Cancer Treatment Developments

FDA Pipeline
Oncology biologics

Population Health
Reducing pediatric hospitalizations

Pharmacy/Formulary
Gene therapy coverage

Technology
Optimizing IT operations

Industry Analysis
What boomers/millennials want
As part of a combination regimen, provide your members with the only FDA-approved treatment for refractory MAC lung disease

ARIKAYCE, through its proprietary liposomal technology PULMOVANCE®, delivers inhaled liposomal amikacin directly to the lungs where the infection resides, and has been shown to penetrate biofilms and macrophages. ARIKAYCE and the Lamira™ Nebulizer System were approved as a drug-device combination and are both processed under pharmacy benefits. The Lamira Nebulizer System is shipped to patients concurrently with their first dose at no additional cost to the patient or health plan.

An animal study analyzed the in vivo uptake of various formulations of amikacin, including ARIKAYCE, IV amikacin, and inhaled IV amikacin. Five to eight times more amikacin was delivered to pulmonary macrophages treated with ARIKAYCE compared with inhaled IV amikacin. The clinical relevance of this is unknown.

FDA-US Food and Drug Administration; IV—intravenous; MAC—Mycobacterium avium complex; NTM—nontuberculous mycobacteria.

INDICATION

LIMITED POPULATION: ARIKAYCE® is indicated in adults, who have limited or no alternative treatment options, for the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. As only limited clinical safety and effectiveness data for ARIKAYCE are currently available, reserve ARIKAYCE for use in adults who have limited or no alternative treatment options. This drug is indicated for use in a limited and specific population of patients.

This indication is approved under accelerated approval based on achieving sputum culture conversion (defined as 3 consecutive negative monthly sputum cultures) by Month 6. Clinical benefit has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitation of Use: ARIKAYCE has only been studied in patients with refractory MAC lung disease defined as patients who did not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. The use of ARIKAYCE is not recommended for patients with non-refractory MAC lung disease.

Hypersensitivity Pneumonitis has been reported with the use of ARIKAYCE in the clinical trials. Hypersensitivity pneumonitis (reported as allergic alveolitis, pneumonitis, interstitial lung disease, allergic reaction to ARIKAYCE) was reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (3.1%) compared to patients treated with a background regimen alone (0%). Most patients with hypersensitivity pneumonitis discontinued treatment with ARIKAYCE and received treatment with corticosteroids. If hypersensitivity pneumonitis occurs, discontinue ARIKAYCE and manage patients as medically appropriate.

Hemoptysis has been reported with the use of ARIKAYCE in the clinical trials. Hemoptysis was reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (17.9%) compared to patients treated with a background regimen alone (12.5%). If hemoptysis occurs, manage patients as medically appropriate.

Bronchospasm has been reported with the use of ARIKAYCE in the clinical trials. Bronchospasm (reported as asthma, bronchial hyperreactivity, bronchospasm, dyspnea, dyspnea exertional, prolonged expiration, throat tightness, wheezing) was reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (28.7%) compared to patients treated with a background regimen alone (10.7%). If bronchospasm occurs during the use of ARIKAYCE, treat patients as medically appropriate.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF INCREASED RESPIRATORY ADVERSE REACTIONS
ARIKAYCE has been associated with an increased risk of respiratory adverse reactions, including hypersensitivity pneumonitis, hemoptysis, bronchospasm, and exacerbation of underlying pulmonary disease that have led to hospitalizations in some cases.
ARIKAYCE®
(amicin liposome inhalation suspension)
590 mg/8.4 mL
Limited Population

Exacerbations of underlying pulmonary disease has been reported with the use of ARIKAYCE in the clinical trials. Exacerbations of underlying pulmonary disease (reported as chronic obstructive pulmonary disease [COPD], infective exacerbation of COPD, infective exacerbation of bronchiectasis) have been reported at a higher frequency in patients treated with ARIKAYCE plus background regimen (14.8%) compared to patients treated with background regimen alone (9.8%). If exacerbations of underlying pulmonary disease occur during the use of ARIKAYCE, treat patients as medically appropriate.

Ototoxicity has been reported with the use of ARIKAYCE in the clinical trials. Ototoxicity (including deafness, dizziness, presyncope, tinnitus, and vertigo) were reported with a higher frequency in patients treated with ARIKAYCE plus background regimen (17%) compared to patients treated with background regimen alone (9.8%). This was primarily driven by tinnitus (7.6% in ARIKAYCE plus background regimen vs 0.9% in the background regimen alone arm) and dizziness (6.3% in ARIKAYCE plus background regimen vs 2.7% in the background regimen alone arm). Closely monitor patients with known or suspected auditory or vestibular dysfunction during treatment with ARIKAYCE. If ototoxicity occurs, manage patients as medically appropriate, including potentially discontinuing ARIKAYCE.

Nephrotoxicity was observed during the clinical trials of ARIKAYCE in patients with MAC lung disease but not at a higher frequency than background regimen alone. Nephrotoxicity has been associated with the aminoglycosides. Close monitoring of patients with known or suspected renal dysfunction may be needed when prescribing ARIKAYCE.

Neuromuscular Blockade: Patients with neuromuscular disorders were not enrolled in ARIKAYCE clinical trials. Patients with known or suspected neuromuscular disorders, such as myasthenia gravis, should be closely monitored since aminoglycosides may aggravate muscle weakness by blocking the release of acetylcholine at neuromuscular junctions.

Embryo-Fetal Toxicity: Aminoglycosides can cause fetal harm when administered to a pregnant woman. Aminoglycosides, including ARIKAYCE, may be associated with total, irreversible, bilateral congenital deafness in pediatric patients exposed in utero. Patients who use ARIKAYCE during pregnancy, or become pregnant while taking ARIKAYCE should be apprised of the potential natazaz to the fetus.

29.0% vs 8.9%
A clinical trial investigated the safety and efficacy of ARIKAYCE - background regimen vs background regimen alone. Efficacy was assessed through a primary endpoint that was based on culture conversion (3 consecutive monthly MAC-negative sputum cultures) by Month 6.
ARIKAYCE - background regimen achieved a 3-fold increase in the percentage of patients who experienced culture conversion by Month 6 [29.0% (60/204) vs 8.9% (17/192) (P<0.0001)] compared with the background regimen alone.
The additional endpoints of 6-minute walk test distance and St George's Respiratory Questionnaire did not demonstrate clinical benefit by Month 6.

Contraindications: ARIKAYCE is contraindicated in patients with known hypersensitivity to any aminoglycoside.

Most Common Adverse Reactions: The most common adverse reactions in Trial 1 at an incidence ≥5% for patients using ARIKAYCE plus background regimen compared to patients treated with background regimen alone were dysphonia (47% vs 1%), cough (39% vs 17%), bronchospasm (29% vs 11%), hemoptysis (13% vs 13%), ototoxicity (17% vs 10%), upper airway irritation (17% vs 2%), musculoskeletal pain (17% vs 8%), fatigue and asthenia (16% vs 10%), exacerbation of underlying pulmonary disease (15% vs 10%), diarrhea (13% vs 5%), nausea (12% vs 4%), pneumonia (10% vs 8%), headache (10% vs 5%), pyrexia (7% vs 5%), vomiting (7% vs 4%), rash (6% vs 2%), decreased weight (6% vs 1%), change in sputum (5% vs 1%), and chest discomfort (5% vs 3%).

Drug Interactions: Avoid concomitant use of ARIKAYCE with medications associated with neurotoxicity, nephrotoxicity, and ototoxicity. Some diuretics can enhance aminoglycoside toxicity by altering aminoglycoside concentrations in serum and tissue. Avoid concomitant use of ARIKAYCE with ethacrynic acid, furosemide, urea, or intravenous mannitol.

Overdosage: Adverse reactions specifically associated with overdose of ARIKAYCE have not been identified. Acute toxicity should be treated with immediate withdrawal of ARIKAYCE, and baseline tests of renal function should be undertaken. Hemodialysis may be helpful in removing amikacin from the body. In all cases of suspected overdosage, physicians should contact the Regional Poison Control Center for information about effective treatment.


Please see the Brief Summary on the following pages.

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ARIKAYCE® (amikacin liposome inhalation suspension)

BRIEF SUMMARY: For complete safety, please consult the full prescribing information.

WARING: RISK OF INCREASED RESPIRATORY ADVERSE REACTIONS

ARIKAYCE has been associated with an increased risk of respiratory adverse reactions including, hypersensitivity pneumonitis, hemoptysis, bronchospasm, exacerbation of underlying pulmonary disease that have led to hospitalizations in some cases (see Warnings and Precautions 5.1, 6.2, 6.3, 5.4).

1 INDICATIONS AND USAGE

LIMITED POPULATION: ARIKAYCE is indicated in adults, who have limited or no alternative treatment options, for the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy. As only limited clinical safety and effectiveness data for ARIKAYCE are currently available, reserve ARIKAYCE for use in adults who have failed or an alternative treatment options. This drug is indicated for use in a limited and specific population of patients.

This indication is approved under accelerated approval based on achieving sputum culture conversion (defined as 3 consecutive negative monthly sputum cultures) by Month 6. Clinical benefit has not yet been established.
Table 1: Adverse Reactions in ≥5% of ARIKAYCE-treated MAC Patients and More Frequent than Background Regimen Alone in Trial 1

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Arikayce plus Background Regimen (n=223)</th>
<th>Background Regimen Alone (n=112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysphoniaa</td>
<td>108 (48)</td>
<td>11 (1)</td>
</tr>
<tr>
<td>Cough</td>
<td>87 (39)</td>
<td>19 (17)</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>64 (29)</td>
<td>12 (11)</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>40 (18)</td>
<td>14 (13)</td>
</tr>
<tr>
<td>Obstructiva</td>
<td>36 (16)</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Upper airway infection</td>
<td>37 (17)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>37 (17)</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Fatigue and asthenia</td>
<td>36 (16)</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Exacerbations of underlying pulmonary diseaseb</td>
<td>30 (14)</td>
<td>11 (10)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>26 (12)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Nausea</td>
<td>26 (12)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>22 (10)</td>
<td>9 (8)</td>
</tr>
<tr>
<td>Headache</td>
<td>22 (10)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Priapism</td>
<td>16 (7)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Vomitinga</td>
<td>15 (7)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Rash</td>
<td>14 (6)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Weight decreased</td>
<td>14 (6)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Change in appetite</td>
<td>12 (5)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>12 (5)</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

aIncludes asthma and dysphonia.
bIncludes cough, productive cough, and upper airway cough syndrome.
cIncludes asthma, bronchial hyperreactivity, bronchospasm, hypoxemia, degree of exertional, prolonged expiration, throat tightness, wheezing.
dIncludes dizziness, drowsiness, memory, visual disturbance, dryness, dyspnea, hyperventilation, vertigo.
eIncludes orthostatic hypotension, syncope, hypotension, syncope, hyperventilation, vertigo.
fIncludes back pain, arthritis, family history, chronic obstructive pulmonary disease.
gIncludes COPD, idiopathic exudative or COPD, idiopathic exacerbation of bronchiectasis.
hIncludes atypical pneumonia, pneumonia, infection not breast of tissue, lower respiratory infection, lung infection, lung infection, pulmonary, pneumonia, pneumonia aspiration, pneumonia pneumatocele, pneumatocele infection, and respiratory tract infection.
iIncludes vomiting and post-tissue vomiting.
jIncludes rash, mucus-popular, drug eruption, and urtica.
kIncludes increased appetite, increased parenchymal, and asymptomatic.

Selected adverse drug reactions that occurred in ≥5% of patients and at higher frequency in ARIKAYCE-treated patients in Trial 1 are presented in Table 2.

Table 2: Selected Adverse Reactions in ≥5% of ARIKAYCE-treated MAC Patients and More Frequent than Background Regimen Alone in Trial 1

<table>
<thead>
<tr>
<th>Arikayce plus Background Regimen (n=223)</th>
<th>Background Regimen Alone (n=112)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>19 (4.5)</td>
</tr>
<tr>
<td>Oral fungal infection</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>8 (3.6)</td>
</tr>
<tr>
<td>Hypersensitivity pneumoniab</td>
<td>6 (3.6)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Respiratory failurec</td>
<td>6 (2.7)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>6 (2.7)</td>
</tr>
<tr>
<td>Neurovascular disorder</td>
<td>5 (2.2)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>5 (2.2)</td>
</tr>
<tr>
<td>Pneumatocele</td>
<td>5 (2.2)</td>
</tr>
<tr>
<td>Exercise intolerance decreased</td>
<td>5 (2.2)</td>
</tr>
<tr>
<td>Balance disorder</td>
<td>3 (1.3)</td>
</tr>
</tbody>
</table>
| Includes oral candidiasis and oral fungal infection.
| Includes allergic incontinence, interstitial lung disease, and pneumatocele.
| Includes acute respiratory failure and respiratory failure.
| Includes musculoskeletal, myopathy, spasticity, and bone disorder.
| Includes pneumonia, pleurisy, pneumonia, and pneumatocele.

Refer to Table 1 and Table 2 for the incidence rate of hypersensitivity pneumoniab, bronchospasm, cough, dyspnoea, exacerbation of underlying disease, hemoptysis, orthostatic upper airway irritation, and inuenmononucleosis (see Warnings and Precautions (5.1, 5.2, 5.3, 5.4, 5.5, 5.6)).

