabetes, and people don't seem to appreciate how overwhelming and difficult it can all be." The clinician should not say: "I understand" or "I hear you" or "Uh-huh." None of those responses tell the patient exactly what the clinician does understand. Plus, it is the patient who should determine whether he or she feels understood—not the clinician.

programs and determine that it's the MI that has effected a change," said Bauer. In addition, MI should not be used in a vacuum; ideally, it is integrated with other quality initiatives, such as the patient-centered medical home.

That is exactly what the Air Force is doing, said Col. Maureen Mintzlaff, USAFR, IMA, NC, a nurse and civilian consultant who has championed the use of MI since she learned about it several years ago. She sees it not only as a tool to change patient behavior, but one that can also improve interactions between healthcare professionals who need to learn how to work as part of a team. After using MI in a small pilot program on smoking cessation, the Air Force is now integrating MI into its patient-centered medical home initiative.

Mintzlaff said MI reinforces the fact that "it's not about me," or about any healthcare provider. "It's about them [the patient], about having empathy, exploring, showing them I care. I can't believe how powerful it is for people to think they can do these things on their own."

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Key Motivational Interviewing Concepts

- Listen for the patient's core concerns and line of reasoning. How does the patient make sense of his or her illness? What does the patient understand to be the risks of not treating the illness? What does the patient think is happening?

- Reflect back the patient's concerns and correct misunderstandings or misinformation without creating defensiveness. For example, if the patient says, "I feel fine and my blood pressure is just 156/110," when asked about nonadherence, the appropriate MI response would be, "So, because you feel fine and your blood pressure is just 156/110, you're wondering, 'What's the big deal?'" That leads into a conversation in which the clinician can say: "That's a great question. Would it be OK if I gave you some information and you let me know what you think?"

  If the patient agrees, the clinician might then explain: "We know that when blood pressure goes below 140/90, your risk for stroke or heart attack goes way down. Your blood pressure is quite a bit above that, which greatly increases your risk for stroke or heart attack. Your medication can lower your blood pressure and lower your risk when taken every day. Where does that leave you now in regard to taking your medicine every day?" Notice that the patient is not told what to do. Instead, the patient is asked to draw his or her own conclusions.

- Participate in an exchange of expertise. This means asking patients what they know and understand (their expertise) and, based on their answers, providing the clinician's expertise, then asking how the new information changes the patient's thinking.

- Understand that genuineness, care, and concern are among the most important MI components.

For your patients with type 2 diabetes who need more than A1C control, choose Levemir® (insulin detemir [rDNA origin] injection)

24/7 GLUCOSE CONTROL

Karen's doctor said taking Levemir® (insulin detemir [rDNA origin] injection) once-daily may get her the control she needs & more

Low rates of hypoglycemia

In 1 study, approximately 45% of patients in each treatment arm achieved A1C <7% with no hypoglycemic events within the last 4 weeks of observation.[1]

- A single major hypoglycemic event was reported in the 70-90 mg/dL group; no major hypoglycemic events in the 80-110 mg/dL group
- Minor hypoglycemia rates were 5.09 (70-90 mg/dL) and 3.16 (80-110 mg/dL) per patient-year*

From a 20-week, randomized, controlled, multicenter, open-label, parallel-group, treat-to-target trial using a self-titration algorithm in insulin-naïve patients with type 2 diabetes, A1C ≥7% and ≤9% on OAD therapy randomized to Levemir® and OAD (1:1) to 2 different fasting plasma glucose (FPG) titration targets (70-90 mg/dL [n=121] or 80-110 mg/dL [n=122]). At study end, in the 80-110 mg/dL group, 55% of patients achieved goal (A1C <7%) with A1C decrease of 0.9%. The mean A1C was 7%.[1]

Covered on more than 90% of managed care plans[2†]

Indications and Usage

Levemir® (insulin detemir [rDNA origin] injection) is indicated to improve glycemic control in adults and children with diabetes mellitus.

Important Limitations of Use:
Levemir® is not recommended for the treatment of diabetic ketoacidosis. Intravenous rapid-acting or short-acting insulin is the preferred treatment for this condition.

Important Safety Information

Levemir® is contraindicated in patients hypersensitive to insulin detemir or one of its excipients.

Do not dilute or mix Levemir® with any other insulin solution, or use in insulin infusion pumps. Do not administer Levemir® intravenously or intramuscularly because severe hypoglycemia can occur.

Hypoglycemia is the most common adverse reaction of insulin therapy, including Levemir®. The timing of hypoglycemia usually reflects the time action profile of the administered insulin formulations. Glucose monitoring is essential for all patients receiving insulin therapy. Any changes to an insulin regimen should be made cautiously and only under medical supervision.

Needles and Levemir® FlexPen® must not be shared.

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including Levemir®. Adverse reactions associated with Levemir® include hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, rash and pruritus. Careful glucose monitoring and dose adjustments of insulin, including Levemir®, may be necessary in patients with renal or hepatic impairment.

Levemir® has not been studied in children with type 2 diabetes, and in children with type 1 diabetes under the age of six.

Please see brief summary of Prescribing Information on adjacent page.

Needles are sold separately and may require a prescription in some states.

*Minor=SMPG <56 mg/dL and not requiring third-party assistance.

† Intended as a guide. Lower acquisition costs alone do not necessarily reflect a cost advantage in the outcome of the condition treated because other variables affect relative costs. Formulary status is subject to change.

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insulin detemir (rDNA origin) injection

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LEVEMIR® (insulin detemir [rDNA origin] injection)

Rx ONLY

BRIEF SUMMARY. Please consult package insert for full prescribing information.

INDICATIONS AND USAGE: LEVEMIR® is indicated to improve glycemic control in adults and children with diabetes mellitus. Important Limitations of Use: LEVEMIR® is not recommended for the treatment of diabetic ketoacidosis. Intravenous rapid-acting or short-acting insulin is the preferred treatment for this condition.

CONTRAINDICATIONS: LEVEMIR® is contraindicated in patients with hypersensitivity to LEVEMIR® or any of its excipients. Reactions have included anaphylaxis.

WARNINGS AND PRECAUTIONS: Dosage adjustment and monitoring: Glucose monitoring is essential for all patients receiving insulin therapy. Changes to an insulin regimen should be made cautiously and only under medical supervision. Changes in insulin strength, manufacturer, type, or method of administration may result in the need for a change in the insulin dose or an adjustment of concomitant anti-diabetic treatment. As with all insulin preparations, the time course of action for LEVEMIR® may vary in different individuals or at different times in the same individual and is dependent on many conditions, including the local blood supply, local temperature, and physical activity. **Administration:** LEVEMIR® should only be administered subcutaneously. Do not administer LEVEMIR® intravenously or intramuscularly. The intended duration of activity of LEVEMIR® is dependent on injection into subcutaneous tissue. Intravenous or intramuscular administration of the usual subcutaneous dose could result in severe hypoglycemia. Do not use LEVEMIR® in insulin infusion pumps. Do not dilute or mix LEVEMIR® with any other insulin or solution. If LEVEMIR® is diluted or mixed, the pharmacokinetic or pharmacodynamic profile (e.g., onset of action, time to peak effect) of LEVEMIR® and the mixed insulin may be altered in an unpredictable manner. **Hypoglycemia:** Hypoglycemia is the most common adverse reaction of insulin therapy, including LEVEMIR®. The risk of hypoglycemia increases with intensive glycemic control. Patients must be educated to recognize and manage hypoglycemia. Severe hypoglycemia can lead to unconsciousness or convulsions and may result in temporary or permanent impairment of brain function or death. Severe hypoglycemia requiring the assistance of another person or parenteral glucose infusion, or glucagon administration has been observed in clinical trials with insulin, including trials with LEVEMIR®. The timing of hypoglycemia usually reflects the time-action profile of the administered insulin formulations. Other factors such as changes in food intake (e.g., amount of food or timing of meals), exercise, and concomitant medications may also alter the risk of hypoglycemia. The prolonged effect of subcutaneous LEVEMIR® may delay recovery from hypoglycemia. As with all insulins, use caution in patients with hypoglycemia unawareness and in patients who may be predisposed to hypoglycemia (e.g., the pediatric population and patients who fast or have erratic food intake). The patient's ability to concentrate and react may be impaired as a result of hypoglycemia. This may present a risk in situations where these abilities are especially important, such as driving or operating other machinery. Early warning symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as longstanding diabetes, diabetic neuropathy, use of medications such as beta-blockers, or intensified glycemic control. These situations may result in severe hypoglycemia (and, possibly, loss of consciousness) prior to the patient's awareness of hypoglycemia. **Hypersensitivity and allergic reactions:** Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including LEVEMIR®. **Renal Impairment:** No difference was observed in the pharmacokinetics of insulin detemir between non-diabetic individuals with renal impairment and healthy volunteers. However, some studies with human insulin have shown increased circulating insulin concentrations in patients with renal impairment. Careful glucose monitoring and dose adjustments of insulin, including LEVEMIR®, may be necessary in patients with renal impairment. **Hepatic Impairment:** Non-diabetic individuals with severe hepatic impairment had lower systemic exposures to insulin detemir compared to healthy volunteers. However, some studies with human insulin have shown increased circulating insulin concentrations in patients with liver impairment. Careful glucose monitoring and dose adjustments of insulin, including LEVEMIR®, may be necessary in patients with hepatic impairment. **Drug interactions:** Some medications may alter insulin requirements and subsequently increase the risk for hypoglycemia or hyperglycemia.

ADVERSE REACTIONS: The following adverse reactions are discussed elsewhere: Hypoglycemia; Hypersensitivity and allergic reactions. Clinical trial experience: Because clinical trials are conducted under widely varying designs, the adverse reaction rates reported in one clinical trial may not be easily compared to those rates reported in another clinical trial, and may not reflect the rates actually observed in clinical practice. The frequencies of adverse reactions (excluding hypoglycemia) reported during LEVEMIR® clinical trials in patients with type 1 diabetes mellitus and type 2 diabetes mellitus are listed in Tables 1-4 below. See Tables 5 and 6 for the hypoglycemia findings.

Table 1: Adverse reactions (excluding hypoglycemia) in two pooled clinical trials of 16 weeks and 24 weeks duration in adults with type 1 diabetes (adverse reactions with incidence ≥ 5%)

	LEVEMIR®, % (n = 767)	NPH, % (n = 388)
Upper respiratory tract infection	26.1	21.4
Headache	22.6	22.7
Pharyngitis	9.5	8.0
Influenza-like illness	7.8	7.0
Abdominal Pain	6.0	2.6

Table 2: Adverse reactions (excluding hypoglycemia) in a 26-week trial comparing insulin aspart + LEVEMIR® to insulin aspart + insulin glargine in adults with type 1 diabetes (adverse reactions with incidence ≥ 5%)

	LEVEMIR®, % (n = 161)	Glargine, % (n = 159)
Upper respiratory tract infection	26.7	32.1
Headache	14.3	19.5
Back pain	8.1	6.3
Influenza-like illness	6.2	8.2
Gastroenteritis	5.6	4.4
Bronchitis	5.0	1.9

Table 3: Adverse reactions (excluding hypoglycemia) in two pooled clinical trials of 22 weeks and 24 weeks duration in adults with type 2 diabetes (adverse reactions with incidence ≥ 5%)

	LEVEMIR®, % (n = 432)	NPH, % (n = 437)
Upper respiratory tract infection	12.5	11.2
Headache	6.5	5.3

Table 4: Adverse reactions (excluding hypoglycemia) in a 26-week clinical trial of children and adolescents with type 1 diabetes (adverse reactions with incidence ≥ 5%)

	LEVEMIR®, % (n = 232)	NPH, % (n = 115)
Upper respiratory tract infection	35.8	42.6
Headache	31.0	32.2
Pharyngitis	17.2	20.9
Gastroenteritis	16.8	11.3
Influenza-like illness	13.8	20.9
Abdominal pain	13.4	13.0
Pyrexia	10.3	6.1
Cough	8.2	4.3
Viral infection	7.3	7.8
Nausea	6.5	7.0
Rhinitis	6.5	3.5
Vomiting	6.5	10.4

Hypoglycemia: Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including LEVEMIR®. Tables 5 and 6 summarize the incidence of severe and non-severe hypoglycemia in the LEVEMIR® clinical trials. Severe hypoglycemia was defined as an event with symptoms consistent with hypoglycemia requiring assistance of another person and associated with either a blood glucose below 50 mg/dL or prompt recovery after oral carbohydrate, intravenous glucose or glucagon administration. Non-severe hypoglycemia was defined as an asymptomatic or symptomatic plasma glucose < 56 mg/dL (<50 mg/dL in Study A and C) that was self-treated by the patient. The rates of hypoglycemia in the LEVEMIR® clinical trials (see Section 14 for a description of the study designs) were comparable between LEVEMIR®-treated patients and non-LEVEMIR®-treated patients (see Tables 5 and 6).

