Managed Healthcare Executive
The C-Suite Advisor

**TOP 10 DISRUPTIVE TRENDS TO WATCH FOR**

- **Drug Pipeline**
  Promising pipeline for hep B

- **Formulary/Pharmacy Development**
  Authorized generics gain popularity

- **Industry Analysis**
  Reduce administrative costs

**Population Health**
#1 PRESCRIBED FOR ADULTS WITH HIV-1 STARTING AND SWITCHING ARV REGIMENS


**INDICATION**

BIKTARVY® is indicated as a complete regimen for the treatment of HIV-1 infection in adults who have no antiretroviral (ARV) treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA <50 copies per mL) on a stable ARV regimen for ≥3 months with no history of treatment failure and no known resistance to any component of BIKTARVY.

**IMPORTANT SAFETY INFORMATION**

**BOXED WARNING: POST TREATMENT ACUTE EXACERBATION OF HEPATITIS B**

- Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of BIKTARVY. Closely monitor hepatic function with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue BIKTARVY. If appropriate, anti-hepatitis B therapy may be warranted.

**Contraindications**

- Coadministration: Do not use BIKTARVY with doxifetilide or rifampin.

**Warnings and precautions (cont’d)**

- **Immune reconstitution syndrome**, including the occurrence of autoimmune disorders with variable time to onset, has been reported.

- **New onset or worsening renal impairment**: Cases of acute renal failure and Fanconi syndrome have been reported with the use of tenofovir prodrugs. In clinical trials of BIKTARVY, there have been no cases of Fanconi syndrome or proximal renal tubulopathy (PRT). Do not initiate BIKTARVY in patients with estimated creatinine clearance (CrCl) <30 mL/min. Patients with impaired renal function and/or taking nephrotoxic drugs (including NSAIDs) are at increased risk of renal-related adverse reactions. Discontinue BIKTARVY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. **Renal monitoring**: Prior to or when initiating BIKTARVY and during therapy, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients as clinically appropriate. In patients with chronic kidney disease, also assess serum phosphorus.

- **Lactic acidosis and severe hepatomegaly with steatosis**: Fatal cases have been reported with the use of nucleoside analogs, including FTC and TDF. Discontinue BIKTARVY if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity develop, including hepatomegaly and steatosis in the absence of marked transaminase elevations.

**Adverse reactions**

- **Most common adverse reactions** (incidence ≥5%; all grades) in clinical studies through week 96 were diarrhea (5%), nausea (6%), and headache (5%).

**Drug interactions**

- **Prescribing information**: Consult the full prescribing information for BIKTARVY for more information on Contraindications, Warnings, and potentially significant drug interactions, including clinical comments.
DHHS RECOMMENDED
As an initial regimen for most adults with HIV-1

EXTENSIVE CLINICAL TRIALS
With >1400 adults, including various age groups and ethnicities

LONG-TERM DATA
Demonstrated efficacy and safety in treatment-naïve adults through Week 96

Drug interactions (cont’d)

- **Enzymes/transporters:** Drugs that induce P-gp or induce both CYP3A and UGT1A1 can substantially decrease the concentration of components of BIKTARYV. Drugs that inhibit P-gp, BCRP, or inhibit both CYP3A and UGT1A1 may significantly increase the concentrations of components of BIKTARYV. BIKTARYV can increase the concentration of drugs that are substrates of OCT2 or MATE1.

- **Drugs affecting renal function:** Coadministration of BIKTARYV with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of FTC and tenofovir and the risk of adverse reactions.

Dosage and administration

- **Dosage:** 1 tablet taken once daily with or without food.
- **Renal impairment:** Not recommended in patients with CrCl <30 mL/min.
- **Hepatic impairment:** Not recommended in patients with severe hepatic impairment.

Dosage and administration (cont’d)

- **Prior to or when initiating:** Test patients for HBV infection.
- **Prior to or when initiating, and during treatment:** As clinically appropriate, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, assess serum phosphorus.

Pregnancy and lactation

- **Pregnancy:** There is insufficient human data on the use of BIKTARYV during pregnancy. An Antiretroviral Pregnancy Registry (APR) has been established. Available data from the APR for FTC shows no difference in the rates of birth defects compared with a US reference population.
- **Lactation:** Women infected with HIV-1 should be instructed not to breastfeed, due to the potential for HIV-1 transmission.

Visit DiscoverBiktarvy.com

Please see Brief Summary of full Prescribing Information for BIKTARYV, including BOXED WARNING, on the following pages.

ARV = antiretroviral; DHHS = Department of Health and Human Services.

BIKTARVY® (bictegravir 50 mg, emtricitabine 200 mg, and tenofovir alafenamide 25 mg) tablets, for oral use

Brief Summary of Full Prescribing Information. See full Prescribing Information. Rx only.