10 OVERDOSAGE

Adverse reactions specifically associated with overdose of ARIKAYCE have not been identified. Acute toxicity should be treated with immediate withdrawal of ARIKAYCE, and basic tests of renal function should be undertaken.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 2-year inhalation carcinogenesis study, rats were exposed to ARIKAYCE for 15–25, 50–70, or 155–170 minutes per day for 90–104 weeks. These provided approximate inhaled doses of 15, 15, and 39 mg/kg/day. Squamous cell carcinomas were observed in the lungs of 1 of 150 rats administered the highest dose tested. Maximum serum AUC levels of amikacin in the rats at steady state were approximately 1.3, 2.9, and 7.6 mg·h/mL at the low, mid, and high doses, respectively, compared with 23.5 mg·h/mL (6.0 to 46.5 mg·h/mL) measured in humans. The squamous cell carcinomas may be the result of a high lung burden of particles in the ARIKAYCE in the rat lung. The reference of the lung tumor findings with regards to humans receiving ARIKAYCE is unknown.

There is no evidence of mutagenicity or genotoxicity was observed in a battery of in vitro and in vivo genotoxicity studies with a transgenic-encapsulated amikacin formulation similar to ARIKAYCE (in vitro microbial mutagenesis test in vitro mouse lymphoma mutation assay, in vitro chromosomal aberration assay, and in vivo micronucleus test in rats).

There were no significant findings associated with interrupted dosing of ARIKAYCE to another animal species, a 12-month inhalation toxicity study was conducted in dogs. Formy alveolar macrophages associated with clearance of the inhaled product were present at dose-related incidence and severity, but they were not associated with inflammation, tissue hypertrophy, or the presence of pneumocyte or pleuropulmonary changes. Dogs were exposed to ARIKAYCE for up to 50 minutes per day, providing inhaled amikacin doses of approximately 5, 10, and 30 mg/kg/day.

Animal reproductive toxicology studies have not been conducted with inhaled amikacin. Subcutaneous administration of amikacin to pregnant rats up to 100 mg/kg/day and to nursing rats up to 100 mg/kg/day during organogenesis was not associated with fetal malformations. Obstetric toxicity was not adequately evaluated in offspring in animal studies.

The estimated background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

Animal reproductive toxicology studies have been conducted with ARIKAYCE or non-liposomal amikacin administered by inhalation. Amikacin was subchronically administered to pregnant rats (Gestation Days 8–14) and mice (Gestation Days 7–11) at doses of 25, 50, or 500 mg/kg to assess developmental toxicity. These doses did not cause fetal visceral or skeletal malformations in mice. The high dose was excessively maternally toxic in rats (neophobia and motility were observed), precluding the evaluation of offspring at this dose. Fetal nasal bone growth restriction was noted at the highest dose tested in the rats and mice exposed to these doses of amikacin in vitro did not differ significantly from control.

Obstetricity was not adequately evaluated in offspring in animal development toxicity studies.

8.2 Lactation

Risk Summary

There is no information regarding the presence of ARIKAYCE in human milk, the effects on the breastfed infant, or the effects on milk production after administration of ARIKAYCE by inhalation. Although limited published data on other routes of administration of amikacin indicate that amikacin is present in human milk, systematic absorption of ARIKAYCE (followed inhalation administration is expected to be low (see Clinical Pharmacology (12.3)). The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for ARIKAYCE and any potential adverse effects on the breastfed child from ARIKAYCE or from the underlying maternal condition.

8.4 Pediatric Use: Safety and effectiveness of ARIKAYCE in pediatric patients below 16 years of age have not been established.

8.5 Hepatic Impairment: ARIKAYCE has not been studied in patients with hepatic impairment. No dose adjustments based on hepatic impairment are required since amikacin is not hepatobiotically metabolized (see Clinical Pharmacology (12.3)).

8.7 Renal Impairment: ARIKAYCE has not been studied in patients with renal impairment. Given the low systemic exposure to amikacin following administration of ARIKAYCE, clinically relevant accumulation of amikacin is unlikely to occur in patients with renal impairment. In patients with known or suspected renal impairment, including elderly patients with potential age-related decreases in renal function (see Warnings and Precautions (5.6), Use in Specific Populations (8.5)).
An Exciting Time for Cancer Care

Cancer care is entering a new, exciting phase. The past few years have seen remarkable lifesaving advances in the treatment of cancer as decades of clinical research become mainstream clinical care.

"Over the last five decades, mortality rates have declined for most cancers, largely due to improvements in prevention, detection, and treatment. These advances have been fueled by breakthrough studies of complex environmental and genetic interactions that can lead to cancer, the identification of targets that drive cancer, and the development of effective interventions against those targets."

Are we on our way to curing cancer? There’s more to do, but one certainty is that new therapies will soon become more routine, meaning healthcare executives need to understand what they are, how they work, the costs, the benefits, and the potential they have to revolutionize cancer treatments and win the war on cancer in the United States.

We know that the impact of new drugs and treatments on cancer outcomes, side effects, and longevity—as well as the impact all of those have on medical costs—is important to you. In Managed Healthcare Executive’s cover story you’ll learn:

- How comprehensive genomic profiling is using next-generation sequencing technology to help match patients to available targeted therapies, immunotherapies, or clinical trial options.
- More about new phase 3 drug candidates offering remarkable promise as a first-line treatment for metastatic colon cancer.
- Why a new chemo-free treatment for leukemia could mark yet another advancement in chemo-free cancer treatment and help take financial and physical burdens off patients.
- How chimeric antigen receptor T-cell therapy is treating other forms of cancer, such as multiple myeloma, and solid tumors of the lung, brain, breast, and colon.

In addition, other great content in this issue will help drive you to value-based solutions. You’ll see novel approaches to cancer pain management; an insider’s look at phase 3 oncology drugs in the pipeline; a game-changing population health initiative at a premier children’s hospital that is reducing the pediatric hospitalization rate; readmission trends for hip and knee replacement; and ways to optimize your information technology operations.

It’s an exciting time for cancer care. We’re here to help you manage all the challenges along the way.

Mike Hennessy, Sr.
Chairman and Founder
Cancer Treatment Developments
Cancer care enters a new, exciting phase, experts say

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Mission: Managed Healthcare Executive* provides healthcare executives at health plans and provider organizations with analysis, insights, and strategies to pursue value-driven solutions.

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Lili Brillstein is a nationally recognized thought leader in the advancement of Episodes of Care as a value-based approach for specialty care. She is the CEO of BCollaborative, which works with stakeholders across the healthcare continuum to successfully make the move from fee for service to value-based healthcare.

Joel V. Brill, MD, is the chief medical officer for Predictive Health, LLC, which partners with stakeholders to improve coverage of value-driven care that optimizes health for people.

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Virginia Calega, MD, is vice president, medical affairs, Facilitated Health Networks at Independence Blue Cross. She oversees utilization management, medical cost, and health outcomes data, and interventions that optimize these outcomes.

Douglas L. Chaet, FACHE, is chief managed care officer, Cleveland Clinic, and chairman, American Association of Integrated Healthcare Delivery Systems.

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Cancer is among the most frightening diagnoses for patients to receive. It is a daunting challenge for oncology treatment specialists, and a persistent challenge for policy makers, payers, and other parties charged with ensuring that high-quality, evidence-based, cost-effective care is delivered consistently for all patients.

In addition to the physical manifestations of oncologic disease and the often very difficult treatment side effects, many patients experience significant financial distress as a result of their diagnosis and treatment. Patients are also often left to navigate a complex and unclear labyrinth of healthcare services on their own during a period of intense physical and emotional vulnerability—the disjointed care that is one of the most unfortunate results of the prevailing fee-for-service payment methodology.

In an attempt to address these issues, many experts are evaluating the potential for adoption of value-based, collaborative care payment models such as Episodes of Care/Bundled Payments as an alternative to fee for service. Value-based models are intended to improve patient outcomes and experiences.

They are also intended to reduce the overall cost of care by shifting focus from each unit of care rendered by every independent practitioner, also known as fee for service, to the comprehensive care rendered to each patient, across a full spectrum of providers.

The goal is to use a collaborative, multidisciplinary care model of providers who work to design practice guidelines and evidence-based algorithms that will reduce variation and optimize care, patient experiences and overall costs of care.

Unlike patients who are having surgical procedures which typically are one-time procedures with discrete triggering events, patients with cancer have wide variability in disease state and progression, significant differences in treatment options and outcomes and varying start and end points of treatment.

Like any other episode of care model, it needs to be structured to clearly define which criteria qualify a patient to be in the episode of care, what services are included in the model and what the start and end points are for the episode.

One of the complicating factors in cancer is that stratification of the patient population requires more information than is typically on the claims data held by the payer. Because cancer—even of the same body part—is not a single diagnosis, it requires integrating clinical data with claims data in order to get to the bio-molecular level of disease for the precision required to allow clinicians to make meaningful decisions for patients with cancer.

This requires even more collaboration among clinicians and administrators than in other episodes.

Collaborative partnerships between providers, payers and other stakeholders engaged in patients’ care are critical to ensure that models are designed to allow clinicians to make the most well-informed decisions based on patients’ specific conditions and genetic and social markers.

With an estimated 1.8 million new cancer diagnoses in 2019, according to the American Cancer Society, and total annual spending on cancer treatment in the United States projected to exceed $170 billion by 2020, it is critical that we assiduously work to develop models that support patients as they navigate this difficult diagnosis.

In addition, it’s important they receive the precise treatment therapies for their particular disease states and situations using the most cost-effective options for care.

These models are designed to improve outcomes, patient experiences, and manage overall costs of care, and they require commitment, transparency, and collaboration among engaged stakeholders.

Lili Brillstein, MPH, an editorial advisor for Managed Healthcare Executive®, is a nationally recognized thought leader in the advancement of Episodes of Care as a value-based approach for specialty care. She is the CEO of BCollaborative, which works with stakeholders across the healthcare continuum to successfully make the move from fee for service to value-based healthcare.
Years before the oldest baby boomers reached retirement age, the healthcare industry began to prepare for the impact of an aging generation.

Healthcare providers and organizations have dedicated time and resources to studying the needs of boomers and adapting to meet them.

Now, as approximately 10,000 baby boomers per day turn 65 years old, the healthcare industry faces the challenge of continuing to deliver targeted care to boomers while simultaneously adopting new practices to meet the care expectations of the largest living adult population in the United States: millennials.

An Intrado survey that compared the healthcare expectations of baby boomers and millennials found that both patient demographics desire more and better communication from their healthcare teams.

However, boomers and millennials have their own unique needs and communication preferences, so it is important to have patient engagement strategies in place for each of these distinct patient groups.

Healthcare teams that do have engagement strategies may be able to increase patient satisfaction and elevate the quality of care for both baby boomers and millennials.

According to Intrado’s survey of 1,036 U.S. adults, nearly two in three baby boomers (64%) say they wish healthcare providers would communicate more often between appointments. Given that older Americans typically have greater healthcare needs, this interest in communication isn’t particularly surprising.

What is surprising is the fact that even more millennials than boomers say they want to engage with their doctors between appointments. More than three in four millennials (76%) wish for more frequent communication from healthcare providers between visits—proving that both age groups of patients want their providers’ attention.

Fortunately, giving them that attention may be simpler than it seems.

TIPS FOR COMMUNICATING WITH BOOMERS, MILLENNIALS

Many healthcare teams already have and use patient engagement technology to send patients messages to remind them about upcoming appointments.

By leveraging the same technology that is used to send appointment reminders, healthcare providers can deliver personalized text, phone and email messages that give baby boomers, and millennials more of the meaningful between-visit communication they crave.

The following examples show a few of the opportunities healthcare teams have to engage boomers and millennials through routine communication:
EMAIL BABY BOOMERS INFORMATION ABOUT MANAGING CHRONIC DISEASE. Unfortunately, 80% of adults age 65 or older have a chronic condition, and 68% have two or more. Sending patients emails to share valuable disease-specific information is a simple and effective way to support baby boomers with at-home chronic disease management. By the year 2030, an estimated one in four baby boomers will have diabetes, and one in three will be obese. Healthcare teams can offer support by sending a series of emails about nutrition, for example, to boomer patients. Baby boomers suggest this type of communication is welcome. According to Intrado’s survey, more than one in three baby boomers (34%) currently feel that healthcare providers do not effectively communicate recommendations that are specific to their individual needs. So, baby boomers would likely welcome disease-specific communications from their healthcare providers.

TEXT MILLENNIALS TO INVITE THEM TO SCHEDULE PREVENTIVE EXAMS. Scheduling wellness exams and preventive procedures is not always a priority for younger adults—particularly if they do not have any known health issues. For busy millennials, it is easy to deprioritize preventive healthcare behind family, work, and play. Because many millennials are not aware when they are due for preventive care, it can be helpful for healthcare teams to send them alerts when they are due for preventive screenings or exams. Text alerts work well for this because they are convenient for patients, and because millennials are adept at texting. Intrado’s survey revealed that 94% of millennials want to receive text, voice calls, or email prompts to schedule appointments or take other similar actions.

SEND BABY BOOMERS MESSAGES TO SUPPORT MEDICATION ADHERENCE. Older Americans often have more prescriptions to keep track of than younger adults. Intrado’s survey revealed that 88% of baby boomers feel that to create ideal healthcare experiences, it is important for healthcare teams to send them reminders when their medications are available to be picked up or when prescriptions need to be refilled. Healthcare teams can easily send automated messages that remind patients to pick up prescriptions, clarify dosage instructions, provide instructions on what to do if side effects become troublesome, or request that patients contact them if they are unable to afford their medications.

CREATE A WELLNESS NEWSLETTER TO SEND TO MILLENNIALS. According to Intrado’s survey, 97% of millennials say they want healthcare providers to support them in managing their health between office visits. If patients are already healthy—and even if they are not—sharing wellness tips and information is a good way to encourage patients to adopt healthy behaviors or make lifestyle improvements. Sending a quarterly newsletter that covers topics such as smoking cessation and weight management, for example, is an easy way to communicate wellness advice to patients and encourage them to take steps to improve their health.