Table 5: Hypoglycemia in Patients with Type 1 Diabetes

		Study A Type 1 Diabetes Adults 16 weeks In combination with insulin aspart		Study B Type 1 Diabetes Adults 26 weeks In combination with insulin aspart		Study C Type 1 Diabetes Adults 24 weeks In combination with regular insulin		Study D Type 1 Diabetes Pediatrics 26 weeks In combination with insulin aspart	
		Twice-Daily LEVEMIR®	Twice-Daily NPH	Twice-Daily LEVEMIR®	Once-Daily Glargine	Once-Daily LEVEMIR®	Once-Daily NPH	Once- or Twice Daily LEVEMIR®	Once- or Twice Daily NPH
Severe hypoglycemia	Percent of patients with at least 1 event (n/total N)	8.7 (24/276)	10.6 (14/132)	5.0 (8/161)	10.1 (16/159)	7.5 (37/491)	10.2 (26/256)	15.9 (37/232)	20.0 (23/115)
	Event/patient/year	0.52	0.43	0.13	0.31	0.35	0.32	0.91	0.99
Non-severe hypoglycemia	Percent of patients (n/total N)	88.0 (243/276)	89.4 (118/132)	82.0 (132/161)	77.4 (123/159)	88.4 (434/491)	87.9 (225/256)	93.1 (216/232)	95.7 (110/115)
	Event/patient/year	26.4	37.5	20.2	21.8	31.1	33.4	31.6	37.0

Table 6: Hypoglycemia in Patients with Type 2 Diabetes

		Study E Type 2 Diabetes Adults 24 weeks In combination with oral agents		Study F Type 2 Diabetes Adults 22 weeks In combination with insulin aspart	
		Twice-Daily LEVEMIR®	Twice-Daily NPH	Once- or Twice Daily LEVEMIR®	Once- or Twice Daily NPH
Severe hypoglycemia	Percent of patients with at least 1 event (n/total N)	0.4 (1/237)	2.5 (6/238)	1.5 (3/195)	4.0 (8/199)
	Event/patient/year	0.01	0.08	0.04	0.13
Non-severe hypoglycemia	Percent of patients (n/total N)	40.5 (96/237)	64.3 (153/238)	32.3 (63/195)	32.2 (64/199)
	Event/patient/year	3.5	6.9	1.6	2.0

Insulin Initiation and Intensification of Glucose Control: Intensification or rapid improvement in glucose control has been associated with a transitory, reversible ophthalmologic refraction disorder, worsening of diabetic retinopathy, and acute painful peripheral neuropathy. However, long-term glycemic control decreases the risk of diabetic retinopathy and neuropathy. *Lipodystrophy:* Long-term use of insulin, including LEVEMIR®, can cause lipodystrophy at the site of repeated insulin injections. Lipodystrophy includes lipohypertrophy (thickening of adipose tissue) and lipoatrophy (thinning of adipose tissue), and may affect insulin adsorption. Rotate insulin injection sites within the same region to reduce the risk of lipodystrophy. *Weight Gain:* Weight gain can occur with insulin therapy, including LEVEMIR®, and has been attributed to the anabolic effects of insulin and the decrease in glucosuria. *Peripheral Edema:* Insulin, including LEVEMIR®, may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy. *Allergic Reactions: Local Allergy:* As with any insulin therapy, patients taking LEVEMIR® may experience injection site reactions, including localized erythema, pain, pruritis, urticaria, edema, and inflammation. In clinical studies in adults, three patients treated with LEVEMIR® reported injection site pain (0.25%) compared to one patient treated with NPH insulin (0.12%). The reports of pain at the injection site did not result in discontinuation of therapy. Rotation of the injection site within a given area from one injection to the next may help to reduce or prevent these reactions. In some instances, these reactions may be related to factors other than insulin, such as irritants in a skin cleansing agent or poor injection technique. Most minor reactions to insulin usually resolve in a few days to a few weeks. *Systemic Allergy:* Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin, including LEVEMIR®, and may be life-threatening. *Antibody Production:* All insulin products can elicit the formation of insulin antibodies. These insulin antibodies may increase or decrease the efficacy of insulin and may require adjustment of the insulin dose. In phase 3 clinical trials of LEVEMIR®, antibody development has been observed with no apparent impact on glycemic control. **Postmarketing experience:** The following adverse reactions have been identified during post approval use of LEVEMIR®. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Medication errors have been reported during post-approval use of LEVEMIR® in which other insulins, particularly rapid-acting or short-acting insulins, have been accidentally administered instead of LEVEMIR®. To avoid medication errors between LEVEMIR® and other insulins, patients should be instructed always to verify the insulin label before each injection.

More detailed information is available upon request.

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Revised: 1/2012

0212-00007333-1 2/2012

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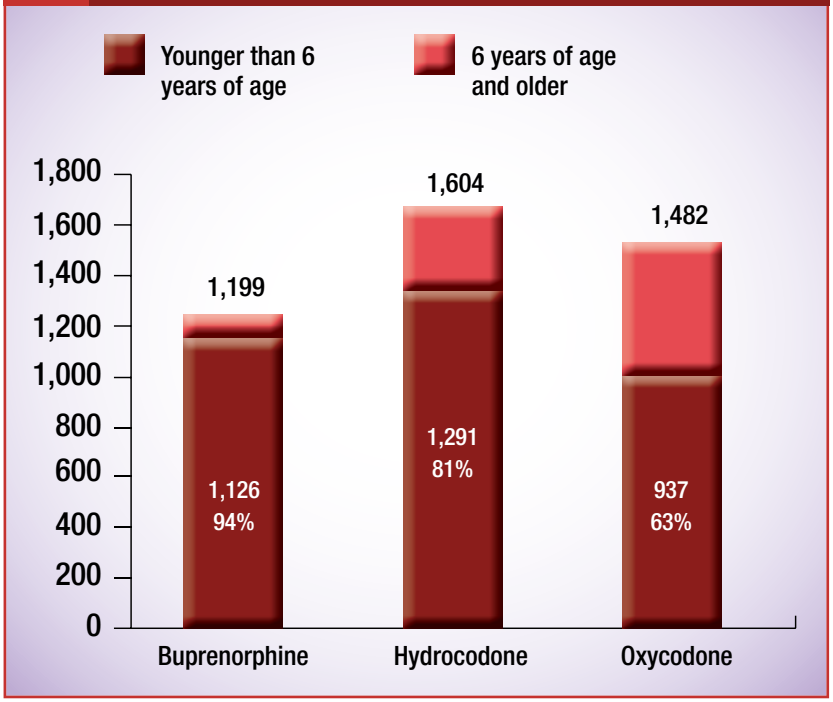
Levemir®
insulin detemir (rDNA origin) injection

Impact of Suboxone® Dosage Forms on Pediatric Exposure

Suboxone® (buprenorphine/naloxone) is a combination product containing a partial opioid agonist (buprenorphine) and an opioid receptor antagonist (naloxone).[1] Comparisons of buprenorphine to full opioid agonists, such as methadone and hydromorphone, suggest that sublingual buprenorphine exhibits typical opioid agonist properties, which are limited by a ceiling effect.[1] This ceiling effect causes the respiratory depression typically seen with excessive opioid dosages to plateau, thereby reducing the dangerous risks of overdosing. The naloxone component in Suboxone® has no significant effect when taken sublingually; however, if the avenue of opioid abuse is intravenous injection, naloxone attenuates the effects of buprenorphine and precipitates opioid withdrawal. These characteristics greatly reduce the risk of overdose, abuse, and toxicity when compared to full opioid agonists and allow Suboxone® to be used safely and effectively for the treatment of opioid dependence on an outpatient basis.

Although Suboxone® was designed to be an abuse-resistant formulation, recent evidence is creating a new cause for concern. According to data from the Drug Abuse Warning Network (DAWN), the estimated number of emergency department (ED) visits due to accidental ingestion of buprenorphine more than doubled from 2008 to 2009.[2] Of the 1,199 buprenorphine-related visits

Fig. 1 **Estimated Number of ED Visits Related to Accidental Ingestion (2009)[2]**



in that year, 94 percent involved children younger than the age of six.[2] This rate of accidental pediatric ingestion can be compared to 81 percent for hydrocodone and 63 percent for oxycodone (Figure 1).[2] The increased incidence of buprenorphine-related accidental ingestions is likely attributable to an increase in utilization patterns.

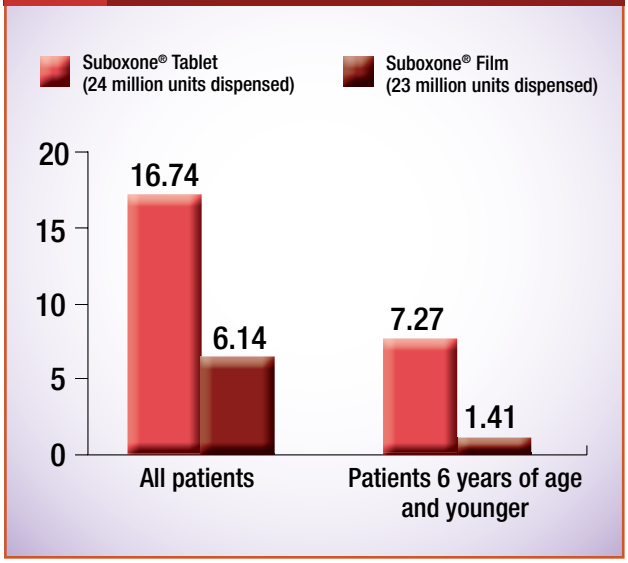
The current dosage formulations that are available may also contribute significantly to increases in accidental ingestion by children. Buprenorphine is available in three formulations: single-ingredient buprenorphine sublingual tablets (Subutex®), buprenorphine/naloxone sublingual tablets (Suboxone® Tablets), and buprenorphine/naloxone sublingual film (Suboxone® Film). While each Suboxone® Film is individually wrapped in a child-resistant package, the two buprenorphine tablet formulations are not traditionally dispensed in unit-dose packaging. Additionally, the tablets are orange in color with a pleasant citrus aroma and could be easily confused for candy by young children, placing children at an increased risk for buprenorphine toxicity.[3] For example, a child who simply puts a sublingual Suboxone® Tablet in his or her mouth can absorb the full dose in as little as five minutes.[3] A 10-kilogram toddler will receive more than a 30-fold overdose by ingesting a single 2mg Suboxone® Tablet, which is the smallest dose commercially available.[3]

Children may develop signs and symptoms of toxicity even if the tablet is rapidly removed from the child's mouth.[3] In a retrospective review of ED admissions for accidental overdoses in children younger than six years of age, all children who ingested greater than 4mg of buprenorphine experienced some clinically relevant effect and were at an increased risk of developing severe symptoms of toxicity.[4] Buprenorphine overdoses have been reported to overwhelm the drug's ceiling effect on respiratory function, which can put young children at risk for sedation, respiratory depression, cerebral anoxia, coma, and death.[3]

Rate of Exposure: Tablet vs. Film

A recent analysis conducted using the Researched Abuse Diversion and Addiction-Related Surveillance (RADARS®) System—a prescription drug abuse, misuse, and diversion surveillance system that collects timely product-specific data—evaluated the rates of Suboxone® exposure reports to poison control centers.[5] Specifically, this analysis compared the rates of Suboxone® Tablet exposure with Suboxone® Film exposure. According to the RADARS® analysis, there was an 81 percent reduction in pediatric (age ≤ 6) exposure for Suboxone® Film compared to Suboxone® Tablets.[5] Additionally, the analysis showed a 63 percent reduction in overall exposure rates for the Suboxone® Film (Figure 2).[5] The results from this analysis demonstrate that utilizing Suboxone® Film as the preferred buprenorphine formulation may be one potential strategy to combat the increasing problems of abuse, diversion, and overdose of Suboxone® within many health plan coverage networks.

Fig. 2 **Suboxone® Exposure Reports to Poison Control Centers—Per Million Units Dispensed[5]**



In addition to promoting the use of individually packaged, child-resistant formulations, there are several other safety measures that could be implemented to help quell the increase in accidental ingestion of buprenorphine in children. Clinicians must take an active role in preventing diversion and counsel patients on proper storage techniques. Buprenorphine-containing medications should always be stored in child-resistant containers and kept out of the reach of children.[3] Also, parents should be educated on the risks associated with buprenorphine overdose and should be able to recognize the signs and symptoms of toxicity in children.