SEND BABY BOOMERS MESSAGES TO HELP CLARIFY FINANCIAL RESPONSIBILITIES. The cost of healthcare is a concern for patients of every age; however, because many baby boomers live on a low or modest income, they may be particularly wary of high-cost healthcare. Following retirement, boomers sometimes have a lot of questions about transitioning from private health insurance to Medicare. To answer questions and help patients overcome financial barriers, healthcare teams can send baby boomers automated messages to share Medicare resources or highlight healthcare services that patients can receive for little or no out-of-pocket cost.

Despite the multitude of opportunities for healthcare teams to communicate with patients, regular between-visit communication is typically uncommon. As a result, fewer than half of baby boomers (45%) and only 66% of millennials surveyed by Intrado said they believe their healthcare providers want to communicate with them between appointments. Fortunately, healthcare teams can easily demonstrate their commitment to supporting patients—from millennials to baby boomers—by using their patient engagement technology to improve and increase communication.

These examples illustrate a small handful of ways healthcare teams can use tailored automated communications to address the needs of both baby boomers and millennials and offer value between in-person appointments.

Nate Brogan currently serves as president of Notification Services at Intrado, where the healthcare mission is to help organizations harness communications to expand the boundaries of where, when, and how healthcare is delivered.
Now Approved for an expanded indication in Diabetic Retinopathy (DR)!

POWER AGAINST

In PANORAMA, EYLEA significantly improved DR severity scores at week 52.

Proportion of patients achieving a ≥2-step improvement in ETDRS-DRSS* score from baseline (primary endpoint).**

80%‡ OF PATIENTS
EYLEA 2 mg every 8 weeks& (n=134)

65%‡ OF PATIENTS
EYLEA 2 mg every 16 weeks& (n=135)

15% OF PATIENTS
sham (n=133)

*p<0.01 vs sham.

The recommended dose for EYLEA in DR is 2 mg (0.05 mL) administered by intravitreal injection every 4 weeks (approximately every 28 days, monthly) for the first 5 injections, followed by 2 mg (0.05 mL) via intravitreal injection every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (approximately every 25 days, monthly), additional efficacy was not demonstrated in most patients when EYLEA was dosed every 4 weeks compared to every 8 weeks. Some patients may need every-4-week (monthly) dosing after the first 20 weeks (5 months).1

Efficacy and safety data of EYLEA in DR are also derived from VISTA and VIVID. The percentage of patients with a ≥2-step improvement on the ETDRS-DRSS from baseline at 100 weeks was 38%, 38%, and 16% in VISTA and 32%, 28%, and 7% in VIVID with EYLEA 2 mg every 8 weeks after 5 initial monthly doses, EYLEA 2 mg every 4 weeks, and control, respectively (secondary endpoint).2

PANORAMA study design: Multicenter, double-masked, controlled study in which patients with moderately severe to severe NPDR (ETDRS-DRSS 47 or 53) without central-involved DME (CI-DME) (N=402; age range: 25-85 years, with a mean of 56 years) were randomized to receive 1) 3 initial monthly EYLEA 2 mg injections, followed by 1 injection after 8 weeks and then 1 injection every 16 weeks; 2) 5 initial monthly EYLEA 2 mg injections, followed by 1 injection every 8 weeks; or 3) sham treatment. Protocol-specified visits occurred every 28±7 days for the first 5 visits, then every 8 weeks (56±7 days). The primary efficacy endpoint was the proportion of patients who improved by ≥2 steps on the ETDRS-DRSS from baseline to week 24 in the combined EYLEA groups vs sham and at week 52 in the EYLEA 2 mg every-16-week and EYLEA 2 mg every-8-week groups individually vs sham. A secondary endpoint was the proportion of patients developing the composite endpoint of proliferative DR (PDR) or anterior segment neovascularization.

VISTA and VIVID study designs: Two randomized, multicenter, double-masked, controlled studies in which patients with DME (N=862; age range: 23-87 years, with a mean of 63 years) were randomized and received 1) EYLEA 2 mg administered every 8 weeks following 5 initial monthly doses; 2) EYLEA 2 mg administered every 4 weeks; or 3) macular laser photoagulation (control), at baseline and then as needed. Protocol-specified visits occurred every 28±7 days. In both studies, efficacy endpoints included the mean change from baseline in best-corrected visual acuity (BCVA), as measured by ETDRS letters, at 52 weeks (primary endpoint) and 100 weeks (secondary endpoint).

INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS
EYLEA is indicated for the treatment of patients with Neovascular (Wet) Age-related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).

CONTRAINDICATIONS
- EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

*Early Treatment Diabetic Retinopathy Study—Diabetic Retinopathy Severity Scale: An established grading scale for measuring the severity of DR.
**Full analysis set.
&5 initial monthly injections, followed by 1 injection every 8 weeks.
&3 initial monthly injections, followed by 1 injection after 8 weeks and then 1 injection every 16 weeks.

EYLEA is a registered trademark of Regeneron Pharmaceuticals, Inc.

REGENERON
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777 Old Saw Mill River Road, Tarrytown, NY 10591

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DISEASE PROGRESSION

EYLEA can help prevent DR vision-threatening complications that can lead to blindness

Significantly fewer patients developed PDR or ASNV with EYLEA at week 52

Composite endpoint of patients who developed PDR or ASNV at week 52 (event rates) (secondary endpoint)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Event Rate</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>EYLEA 2 mg every 8 weeks (n=134)</td>
<td>2.4%‡</td>
<td>0.12</td>
</tr>
<tr>
<td>EYLEA 2 mg every 16 weeks (n=135)</td>
<td>4.0%‡</td>
<td>0.15</td>
</tr>
<tr>
<td>sham (n=133)</td>
<td>20.1%</td>
<td></td>
</tr>
</tbody>
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*P<0.01 vs sham.

All patients were treatment-naive to focal or grid laser photocoagulation, panretinal photocoagulation, and any anti-vascular endothelial growth factor (anti-VEGF) treatment. Composite endpoint of developing PDR or anterior segment neovascularization (ASNV) was diagnosed by either the reading center or investigator through week 52. Event rate was estimated using the Kaplan-Meier method.

WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.

- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

- There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

ADVERSE REACTIONS

- Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.

- The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

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

BRIEF SUMMARY—Please see the EYLEA® full prescribing Information available on HCPEYLEA.us for all additional product information.

1 INDICATIONS AND USAGE
EYLEA® (afibrentinal) Injection
For Intravitreal Injection

Macular Edema (Age-Associated Macular Degeneration) (AMD), Macular Edema Following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR).

4 CONTRAINDICATIONS

4.1 Prior Intravitreal Injections
EYLEA® is contraindicated in patients with active or pericentral infections.

4.2 Active Intravitreal Inflammation
EYLEA® is contraindicated in patients with active intravitreal inflammation.

4.3 Hypersensitivity
EYLEA® is contraindicated in patients with known hypersensitivity to EYLEA® or any of the excipients in EYLEA®. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. [see Patient Counseling Information (8.6)].

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal detachments
Intravitreal injections, including those with EYLEA®, have been associated with endophthalmitis and retinal detachments (see Adverse Reactions [6.1]). Proper aseptic injection technique must always be used when administering EYLEA®. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. [see Patient Counseling Information (8.6)].

5.2 Increase in Intraocular Pressure
Acute increases in intraocular pressure have been seen in 60 minutes of intravitreal injection, including with EYLEA® (see Adverse Reactions [6.1]). Systemic increases in intraocular pressure have also been reported after repeated intravitreal bolus with venous restriction (HVR) injection. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

5.3 Hemorrhagic Events
There is a potential for mild to severe intravitreal hemorrhage events (ATLAS) following intravitreal use ofVEGF inhibitors, including EYLEA®. ATLAS are defined as nonfocal, nonretinal neovascularization, or vitreous death (including deaths of unknown cause). The incidence of reported intravitreal hemorrhage events in wet AMD studies during the first year was 13.2% (9/69) in 2014) in the combined group of patients treated with EYLEA® compared with 15.6% (9/58) in patients treated with ranibizumab through 96 weeks. In the second phase 1-2 renal data through 52 weeks in the DME studies from baseline to week 52 was 3.2% (9/281) in the combined group of patients treated with EYLEA® compared with 4.0% (12/295) in the control group. These events were reported to be less common in the DME studies.

6 ADVERSE REACTIONS

6.1 Adverse Reactions
The following adverse reactions are described elsewhere in the labeling:

- Hypersensitivity (see Contraindications [4.3])
- Endophthalmitis and retinal detachments (see Warnings and Precautions [5.1])
- Increase in intraocular pressure (see Warnings and Precautions [5.2])
- Intravitreal hemorrhage events (see Warnings and Precautions [5.3])

6.2 Clinical Trials Experience
Because clinical trials are conducted under very varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in other clinical trials of the same drug, or another drug and may not reflect the rates observed in practice.

9.1 Macular Edema (Age-Associated Macular Degeneration) (AMD)
The data described below reflect exposure to EYLEA® in 1424 patients with AMD, including 272 patients treated with the 2 mg dose in 2-mg double-masked, controlled clinical studies (WAVE and VIATORI) for 24 months (with active control in arms 1 and 2).

9.2 Macular Edema Following Retinal Vein Occlusion (RVO)
The data described below reflect 5 months of exposure in EYLEA® with a monthly 2 mg dose in 24 patients following the CRN2 study in 2 clinical studies (COWEBS) and 468 and 98 patients in one clinical study (CHART).
Magellan Rx Management, the full-service pharmacy benefits management division of Magellan Health, Inc., released its fourth annual Medicaid Pharmacy Trend Report, developed through in-depth data analysis and supported by Magellan’s experience in managing fee-for-service (FFS) Medicaid pharmacy programs.

The report outlines emerging and innovative state strategies for managing high-cost Medicaid prescription drugs. The report also includes a forecast of the top key conditions in Medicaid along with a pipeline analysis of drugs expected to impact the Medicaid program.

Key findings in this year’s report include:

- The specialty net trend of 6.1%, up slightly over last year, continued to contribute positively to the overall net trend, but is well below the 20.5% net trend seen in 2016.

- Traditional net trend declined from -5.1% in 2016 to -2.6% in 2018. Even with the negative trend, it is not declining at the same pace as the previous two years.

- The average net cost per claim was nearly flat at 0.8% change, compared with -4.4% in 2017.

- Magellan Rx’s new analytics product, MRx Predict, shows the overall gross trend is expected to marginally rise from 2018 as new, groundbreaking therapies and specialty drugs continue to create upward pressure.

“The Medicaid Pharmacy Trend Report is an effective tool in providing states with data and solutions to better manage cost trends and improve budget predictability for their Medicaid FFS pharmacy benefit management program,” says Doug Brown, vice president and chief strategy officer, government markets, Magellan Health. “The report examines drug classes with the largest effect on Medicaid net spend, cost-saving opportunities, and a detailed look at how recent legislative and state program innovation has and will affect the Medicaid program.”

Report Details Trends in Medicaid Fee-for-Service Pharmacy Programs

by MHE STAFF
New ways to win the war on cancer include novel methods of diagnosing and treating it. Here’s a look at some developments in the pipeline as well as ones that recently got FDA’s stamp of approval.

1. **Comprehensive genomic profiling**

Comprehensive genomic profiling (CGP) tests analyze tumor tissue or blood samples for molecular changes in genes. Using next-generation sequencing technology to analyze DNA mutations, CGP can help match patients to available targeted therapies, immunotherapies, or clinical trial options.

CGP can be used to manage all types of advanced cancer, says Brian Alexander, MD, MPH, chief medical officer of Foundation Medicine, and associate professor of radiation oncology at Harvard Medical School, both based in Cambridge, Massachusetts.

Unlike single-marker assays that only test for a few cancer-driving mutations, CGP can...
Cancer care enters a new, exciting phase, experts say

**1 New screening method for prostate cancer**

Ezra is a novel artificial intelligence (AI) technology that can aid radiologists in detecting lesions or tumors on the prostate. "It is designed to help radiologists detect prostate cancer with additional accuracy, as well as streamline their workload," says Azra Raza, MD, professor of medicine, and director of Myelodysplastic Syndrome Center, Columbia University Medical Center, and New York Presbyterian Hospital, both in New York City. "We plan to build additional AI for other organs, and ultimately create technology that can perform a full-body MRI scan."

Ezra’s engineers created an AI algorithm to detect prostate cancer using MRI images from 346 patients obtained from a cancer imaging archive data portal. The AI uses advanced neural network architecture to learn from a radiologist’s assessment of prostate lesions on MRIs. “The AI can predict lesion locations that could be clinically significant cancers on images that it has not previously seen,” says Raza, who is on the board of medical advisors at Ezra and uses the technology.

In April 2019, a study published in the *International Journal for Computer Assisted Radiology and Surgery* showed that Ezra could detect lesions with 93% accuracy.

**2 Novel colorectal cancer treatment**

Arfolitixorin is a drug candidate being tested in a phase 3 clinical study across 80 sites in the United States and Europe as part of a first-line treatment regimen for metastatic colorectal cancer.

Arfolitixorin is the first pure form of a molecule called MTHF, an active ingredient that can improve standard chemotherapy’s effectiveness. MTHF helps prevent cancer cell growth by working with other chemotherapy agents to block DNA replication that’s needed to produce new cancer cells, says Karin Ganlöv, MD, chief medical officer of Isofol Medical, a health system in Gothenburg, Sweden. Unlike existing chemotherapy additives, which are only effective in a small percentage of patients, MTHF can benefit almost everyone with advanced colorectal cancer who receives chemotherapy.

Ganlöv says arfolitixorin is the first major innovation to the first-line metastatic colorectal cancer treatment regimen in decades. "For years researchers have unsuccessfully tried to produce pure MTHF, knowing that this molecule is necessary to improve chemotherapy’s effectiveness,” she says. As the first treatment that someone with metastatic colorectal cancer would receive, the drug could potentially benefit a large number of people, Ganlöv says. Arfolitixorin could also be used in other cancer types like gastric, pancreas, and head and neck cancers. In a previous study, patients had a greater than 30% reduction in tumor size from baseline when taking the drug.

**3 New treatment for lung cancer and more**

KEYNOTE-671 is a phase 3 clinical study evaluating the role of adding immunotherapy to standard chemotherapy in high-risk patients with early stage lung cancer, prior to having surgery. Immunotherapy activates the patient’s immune system to allow it to successfully fight cancer. "Cancer cells have a cloak that allows them to hide from a patient’s own immune system,” says Dan Costin, MD, FACP, director of the White Plains Hospital, Center for Cancer Care, in White Plains, New York, which is a member of the Montefiore Health System. “Modern immunotherapy targets both cancer and immune cells, removes the cloak protecting the cancer cells, and exposes cancer cells to the immune system. This allows a patient’s own immune cells to eradicate the now vulnerable cancer cells.”

Preliminary data prior to starting the study suggested that treating these high-risk patients prior to surgery with both immunotherapy and chemotherapy resulted in the eradication of more than 90% of the cancer in the vast majority of patients treated. “This is an astonishing outcome, which is rarely seen in modern oncology,” Costin says.

**4 Arfolitixorin**

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Cancer developments

"If these findings are confirmed in larger phase 3 studies, including KEYNOTE-671, then the landscape of cancer therapy may forever be changed," Costin says. "Patients will require less aggressive surgical procedures, less toxic treatment protocols, and will have dramatically improved survival compared to historical expectations." Similar phase 3 studies using comparable approaches to treatment are now ongoing in patients with triple negative breast cancer, kidney cancer, and head and neck cancer.

5 Help for non-Hodgkin lymphoma patients

Non-Hodgkin lymphomas (NHLs) are divided into more than 80 subtypes. Diffuse large B-cell lymphoma (DLBCL) comprises nearly 30% of NHLs. Front-line therapy with a chemotheraphy regimen called RCHOP can effectively cure about two-thirds of DLBCL patients, but the remaining patients either don’t respond or relapse soon after receiving it.

Polatuzumab is a novel targeted antibody-drug conjugate that has had impressive results in relapsed and refractory (R/R) patients with DLBCL who have failed standard chemotherapy. In a phase 2 study in R/R DLBCL patients with aggressive lymphomas, polatuzumab was combined with rituximab (an antibody therapy) and a less intensive chemotherapy called bendamustine. "The combination was well tolerated and showed tremendous response and survival rates," says Manali Kamdar, MD, MBBS, assistant professor and clinical director of lymphoma services, at University of Colorado, Anschutz Cancer Center, in Denver.

Given this, the FDA granted accelerated approval of polatuzumab vedotin-piiq (POLIVY, manufactured by Genentech, Inc.) in June 2019.

Polatuzumab targets a protein called CD79b, which is expressed on most B cell NHLs, such as DLBCL. Polatuzumab targets this protein, gets internalized, and releases a chemotherapy toxin that causes death of lymphoma cells. "The idea is to target cancer cells alone and spare normal fast-growing cells, thus decreasing toxicity without decreasing efficacy," Kamdar says.

Spectrum Health in Grand Rapids, Michigan, is also having success treating R/R DLBCL. Stephanie Williams, MD, division chief of the Adult Blood and Marrow Transplant program, says chimeric antigen receptor (CAR) T-cell therapy, a type of immunotherapy, uses a patient’s own white blood cells to combat cancer cells. "Results have been so positive, that the FDA rapidly approved its use for adults with advanced lymphomas and children with acute lymphoblastic leukemia," she says. CAR T-cell therapy is the first cellular immunotherapy approved by the FDA.

Specifically, T-cells are removed from a patient’s bloodstream and are genetically engineered with CARs to become “killer cells” directed toward the patient’s lymphoma. The engineered cells are infused into the patient in order to seek and destroy cancer cells.

Patients who undergo CAR T-cell therapy have tried other treatments that were unsuccessful. More than half of the patients treated with this therapy enter remission and retain it beyond 18 months. "With this type of lymphoma, no other therapy gives these types of results," Williams says.

Researchers are investigating whether CAR T-cell therapy can be effective in treating other forms of cancer, such as multiple myeloma, and solid tumors of the lung, brain, breast, and colon.

6 Chemo-free treatment for leukemia

In January 2019, FDA approved ibrutinib in combination with the drug obinutuzumab as a first-line therapy for newly diagnosed chronic lymphocytic leukemia (CLL) patients, making it the first non-chemotherapy combination for CLL. "This marks another advancement in the growing trend toward chemo-free cancer regimens," says Lee Greenberger, MD, chief scientific officer for The Leukemia & Lymphoma Society.

Ibrutinib is the first of a category of drugs that target the Bruton tyrosine kinase (BTK) proteins found in several types of blood cancers including CLL, mantle cell lymphoma, and Waldenstrom macroglobulinemia, a type of non-Hodgkin lymphoma. When they mutate, these proteins cause an overgrowth of cancer cells. These drugs suppress the activity of the mutated BTK protein and stop the signal for the cancer cells to grow.

These drugs are targeted therapies that attack cancer cells directly while sparing healthy cells from harm and they have fewer side effects. "For patients, this eases the physical and financial strains that are often tied to chemotherapy," Greenberger says. "Patients can take a pill purchased at their local pharmacy and don’t have to visit a clinic to receive treatment."

WHAT THE FUTURE HOLDS

Cancer care has entered a new, exciting, and constantly improving phase. "Decades of clinical research have finally begun to bear fruit, ushering in a surge in effective medications enhanced by the FDA. Patients are living longer and have much more treatment options to choose from. Patients are empowered with information, allowing more informed decisions for their treatment," says Manali Kamdar, MD, MBBS, assistant professor and clinical director of lymphoma services, at University of Colorado, Anschutz Cancer Center, in Denver.

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These drugs are targeted therapies that attack cancer cells directly while sparing healthy cells from harm and they have fewer side effects. "For patients, this eases the physical and financial strains that are often tied to chemotherapy," Greenberger says. "Patients can take a pill purchased at their local pharmacy and don’t have to visit a clinic to receive treatment."

WHAT THE FUTURE HOLDS

Cancer care has entered a new, exciting, and constantly improving phase. "Decades of clinical research have finally begun to bear fruit, ushering in a surge in effective medications enhanced by the FDA. Patients are living longer and have much more treatment options to choose from. Patients are empowered with information, allowing more informed decisions for their treatment," says Manali Kamdar, MD, MBBS, assistant professor and clinical director of lymphoma services, at University of Colorado, Anschutz Cancer Center, in Denver.
such as targeted antibodies, immunotherapy, and non-chemotherapy pills,” Kamdar says. “The eventual goal is to cure cancer.”

In order to do that, clinical investigators are trying to figure out mechanisms of tumor destruction that not only increase tumor killing, but do so without inducing undue toxicities to patients. “Themes gaining momentum and showing great promise in clinical trials are combining anticancer drugs, which are synergistic, effective as single drugs, and don’t have overlapping toxicities when used in combinations,” Kamdar says.

Cancer research is also focused on early diagnosis and detection of relapse. The concept of molecular detection of cancer is gaining traction in the form of minimal residual disease (MRD) monitoring in blood. MRD analysis at diagnosis, and tracking the tumor cell population during therapy and post completion of therapy to detect relapse, is being tested in several clinical trials. “This has great potential in managing some types of cancers like lymphomas,” Kamdar says.

**IMPACT OF LARGE DATA SETS**

On another front, the availability of large amounts of real-world data and analytics will fundamentally change the way that cancer care is practiced. “Over the past few decades, the pace of information growth has rapidly increased,” Alexander says. “In the next few years, the amount of data generated from multiple sources will increase exponentially, and the availability of increasingly large data sets from which to learn will grow in parallel.”

Molecular profiling, including CGP and the ability to generate that data from blood, will be increasingly available, as will machine learning algorithms that can unlock hidden information in radiology data sets—which are now only seen as images through transformation and pathology images.

Alexander foresees a transition to more of a “learning health system,” where insights will be generated from observational data and essential trial elements, such as randomization, will become more embedded into clinical practice.

“Technology that enables the aggregation and interpretation of such volumes of information will allow for doctors and patients to make better decisions at the point of care, and regulators and payers to better understand the risk/benefit/cost implications of new therapies in specific populations much faster,” Alexander says.

**TREATMENTS FOR BROADER POPULATIONS**

While most current research efforts are invested in personalized and targeted cancer treatments, Ganlov believes the future of cancer treatment will also involve advancements in treatment that can be effective in broader populations affected by cancer. “We’re already seeing this with CAR T therapies, where the first-generation CAR Ts target selective cancer types, but next-generation CAR Ts use a novel approach that can be easily produced and administered to many cancer patients at once. This drug development mindset will be seen in other areas of oncology drug development as researchers look for ways to make tangible benefits for large cancer indications or for many cancer patients rather than a few.”

**DNA TESTING PLAYS A GREATER ROLE**

In the future, Costin expects that most cancer diagnoses will be done by testing tumor cells’ DNA. Treatment decisions will be based both on the cancer’s origin and the DNA drivers of the cancer. “Many cancers will be treated initially with neoadjuvant therapy (therapy that is given prior to surgery),” he says. “Neoadjuvant treatments will almost always consist of a combination of several treatment modalities, with a focus on immunotherapy and targeted therapy.”

Over time, chemotherapy won’t disappear but will become much less important as both immunotherapy and targeted treatments will most likely become more effective and be less toxic.

Karen Appold is a medical writer in Lehigh Valley, Pennsylvania.
Cancer-related pain doesn’t always stop when active treatment ends. Patients with stabilized disease or who are in remission are living longer due to earlier detection and better treatments. Managing chronic pain (six months or longer) is increasingly important. About 5% of the U.S. population, or 15.5 million people, are cancer survivors, according to “Pain in Cancer Survivors: How to Manage,” published June 2019 in Current Treatments in Oncology. Cancer-related pain can be from the disease itself, or due to treatment. Most cancer patients will experience pain at some point during their illness, says Jacob Strand, MD, chair of palliative care medicine at the Mayo Clinic in Rochester, Minnesota. About 80% to 90% of those with metastases, who are incurable, will have cancer-related pain, Strand says, as will up to 40% of cancer survivors overall.

Ideally, treating pain involves a multi-prong approach. That might mean some combination of physical therapy, behavioral therapy, blocks/injections, and medication. Not all health insurance covers an extensive approach, though under-treating pain impacts a patient’s health and quality of life substantially. As patients live longer after active treatment, oncologists see the patients less, leaving pain management in the hands of PCPs, who may not feel equipped to treat cancer-related pain.

CANCER PAIN ASSESSMENT

A typical assessment for pain management includes pain assessment, functional assessment, and then risk assessment, says Judith Paice, PhD, RN, director of the Cancer Pain Program in the Hematology-Oncology division at Northwestern University in Chicago.

The risk assessment is newer and still not performed by most oncologists, Paice says. It includes questions about smoking, alcohol use, and prescription substance use not as prescribed. It also includes a family history of substance abuse to give a “crude understanding of genetic risk” and to understand what substance issues might exist in the home. She takes all the answers into account, while trying to determine if their pain is likely to respond to opioids, and if they’re at risk for abuse.

A cancer patient can suffer from various types of pain. Tumor-related pain can be from a tissue injury, like a mass effect from the tumor pressing against the bone or nerves. Pain can be treat-
ment-related, like pain after surgery, or associated with radiation therapy. As radiation gets more precise, patients are experiencing less pain. "Unfortunately, pain associated with chemotherapy is increasing, as more and more agents are causing peripheral neuropathy," Paice says. Steroid use can cause avascular necrosis and bone fragility. Aromatase inhibitors and hormonal therapies for prostate and breast cancers can cause pain. "If one in eight women with breast cancer are estrogen positive, they're likely on aromatase inhibitors for five to 10 years," Paice says. Stem cell transplant can lead to graft-versus-host disease. With new treatments always arising, pain management is a moving target, she says.

ASSESSING AND TREATING FUNCTION, NOT PAIN SEVERITY

Pain used to be assessed and treated based on intensity scores, with patients rating their pain on a 0-10 scale, and trying to lower the pain to a different number. That is changing. Clinicians are now focused on functionality: what the patient can do after pain management that they couldn’t do before it. Clinicians ask patients about their physical and emotional goals, understanding what improved function and quality of life looks like.

Improved functionality could be performing activities of daily living that they couldn’t do because of pain, Strand says. "That shift is particularly important in chronic cancer-related pain, where there’s no cure for the underlying problem," he says.

Multimodal therapy is the preferred approach. While medications work well for some, a medication may be contraindicated due to a patient’s other medical issues. And not all pain can be addressed with pharmacological treatments. Treatments like physical and occupational therapy, and cognitive behavioral therapy (CBT) are often helpful, though CBT sometimes carries a stigma. "I try to reframe it," Paice says. She tells patients "our psychologist here is not for crazy people. It’s for normal people going through crazy times." She tells them they are going through a difficult time, but have an inner strength that the therapist will help them find.