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Contraception Mandate:
Managed Care Perceptions and Implications

Shawn Barger, PharmD, Director of Pharmacy, AvMed; Todd C. Lord, PharmD, Manager of Managed Markets Solutions, CDMI; and Russell C. Dunn, PharmD Candidate, University of Rhode Island

In the United States, approximately half of all pregnancies are unplanned.[1] The management of the resulting births, miscarriages, and abortions significantly increases overall resource utilization and costs the healthcare system more than $5 billion annually; the average direct medical cost for a single unintended pregnancy is estimated to be $1,600.[2] The majority of these pregnancies occur in single women in their 20s, and nearly two-thirds of the healthcare expenditure falls into the hands of Medicaid and other publicly funded insurance programs.[3,4] Unplanned pregnancies also significantly increase the risk of preterm birth, low birth weight, low socioeconomic status, low cognitive ability, and cause greater conflict in relationships.[5,6,7] These consequences have been known for many years, as Brown and Eisenberg identified in 1995:

"With an unwanted pregnancy especially, the mother is more likely to seek prenatal care after the first trimester or not to obtain care. She is more likely to expose the fetus to harmful substances by smoking tobacco and drinking alcohol. The child of an unwanted conception is at greater risk of weighing less than 2,500 grams at birth, of dying in its first year of life, of being abused, and of not receiving sufficient resources for healthy development. The mother may be at greater risk of physical abuse herself, and her relationship with her partner is at greater risk of dissolution. Both mother and father may suffer economic hardship and fail to achieve their educational and career goals. The health and social risks associated with a mistimed conception are similar to those associated with an unwanted conception, although they are not as great."[8]

Contraceptive use in the United States has been shown to save $19 billion in direct medical costs every year.[9] For every $1 spent on family planning services, more than $4 are saved.[10] In 2001, the Centers for Medicare & Medicaid Services (CMS) began a study that expanded contraceptive coverage to women who were normally ineligible in certain states.[11] Originally projected to be budget-neutral, net Medicaid savings were upwards of $76 million in California after two years.[11] Further analysis of the data predicted that the net savings would be greater than $700 million over ten years if the program was made available to the entire United States population.[11]

Effective August 1, 2012, the controversial contraceptive mandate will be enacted as part of the Patient Protection and Affordable Care Act (PPACA).[12] The plan, developed by the Institute of Medicine (IOM), requires private insurers to cover a variety of preventive services without charging their beneficiaries a copayment or cost-sharing of any kind.[12] The preventive services included in the plan are supported by strong evidence demonstrating improvements in health outcomes. The intent of the mandate is to increase access to preventive care services for women in an attempt to reduce unnecessary

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resource utilization and negative health outcomes. Mammograms, gestational diabetes screenings, cervical cancer screenings, and all U.S. Food and Drug Administration (FDA)–approved contraceptive methods will be required to be available at no patient cost-sharing.[12] Although most of the screenings will be offered annually with no out-of-pocket expense, contraceptives will be available on an "as prescribed" frequency.[12] Oral contraceptives, the Ortho Evra patch, and the NuvaRing are all included, as well as intrauterine devices (IUDs) and emergency oral contraceptives.[12] These requirements will apply to all private health plans, with the exception of those groups that maintain a grandfathered status. Plans with grandfathered groups must have been in existence prior to March 23, 2010, and cannot make significant changes to their coverage, such as cutting benefits or raising cost-sharing.[12] The Department of Health and Human Services (HHS) believes most plans that meet this grandfather clause criteria will likely lose the protected status within a few years.[13] Once a plan loses its grandfathered status, it will be forced to comply with the preventive care service requirements of the PPACA.

Managed Care Consensus

A recent survey of pharmacy and medical directors from 15 of the nation's leading insurers (HMOs, IDNs, and ACOs) was conducted by CDMI to gain managed care perceptions regarding the upcoming contraception mandate and how organizations are planning to comply with the required regulations. The insurers included in this research are responsible for providing prescription drug coverage to more than 55 million beneficiaries across the country.

Within managed care, the general consensus regarding the law is that it will have a negligible impact on unintended pregnancies. This leads to the fundamental question of the mandate: Will the increased access to contraceptive medications lower the rate of unplanned pregnancies in the United States? Some experts argue that out-of-pocket cost to patients is one of the largest factors preventing many women in the country from using effective birth control.[14] Whether this mandate will lower pregnancy rates is yet to be seen. If the rate of unplanned pregnancies does not drop significantly, the increased financial burden on insurers could hinder what the statute set out to achieve.

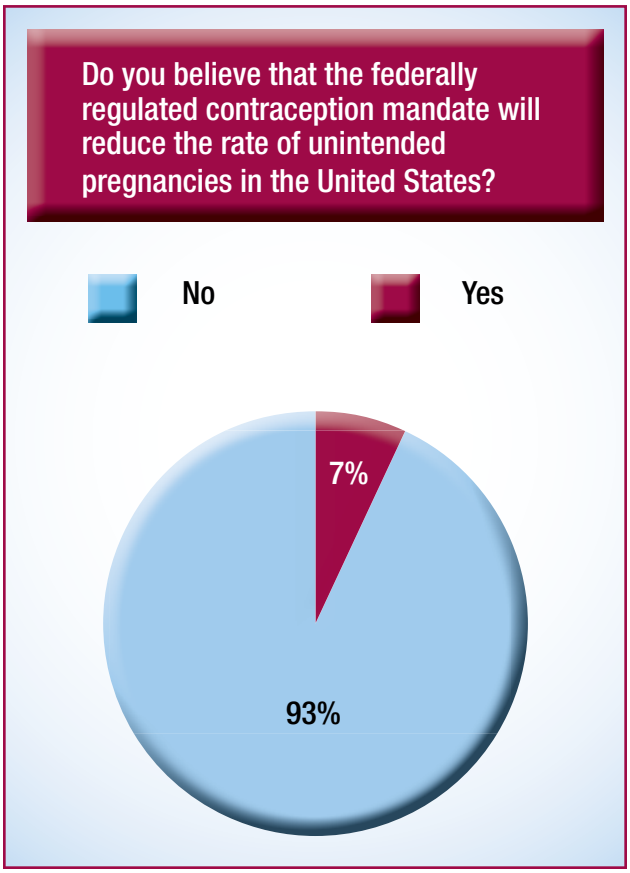
Similar to other PPACA reforms, insurers must comply with this federal mandate regardless of their stance on its effectiveness. Plans with confirmed grandfathered groups fear that this position will only offer minimal protection and be temporary, especially since national compliance is anticipated within the next year. The law includes some vague and interpretable language, which most managed care organizations are currently analyzing within their legal departments to ensure full compliance when the program goes live.

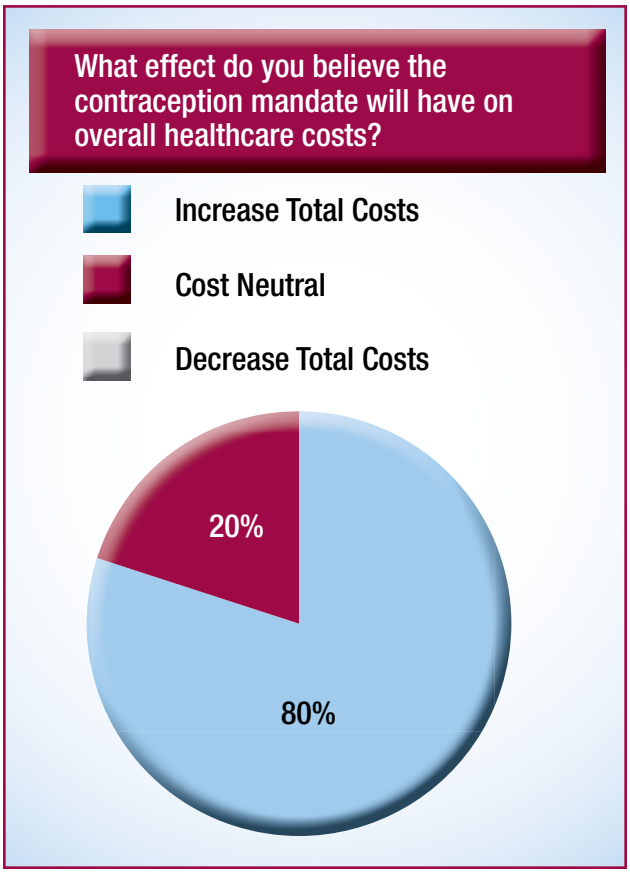
Formularies and Processes

From a structural standpoint, the law is not foreseen to drastically modify any insurer's formularies or processes. The majority of organizations already cover all FDA-approved contraceptive products and devices, although they are usually separated by copay differentials or specific levels of cost-sharing. While some insurers may choose to provide all contraceptive products and devices (including generics and multisource brands) at a zero dollar copay, the majority will adhere to a more traditional formulary structure. The mandate contains language that highlights the importance of using "reasonable medical management techniques" during the formulary decision-making process to ensure appropriate utilization and patient safety. The proposed rule from the HHS states:

"The use of reasonable medical management techniques allows plans and issuers to adapt these recommendations and guidelines to coverage of specific items and services where cost-sharing must be waived. Thus, under these interim final regulations, a plan or issuer may rely on established techniques and the relevant evidence base to determine the frequency, method, treatment, or setting for which a recommended preventive service will be available without cost-sharing requirements to the extent not specified in a recommendation or guideline."[15]

Managed care organizations are interpreting this differently. The majority believe that this statement supports the use of appropriate formulary controls and, when necessary to inspire appropriate utilization, the use of cost-sharing for branded products. Although generic contraceptive products will be available without an out-of-pocket expense to patients, branded medications with FDA-approved generic equivalents will be placed at higher tiers and many insurers will require a certain level of cost-sharing.





To further promote appropriate utilization and help contain potential cost increases, plans are examining the effectiveness of specific formulary controls and other medical management strategies. Some plans are considering setting a days supply limitation on contraceptive products to reduce the likelihood of unnecessary refills and potential waste. This same rationale supports the use of quantity limits that will restrict each fill/refill to either a one-month or three-month supply. Many organizations are also considering implementing a generic step program. This would guide patients to begin contraceptive therapy using a FDA-approved generic medication and have step-edits against branded products. As the use of generic medication is strongly supported by the FDA, this is an effective strategy to promote appropriate and efficacious treatment options while simultaneously minimizing the potential financial burden and improper drug utilization.

Due to the vague nature of the legislation, many plans are still evaluating how their organizations will respond to the mandate; however, a variety of medical management strategies designed to improve patient outcomes and ensure patient safety are being evaluated by many organizations. These management strategies not only will inspire appropriate utilization, but also will help to contain the anticipated cost increase derived from the mandate.

Managed Care Concerns

Managed care organizations have a variety of concerns with the new mandate. Inappropriate utilization of contraceptives, such as early and unnecessary refills, is cause for alarm. Insurers believe that this not only will affect community pharmacies, but also mail order. Mail-order pharmacies could use the mandate to increase their prescription volume by automatically filling these medications. With no price barrier, the incentive to cancel unnecessary refills and deliveries is negligible, which results in limited medical benefits for patients and increases the cost burden for insurers. Increased pharmacy costs due to the lack of copay and increased volume of prescriptions is expected, but the organizations are willing to accept this if medical costs fall as a result. Unfortunately, the majority of managed care executives do not believe the mandate will result in reductions in overall resource utilization. One potential method to promote appropriate utilization is to increase the use of IUDs or other surgical procedures. These are very effective methods of contraception and,

with years between replacing devices or a one-time treatment, overutilization becomes less of a concern.

Pharmaceutical companies present another concern. With the mandate requiring coverage of all FDA-approved contraceptive methods, drug manufacturers will not have an incentive to offer competitive contracts. Similarly, pharmaceutical companies with single-source, brand-name medications could raise their prices significantly, knowing that insurers have a limited ability to place controls against the class. Fortunately for many insurers, brand-name contraceptives with available generic equivalents will remain at a higher tier with an associated cost-sharing, and there are only a few single-source brands currently available. Nevertheless, organizations examining the law feel that there are too many financial risks with only a small chance for potential savings. Overall, this mandate is expected to result in increased costs to payors with no clear clinical benefit to patients, as well as the possibility of higher premiums.

With some organizations expecting costs to comply with the reform to exceed tens of millions, many have begun to theorize how to mitigate expenses. The Academy of Managed Care Pharmacy (AMCP) publicly addressed the HHS with a request to clarify the requirements to ensure proper interpretation and acceptance of the mandate. AMCP requested more information on whether health plans may use formulary decision-making strategies to determine which oral contraceptives to cover. They argued that formularies are a well-established medical management process that promotes clinically sound and cost-effective medical therapy and positive therapeutic outcomes. AMCP went on to request that the mandate clarify the cost-sharing requirements in regard to over-the-counter (OTC) contraceptives, such as Plan B. As these medications are typically available on demand, AMCP suggests the zero copay should be applicable only with a valid prescription. Without proper evaluation by a medical provider, patients could potentially use the product incorrectly or distribute the product to others. Requiring a prescription for OTC products under this mandate is a step in the right direction not only for cost-savings, but also for proper usage.

AMCP also highlighted the cost-saving potential of using generic medications. The request to the HHS cited an *Express Scripts Drug Trend Report* demonstrating that increasing the generic fill rate of oral contraceptives by 25 percent nationally can save commercial insurers an estimated $454 million annually.[16] While considering that the volume of contraception prescriptions is likely to rise without cost-sharing, these savings would be substantial.

There are conflicting reports on what is expected to occur when the mandate is enacted. The fear within managed care is that there is only a small chance of success with huge financial risks. Improper utilization of contraceptives, coupled with price increases from manufactures, will almost inevitably raise premiums, unless medical bills from unplanned pregnancies fall. CMS and the HHS believe this mandate has the potential to increase savings, as it has shown to accomplish in some preliminary pilot research. If cost-sharing is truly the largest barrier to proper contraception, the mandate may prove successful in reducing negative outcomes for many women. However, the true cost implications associated with these regulations will likely take more than a year to fully evaluate. Until that time, private insurers will be obligated to comply with the federal mandate and provide all FDA-approved contraceptive methods without charge to their beneficiaries.

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The Pioneer ACO Model: HealthCare Partners' Integrated Approach to Accountable Care

Robert J. Klein, Vice President, Marketing and Communications, HealthCare Partners; and Judith S. Hurley

Robert J. Klein

Providing high-quality patient care while controlling medical costs is the holy grail of healthcare. For more than two decades, HealthCare Partners (HCP), a physician-led healthcare delivery organization with staff-model medical groups and independent practice associations (IPAs) in California, Nevada, and Florida, has embraced that goal through a commitment to both clinical excellence and coordination of patient care. HCP has been highly engaged in the national dialogue on accountable care, and was recently selected to participate in the Pioneer Accountable Care Organization (ACO) Program, an initiative of the Centers for Medicare & Medicaid Services (CMS).

HCP believes the ACO model, which focuses on care coordination across providers and healthcare settings, is a compelling approach. "In the fee-for-service world, care is often fragmented and utilizes resources unnecessarily," said Jamie Phillips, HCP's Vice President of Regional Operations. "This adds confusion to the whole patient experience. We believe applying coordinated care principles to the Medicare fee-for-service population leads to better care for the patient. That is essentially what we have been doing with our Medicare Advantage population for many years."

The Pioneer ACO Model

An ACO consists of medical groups, hospitals, long-term care facilities, and other providers and suppliers that have banded together to coordinate care for the patients they serve.[1] The Patient Protection and Affordable Care Act (PPACA) contains provisions for an ACO initiative centered on Medicare fee-for-service (FFS) beneficiaries; this has led to the development of the Shared Savings Program, the Advanced Payment ACO Model, and the Pioneer ACO Model (see Table 1, page 34), which are all administered by the Center for Medicare & Medicaid Innovation (CMI).[1,2]

Like the other ACO initiatives administered by CMI, the Pioneer ACO Model aims to test payment arrangements that lead to improved care, reduced waste, and cost-savings to Medicare. In contrast to the Shared Savings Program, however, the Pioneer ACO Model was designed specifically for high-performing health systems with proven skills in coordinating care across multiple treatment settings and managing patients with complex medical needs.[2] Although the Pioneer ACO Model is associated with a higher degree of risk for the participating organizations, the savings potential is also greater. Additionally, it allows providers to move relatively quickly from a shared savings to a population-based payment model.

That approach was attractive to HCP. "We wanted to rapidly, rather than gradually, get to a sharing of risk and being accountable for the population," said Phillips. "The shared savings version didn't allow us to get there as aggressively as we wanted."

Applicant ACOs were permitted to choose among five payment options, including a 50, 60, or 70 percent shared savings model in year one and a 60, 70, or 75 percent shared savings model in year two.[3] ACOs that have met the minimum criteria for savings in years one and two will transition to a partial or full population-based payment model in year three. If an ACO is successful, program participation may be extended for two additional years using the year three payment model. The quality of care provided by the ACOs will be evaluated using 33 performance measures; organizations that do not meet specific quality benchmarks will be ineligible to share in the generated savings.[4] Each Pioneer ACO aims to include at least 15,000 Medicare FFS beneficiaries (5,000 in the case of rural ACOs).[5] Thirty-two organizations were selected to participate in the Pioneer ACO Model, which began in January 2012.[6]

The HCP Pioneer ACO

The HCP Pioneer ACO in California currently includes 30,000 Medicare FFS beneficiaries. Two-thirds of the beneficiaries are seen by HCP IPAs. The initial subset of participating IPA providers includes 685 primary care providers and 153 specialists. The HCP staff-model medical group, which employs 700 physicians practicing out of 60 clinics and offices, sees the remaining third of the Pioneer patients. The HCP groups in Florida and Nevada were also selected as Pioneer ACOs and have separate agreements with CMI; those ACOs include 12,000 and 21,000 Medicare FFS beneficiaries, respectively.

A HCP steering committee provides policies and guidance to the Pioneer ACO. Separate working teams coordinate patient messaging, provider engagement, medical management, meaningful use of electronic health records (a required component of Medicare ACOs), and other tasks. Most teams were already part of HCP's operating structure, and it is anticipated that they will be able to incrementally absorb much of the work related to the Pioneer ACO patients.

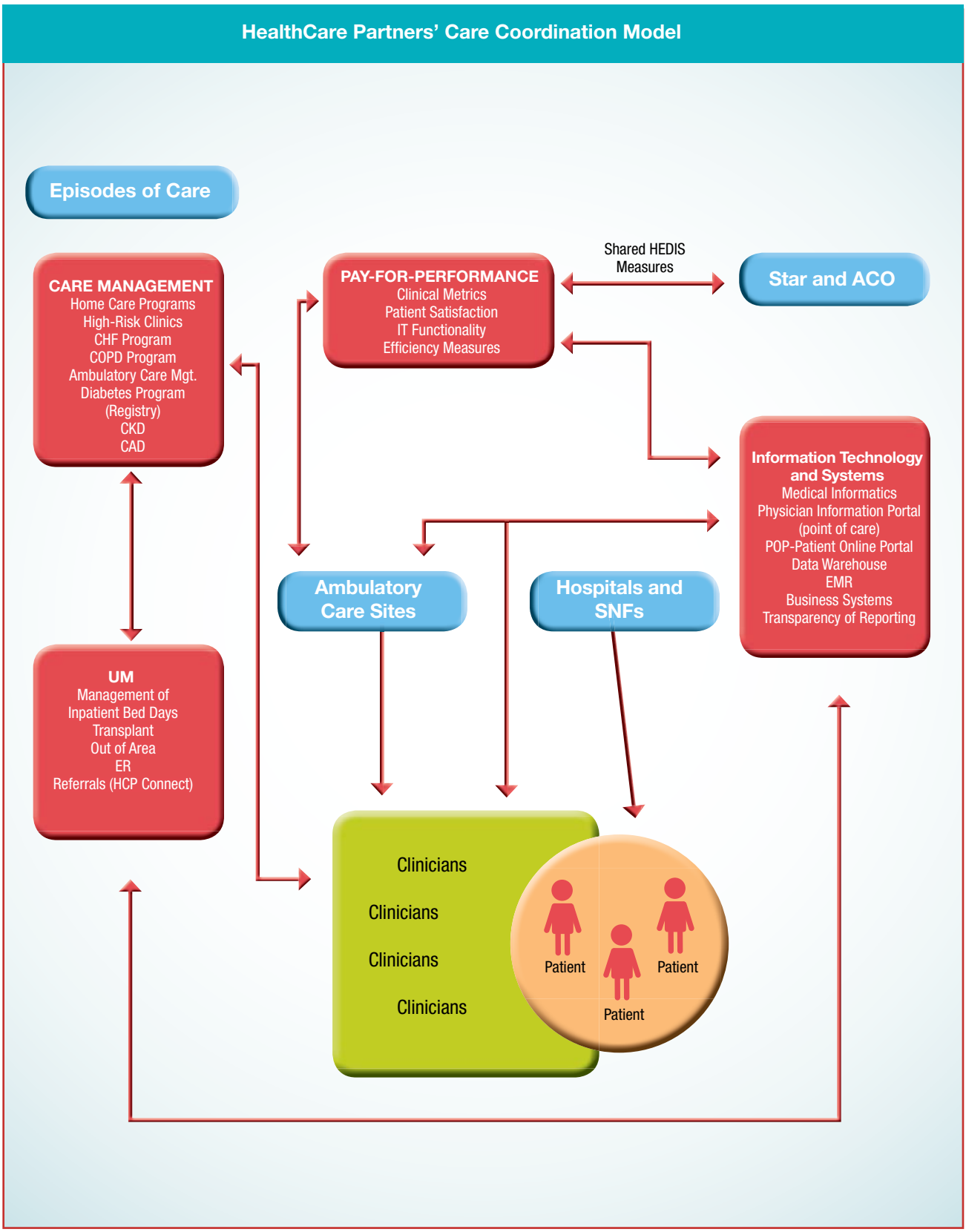
In this first year of the Pioneer program, HCP is focusing on provider and patient engagement and adding program resources where needed. Recruiting IPA providers to participate in the ACO took place through a focused effort that was made easier by the fact that many were already taking advantage of HCP's existing clinical programs and patient management tools. The participating IPA and group physicians believe the program to be an important step to improve Medicare FFS measures, reduce waste, and slow the cost trend.

Meeting year one patient engagement goals was challenging, since identifying and contacting eligible patients was a multi-step process. Once HCP identified participating providers in early 2012, CMI had to analyze the utilization records of the associated patients and apply algorithms to align patients and providers. Accurate attribution of a patient to a given primary care provider is critical, since it identifies who is responsible for coordinating the patient's care and affects provider-specific reports on performance measures. CMI also requires the ACOs to use specific protocols and materials to inform patients about the program and offer them the opportunity to opt out of sharing their health information with the ACO. On the whole, beneficiary response has been positive, and HCP anticipates that the ACO population will grow as the program moves forward.

In the ACO model, access to care is "without walls." Medicare FFS beneficiaries remain free to see any provider they wish, whether or not that provider is part of the ACO. Thus, ACOs have a strong incentive to keep patients engaged with their organization and satisfied with their providers in order to manage their care and control costs. Meeting patient needs will therefore be critical to an ACO's

ACCOUNTABLE CARE ORGANIZATIONS

continued



"In the fee-for-service world, care is often fragmented and utilizes resources unnecessarily. This adds confusion to the whole patient experience. We believe applying coordinated care principles to the Medicare fee-for-service population leads to better care for the patient. That is essentially what we have been doing with our Medicare Advantage population for many years."

–Jamie Phillips, Vice President of Regional Operations, HealthCare Partners

success. Specific patient interventions will bring to life the benefits of the ACO's enhanced care coordination. In addition to physician letters and front office education, HCP plans to use videos and social media to inform and engage patients. Patient satisfaction surveys are included in the Pioneer ACO performance measures and, along with retention rates, are part of HCP's data-driven clinical model.

Tools and Tactics

HCP has a track record of effectively and efficiently managing patient care, one of the characteristics that made it eligible to be a Pioneer ACO. For example, among Medicare beneficiaries, HCP's rate of hospital admissions is about a third lower than the national average and its 2010 30-day readmission rate was 13.9 percent in California, 14.0 percent in Nevada, and 14.8 percent in Florida, compared to a national average of 19.6 percent.[7,8] Several strategies and tools have been critical to reducing these high-cost events and will be utilized to coordinate the care of Pioneer ACO patients and promote higher patient and family member satisfaction.

On the technology side, a comprehensive data warehouse aggregates administrative, financial, and clinical data for multiple uses, including identification and stratification of high-risk and high-cost patients.[9] The Physician Information Portal, a secure Web-based platform, is a point-of-care tool for sharing patient medical history, medications, allergies, lab results, procedures, vital signs, and referrals among HCP providers caring for the patient.[9] Providers can view outstanding action items and track the patient's encounters throughout the health system. The portal also contains performance metrics aggregated at the regional, office, and provider levels, allowing a provider to track and compare his or her own performance on measures of quality and care coordination.[9] A clinical decision-support platform is being developed that will systematize clinical guidelines for ready access and permit HCP providers to monitor related referral practices.[9] Finally, a patient portal is available to medical group patients for scheduling appointments, viewing lab results, requesting prescription refills, and sending secure messages to their providers. This tool will be rolled out to IPA patients in year two of the ACO performance period.