The idea behind using multiple interventions is to provide the best outcomes with the fewest side effects and least risk. Not all therapy types are indicated for each patient, but it’s important to consider different treatment modes. In the best scenario, patients have access to various therapies to help them move appropriately and with emotions. "It’s really tough to get all of that paid," Paice says.

WHO SHOULD TREAT PAIN MANAGEMENT?

Five years out from cancer treatment, many patients are no longer seeing their oncologist more than once annually, if at all. Some academic medical centers develop care plans for PCPs to follow, but they mostly recommend screening practices, not pain management. That can leave PCPs in the uncomfortable position of treating cancer-related pain, without the knowledge.

“Clinicians have historically not been well trained to manage cancer pain at all stages of their diagnosis, illness, survivorship, and end of life.”
— JACOB STRAND, MD, MAYO CLINIC

Palliative care clinicians tend to see more difficult cases, Strand says, either those with a complicated medication regimen, or patients with coexisting symptoms like mood disorders, or patients with a high risk of relapse.

One concern that cancer patients have is the fear of cancer recurrence. A new pain complaint is stressful to patients, given the uncertainty of the disease returning. A clinician treating a cancer survivor for pain should be aware of that.

TYPES OF TREATMENTS

Clinicians try to optimize use of non-opioid medications for chronic pain, Paice says. That can include nonsteroidal anti-inflammatory drugs. Steroid injections and nerve blocks are useful, especially for abdominal pain related to pancreatic cancer, says David Craig, PharmD, clinical pharmacist in pain management/palliative care at H. Lee Moffitt Cancer Center in...
Tampa, Florida. “Drugs are not very good at managing abdominal or neuropathic pain,” he says.

But 30% to 50% of those getting antineoplastic therapy, and 75% to 90% of those with advanced disease, have pain best treated by opioids, according to UpToDate. Opioids have received a lot of negative press lately. “Our first goal as physicians is to do no harm,” Strand says. And that means being thoughtful about how medications are used and how patients are monitored, to minimize even unintentional harm.

Not only are some clinicians reticent to prescribe opioids when indicated, but patients are afraid to take them. “We need to be really direct and ask them if they’re worried about becoming addicted,” Paice says. Patients may not take prescribed opioids out of fear, or because they receive negative messages from family members. That contributes to undertreatment of pain.

Part of Strand’s risk screening process includes checking the state prescription monitoring database, to see if the patient may be at risk for substance abuse. Closely monitoring outcomes and patient function, as opposed to pain level, helps with safer prescribing. “We can provide it safely and still manage pain effectively,” Strand says. He tells patients that part of his job is to make sure they’re safe, and that can help them overcome some fear of addiction. The number of patients in his practice who benefit from opioid treatment far outweigh the number of patients harmed from it, he says.

Clinicians disagree about the utility of cannabis in pain management. Craig does not recommend it to his patients, as he says there’s not enough data to support it, and patients think they can buy it from someone off the street, smoke it, and it will work. “We don’t disallow it, but we don’t recommend it,” he says.

A 2018 study, “Medical Oncologists’ Beliefs, Practices, and Knowledge Regarding Marijuana Used Therapeutically: A Nationally Representative Survey Study,” in the Journal of Clinical Oncology reported that up to 80% of oncologists have discussed medical cannabis use with patients, though only 30% felt informed enough to recommend it. The study, which surveyed 400 medical oncologists in 2016, showed that 67% of oncologists thought it was a helpful addition to standard pain management options. The American Cancer Society noted that some studies found that inhaled marijuana was helpful for neuropathic pain, and that those using marijuana extracts in clinical trials needed less pain medication.

Strand has comprehensive discussions with his patients about medical cannabis, as he knows patients will ask about it. He says the data on effectiveness in pain management for cancer pain is mixed. In his practice he’s seen patients benefit from it, and those who don’t. Like many treatments, clinicians need to determine how cannabis fits into treatment, and monitor it closely for side effects.

“They’re not the savior to our problems with pain, but they should also not be discarded,” he says.

Before a patient uses cannabis for pain management, he asks them to track it in a pain diary, just as they would with any other pain medication.

THE PROBLEM WITH UNDERTREATMENT

Undertreating pain is a problem, as is overtreatment. Pain management allows a person to be functional. “They need to move to prevent lung complications, blood clots, and improve their general quality of life,” Paice says. “We don’t want people isolated in their homes because the pain is too bad to move.” This happens due to access to care, as well as for those afraid to use opioids.

Undertreatment can also affect survival. “Sometimes symptoms that are poorly controlled can lead patients to discontinue therapy,” Strand says. He tells patients that if their pain is preventing them from getting out of their chair, they’ll have a worse outcome than if they were functional individuals.

Deborah Abrams Kaplan covers medical and practice management topics.
In the study, “Improving Quality and Decreasing Cost by Reducing Readmissions in Patients Undergoing Total Joint Arthroplasty,” conducted by the Nebraska Medical Center, several risk factors such as obesity, diabetes, and malnutrition, have been found to contribute to the complication and readmission rates following total joint arthroplasty (TJA).

A. Brion Gardner, MD, an orthopaedic surgeon for The Centers for Advanced Orthopedics in Bethesda, Maryland, says there are a variety of reasons that an individual with a hip or knee replacement may be readmitted. The most serious cause is experiencing a heart attack shortly after surgery, and some patients with preexisting conditions may be more at risk for this.

“Other grounds for readmission include uncontrolled pain, a wound that has drained or is infected, or a blood clot,” he says. “Patients may also be readmitted if there is suspicion of a blood clot or preliminary infection.”

Brian Hallstrom, MD, is co-director of Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI), a Blue Cross Blue Shield of Michigan-sponsored, statewide collaborative of hospitals, orthopaedic surgeons, and medical professionals; and clinical assistant professor of orthopaedic surgery at the University of Michigan.

“The most common reasons for hip replacement readmission are fracture, dislocation, blood clots, or other medical complications,” he says. “Knee replacement patients are more likely to come in with pain or blood clots. In both cases, the medical returns are often associated with the patients who experience other medical issues, such as diabetes or heart disease.”

Further, constipation is a common problem among postsurgical patients who are placed on opioids, and bowel problems can also be a reason for return to the emergency department (ED) and readmission to the hospital.

Reimbursement trends for hip and knee replacement

The Centers for Advanced Orthopaedics is contracted with Medicare and uses a bundled payment method that has a direct relationship with reimbursement, Gardner says.

“Given that readmissions increase the total cost of care for a 90-day period, this could ultimately impact the organi-
zation’s bottom line, depending on what happened and why,” he says. “Also, if the cost of care is too high throughout a set period of time, money may be owed to the government since it then exceeds the target price in the bundled agreement.”

However, when it comes to commercial insurance, readmission is not yet having an impact on reimbursement. Gardner believes in the future, payment may be dependent on performance and quality of care, where reimbursement is withheld for poor outcomes.

At Blue Cross Blue Shield of Michigan, Tom Leyden, director II, value partnerships program, said it has developed variable value-based reimbursement (VBR) opportunities for primary care physicians and all specialty types participating in its quality improvement programs.

“For the inaugural program year, we saw 147 orthopaedic surgeons participating in MARC-QI receive VBR payments tied to improvements in patients receiving functional assessments and reductions in the percentage of total knee/hip arthroplasty patients sent to ECF/SNFs [Extended Care Facility/Skilled Nursing Facilities] postsurgery,” he says. “In fact, many of our hospitals are now sending 0% of their patients to SNFs after surgery.”

The second VBR opportunity for orthopaedic surgeons is tied to improvements in overall per member per month (PMPM) medical/surgical cost of care + pharmacy cost; change in cost of care PMPM from the prior year; a single composite score comprised of quality metrics from across many Physician Group Incentive Program initiatives; proportion of visits with primary diagnosis of low back pain receiving an imaging study; and adult MRI and CT imaging per 1,000 member years.

“Finally, we have piloted a bundled payment arrangement for noncomplicated hip and knee replacement procedures,” Leyden
Readmission trends | Population Health Management

Hallstrom says there are sites participating in MARCQI that have staff dedicated to focusing on pain management. This includes early follow-up phone calls from nurse coordinators.

“The intent of these calls is to catch trouble early, assist the patient, and avoid returns to the hospital,” he says. “Other Michigan sites have focused on reducing opioid-related constipation with education and by providing stool softener kits to patients. When patients receive better care, and have better outcomes, there is less opportunity for complications and a need to return to the hospital.”

Leyden says the MARCQI collaborative has engaged in an ongoing effort to improve the quality of care for all patients undergoing hip and knee replacement in Michigan and these efforts succeed because the surgeons, nurses, data abstractors, quality teams, and other participants work together to achieve meaningful quality improvement goals.

The collaboration allows for efforts to continually be refined, driving further progress, which is evident in the results MARCQI has experienced to-date, including 18% reduction in 30-day readmissions; 17% reduction in ED visits within 30 days (hip); 52% reduction in venous thromboembolism events; and 88% reduction in infections.

Managing risk factors to drive down hip and knee replacement 30-day readmissions

The preoperative evaluation done with the patient’s primary care doctor is essential for identifying and treating any risk factors, Gardner says. With hip and knee replacements, there are well-known perimeters.

“For example, a BMI over 40 increases the risk of blood clots, wound complications, dislocations, and nerve injury,” he says. “In diabetics, a hemoglobin A1c that is above 8% significantly increases the potential risks and must be lowered before proceeding with surgery. In addition, if the absolute levels of protein in the body are not high enough, we would postpone surgery until the lab values are below the threshold for minimizing risk factors.”

Stephen Fealy, MD, leading orthopaedic surgeon at Hospital for Special Surgery in New York, says one of the best ways to manage and mitigate the risk of readmission after orthopaedic surgery is to ensure patients have access to and receive physical therapy as expeditiously as possible.

“When you’re dealing with musculoskeletal injuries and surgeries, the healing process can be complex, long-term, and often requires recurring specialized attention and practice, such as safe incremental exercise to help patients gain back and maintain their strength and range of motion,” he says. “The sooner this can start, the better off the patient will be in both the near- and long-term.”

Hallstrom notes the first, and best, step is optimizing patients prior to surgery. Things like weight loss, smoking cessation, and controlling diabetes before surgery are all ways to help avoid postoperative problems.

Keith Loria is an award-winning journalist who has been writing for major newspapers and magazines for close to 20 years.
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Cincinnati Children's Hospital Medical Center has called Avondale, Ohio, home since 1926. The hospital has been on a decades-long mission to lead, advocate, and collaborate in order to improve the health of local children and reduce health disparities in targeted populations.

Two such population groups were the focus of a health initiative aimed at reducing the inpatient bed-day rate by at least 10% by mid-2020 for children from two nearby neighborhoods, and to narrow the gap between those neighborhoods and healthier ones.

“This was not a simple or straightforward program,” says the initiative’s lead researcher Andrew F. Beck, MD, attending physician, in the Division of General and Community Pediatrics, and Division of Hospital Medicine at the health system. “Rather, it was complex, involving active collaboration with community partners.”

Beck and fellow researchers explored common elements that underpin morbidity across conditions and serve as key contributors to hospital days and disparities. This focus allowed them to bring the right hospital resources and community partners to the table to tackle the most problematic conditions.

The multilevel approach involved analyzing real-time electronic health records (EHRs) to identify neighborhood “hot spots” in need of additional support for children living within those neighborhoods; optimizing chronic disease management by closing care gaps during hospitalizations and after discharge; mitigating social risks such as housing instability and limited access to medications and personal hygiene supplies; and helping children transition out of the hospital. The researchers hoped to develop, test, and refine a theory for how to narrow equity gaps across broader geographic areas.

“As healthcare systems evolve toward value-based payment models to address the nation’s healthcare cost crisis, more attention has shifted to population health outcomes, especially for lower-income patients,” Beck says. “Healthcare leaders are looking for ways to increase preventive care and reduce admissions (and readmissions)—key metrics that play important roles in maximizing reimbursements and ensuring we can continue to provide care for all those we serve and drive innovation that will improve the lives of generations to come.”

Furthermore, leaders recognize the moral imperative to address health disparities and improve access to quality care and they know they are accountable to more than just the people who walk through their doors, according to Beck.

“They have an obligation to serve their communities and all those who look to health systems for support, regardless of patients’ social status,” he says. “This outlook is often woven into healthcare organizations’ mission statements.”

Societal factors
In many neighborhoods like Avondale and Price Hill, access to pharmacies, grocery stores, green spaces, and adequate transportation can be limited. Housing may have exposures known to adversely affect health (e.g., pests, mold). This constellation of social, economic, and environmental factors influences short- and long-term health outcomes at the patient level, researchers say.

Beck and his team defined a goal in spring 2015: to reduce the inpatient bed-day rate for children from Avondale and Price Hill by at least 10% by June 30, 2020. Meeting this goal required being accountable for an entire population and focusing on the root causes of place-based inequities, he says.

Improvement efforts began in July of that year, with the assembly of a multidisciplinary team that included inpatient and outpatient
medical providers, social workers, community partners (such as legal aid), and parents of neighborhood children. This initiative focused on roughly 8,000 children living in the high-morbidity, high-poverty Avondale and Price Hill neighborhoods. Children from these communities disproportionately experienced morbidity across nearly every condition and pediatric subspecialty.

The study period was between July 2012 and June 2018, with July 2012–June 2015 as the baseline phase and July 2015–June 2018 as the improvement phase.

Across the entirety of the study period there were a total of 38,583 hospitalizations for in-county children, of which 37,337 (97%) lasted less than 14 days. Hospitalizations that met diagnostic and length-of-stay inclusion criteria contributed 76,759 inpatient bed-days. The county’s inpatient bed-day rate was 5.6 days per 1,000 children per month. The baseline rate for Avondale and Price Hill was 8.4 days per 1,000 children per month. This equated to neighborhood children collectively spending about 75 days each month and 900 days each year on inpatient units in Cincinnati Children’s Hospital Medical Center before improvement efforts began in the summer of 2015.

By the end of the study period in 2018, the average monthly inpatient bed-day rate decreased to 6.9 per 1,000 children, or 18% fewer in-hospital days than at baseline (July 2012–June 2015). There was no similar decrease in the rate for control neighborhoods, where the rate remained at 7.6 inpatient bed-days per 1,000 children per month throughout the study period.

The rate reduction in Avondale and Price Hill was likely driven by fewer hospitalizations instead of shorter lengths-of-stay. The hospitalization rate dropped 20%—from 4.1 events per 1,000 children per month to 3.3 events—again beginning during the summer of 2015.

Finally, researchers assessed the degree to which the efforts narrowed equity gaps relative to the rest of the county. For the baseline period, Avondale had the fourth-highest and Price Hill the 11th-highest inpatient bed-day rates out of 80 county neighborhoods. In that period, Avondale and Price Hill children spent 2,720 days in the hospital, compared with 2,145 in the improvement period (July 2015–June 2018). The number of hospitalizations decreased from 1,344 to 1,041. Indicative of a move toward equity, Avondale improved to the ninth-highest and Price Hill to the 15th-highest inpatient bed-day rates.

**Expanding pop health**

Beck and his team have been encouraged by the marked, statistically significant improvements in Avondale and Price Hill when comparing two key metrics from the 2012-2015 benchmark to their results in 2015-2018: the inpatient bed-day rate and hospitalizations. “This meant children spend hundreds of additional days at school and at home instead of in the hospital,” Beck says.

However, there is still progress to be made. “We are taking what we have learned from our efforts in Avondale and Price Hill into account as we plan for scale and spread across additional local neighborhoods. We believe that the theories and methods used to decrease bed-day rates and hospitalizations could serve as a relevant example to other pediatric population health improvement projects—locally as well as nationally,” Beck says.

Tricia Krizner is a Cleveland-based writer.

These findings were recently published in *Health Affairs.*

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**Avondale and Price Hill Neighborhoods, 2012-2018**

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<td><strong>Inpatient bed-day rate days per 1,000 children per month</strong></td>
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<td>Total number of hospitalizations</td>
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<td>Avondale inpatient bed-day rate ranking out of 80 county neighborhoods</td>
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<tr>
<td>Price Hill inpatient bed-day rate ranking out of 80 county neighborhoods</td>
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Managed Healthcare Executive.com
Although investing in housing construction and rehabilitation is relatively new for most hospitals and health systems, a new guide argues that hospitals’ institutional assets, focus on health outcomes, and position as anchor institutions make them well-positioned to invest in affordable housing.

The Urban Institute surveyed non-profit hospitals to learn more about current practice and motivations, considerations, and challenges they face in addressing housing needs of their patients and communities.

“...To our knowledge, our survey was a first attempt to systematically understand how nonprofit hospitals and health systems are approaching housing-related activities, including investments,” says Kathryn Reynolds, policy program manager for the Research to Action Lab at the Urban Institute.

Overall, 45 nonprofit hospitals and health systems participated in the survey. Due to the small number of study participants, some experiences and insights may not have been captured, and findings are not generalizable and representative. “However,” Reynolds says, “these findings resonated well in our subsequent roundtable discussions with experts and hospital administrators and gave us some sense of the information and tools that may be needed to encourage more nonprofit hospitals and health systems to consider housing investments.”

Key findings include the following:

- Nonprofit hospitals are largely aware of housing needs in their communities or within their patient population and many hospitals are undertaking efforts to address the issue.
- Hospitals see housing as a platform for addressing social determinants of health but are concerned about the time and resources needed.
- Hospitals most often dedicate health services, administrative capabilities, and political leverage to support housing initiatives.
- Hospitals seem less interested in direct financial investments in housing.
Affordable housing  |  Population Health Management

- Hospitals involved in affordable housing development most often provide funding, but at modest levels.
- Hospitals that make affordable housing investments partner with financial intermediaries.
- Hospitals may need more information about the implications of federal policies for housing investments.

Many case studies highlight health systems and hospitals that have made early, innovative investments in community development and housing.

"However, little is known about the nonprofit hospitals and health systems that are exploring or starting to implement housing-related projects, or what could help motivate the hospitals and health systems that are not involved to make housing investments," Reynolds says. "Further, federal, state, and local funding to create, preserve, and operate affordable apartments falls far short of the need across the country, leading to a shortage of affordable and quality housing, especially for low- and moderate-income families.

"Nonprofit hospitals and health systems, as anchor institutions rooted in place and with missions to improve community health, are well-suited to contribute funding to alleviate this problem," she says.

A guide
The Urban Institute publication provides guidance to hospitals and health systems that wish to invest in affordable housing development projects. The resource shares actionable, research-informed strategies and examples of how nonprofit hospitals and health systems can help fill the financing gap that often prevents affordable housing from being built or rehabilitated. The guide describes key steps to consider when planning and implementing an investment strategy:

- Assess social determinants of health in the community.
- Identify the target population or community for housing investment.
- Engage with the community who will be directly impacted.
- Understand the policy context that drives the institution’s investment actions.
- Determine an affordable housing investment strategy.
- Select an implementation partner or partners to assist in reaching the goal.
- Identify internal champions.
- Measure the progress made.

Three concrete ways in which hospitals and health systems can support a housing investment project, include:

- Donating land or buildings or swapping land with a housing developer;
- Using their financial position to enhance credit or lowering borrowing costs, or provide a direct loan for construction, renovation, or rehabilitation costs; and
- Contributing staff time or capital to encourage others to invest in affordable housing development.

There are three things health care executives should know, according to Reynolds:

1. Affordable housing is a proven asset class with a demonstrated history of predictable returns and a well-developed network of developers and intermediaries. An investment in housing allows health institutions to serve their mission and address upstream social determinants of health while allowing the hospital to make subsequent investments in future projects with “revolving” dollars, according to Reynolds.

2. Nonprofit hospitals and health systems have institutional assets that make them especially well-suited to making investments in affordable housing, especially with a knowledgeable partner, such as a community development financial institution or a non-profit developer. These assets include:

a. Financial assets for charitable investments, such as endowments, pensions, and insurance reserves;

b. Nonfinancial assets that can be used to offset costs for development, such as land and buildings; and

c. Their financial strength which can enhance credit or reduce risk of investments.

3. Evaluation is a critical component to measuring success in any project, "but our survey and conversations with many hospital and health system administrators suggest that few housing investments—including those designed with specific health outcomes in mind—are systematically tracked and measured," Reynolds says. "An evaluation would not only allow hospital leadership to understand the impact of their investment on patients and communities, but would also contribute to knowledge base of ‘what works’ to alleviate population or community-based housing-related issues."
American healthcare costs are skyrocketing. As such, both payer and provider organizations are looking for creative, sustainable ways to reduce waste and improve the quality of care for patients, especially those who are living with chronic or complex medical conditions. With CMS already collecting data for its first oncology performance measure, OP-35: Admissions and Emergency Department Visits for Patients Receiving Outpatient Chemotherapy, which will affect payments come 2020, many healthcare organizations are taking a long, hard look at where they can prevent, or at least significantly reduce, cancer readmissions.

It’s not a surprise. As noted by the Agency for Healthcare Research and Quality, hospital readmissions, regardless of condition, are remarkably expensive, with collective costs hovering just over $41 billion a year for patients who return to the hospital within 30 days of discharge. But Alok Khorana, MD, medical oncologist at the Cleveland Clinic, in Cleveland, says readmissions are becoming more of a focal issue for cancer care, as more patients are treated in an outpatient setting.

“In the past, cancer patients were generally admitted while they were worked up, staying in the hospital for 10 to 14 days,” he explains. “Today, there is pressure to make hospital stays as brief as possible, which means that many patients are discharged without all of their issues being completely resolved. Since cancer is such a complex condition, with both acute and chronic elements, we often see that readmission rates in the cancer population are higher than those in the general medical population.”

But given cancer’s complexity, what can healthcare stakeholders across the industry do to better prevent cancer readmissions?

**Consider care transitions**

Given how little time patients stay in the hospital today, the Cleveland Clinic embarked on a process improvement project to improve outpatient care transitions. Khorana says the project started as a way of looking at “common sense” steps to reduce readmissions. He said their first lesson learned was that a significant portion of cancer readmissions are simply inevitable given this disease’s level of complexity.

“This is important for regulators and for payer organizations to understand,” he says. “In many cases, readmission is the right thing to do for patients. It cannot be avoided no matter what the provider may do.”

Yet, to help reduce the number of readmissions in cases that were preventable, he and his colleagues focused on improving care transitions, providing patients with more support once they were discharged.

“Cancer patients receive really intensive care while they are in the hospital, from a variety of different clinical staff,” he explains. “The key is to not take all of that away once they went home. We started a program where an oncology nurse checked in with patients within 48 hours of discharge, and then they had a follow-up appointment with the provider within five days of discharge, to help provide continuity of care and answer any questions. We discovered that there were a lot of areas where we could help prevent readmissions just by adding in those extra contacts.”

In fact, by putting this standardized discharge protocol in place, the Cleveland Clinic was able to reduce the readmission rate in medical oncology by approximately 4.5%.

“It was a modest improvement—but a sustainable one,” he says. “In terms of dollars, we are
talking about millions of dollars in savings over the long term. And the patients, of course, have the benefit of not ending up back in the hospital.”

**Predict high-risk patients**

But, given that some cancer readmissions are unavoidable, how might healthcare organizations better predict who is at the highest risk of a readmission?

Carl Schmidt, MD, a surgical oncologist at West Virginia University Cancer Institute, in Morgantown, West Virginia, hoped to develop a model that could estimate the risk of readmission for individual patients. With such a model in place, oncologists could better determine where to best put care management resources after discharge.

“In our original analysis, we estimated that probably about one in five readmissions was preventable,” he says. “So, in that 20%, there may be things we can do to stop them from happening. Those patients may just need more interventions. But since some of those interventions are costly, you don’t want to give them to everyone. You want to figure out who really needs them.”

He and a team of colleagues developed a logistic regression model using high-risk factors including abnormal sodium levels, low white blood cell count, solid malignancy, and emergency department visits, among others. When they validated the model, it could reliably predict which patients would go on to be readmitted with about 70% accuracy. He believes future models could use artificial intelligence (AI) tools to improve that percentage.

“Our model was pretty simple, but it still allowed us to flag patients who might need some additional support,” he says. “But healthcare organizations, particularly academic centers with the resources, could come up with a better predictive model using neural networking or other AI methods that offer more precise predictions.”

**The right path forward**

Justin Bekelman, MD, a radiation oncologist at the University of Pennsylvania’s Perelman School of Medicine in Philadelphia, who has studied how to reduce unplanned acute care for patients with cancer, including hospital readmissions, says there is a huge opportunity for healthcare stakeholders to think creatively about how address cancer readmissions. He agrees with Schmidt that predictive analytics will likely play an integral role.

“Today, there are not truly validated predictive analytics that can identify patients who are at the highest risk of readmission,” he says. “But in addition, healthcare organizations can also use those kind of big data approaches to simple find ways to dramatically improve the care of patients with cancer—that will reduce readmissions, too.”

Bekelman, as well as Schmidt and Khorana, all argue that addressing this issue isn’t something that healthcare organizations can do alone. There is a role for payers, too—either by funding larger scale research efforts or by providing predictive models and tools for their provider partners to use to improve care for this patient population. Jessica Saba, PharmD, director of Value Based and Population Health at Highmark, Inc., a large Blue Cross Blue Shield plan serving Pennsylvania, West Virginia, and Delaware, says it’s certainly something that health plans like hers are actively working on.

“Cancer care, traditionally, represents quite a large bit of healthcare spend—and there are many direct and indirect ways to try to manage that,” she says. “And, certainly, analytics is an emerging area for Highmark and we are looking at ways that data can help. We are working quite hard to provide more tools and insights to our physician partners so they can more effectively manage these cases.”

“Cancer patients receive really intensive care while they are in the hospital, from a variety of different clinical staff. The key is to not take all of that away once they went home.”

— ALOK KHORANA, MD, CLEVELAND CLINIC

“Trying to reduce them in payer contracts or with quality metrics that say something like, ’Oh, you need to drop your readmission rate from 14% to 13.2%, isn’t going to work,” she says. Healthcare stakeholders need to collaborate and come up with better, smarter models so we can understand and undertake evidence-based measures that will provide the best quality care for our patients—and, with that, reduce readmissions along the way.”

Kayt Sukel is a science and health writer based outside Houston.

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For his part, Schmidt says he is buoyed by the amount of academic research being done on this issue. And he hopes that healthcare organizations, both of the provider and payer variety, are not only paying close attention to the studies—but looking for ways that they can get involved to help.

“This is about a lot more than just readmission numbers,” he says. “Trying to reduce them in payer contracts or with quality metrics that say something like, ‘Oh, you need to drop your readmission rate from 14% to 13.2%, isn’t going to work,'” she says. Healthcare stakeholders need to collaborate and come up with better, smarter models so we can understand and undertake evidence-based measures that will provide the best quality care for our patients—and, with that, reduce readmissions along the way.”
8 Ways to Optimize Your IT Operations

Ensuring your IT plan is aligned with the organization’s strategy can be critical to success. Here are eight things to keep in mind.

by LINDA WILSON

From the adoption of value-based, consumer-centric care to the arrival of new industry players, such as retailers, change seems constant in the healthcare industry. That’s why it’s more important than ever for organizations to deploy technology wisely to support their business vision and strategy.