Population health management lies at the heart of accountable care. Existing strategies at HCP include disease management (DM) programs for costly conditions: diabetes, congestive heart failure, coronary artery disease, asthma, and chronic obstructive pulmonary disease (COPD).[9] The DM care teams manage symptoms; provide care coordination, follow-up, and education; and monitor patients and expedite access to care after hospitalizations. These programs can have a significant impact. In a one-year evaluation of a patient-centered, COPD management program that included training in self-management skills, nurse telephonic outreach, and an action plan for symptom exacerbation, HCP observed a 34 percent reduction in costs and a 46 percent ROI.[10]

Additional services are provided to high-risk patients to better coordinate care across multiple providers and foster treatment adherence and self-management skills. HCP recently opened five comprehensive care centers in which multidisciplinary teams stabilize and manage high-risk patients. It also has a home-visit program for seniors. Both strategies help prevent unnecessary hospitalizations.[9]

A long-standing commitment to evidence-based inpatient care has been another important cost-containment strategy. HCP directly employs hospitalists, who provide clinical services to hospitalized patients, keep PCPs abreast of patient status, and strive to reduce unnecessary utilization.[9] To prevent readmissions, they meet with PCPs and skilled nursing facility physicians to develop comprehensive post-discharge care plans. Given HCP's successes to date in managing population health among Medicare Advantage Plan enrollees, it anticipates achieving its Pioneer program

continued

Table 1 — Key Features of the Pioneer ACO Program

Length of agreement	Three years, with possible extensions to fourth and fifth years
Medicare fee-for-service beneficiaries	15,000 beneficiaries minimum (5,000 for rural ACOs). Beneficiaries are prospectively identified and aligned with a PCP. New beneficiaries have 30 days at the start of the year to opt out of healthcare data sharing. CMS provides historical claims data to aid in risk management and care planning.
Alignment with provider	Both MD and non-MD PCPs are allowed; alignment with certain specialists is allowed if less than 10 percent of the beneficiary's care is from a PCP.
Health information technology	ACO must show meaningful use of electronic health records by 50 percent of PCPs by the start of year two.
Performance-based contracts	ACO must enter into performance-based contracts with other payors, such as insurers and employer health plans. More than 50 percent of the ACO's revenues must be derived from such payment arrangements by the end of year two.
Performance metrics	Quality scores are based on 33 measures in four domains: patient experience (CAHPS), care coordination/patient safety, preventive health, and at-risk population.
Payment model	ACOs choose from among five payment options that include: **Year one:** One-sided or two-sided risk; shared savings/losses of 50-70 percent, depending on option **Year two:** Two-sided risk; shared savings/losses of 60-75 percent, depending on option **Year three:** Population-based payment of 50 percent of expected Part A and B revenue or 100 percent of expected Part B revenue (plus shared risk for remaining care not covered by the population-based payment) or 100 percent of expected Part A and B revenue, depending on option For all options, minimum savings rate requirements and sharing and loss caps apply. Quality scores affect payment eligibility and amounts.

Sources:
Center for Medicare & Medicaid Innovation. Alternative Payment Arrangements for the Pioneer ACO Model. **http://innovations.cms.gov/Files/x/Pioneer-ACO-Model-Alternative-Payment-Arrangements-document.pdf.**
Centers for Medicare & Medicaid Services. Pioneer Accountable Care Organization (ACO) Model Request for Application. May 17, 2011. **http://innovations.cms.gov/Files/x/Pioneer-ACO-Model-Alternative-Payment-Arrangements-document.pdf.**

objectives, including transitioning to the full-risk payment option in year three, although several challenges lie ahead.

Meeting Challenges

The IPAs are critical to HCP's Pioneer ACO. Much of the company's efforts in managing the ACO will center on supporting the IPA providers and patients with the more robust tools and infrastructure commonly used on the medical group side. The Physician Information Portal will be expanded to include FFS beneficiaries and give IPA providers access to additional layers of clinical and performance data. Gaining access to third-party laboratory data, which is needed in order to have a complete clinical picture of IPA patients, presents difficult technical issues that need to be solved.

Although HCP's hospitalists take care of medical group FFS patients, the practice is less prevalent on the IPA side. Many IPA providers see their own patients in the hospital, and encouraging the use of HCP's hospitalists and discharge teams will require further dialogue with the IPA providers. IPA leadership and collaboration has been important during year one of the Pioneer ACO and will be even more so during years two and three.

The ACO model gives HCP responsibility for coordinating the care of FFS patients, who are free to go outside the ACO. Thus, one of its biggest challenges is to make the patient experience so extraordinary that patients do not want to go anywhere else. Straightforward steps, such as having someone who sets up appointments as part of post-discharge planning, can create patient satisfaction, and the IPA physicians also see this as a value-added service. HCP will be looking at a number of proactive strategies for keeping FFS patients satisfied with their patient experience and engaged with the organization.

Moving Forward

As a healthcare delivery organization that embraces care coordination principles and is participating in the accountable care model, HCP recognizes that there are several organizational components that increase the likelihood of success:

- The commitment and infrastructure needed to improve the quality and coordination of patient care grows out of strong physician leadership and a culture that supports clinical excellence.
- Improving the management of population health is data driven, and requires an appropriate investment in technology infrastructure.
- The ACO model requires thinking beyond the walls of the organization and finding new ways to engage stakeholders, providers, vendors, and patients.
- The organization has to be in it for the long haul. These programs take time and investment and may not show an immediate return.

The Pioneer ACO model is consistent with HCPs' long-standing mission to be the role model for integrated and coordinated care and to lead the transformation of the national healthcare delivery system to assure quality, access, and affordable care for all. The multilayered and collaborative strategies of accountable care require rethinking and retooling current approaches, but the model may prove to be a major step forward in improving the quality, experience, and affordability of healthcare.

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PIPELINE TRENDS

NEW DRUG APPROVALS

GENITOURINARY

Stendra™ (avanafil)
AWP: TBA
WAC: TBA
Approved: April 27, 2012
Formulation: Tablet
Manufacturer: Vivus, Inc.
Indication: Stendra™ (avanafil) is a fast-acting phosphodiesterase type 5 (PDE5) inhibitor for the treatment of erectile dysfunction.

NEW FDA-APPROVED INDICATIONS

Drug Name	Approved	New Indication
Levaquin® (levofloxacin)	April 27, 2012	Approved for use in the treatment of plague infection
Levemir® (insulin detemir)	March 29, 2012	Approved for a pregnancy category B classification

NEW FORMULATIONS AND DOSAGE FORMS

Drug Name	Manufacturer	Approved	Pricing	Advertised Advantage
Binosto® (alendronate) effervescent tablet	EffRx Pharmaceuticals SA	March 14, 2012	AWP: TBA WAC: TBA	New, once-weekly effervescent tablet formulation of alendronate offers patients an alternative in the treatment of osteo-porosis
Dymista® (azelastine and fluticasone) nasal spray	Meda Pharmaceutical, Inc.	May 1, 2012	AWP: $173.75* WAC: $139.00*	The first nasal spray that combines a H1-receptor antagonist and corticosteroid for the relief of symptoms associated with seasonal allergic rhinitis
Fabior® (tazarotene) foam	Stiefel Laboratories, Inc.	May 11, 2012	AWP: TBA WAC: TBA	A novel dosage form of retinoid tazarotene indicated for the topical treatment of acne vulgaris
Pertzye® (pancrelipase) delayed-release capsule	Digestive Care, Inc.	May 17, 2012	8,000 Units AWP $1.9875^ WAC $1.59^ 16,000 Units AWP $3.9875^ WAC $3.19^	A pancreatic enzyme product with a unique releasing mechanism indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions
QNASL® (beclomethasone diproprionate) nasal aerosol	TEVA Pharmaceuticals	March 26, 2012	AWP: $128.39* WAC: $106.99*	A novel, non-aqueous, “dry” nasal aerosol indicated for the treatment of nasal symptoms associated with seasonal and perennial allergic rhinitis in those patients 12 years of age and older

*Package price, ^Price per capsule

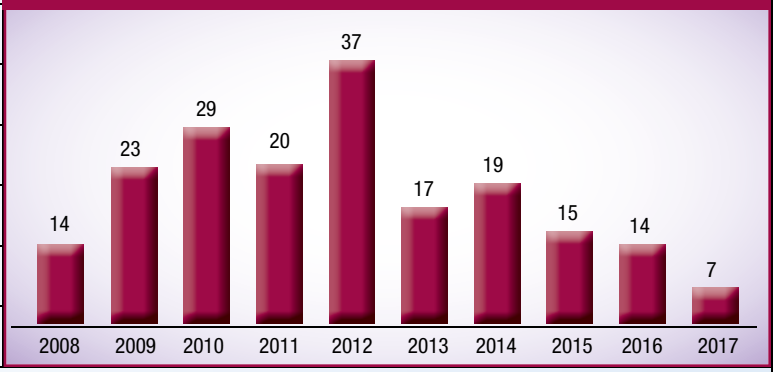
Atorvastatin Generic Launches

Atorvastatin, the generic version of the $13 billion blockbuster Lipitor, is presently being sold in the U.S. by two generic manufacturers, Ranbaxy and Watson. With the Ranbaxy 180-day exclusivity period coming to an end this past May, the atorvastatin market is now open for several other manufactures to share in the national sales. During the exclusivity period, Ranbaxy made about $600 million off the generic product. Although generic manufacturers Dr. Reddy’s and Aurobindo are awaiting FDA approval, one manufacturer decided not to pursue a generic atorvastatin product: TEVA. Originally, it was anticipated that very few generic manufacturers would be able to market this product, but it is now projected that up to eight manufacturers will have generic atorvastatin products FDA-approved in the near future. Many managed care organizations were concerned that the cost of generic atorvastatin would only be minimally less expensive than the branded agent, but this additional competition is projected to drastically reduce atorvastatin costs for payors.

Disclosures: The information contained in Pipeline Trends is current as of June 2012. Estimated dates are subject to change according to additional indication/approvals, patents, patent litigation, etc. Information available from **www.fda.gov** and **pricerx.medispan.com.**

NEW FIRST-TIME GENERIC DRUG APPROVALS	PROJECTED FIRST-TIME GENERIC ENTRY
Clopidogrel (Plavix®) Launched: May 17, 2012	Montelukast (Singulair®) August 2012
Carbidopa/levodopa/entacapone (Stalevo®)† Launched: April 4, 2012 (100mg and 150mg tablets) April 23, 2012 (50mg, 75mg, 125mg, and 200mg tablets)	Pioglitazone (Actos®) August 2012
Escitalopram oxalate tablet (Lexapro®)‡ Launched: March 14, 2012	Rivastigmine (Exelon®) August 2012
Escitalopram oxalate oral solution (Lexapro®) Launched: March 14, 2012	Sildenafil (Revatio®) September 2012
Ibandronate tablet (Boniva®) Launched: March 19, 2012	Valsartan (Diovan®) September 2012
Irbesartan tablet (Avapro®)‡ Launched: March 30, 2012	Valsartan-hydrochlorothiazide (Diovan HCT®) September 2012
Irbesartan-hydrochlorothiazide tablet (Avalide®)‡ Launched: March 30, 2012	
Modafinil tablet (Provigil®)^ Launched: March 30, 2012	
Quetiapine tablet (Seroquel®) Launched: March 27, 2012	
Ropinirole extended-release (Requip® XL) Launched: May 17, 2012	
Tinidazole tablet (Tindamax®) Launched: April 30, 2012	
Vancomycin capsule (Vancocin®) Launched: April 9, 2012	
Ziprasidone capsule (Geodon®) Launched: March 2, 2012	

Number of Branded Patent Expirations per Year

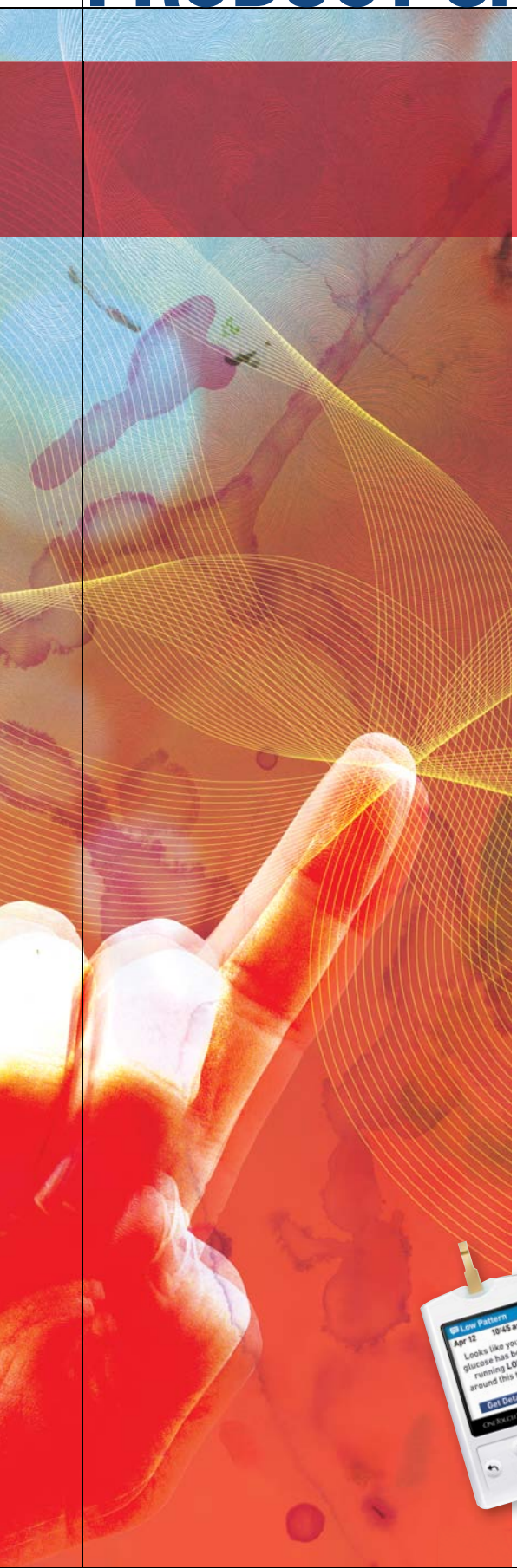


† Sun Pharma Global FZE has 180 days exclusivity, ‡Teva has 180 days exclusivity, ^ Authorized generic launched by Teva

COMING SOON . . .

Drug Name	Manufacturer	Filing Status	Proposed Indication
CARDIOVASCULAR			
AMR101 (ethyl isosapentate)	Amarin Corporation	PDUFA July 26, 2012	Oral treatment of very high triglycerides (>500 mg/dL)
Lomitapide	Aegerion Pharmaceuticals, Inc.	NDA filed February 29, 2012	Oral MTP-1 inhibitor for homozygous familial hypercholesterolemia
Kynamro (mipomersen)	sanofi-aventis	NDA filed March 29, 2012	Apo-B synthesis inhibitor for the treatment of homozygous familial hypercholesterolemia
MK-0524A (niacin ER and laropiprant)	Merck & Co., Inc.	Refilling expected late 2012	Oral combination product with an anti-flushing agent for the treatment of primary hypercholesterolemia
DIABETES			
Insulin Degludec	Novo Nordisk A/S	PDUFA October 29, 2012	Long-acting basal insulin analogue for the treatment of Diabetes Mellitus
Canagliflozin	Johnson & Johnson	NDA filed May 31, 2012	Oral SGLT-2 inhibitor for the treatment of Type 2 Diabetes Mellitus
Lyxumia (lixisenatide)	sanofi-aventis	NDA filing expected late 2012	Once-daily GLP-1 analogue for the treatment of Type 2 Diabetes Mellitus
RESPIRATORY			
Eklira (aclidinium)	Almirall and Forest Laboratories, Inc.	PDUFA July 30, 2012	Twice-daily muscarinic antagonist inhaler for maintenance treatment of bronchospasm associated with COPD
GASTROINTESTINAL			
Linaclotide	Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc.	PDUFA September 2012	Oral medication for chronic constipation and irritable bowel syndrome with constipation

PRODUCT SPOTLIGHT



OneTouch® Verio®IQ
Blood Glucose Monitor

The prevalence of diabetes in the United States continues to grow, affecting an estimated 25.8 million Americans in 2011.[1] Diabetes is a progressive disease that requires frequent monitoring, pharmacologic therapy, and nutritional education in order to achieve appropriate glycemic control. Poor management of blood glucose can result in acute and long-term complications, such as cardiovascular disease, microvascular damage, and kidney failure. Diabetes and its associated complications, particularly those of micro- and macro-vascular disease, accounted for an economic burden of $174 billion in 2007.[2] Healthcare costs for patients with diabetes is 2.3 times greater than the general population after combining costs of medications, testing supplies, and related complications.[2] A large proportion of these costs is derived from the Medicare population, which is projected to expand over the next several years. In response to this, managed care organizations (MCOs) must develop strategies to minimize diabetes-related complications for their beneficiaries by promoting best-practice guidelines and supplying patients and physicians with the appropriate resources to achieve glycemic control.

Self-monitoring of blood glucose (SMBG) has been a mainstay of diabetic treatment for nearly 30 years. For patients on insulin, the American Diabetes Association (ADA) recommends that SMBG be performed at least three times per day.[3] The key to effective use of SMBG in clinical practice is pattern management, regardless of the monitoring regimen. Pattern management is a systematic approach to identifying glycemic patterns within SMBG data and taking appropriate action based upon those results. To be effective at pattern management, patients and their clinicians must establish pre- and postprandial glucose targets and obtain data on glucose levels, carbohydrate intake, medication administration, activity levels, and physical and emotional stress. This data must then be analyzed to identify patterns of glycemic excursions and assess any influential factors. Once patterns have been established, patients and clinicians can begin implementing appropriate therapeutic actions. Patients must continue performing SMBG in order to assess the impact of these therapeutic modifications. Studies have shown that the

The OneTouch® Verio®IQ is a blood glucose meter that incorporates innovative technology to help patients and providers easily identify patterns in glucose regulation.

"All meters will tell you your blood sugar level at a particular moment in time. But the OneTouch® Verio®IQ system is the only one to compare your current result with your previous results and to proactively alert you to important patterns you might not even be aware exist. Our goal is to make a real difference for people with diabetes by providing simple tools that help patients discover ways to improve their glycemic control. By analyzing the information after each test and identifying patterns as they occur, this system helps patients and their healthcare professionals focus on fixing a potential problem instead of trying to find it."

– Michael Pfeifer, Chief Medical Officer, LifeScan, Inc.

appropriate use of pattern management results in lower HbA_{1c} levels and improved outcomes.[5]

While comprehensive pattern management is an effective way to achieve HbA_{1c} goals, it also presents several challenges for patients. Pattern management requires patients to be diligent in their documentation of medication administration, dietary intake, time of SMBG, and resulting blood glucose values. For patients new to the concept of pattern management, this requires a substantial time commitment, and is often viewed as an imposition to their daily routines. Other barriers to appropriate pattern management and attainment of glycemic goals include poor health literacy, lack of knowledge about the disease state, disbelief that these practices are beneficial, and patients' unwillingness to take responsibility for their treatment.[6]

Introduction to an Innovative Pattern Management Technology

A new product recently released by LifeScan, a Johnson & Johnson company, aims to provide a solution to help patients improve their SMBG practices and overall understanding of blood glucose values. The OneTouch® Verio®IQ is a blood glucose meter that incorporates innovative technology to help patients and providers easily identify patterns in glucose regulation. The OneTouch® Verio®IQ is specifically designed for diabetic patients who are taking daily injections of insulin. Patients on insulin have the highest risk of experiencing hypoglycemic episodes, which can have a substantial negative impact on morbidity. Unfortunately, hypoglycemia acts as a deterrent for intensifying therapy for patients with diabetes. Due to the progressive nature of the disease, it is important to continue modifying therapy in order to appropriately manage glycemic levels. The OneTouch® Verio®IQ can be used as a tool to help reduce the clinical inertia that prevents the intensification of diabetes treatment. By appropriately utilizing the OneTouch® Verio®IQ system, physicians will be able to automatically identify trends in their patients' glucose regulation and proactively modify therapy to reduce the presence of hypoglycemic patterns. This device also helps patients to understand the meaning behind their glucose values and how changes in their daily routines can result in high and potentially dangerous low glycemic patterns.

The OneTouch® Verio®IQ also serves as a helpful tool to assist patients and physicians with initiating a pattern management program to better control glucose levels. The OneTouch® Verio®IQ system features a proprietary pattern identification technology, which is known as PatternAlert™. This technology finds patterns that are relevant to the patient's diabetes management without producing excessive alerts. With every test, the OneTouch® Verio®IQ searches for high and low glycemic patterns and notifies the patient when one is found. The patterns are identified based on the following descriptions:

High Glucose Pattern: Three before-meal high readings within the same three-hour window over the past five days. High before-meal results are preset to 130 mg/dL or higher to match current ADA guidelines. However, preset reading cut-offs can also be personalized to any result at or higher than 100 to 160 mg/dL.

Low Glucose Pattern: Two low readings within the same three-hour window over the past five days. Low results are preset to 70 mg/dL or lower to match current ADA guidelines and can also be personalized to any result at or lower than 50 to 90 mg/dL.

Another major advantage of the OneTouch® Verio®IQ system is the testing strips that are compatible with the device. The OneTouch® Verio®IQ system requires the new OneTouch® Verio® Gold Test Strips. These Test Strips are

PRODUCT SPOTLIGHT *continued*

FEATURES OF TOP GLUCOSE METERS						
	OneTouch VerioIQ	OneTouch Ultra 2	Accu-Chek Aviva Plus	Freestyle Lite	Contour Breeze 2	Nipro TrueTrack
Test Sites	■ Fingertip	■ Fingertip ■ Forearm ■ Palm	■ Upper arm ■ Forearm ■ Palm ■ Fingertip ■ Thigh ■ Calf	■ Upper arm ■ Forearm ■ Palm ■ Fingertip ■ Thigh ■ Calf	■ Fingertip ■ Forearm ■ Palm	■ Fingertip ■ Forearm
Sample Size	0.4µL	1µL	0.6µL	0.3µL	1µL	1µL
Coding	No	Yes	No	No	No	No
Additional Features	■ PatternAlert™ ■ SmartScan™ ■ Stores 750 results ■ 7,14,30,90 day averages ■ Rechargeable battery ■ Illuminated test area	■ 7,14,30 day averages ■ Stores 500 results ■ Meal tags	■ 7,14,30 day averages ■ Stores 500 results ■ Customizable test reminders	■ Strip port light	■ 10-test disk strips	

designed for both accuracy and precision, and exceed the ISO3 accuracy criteria for blood glucose monitoring. The OneTouch® Verio® Gold Test Strips feature SmartScan™ technology, which tests each blood sample 500 times and provides results within five seconds. The strips are also complete with visual confirmation of blood application and require only a small amount of blood (0.4 µL) to accurately determine results.

In addition to the PatternAlert™ and SmartScan™ technologies that are incorporated into this meter, the OneTouch® Verio®IQ system offers several other simple and convenient features to help promote appropriate blood glucose testing.

- **Illuminated Testing Area:** After a test strip is inserted, the color screen and meter cap light up. This allows for testing in dimly lit or dark conditions.
- **Intuitive Interface:** The meter is controlled by four simple and easy-to-use buttons. The meter also has user-friendly menus and color-coded messages that are available in English or Spanish.
- **Memory/Averages:** The meter stores 750 test results and 50 pattern messages. Blood glucose averages can be displayed as 7-, 14-, 30-, and 90-day values.
- **Eco-friendly Rechargeable Battery:** The battery life lasts up to two weeks between charges and can be easily charged with an AC adapter or mini USB cable (both included).
- **A Companion Pattern Guide:** This is an easy-to-follow guidebook that offers possible causes and potential solutions for high and low patterns based on the guidance provided by leading diabetes experts. This guide can be made available to patients from their healthcare providers or by contacting LifeScan directly at **888-567-3003.**

As healthcare costs continue to rise, managed care organizations must put an emphasis on proper chronic disease management in order to prevent complications and additional expenses. Technologies like LifeScan's OneTouch® Verio®IQ can help make managing diabetes easier, and can alert patients and physicians when changes in care are necessary. Tighter glycemic control will allow patients to suffer fewer complications and slow the progression of the disease state. The use of new technologies such as the OneTouch® Verio®IQ system can contribute to lowering healthcare costs for MCOs by helping patients better manage their diabetes and prevent further disease-related complications.

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Victoza® (liraglutide [rDNA origin] injection)

Rx Only

BRIEF SUMMARY. Please consult package insert for full prescribing information.

WARNING: RISK OF THYROID C-CELL TUMORS: Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or nonclinical studies. Victoza® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors *[see Contraindications and Warnings and Precautions]*.

INDICATIONS AND USAGE: Victoza® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. **Important Limitations of Use:** Because of the uncertain relevance of the rodent thyroid C-cell tumor findings to humans, prescribe Victoza® only to patients for whom the potential benefits are considered to outweigh the potential risk. Victoza® is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise. In clinical trials of Victoza®, there were more cases of pancreatitis with Victoza® than with comparators. Victoza® has not been studied sufficiently in patients with a history of pancreatitis to determine whether these patients are at increased risk for pancreatitis while using Victoza®. Use with caution in patients with a history of pancreatitis. Victoza® is not a substitute for insulin. Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings. The concurrent use of Victoza® and insulin has not been studied.