The information technology (IT) operation “needs to move from a cost center to more of a value center,” says Subra Sripada, managing director in the healthcare practice at Navigant Consulting. “Simply said, the IT tactical plan needs to align closely with the strategic plan,” he says.

While this is not a new concept, achieving it isn’t easy. So Sripada, former chief information officer and chief transformation officer at Beaumont Health in Southeast Michigan, and other experts share eight recommendations about how to align the work of information technology with the organization’s strategy.

1 CREATE A STRUCTURED GOVERNANCE PROCESS

At FHN—a rural health system based in Freeport, Illinois—an IT governance group composed of C-suite executives meets throughout the year to make sure the IT department’s portfolio of projects supports the organization’s strategy to become a consumer-centric health network. “It really needs to be owned by the IT governance council because the IT department needs the support of senior executives to really get what they need: the resources to get things done,” explains Mark Gridley, president and CEO of FHN, which includes a 100-bed hospital.

Carol Chouinard, vice president of provider technology at Optum Advisory Services, says regular governance meetings provide a venue for C-suite executives to learn about the work of the IT department throughout the year. “Too many CIOs go through this decision-making process, and then they walk away. Then there are these surprises and frustrations the next time they get to the table,” he says.

2 ADOPT PROJECT MANAGEMENT FOR THE ENTIRE ENTERPRISE

While many healthcare organizations use a project management process within the IT department to vet, manage, and track projects, fewer of them have adopted a process that encompasses the entire organization.

But that’s what executives at Albany Medical Center in New York decided to do earlier this year. In March, the academic medical center launched an enterprise program management office. The office coordinates and tracks all initiatives from departments across the organization, such as IT, facilities, and clinical service lines, as well as cross-functional projects.

Projects are completed on a day-to-day perspective at the department level, but the project details from IT and other departments also are fed into the enterprise program management process. “It is completely bidirectional,” says George Hickman, executive vice president, CIO, and chief analytics officer at Albany Medical Center.

“We can see all the interrelationships,” Hickman continues. “Frankly, it makes the prioritization process transparent and fundamentally clear to all of senior management.” Because many projects compete for the same people and financial resources, centralized project management
helps executives balance competing priorities, he notes.

A team from IT and finance manages the enterprise program management office. The team reports to a leadership group that oversees Albany Medical Center’s overall strategic plan—an effort the organization calls “Pillars 22,” Hickman says.

3 EMBRACE THE ANNUAL BUDGET PROCESS

During the annual budget process, CIOs should help other members of the C-suite decide how to deploy technology to fix business problems. They should also provide their peers with insight about the benefits and risks of each option.

As Gridley explains, “For myself as the CEO, I may have a vision for where I think things need to be, but my IT team is the one that needs to help frame the vision.”

For example, he says, FHN’s executives wanted to provide telehealth services as an alternative to in-office visits for patients. After evaluating the risks and benefits of developing a telehealth program in-house, FHN decided to contract with MDLive, which manages the virtual technology and remote providers but brands the service as an FHN entity. The new service has been live for several months.

4 BE FLEXIBLE

“The mature CIOs will always anticipate and be able to manage through changes in the project portfolio. We are in an industry where things change,” Chouinard explains. “The most common is budget pressure and budget priority changes. The second is around M&A activity. The third is leadership changes. New folks come in and they have new priorities.”

For example, he says he worked with a large health system that pulled the plug on a Cerner electronic medical record (EMR) deployment in one local market because a large, important medical group insisted that the organization’s local hospitals use Epic’s EMR.

5 MANAGE FINANCIAL RESOURCES

Most IT departments need to improve how they manage budgeting, forecasting and spending revisions for the projects in their portfolios, Chouinard says. Even more important, they need to think about IT spending in a strategic way. He explains the strategic thought process as, “What is the right level of affordability? How much can we do with the money we have?”

6 ENGAGE STAFF

Sripada encourages his clients to hold town hall meetings to report back to their staff about the progress the IT department is making to support the organization’s strategic goals. “I’ve always felt that gives a sense of purpose to the IT team,” Sripada says.

Hickman says members of the data analytics team are assigned to Albany Medical Center’s process improvement projects, so they become familiar with the organization’s corporate strategy through their day-to-day work.

Beyond that, Hickman says he includes an agenda item on Albany Medical Center’s strategy at IT department meetings. He also encourages information sharing at meetings. “I try to create venues—whether I am there or not—where we go around the table and talk about what we are working on, and the approaches we are taking,” he says.

7 ALIGN THE IT PROJECT PORTFOLIO TO THE CORPORATE CULTURE

Organizations have different appetites for the amount of risk they are willing to take on and the rate of change they are comfortable managing. CIOs should fully understand those cultural dynamics before embarking on large initiatives or changing the mix of existing projects, Sripada advises.

Just because there are technologies available to solve a business problem doesn’t mean the organization is ready to adopt it and benefit from it, he says.

During his last four years at Beaumont Health, Sripada oversaw the day-to-day activities involved in merging three health systems into one—a process that subject- ed employees to a rapid pace of change. In hindsight, “we are glad we did it the way we did it,” he says, while also saying that it was a challenging process. “There were a lot of balls that were in the air.”

8 KEEP AN EYE OF THE FUTURE STATE

The IT team needs to keep abreast of new technologies that could help the corporate organization reach its strategic goals, such as third-party apps for consumers. The department also needs to plan for changes to the underlying infrastructure, such as the EMR to support future IT investments.

“It is so easy to get lost in the 400 requests that we get, and we have to manage on a regular basis,” Chouinard says. “There is a risk that we will lose sight of what the bigger picture is.”

Linda Wilson is an experienced writer and editor specializing in the healthcare industry.
As the opioid crisis rages on, the healthcare industry is looking for alternatives to pain management. The crisis has spurred people from all over the industry, from pharmacists to physicians to healthcare technology companies to pharmaceutical manufacturers, to reconsider their approach.

This type of approach is undoubtedly necessary: Deaths related to opioid doses number about 150 every day, according to the National Institutes of Health (NIH). One recent study found that Americans are prescribed opioids far more often for surgery than in other similar countries—in Sweden, 11% of patients received opioids after surgery, compared to over 70% in the United States. This is a problem, because around 21% to 29% of patients prescribed opioids develop an addiction.

The good news, however, is that opioid prescription rates are declining. According to the CDC, opioid prescribing rates have been falling in recent years, from a high of 81.3 prescriptions per 100 persons in 2012 to 58.7 prescriptions in 2017.

However, lowering prescribing rates only solves one part of the equation. Patients still need a way to cope with pain, leading many to consider alternate solutions. From acupuncture to novel electrotherapies, here are some ways healthcare is rethinking pain management.

**Acupuncture**

Acupuncture is old—very old. Archeologists have found evidence of sharpened bones and rocks that they believe were used for acupuncture as long as 8,000 years ago. Now commonly associated with traditional Chinese medicine, the practice was and has been somewhat on the fringes in Western medicine (and for a significant length of time in China, it was outlawed in 1929 and reinstated in 1949).

In the 1990s, however, acupuncture began to receive more attention. In a 1997 *JAMA* article, the NIH gave “cautious approval of some applications of acupuncture.” After looking at the research, NIH concluded that there is evidence the practice helps with post-operative nausea and vomiting, as well as those same symptoms caused by chemotherapy and post-operative dental pain.

Currently, the NIH website says of acupuncture: “Although millions of Americans use acupuncture each year, often for chronic pain, there has been considerable controversy surrounding its value as a therapy and whether it is anything more than placebo. Research exploring a number of possible mechanisms for acupuncture’s pain-relieving effects is ongoing.”

But with the opioid crisis comes a need for alternative, nonaddictive approaches to pain management, and many believe acupuncture could be a viable solution.

Perhaps the greatest indication that acupuncture has hit the mainstream is a three-year program sponsored by the Defense and Veterans Center for Integrative Pain Management (DVCIPM), part of the Department of Defense focusing on pain relief. The program trained over 2,800 clinicians—including a number of pharmacists—in what’s known as battlefield acupuncture (BFA).

BFA was developed by Air Force physician Richard Niemtzow in 2001 as a method of relief for chronic pain. It was first tested on U.S. soldiers in Iraq and Afghanistan for efficacy—Niemtzow called it BFA because unlike other therapies, it is easy to administer and transport. It works by putting small studs in specific points on the ear in the hope that they will relieve pain. While Niemtzow says, according to a recent *Military Times* article, that he hopes the treatment could provide alternatives to opioids and that he has seen significant, helpful results in pain patients, this is just one new tool in the arsenal against pain—often encouraging patients to seek other complementary treatments or oral therapies.
Another sign that acupuncture may be hitting the mainstream comes from CMS, which is currently considering covering acupuncture to treat chronic lower back pain under Medicare.

Shital Parikh Mars, CEO of Progressive Care, a pharmacy and technology company, based in Hallandale Beach, Florida, says, “Medicare beginning to open these doors for patients is a great thing, because physical therapies like chiropractic care, acupuncture, and massage are less toxic to the body when performed by fully qualified professionals. These therapies can help manage pain before the patient seeks opioid treatment or even does bodily damage from long term frequent nonsteroidal anti-inflammatory drug [NSAID] use.”

Mars’ experience with acupuncture is personal: She suffered from stress-induced neck and back pain, of which acupuncture “worked better for me than alternatives that I have tried.” She says healthcare in the future will likely be experimenting with these alternative therapies, and it would “behoove most standard medicine practitioners to open up their service offerings and begin presenting these alternative treatments to their patients. But first and foremost, education is necessary so that both doctors and patients understand the diagnosis, what options are available, what success and results look like, treatment durations, risks, costs, etc.”

**New technologies**

Looking to the past isn’t the only available option for those looking for opioid alternatives.

One of the new trends for pain relief seekers is the use of electrical therapy to stimulate nerves. A recently approved example is Nervio from Theranica. Nervio is an app-connected device worn as an armband that utilizes Remote Electrical Neuro modulation (REN) to treat migraines. The device is worn for 45 minutes on the upper arm where it stimulates mainly small skin nerves.

The results speak for themselves: a study published in the *Journal of Headache and Medicine* that compared REN with traditional, patient-preferred therapies, researchers found that two-thirds (66.7%) of patients undergoing REN therapy experienced relief compared to 52.5% of those who underwent traditional therapies. Based on these findings, the researchers concluded the REN is an effective alternative and may even be worth looking at as a first-line treatment.

Other migraine technologies relying on electrical stimulation include Cefaly, sTMS mini, and gammaCore. This is good news for patients looking to get away from opioids or other medications. While migraine-specific drugs—as well as more common approaches like over-the-counter NSAIDS (which are themselves responsible for a large number of side effects)—are available, opioids continue to be prescribed for migraines at high rates, according to the American Headache Society.

Perhaps it’s unsurprising then, that the market for this kind of technology is expected to boom in coming years. While issues of reimbursement and access still exist, one report from Global Market Insights found that the worldwide market for neurostimulation devices is set to hit $16 billion by 2024, growing at a compound annual growth rate of 15%. While part of that growth is for non-pain-related treatments for neurological conditions (e.g., Parkinson disease, epilepsy, dementias), much of that growth will be driven by patients in pain resulting from failed back surgery, as well as by chronic pain sufferers.

Nicholas Hamm is managing editor of our sister publication Drug Topics®, where the story first appeared.
Costs for oncology medications continue to increase in the United States, with spending on all drugs reaching almost $150 billion in 2018. According to a study published in the *Journal of Managed Care & Specialty Pharmacy*, there are challenges for managing cancer drug costs even with new innovative technology tools. There are a variety of direct costs associated with treating cancer, which include physician visits, laboratory and imaging tests, radiation treatment, hospital stays, home care, and medication expenses. Here are oncology drugs that are in phase 3 development and biosimilars on the horizon.

**Phase 3 oncology drugs in the pipeline**

There are a variety of phase 3 drugs in the pipeline with some innovative approaches to cancer treatment. Celgene is planning to submit the biologics license application for liso-
cabtagene maraleucel (liso-cel) in the fourth quarter of 2019 for diffuse large B-cell lymphoma, the most common type of non-Hodgkin lymphoma (NHL), with more than 18,000 individuals diagnosed annually. The ongoing phase 3 TRANSFORM (NCT03575351) trial is evaluating liso-cel in patients with B-cell NHL, and the expected study completion date is 2023.

Entinostat is being studied by Syndax Pharmaceuticals for the treatment of advanced hormone receptor-positive breast cancer, which has a novel mechanism of action as a histone deacetylase (HDAC) inhibitor. Evidence suggests that HDAC inhibitors can inhibit tumor growth, resulting in cancer cell death with little effect on normal tissue. Entinostat received breakthrough therapy status from the FDA after a phase 2 randomized placebo-controlled study demonstrated significant improvement in overall survival in combination with exemestane versus exemestane as monotherapy. Entinostat is currently being studied in a phase 3 trial (NCT02115282) including about 600 patients with recurrent hormone receptor-positive breast cancer, and the results are expected sometime in 2019.

Novartis is currently studying asciminib in patients with chronic myeloid leukemia through a phase 3 multicenter trial, with results expected in 2025. Asciminib has a novel mechanism of action in that it binds to a different site of the protein than tyrosine kinase inhibitors (TKIs) called the ABL1 myristoyl pocket, making it a promising option for patients that are intolerant/resistant to currently available TKIs.

**Biosimilar drugs and implications in therapy**

Biosimilar approval may help to decrease oncology drug costs for patients as patent expirations of major biologics occur. According to Express Scripts, biosimilars could bring approximately $250 billion in savings by 2024. "Biosimilars have revolutionized oncology treatment modalities available to patients with serious health conditions in the last two decades," says Jorge J. Garcia, PharmD, assistant vice president/System Oncology Pharmacy Service Line, Miami Cancer Institute/Baptist Health South Florida.