CONTRAINDICATIONS: Victoza® is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

WARNINGS AND PRECAUTIONS: Risk of Thyroid C-cell Tumors: Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice. Malignant thyroid C-cell carcinomas were detected in rats and mice. A statistically significant increase in cancer was observed in rats receiving liraglutide at 8-times clinical exposure compared to controls. It is unknown whether Victoza® will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors could not be determined by clinical or nonclinical studies *[see Boxed Warning, Contraindications]*. In the clinical trials, there have been 4 reported cases of thyroid C-cell hyperplasia among Victoza®-treated patients and 1 case in a comparator-treated patient (1.3 vs. 0.6 cases per 1000 patient-years). One additional case of thyroid C-cell hyperplasia in a Victoza®-treated patient and 1 case of MTC in a comparator-treated patient have subsequently been reported. This comparator-treated patient with MTC had pre-treatment serum calcitonin concentrations >1000 ng/L suggesting pre-existing disease. All of these cases were diagnosed after thyroidectomy, which was prompted by abnormal results on routine, protocol-specified measurements of serum calcitonin. Four of the five liraglutide-treated patients had elevated calcitonin concentrations at baseline and throughout the trial. One liraglutide and one non-liraglutide-treated patient developed elevated calcitonin concentrations while on treatment. Calcitonin, a biological marker of MTC, was measured throughout the clinical development program. The serum calcitonin assay used in the Victoza® clinical trials had a lower limit of quantification (LLOQ) of 0.7 ng/L and the upper limit of the reference range was 5.0 ng/L for women and 8.4 ng/L for men. At Weeks 26 and 52 in the clinical trials, adjusted mean serum calcitonin concentrations were higher in Victoza®-treated patients compared to placebo-treated patients but not compared to patients receiving active comparator. At these timepoints, the adjusted mean serum calcitonin values (~ 1.0 ng/L) were just above the LLOQ with between-group differences in adjusted mean serum calcitonin values of approximately 0.1 ng/L or less. Among patients with pre-treatment serum calcitonin below the upper limit of the reference range, shifts to above the upper limit of the reference range which persisted in subsequent measurements occurred most frequently among patients treated with Victoza® 1.8 mg/day. In trials with on-treatment serum calcitonin measurements out to 5-6 months, 1.9% of patients treated with Victoza® 1.8 mg/day developed new and persistent calcitonin elevations above the upper limit of the reference range compared to 0.8-1.1% of patients treated with control medication or the 0.6 and 1.2 mg doses of Victoza®. In trials with on-treatment serum calcitonin measurements out to 12 months, 1.3% of patients treated with Victoza® 1.8 mg/day had new and persistent elevations of calcitonin from below or within the reference range to above the upper limit of the reference range, compared to 0.6%, 0% and 1.0% of patients treated with Victoza® 1.2 mg, placebo and active control, respectively. Otherwise, Victoza® did not produce consistent dose-dependent or time-dependent increases in serum calcitonin. Patients with MTC usually have calcitonin values >50 ng/L. In Victoza® clinical trials, among patients with pre-treatment serum calcitonin <50 ng/L, one Victoza®-treated patient and no comparator-treated patients developed serum calcitonin >50 ng/L. The Victoza®-treated patient who developed serum calcitonin >50 ng/L had an elevated pre-treatment serum calcitonin of 10.7 ng/L that increased to 30.7 ng/L at Week 12 and 53.5 ng/L at the end of the 6-month trial. Follow-up serum calcitonin was 22.3 ng/L more than 2.5 years after the last dose of Victoza®. The largest increase in serum calcitonin in a comparator-treated patient was seen with glimepiride in a patient whose serum calcitonin increased from 19.3 ng/L at baseline to 44.8 ng/L at Week 65 and 38.1 ng/L at Week 104. Among patients who began with serum calcitonin <20 ng/L, calcitonin elevations to >20 ng/L occurred in 0.7% of Victoza®-treated patients, 0.3% of placebo-treated patients, and 0.5% of active-comparator-treated patients, with an incidence of 1.1% among patients treated with 1.8 mg/day of Victoza®. The clinical significance of these findings is unknown. Counsel patients regarding the risk for MTC and the symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea or persistent hoarseness). It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate the potential risk of MTC, and such monitoring may increase the risk of unnecessary procedures, due to low test specificity for serum calcitonin and a high background incidence of thyroid disease. Patients with thyroid nodules noted on physical examination or neck imaging obtained for other reasons should be referred to an endocrinologist for further evaluation. Although routine monitoring of serum calcitonin is of uncertain value in patients treated with Victoza®, if serum calcitonin is measured and found to be elevated, the patient should be referred to an endocrinologist for further evaluation. **Pancreatitis:** In clinical trials of Victoza®, there were 7 cases of pancreatitis among Victoza®-treated patients and 1 case among comparator-treated patients (2.2 vs. 0.6 cases per 1000 patient-years). Five cases with Victoza® were reported as acute pancreatitis and two cases with Victoza® were reported as chronic pancreatitis. In one case in a Victoza®-treated patient, pancreatitis, with necrosis, was observed and led to death; however clinical causality could not be established. One additional case of pancreatitis has subsequently been reported in a Victoza®-treated patient. Some patients had other risk factors for pancreatitis, such as a history of cholelithiasis or alcohol abuse. There are no conclusive data establishing a risk of pancreatitis with Victoza® treatment. After initiation of Victoza®, and after dose increases, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, Victoza® and other potentially suspect medications should be discontinued promptly, confirmatory tests should be performed and appropriate management should be initiated. If pancreatitis is confirmed, Victoza® should not be restarted. Use with caution in patients with a history of pancreatitis. **Use with Medications Known to Cause Hypoglycemia:** Patients receiving Victoza® in combination with an insulin secretagogue (e.g., sulfonylurea) may have an increased risk of hypoglycemia. In the clinical trials of at least 26 weeks duration, hypoglycemia requiring the assistance of another person for treatment occurred in 7 Victoza®-treated patients and in two comparator-treated patients. Six of these 7 patients treated with Victoza® were also taking a sulfonylurea. The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea or other insulin secretagogues *[see Adverse Reactions]*. **Renal Impairment:** Victoza® has not been found to be directly nephrotoxic in animal studies or clinical trials. There have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis in Victoza®-treated patients *[see Adverse Reactions]*. Some of these events were reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration *[see Adverse Reactions]*. Some of the reported events occurred in patients receiving one or more medications known to affect renal function or hydration status. Altered renal function has been reversed in many of the reported cases with supportive treatment and discontinuation of potentially causative agents, including Victoza®. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment. **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with Victoza® or any other antidiabetic drug.

ADVERSE REACTIONS: Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The safety of Victoza® was evaluated in a 52-week monotherapy trial and in five 26-week, add-on combination therapy trials. In the monotherapy trial, patients were treated with Victoza® 1.2 mg daily, Victoza® 1.8 mg daily, or glimepiride 8 mg daily. In the add-on to metformin trial, patients were treated with Victoza® 0.6 mg, Victoza® 1.2 mg, Victoza® 1.8 mg, placebo, or glimepiride 4 mg. In the add-on to glimepiride trial, patients were treated with Victoza® 0.6 mg, Victoza® 1.2 mg, Victoza® 1.8 mg, placebo, or rosiglitazone 4 mg. In the add-on to metformin + glimepiride trial, patients were treated with Victoza® 1.8 mg, placebo, or insulin glargine. In the add-on to metformin + rosiglitazone trial, patients were treated with Victoza® 1.2 mg, Victoza® 1.8 mg or placebo. *Withdrawals:* The incidence of withdrawal due to adverse events was 7.8% for Victoza®-treated patients and 3.4% for comparator-treated patients in the five controlled trials of 26 weeks duration or longer. This difference was driven by withdrawals due to gastrointestinal adverse reactions, which occurred in 5.0% of Victoza®-treated patients and 0.5% of comparator-treated patients. The most common adverse reactions leading to withdrawal for Victoza®-treated patients were nausea (2.8% versus 0% for comparator) and vomiting (1.5% versus 0.1% for comparator). Withdrawal due to gastrointestinal adverse events mainly occurred during the first 2-3 months of the trials. Tables 1, 2 and 3 summarize the adverse events reported in ≥5% of Victoza®-treated patients in the six controlled trials of 26 weeks duration or longer.

Table 1: Adverse events reported in ≥5% of Victoza®-treated patients or ≥5% of glimepiride-treated patients: 52-week monotherapy trial

	All Victoza® N = 497	Glimepiride N = 248
Adverse Event Term	(%)	(%)
Nausea	28.4	8.5
Diarrhea	17.1	8.9
Vomiting	10.9	3.6
Constipation	9.9	4.8
Upper Respiratory Tract Infection	9.5	5.6
Headache	9.1	9.3
Influenza	7.4	3.6
Urinary Tract Infection	6.0	4.0
Dizziness	5.8	5.2
Sinusitis	5.6	6.0
Nasopharyngitis	5.2	5.2
Back Pain	5.0	4.4
Hypertension	3.0	6.0

Table 2: Adverse events reported in ≥5% of Victoza®-treated patients and occurring more frequently with Victoza® compared to placebo: 26-week combination therapy trials

Add-on to Metformin Trial			
	All Victoza® + Metformin N = 724	Placebo + Metformin N = 121	Glimepiride + Metformin N = 242
Adverse Event Term	(%)	(%)	(%)
Nausea	15.2	4.1	3.3
Diarrhea	10.9	4.1	3.7
Headache	9.0	6.6	9.5
Vomiting	6.5	0.8	0.4
Add-on to Glimepiride Trial			
	All Victoza® + Glimepiride N = 695	Placebo + Glimepiride N = 114	Rosiglitazone + Glimepiride N = 231
Adverse Event Term	(%)	(%)	(%)
Nausea	7.5	1.8	2.6
Diarrhea	7.2	1.8	2.2

Constipation	5.3	0.9	1.7
Dyspepsia	5.2	0.9	2.6
Add-on to Metformin + Glimepiride			
	Victoza® 1.8 + Metformin + Glimepiride N = 230	Placebo + Metformin + Glimepiride N = 114	Glargine + Metformin + Glimepiride N = 232
Adverse Event Term	(%)	(%)	(%)
Nausea	13.9	3.5	1.3
Diarrhea	10.0	5.3	1.3
Headache	9.6	7.9	5.6
Dyspepsia	6.5	0.9	1.7
Vomiting	6.5	3.5	0.4
Add-on to Metformin + Rosiglitazone			
	All Victoza® + Metformin + Rosiglitazone N = 355	Placebo + Metformin + Rosiglitazone N = 175	
Adverse Event Term	(%)	(%)	
Nausea	34.6	8.6	
Diarrhea	14.1	6.3	
Vomiting	12.4	2.9	
Decreased Appetite	9.3	1.1	
Anorexia	9.0	0.0	
Headache	8.2	4.6	
Constipation	5.1	1.1	
Fatigue	5.1	1.7	

Table 3: Treatment-Emergent Adverse Events in 26 Week Open-Label Trial versus Exenatide (Adverse events with frequency ≥5% and occurring more frequently with Victoza® compared to exenatide are listed)

	Victoza® 1.8 mg once daily + metformin and/or sulfonylurea N = 235	**Exenatide 10 mcg twice daily + metformin and/or sulfonylurea** N = 232
Preferred Term	(%)	(%)
Diarrhea	12.3	12.1
Dyspepsia	8.9	4.7
Constipation	5.1	2.6

Gastrointestinal adverse events: In the five clinical trials of 26 weeks duration or longer, gastrointestinal adverse events were reported in 41% of Victoza®-treated patients and were dose-related. Gastrointestinal adverse events occurred in 17% of comparator-treated patients. Events that occurred more commonly among Victoza®-treated patients included nausea, vomiting, diarrhea, dyspepsia and constipation. In a 26-week study of Victoza® versus exenatide, both in combination with metformin and/or sulfonylurea overall gastrointestinal adverse event incidence rates, including nausea, were similar in patients treated with Victoza® and exenatide. In five clinical trials of 26 weeks duration or longer, the percentage of patients who reported nausea declined over time. Approximately 13% of Victoza®-treated patients and 2% of comparator-treated patients reported nausea during the first 2 weeks of treatment. In a 26 week study of Victoza® versus exenatide, both in combination with metformin and/or sulfonylurea, the proportion of patients with nausea also declined over time. *Immunogenicity:* Consistent with the potentially immunogenic properties of protein and peptide pharmaceuticals, patients treated with Victoza® may develop anti-liraglutide antibodies. Approximately 50-70% of Victoza®-treated patients in the five clinical trials of 26 weeks duration or longer were tested for the presence of anti-liraglutide antibodies at the end of treatment. Low titers (concentrations not requiring dilution of serum) of anti-liraglutide antibodies were detected in 8.6% of these Victoza®-treated patients. Sampling was not performed uniformly across all patients in the clinical trials, and this may have resulted in an underestimate of the actual percentage of patients who developed antibodies. Cross-reacting anti-liraglutide antibodies to native glucagon-like peptide-1 (GLP-1) occurred in 6.9% of the Victoza®-treated patients in the 52-week monotherapy trial and in 4.8% of the Victoza®-treated patients in the 26-week add-on combination therapy trials. These cross-reacting antibodies were not tested for neutralizing effect against native GLP-1, and thus the potential for clinically significant neutralization of native GLP-1 was not assessed. Antibodies that had a neutralizing effect on liraglutide in an *in vitro* assay occurred in 2.3% of the Victoza®-treated patients in the 52-week monotherapy trial and in 1.0% of the Victoza®-treated patients in the 26-week add-on combination therapy trials. Among Victoza®-treated patients who developed anti-liraglutide antibodies, the most common category of adverse events was that of infections, which occurred among 40% of these patients compared to 36%, 34% and 35% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. The specific infections which occurred with greater frequency among Victoza®-treated antibody-positive patients were primarily nonserious upper respiratory tract infections, which occurred among 11% of Victoza®-treated antibody-positive patients; and among 7%, 7% and 5% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. Among Victoza®-treated antibody-negative patients, the most common category of adverse events was that of gastrointestinal events, which occurred in 43%, 18% and 19% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. Antibody formation was not associated with reduced efficacy of Victoza® when comparing mean HbA_{1c} of all antibody-positive and all antibody-negative patients. However, the 3 patients with the highest titers of anti-liraglutide antibodies had no reduction in HbA_{1c} with Victoza® treatment. In clinical trials of Victoza®, events from a composite of adverse events potentially related to immunogenicity (e.g. urticaria, angioedema) occurred among 0.8% of Victoza®-treated patients and among 0.4% of comparator-treated patients. Urticaria accounted for approximately one-half of the events in this composite for Victoza®-treated patients. Patients who developed anti-liraglutide antibodies were not more likely to develop events from the immunogenicity events composite than were patients who did not develop anti-liraglutide antibodies. *Injection site reactions:* Injection site reactions (e.g., injection site rash, erythema) were reported in approximately 2% of Victoza®-treated patients in the five clinical trials of at least 26 weeks duration. Less than 0.2% of Victoza®-treated patients discontinued due to injection site reactions. *Papillary thyroid carcinoma:* In clinical trials of Victoza®, there were 6 reported cases of papillary thyroid carcinoma in patients treated with Victoza® and 1 case in a comparator-treated patient (1.9 vs. 0.6 cases per 1000 patient-years). Most of these papillary thyroid carcinomas were <1 cm in greatest diameter and were diagnosed in surgical pathology specimens after thyroidectomy prompted by findings on protocol-specified screening with serum calcitonin or thyroid ultrasound. *Hypoglycemia:* In the clinical trials of at least 26 weeks duration, hypoglycemia requiring the assistance of another person for treatment occurred in 7 Victoza®-treated patients (2.6 cases per 1000 patient-years) and in two comparator-treated patients. Six of these 7 patients treated with Victoza® were also taking a sulfonylurea. One other patient was taking Victoza® in combination with metformin but had another likely explanation for the hypoglycemia (this event occurred during hospitalization and after insulin infusion) (Table 4). Two additional cases of hypoglycemia requiring the assistance of another person for treatment have subsequently been reported in patients who were not taking a concomitant sulfonylurea. Both patients were receiving Victoza®, one as monotherapy and the other in combination with metformin. Both patients had another likely explanation for the hypoglycemia (one received insulin during a frequently-sampled intravenous glucose tolerance test, and the other had intracranial hemorrhage and uncertain food intake).

Table 4: Incidence (%) and Rate (episodes/patient year) of Hypoglycemia in the 52-Week Monotherapy Trial and in the 26-Week Combination Therapy Trials

	Victoza® Treatment	**Active Comparator**	**Placebo Comparator**
Monotherapy	**Victoza®** (N = 497)	**Glimepiride** (N = 248)	**None**
Patient not able to self–treat	0	0	—
Patient able to self–treat	9.7 (0.24)	25.0 (1.66)	—
Not classified	1.2 (0.03)	2.4 (0.04)	—
Add-on to Metformin	**Victoza® + Metformin** (N = 724)	**Glimepiride + Metformin** (N = 242)	**Placebo + Metformin** (N = 121)
Patient not able to self–treat	0.1 (0.001)	0	0
Patient able to self–treat	3.6 (0.05)	22.3 (0.87)	2.5 (0.06)
Add-on to Glimepiride	**Victoza® + Glimepiride** (N = 695)	**Rosiglitazone + Glimepiride** (N = 231)	**Placebo + Glimepiride** (N = 114)
Patient not able to self–treat	0.1 (0.003)	0	0
Patient able to self–treat	7.5 (0.38)	4.3 (0.12)	2.6 (0.17)
Not classified	0.9 (0.05)	0.9 (0.02)	0
Add-on to Metformin + Rosiglitazone	**Victoza® + Metformin + Rosiglitazone** (N = 355)	**None**	**Placebo + Metformin + Rosiglitazone** (N = 175)
Patient not able to self–treat	0	—	0
Patient able to self–treat	7.9 (0.49)	—	4.6 (0.15)
Not classified	0.6 (0.01)	—	1.1 (0.03)
Add-on to Metformin + Glimepiride	**Victoza® + Metformin + Glimepiride** (N = 230)	**Insulin glargine + Metformin + Glimepiride** (N = 232)	**Placebo + Metformin + Glimepiride** (N = 114)
Patient not able to self–treat	2.2 (0.06)	0	0
Patient able to self–treat	27.4 (1.16)	28.9 (1.29)	16.7 (0.95)
Not classified	0	1.7 (0.04)	0

In a pooled analysis of clinical trials, the incidence rate (per 1,000 patient-years) for malignant neoplasms (based on investigator-reported events, medical history, pathology reports, and surgical reports from both blinded and open-label study periods) was 10.9 for Victoza®, 6.3 for placebo, and 7.2 for active comparator. After excluding papillary thyroid carcinoma events *[see Adverse Reactions]*, no particular cancer cell type predominated. Seven malignant neoplasm events were reported beyond 1 year of exposure to study medication, six events among Victoza®-treated patients (4 colon, 1 prostate and 1 nasopharyngeal), no events with placebo and one event with active comparator (colon). Causality has not been established. **Laboratory Tests:** In the five clinical trials of at least 26 weeks duration, mildly elevated serum bilirubin concentrations (elevations to no more than twice the upper limit of the reference range) occurred in 4.0% of Victoza®-treated patients, 2.1% of placebo-treated patients and 3.5% of active-comparator-treated patients. This finding was not accompanied by abnormalities in other liver tests. The significance of this isolated finding is unknown. **Post-Marketing Experience:** The following additional adverse reactions have been reported during post-approval use of Victoza®. Because these events are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Gastrointestinal: nausea, vomiting and diarrhea sometimes resulting in dehydration *[see Warnings and Precautions]*. Renal and Urinary Disorders: increased serum creatinine, acute renal failure or worsening of chronic renal failure, which may sometimes require hemodialysis *[see Warnings and Precautions]*.

OVERDOSAGE: In a clinical trial, one patient with type 2 diabetes experienced a single overdose of Victoza® 17.4 mg subcutaneous (10 times the maximum recommended dose). Effects of the overdose included severe nausea and vomiting requiring hospitalization. No hypoglycemia was reported. The patient recovered without complications. In the event of overdosage, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms.

More detailed information is available upon request.

For information about Victoza® contact: Novo Nordisk Inc., 100 College Road West, Princeton, New Jersey 08540, 1–877-484-2869

Date of Issue: May 18, 2011 **Version: 3**

Manufactured by: Novo Nordisk A/S, DK-2880 Bagsvaerd, Denmark

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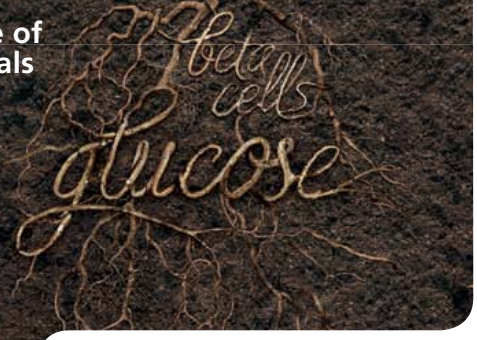
VICTOZA®
liraglutide (rDNA origin) injection

Help adult patients with type 2 diabetes gain greater access

Get to know Victoza® on a deeper level.

Powerful reductions in A1C from -0.8% to -1.5%*



Low rate of hypoglycemia

Flexible dosing any time of day, independent of meals

May reduce weight
—Victoza® is not indicated for the management of obesity, and weight change was a secondary end point in clinical trials

VictozaCare™ helps patients stay on track with ongoing support
—Patients enrolled in **VictozaCare™** were more adherent to Victoza® than those not enrolled†

To see how Victoza® works for your patients, visit **VictozaPro.com/GLP1.**

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VICTOZA®
liraglutide (rDNA origin) injection

Indications and usage

Victoza® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Because of the uncertain relevance of the rodent thyroid C-cell tumor findings to humans, prescribe Victoza® only to patients for whom the potential benefits are considered to outweigh the potential risk. Victoza® is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise.

In clinical trials of Victoza®, there were more cases of pancreatitis with Victoza® than with comparators. Victoza® has not been studied sufficiently in patients with a history of pancreatitis to determine whether these patients are at increased risk for pancreatitis while using Victoza®. Use with caution in patients with a history of pancreatitis.

Victoza® is not a substitute for insulin. Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

The concurrent use of Victoza® and insulin has not been studied.

Important safety information

Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or nonclinical studies. Victoza® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors.

If pancreatitis is suspected, Victoza® should be discontinued. Victoza® should not be re-initiated if pancreatitis is confirmed.

When Victoza® is used with an insulin secretagogue (e.g. a sulfonylurea) serious hypoglycemia can occur. Consider lowering the dose of the insulin secretagogue to reduce the risk of hypoglycemia.

Renal impairment has been reported postmarketing, usually in association with nausea, vomiting, diarrhea, or dehydration, which may sometimes require hemodialysis. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment.

There have been no studies establishing conclusive evidence of macrovascular risk reduction with Victoza® or any other antidiabetic drug.

The most common adverse reactions, reported in ≥5% of patients treated with Victoza® and more commonly than in patients treated with placebo, are headache, nausea, diarrhea, and anti-liraglutide antibody formation. Immunogenicity-related events, including urticaria, were more common among Victoza®-treated patients (0.8%) than among comparator-treated patients (0.4%) in clinical trials.

Victoza® has not been studied in type 2 diabetes patients below 18 years of age and is not recommended for use in pediatric patients.

Victoza® should be used with caution in patients with hepatic impairment.

Please see brief summary of Prescribing Information on adjacent page.

*Victoza® 1.2 mg and 1.8 mg when used alone or in combination with OADs.
†Crossix ScoreBoard™ Report, September 2011. Adherence measured by number of actual Victoza® prescriptions filled for existing Victoza® patients enrolled in **VictozaCare™** versus a match-pair control group not enrolled in **VictozaCare™** through first 8 months of enrollment.

1111-00006045-1 January 2012

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If pancreatitis is suspected, Victoza® should be discontinued. Victoza® should not be re-initiated if pancreatitis is confirmed.

When Victoza® is used with an insulin secretagogue (e.g. a sulfonylurea) serious hypoglycemia can occur. Consider lowering the dose of the insulin secretagogue to reduce the risk of hypoglycemia.

Renal impairment has been reported postmarketing, usually in association with nausea, vomiting, diarrhea, or dehydration, which may sometimes require hemodialysis. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment.

There have been no studies establishing conclusive evidence of macrovascular risk reduction with Victoza® or any other antidiabetic drug.

The most common adverse reactions, reported in ≥5% of patients treated with Victoza® and more commonly than in patients treated with placebo, are headache, nausea, diarrhea, and anti-liraglutide antibody formation. Immunogenicity-related events, including urticaria, were more common among Victoza®-treated patients (0.8%) than among comparator-treated patients (0.4%) in clinical trials.

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1111-00006045-1 January 2012