Cancer Institute/Baptist Health South Florida. Garcia says that biosimilars are defined as biologic agents that are not chemically identical; but are highly similar to an approved reference biologic agent.

Filgrastim-sndz, the first biosimilar approved by the FDA and launched in the United States, "has achieved and maintained market share in its drug class, providing discounts in the vicinity of 30%,” Garcia says. Long-acting granulocyte colony stimulating factor (G-CSF) biosimilars have most recently entered the market (e.g., pegfilgrastim-cbqv and pegfilgrastim-jmdb) driving discounts on highest cost G-CSF products. Additionally, there are more pegfilgrastim biosimilars expected to enter the market in the future, which could potentially further drive down costs.

"Bevacizumab-awwb and trastuzumab-anns are the first oncology therapeutic biosimilars to launch in the United States this summer, both of which are expected to make a significant dent on the oncology cost curve,” Garcia says.

However, it is anticipated that providers will be more reluctant to use therapeutic biosimilars compared with supportive care biosimilars (e.g., G-CSF). More significant cost savings are expected as several other bevacizumab and trastuzumab biosimilars enter the U.S. market in the near future.

Jennifer Gershman, PharmD, CPh, is a pharmacist and medical writer residing in South Florida.

“Biologics have revolutionized oncology treatment modalities available to patients with serious health conditions in the last two decades.”

— JORGE J. GARCIA, PHARM.D, MIAMI CANCER INSTITUTE/BAPTIST HEALTH SOUTH FLORIDA
Top 4 Drugs in the Pipeline

by CHRISTINE BLANK

Among the top pipeline drugs is a new treatment for type 2 diabetes and a novel acute migraine drug, according to OptumRx’s “Drug Pipeline Insight Report” for third quarter of 2019.

The top four drugs under development, according to the report, include:

1. **UBROGEPANT** (Allergan), a new oral migraine treatment based on the calcitonin gene-related peptide (CGRP) mechanism of action—the first oral medication in its class. Ubrogepant has been accepted for FDA review, and it is expected to be approved in late 2019.

   Currently, three injectable CGRP inhibitors are available for patients to take preventively, while new oral CGRP inhibitors, such as ubrogepant, treat the acute symptoms of a migraine and are not preventive, Dutta says.

   “The difference in indication and administration are important distinctions,” he says. “Pricing is also a concern since most triptans are available generically and cost as low as $20 to $30 per month or prescription.”

   Meanwhile, the injectable CGRPs have a list price at about $6,900 a year or $575 monthly.

2. **CABOTEGRAVIR AND RILPIVIRINE** (Cabenuva, Viiv Healthcare), a two-drug regimen for treating HIV-1 in adults. If approved, Cabenuva would be the first long-acting, injectable treatment for adults living with HIV, potentially changing the way many patients living with HIV are managed and treated, according to OptumRx.

   It was estimated 1.1 million individuals, in 2016, aged 13 and older are positive for HIV infection, with an additional 162,000 whose infections are not diagnosed.

   “The current standard of care for HIV is a daily, oral, three-drug regimen of antiretroviral therapy (ART). However, two global phase 3 studies have shown once per month injections of cabotegravir/rilpivirine are as effective as a standard ART, the report says.

3. **LUSPATERCEPT** (Acceleron Pharma and Celgene), an investigational agent to treat anemia in adult patients with very low to intermediate-risk myelodysplastic syndromes (MDS) and beta-thalassemia. Both conditions often require regular blood transfusions, which are costly, and associated with their own set of side effects, including risk of infection and iron overload toxicity. The only curative treatment is stem cell transplantation, OptumRx says.

   “It is estimated that MDS is diagnosed in at least 10,000 people each year in the United States, with more than 60,000 people living with the disease today,” Dutta says.

   Industry analysts are projecting that luspatercept will reach sales in excess of $2 billion, based on its ability to treat MDS and beta thalassemia.

   FDA has set target action dates of December 4, 2019, for the beta thalassemia indication (priority review) and April 4, 2020, for the MDS indication.

4. **BROLUCIZUMAB** (Novartis) to treat wet age-related macular degeneration (AMD), also known as neovascular AMD, or nAMD. Wet AMD is a leading cause of blindness, estimated to affect up to 1.75 million people in the United States by 2020, according to OptumRx.

   Analysts predict that brolucizumab will reach annual sales over $1 billion globally by 2021, and that it will become the most profitable AMD drug by 2026.

   “However, the U.S. patents on both Lucentis and Eylea will expire in 2020, and biosimilars for both are in development. These forecasts depend on the biosimilar drugs that are currently in various stages of development for the existing AMD drugs. If these should come to market, there could be additional price competition in the class,” OptumRx says.

Christine Blank is a freelance writer based in Orlando, Florida.
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Accessibility and Affordability of Gene Therapy

Payers are finding ways for members to afford expensive specialty drug treatments

by MARI EDLIN

The race to decrease drug costs is heating up across America. The Trump administration has one idea, Speaker of the House Nancy Pelosi has her solution, and big pharma has proposed a resolution to the problem. But some insurers are now rising to the occasion and finding ways for members to afford expensive specialty drug treatments, such as gene therapy.

The cost of gene therapies is expected to reach more than $16 billion in the United States by 2024. While only two therapies have yet been approved, they are indicative of the high price tag.

Luxturna (voretigene neparvovec-rzyl), the first FDA-approved prescription gene therapy for people with inherited retinal disease leading to blindness, costs $415,000 per eye. Zolgensma (onasemnogene abeparvovec-xioi), for children under two years old with spinal muscular atrophy, is set at $2.1 million.

Embarc eliminates copayments

Cigna has developed a coverage program, Embarc Benefit Protection, for the two therapies that don’t require any out-of-pocket (OOP) payments related to the cost of the medicine. It is expected to go live by January 2020.

Payers pay a per-member per-month (PMPM) fee to access Embarc’s gene therapy network. Physicians are required to submit prior authorization requests for patient eligibility. Steve Miller, MD, chief medical clinical officer for Cigna, hopes that PMPM will reach $1.

He says that Cigna chose gene therapy because of the integral part it will play in overall healthcare. He also is concerned by the history of gene therapies: Two of which were approved in Europe and have since been taken off the market because they are cost prohibitive. “Without patient access, a product can become a tremendous market failure,” Miller says.

“Some plans are writing policies to exclude gene therapy, while stop-loss insurers are capping their exposure,” he adds.

“Although gene therapy is not yet urgent or presenting any threat, we want to capture the market before insurers decide to exclude these treatments from their benefits,” Miller says. He wants to eliminate all barriers to joining the Embarc coalition of subsidiaries and affiliates so that patients are not forced into government insurance. The program initially will target Cigna members followed by Express Scripts’ book of business, then Evicor and finally nonaffiliated health plans.

Brian Duffant, vice president at BluePath Solutions, a market access and health economics/outcomes research consulting firm based in Los Angeles, says payers are developing new
payment programs to address the projected future increase in demand for gene therapies based on the burgeoning gene therapy pipeline.

The addressable market for gene therapies could grow as large as 2.4 billion patients worldwide, according to Guggenheim Securities.

Miller says Embarc will combine Cigna’s innovative payment with the health services, medical benefit management, and specialty pharmacy expertise of Express Scripts, a pharmacy benefits manager; eviCore, a healthcare management company; Accredo specialty pharmacy; and Curascript SD, a specialty pharmaceutical dispensing and distribution company.

AveXis, a subsidiary of Novartis Corp. that developed Zolgensma, also is partnering with Cigna’s coalition members offering payers pay-over-time options up to five years and outcomes-based agreements up to five years for the drug. In the same vein, the Cigna partnership will envelop Spark Therapeutics, the producer of Luxturna.

New kind of paradigm

“There wasn’t a paradigm in the private sector for this kind of coverage, but we wanted to get something out there,” Miller says.

Cigna chose an approach that considers the impact Embarc will have on all stakeholders, including manufacturers, providers, payers, and patients.

Embarc will create:

- Value-based contracting
- Limits on barriers to access, eliminating the need for copayments
- Patient encouragement to make the best choice without financial support playing a role

Cigna anticipates providing best prices and value-based pricing, will keep the price of Zolgensma for example, within the range of traditional cost-effectiveness thresholds used by the Institute for Clinical and Economic Review (ICER), not just what the market will bear, Miller says. ICER produces cost-effectiveness analyses.

"Without patient access, a product can become a tremendous market failure.”

— STEVE MILLER, MD, CIGNA

For payers—employers, insurers, and unions—Embarc expects to provide low prices with pass-through and transparency; spread overhead among as many patients as possible; use uniform utilization management criteria so there is no adverse selection, which gives payers 100% predictability; and establish a flat PMPM not based on usage.

Cigna will enable payers to use Embarc as a white label, payment product to build Cigna’s coalition, Miller says.

Patients should receive speedy treatment without any copayments, while providers are expected to be part of centers of excellence to keep costs down.

Miller says patients will pay little—perhaps an administrative fee—to nothing for the new available gene therapies. By negotiating best prices with manufacturers, he anticipates it will be possible to buy down copayments.

“What is clear is that payers will likely use a combined approach to manage gene therapy utilization, including use of centers of excellence; population risk-pooling; and short- and long-term, outcomes-based contracts with manufacturers, reinsurance, and programs intended to pay for gene therapy over time as opposed to one up-front payment,” Duffant explains.

A report developed by the PwC Health Research Institute (HRI) outlines a menu of contracting and price-assistance models that could make gene therapy more accessible and affordable.

However, HRI, found in a survey that just 56% of pharmaceutical executives reported using at least one value-based drug contract, while only 14% of payers said they engaged in outcomes-based agreements with biopharmaceutical companies.

Cigna is working on version two of Embarc that will target patients most likely to benefit from gene therapy to limit adverse risk.

“The product will begin to look more traditional as more patients are involved and prices decrease,” Miller says.
Coverage challenges lurk
Duffant is concerned that if a small employer has even one patient who needs gene therapy, this could have a catastrophic impact on employers’ overall healthcare spend. “Payers need a way to manage a new paradigm of gene therapies with a high one-time upfront cost and uncertain clinical benefits over the long-term,” he says.

He recommends using clinical management tools to target the right persons with the right therapies. Although it is a new way of financing specialty pharmacy and gene therapy, it doesn’t get to the challenge posed by these expensive drugs; it doesn’t address long-term sustainability; it is out of line with economic and wage growth,” Wojcik says. “It is similar to covering college expenses while not addressing inflation.”

He concedes that patients are shielded from cost sharing, but acknowledges an underlying payment exists. He is concerned that smaller employers are apt to face higher premiums to offset the pricing arrangement. “There are already limits on OOP payments,” Wojcik says.

While he doesn’t expect a big impact initially with these payment programs, he believes that as more gene therapies hit the marketplace and affect a wider population, the result could have more significance and provide affordable healthcare.

Other insurers to jump on coverage bandwagon
Ethan Slavin, spokesperson for Aetna, says the insurer is working hard to effectively manage the cost of these therapies for its clients and members. For example, Aetna is currently developing:

- Refined pharmacy benefit management strategies, including formulary and utilization management programs, for therapy classes with high-cost entrants that have available alternatives.
- Stop-loss products for clients looking to better control medical costs, including an innovative reinsurance instrument specifically designed for gene therapies.
- Alternative payment models, including annuity payments that spread the cost of ultra-high cost drugs over a period of time, and may provide some clients with options to control spending in a single year.

The health plan also is exploring outcomes-based contracts with manufacturers to ensure patients and customers derive clinical benefit and value from gene therapy products. In addition, Aetna is advancing a network strategy that ensures patients receive treatment at high-value sites of care in terms of both clinical quality and cost.

According to an article published by the Advisory Board, Anthem has a product under consideration that includes reimbursement or stop-loss options that would protect employers from the negative financial repercussions of gene therapies.

Mari Edlin, a frequent contributor to Managed Healthcare Executive®, is based in Sonoma, California.
Industry Analysis

Cultural Competence

31.7% The percentage of non-Hispanic black adults who think it is important to have a healthcare provider who shared or understood their culture.

The importance of having a healthcare provider who shares or understands cultural differences.

<table>
<thead>
<tr>
<th>Importance</th>
<th>Hispanic</th>
<th>non-Hispanic</th>
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<tbody>
<tr>
<td>very important</td>
<td>32.9%</td>
<td>27.0%</td>
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<tr>
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<tr>
<td>slightly important</td>
<td>28.4%</td>
<td>32.6%</td>
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</table>

Source: CDC

Community Health Crunch

Facing a potential funding crunch, community health centers in medically underserved areas around the country report they are considering reductions in staffing and services that would limit patients’ access to care. In response to federal funding uncertainty, actions being considered include instituting:

52% hiring freeze
45% spending down reserves
42% cancelling or delaying planned facility renovation or expansion
38% laying off staff

Source: KFF/GWU

Smoking Trends

adults aged 18 to 24 years who:

<table>
<thead>
<tr>
<th>Year</th>
<th>smoked cigarettes</th>
<th>used electronic cigarettes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
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<td>5.1%</td>
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<tr>
<td>2018</td>
<td>7.8%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

Source: National Health Interview Survey

“What is clear is that payers will likely use a combined approach to manage gene therapy utilization, including use of centers of excellence; population risk-pooling; and short- and long-term, outcomes-based contracts with manufacturers, reinsurance, and programs intended to pay for gene therapy over time as opposed to one up-front payment.”

—Brian Duffant, vice president at BluePath Solutions

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