WARNING: POST-TREATMENT ACUTE EXACERBATION OF HEPATITIS B

Severe acute exacerbations of hepatitis B have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing emtricitabine (FTC) and/or tenofovir disoproxil fumarate (TDF), and may occur with discontinuation of BIKTARVY. Closely monitor hepatic function with both clinical and laboratory follow-up for at least several months in patients who are coinfected with HIV-1 and HBV and discontinue BIKTARVY. If appropriate, anti-hepatitis B therapy may be warranted [see Warnings and Precautions].

INDICATIONS AND USAGE

BIKTARVY is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 3 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of BIKTARVY.

DOSEAGE AND ADMINISTRATION

Also see Warnings and Precautions and Use in Specific Populations.

Testing Prior to or When Initiating: Test patients for HBV infection.

Testing Prior to or When Initiating, and During Treatment:

As clinically appropriate, assess serum creatinine, estimated creatinine clearance (CrCl), urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus.

Doseage: One tablet taken once daily with or without food.

Renal Impairment: BIKTARVY is not recommended in patients with CrCl <30 mL/min.

Hepatic Impairment: BIKTARVY is not recommended in patients with severe hepatic impairment.

CONTRAINdications

Also see Drug Interactions.

BIKTARVY is contraindicated to be co-administered with:

• dofetilide due to the potential for increased dofetilide plasma concentrations and associated serious and/or life-threatening events

• rifampin due to decreased BIC plasma concentrations, which may result in the loss of therapeutic effect and development of resistance to BIKTARVY

WARNINGS AND PRECAUTIONS

Also see BOXED WARNING, Contraindications, Adverse Reactions, and Drug Interactions.

Severe Acute Exacerbation of Hepatitis B in Patients Coinfected with HIV-1 and HBV: Patients with HIV-1 should be tested for the presence of chronic hepatitis B virus (HBV) before or when initiating ARV therapy. Severe acute exacerbations of hepatitis B (e.g., liver decompensation and liver failure) have been reported in patients who are coinfected with HIV-1 and HBV and have discontinued products containing FTC and/or TDF, and may occur with discontinuation of BIKTARVY. Patients coinfected with HIV-1 and HBV who discontinue BIKTARVY should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, anti-hepatitis B therapy may be warranted, especially in patients with advanced liver disease or cirrhosis since post-treatment exacerbation of hepatitis may lead to hepatic decompensation and liver failure.

Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions: Coadministration of BIKTARVY with certain other drugs may result in known or potentially significant drug interactions; this may lead to loss of efficacy and development of resistance to BIKTARVY or clinically significant adverse reactions from prior exposures of concomitant drugs. Consider the potential for drug interactions and review concomitant medications prior to and during therapy. Monitor for adverse reactions associated with concomitant drugs.

Immune Reconstitution Syndrome (IRS): IRS has been reported in patients treated with combination ARV therapy. During the initial phase of treatment, patients whose immune systems respond may develop an inflammatory response to indolent or residual opportunistic infections, which may necessitate further evaluation and treatment. Autoimmune disorders have been reported to occur in the setting of immune reconstitution; the time to onset is variable, and can occur many months after initiation of treatment.

New Onset or Worsening Renal Impairment: Renal impairment, including acute renal failure and Fanconi syndrome, has been reported with the use of tenofovir prodrugs in animal studies and human trials. In clinical trials of BIKTARVY in subjects with no antiretroviral treatment history with eGFRs >30 mL/min and in virologically suppressed subjects switched to BIKTARVY with eGFRs >50 mL/min, renal serious adverse events were encountered in less than 1% of subjects treated with BIKTARVY through Week 48. BIKTARVY is not recommended in patients with CrCl <30 mL/min. Patients taking tenofovir prodrugs who have renal impairment and/or are taking nephrotoxic agents including NSAIDs are at increased risk of developing renal-related adverse reactions. Discontinue BIKTARVY in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Renal Monitoring: Prior to or when initiating BIKTARVY, and during treatment with BIKTARVY, assess serum creatinine, CrCl, urine glucose, and urine protein in all patients as clinically appropriate. In patients with chronic kidney disease, also assess serum phosphorus.

Lactic Acidosis/Severe Hepatomegaly with Steatosis:

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including FTC and TDF. Treatment with BIKTARVY should be suspended in any individual who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity, including hepatomegaly and steatosis in the absence of marked transaminase elevations.

ADVERSE REACTIONS

Also see BOXED WARNING and Warnings and Precautions.

In Adults with No ARV Treatment History:

The safety assessment of BIKTARVY is based on Week 48 data from two randomized, double-blind, active-controlled trials: 1489 (n=314) and 1490 (n=320), in HIV-1 infected, ARV treatment-naïve adults. Through Week 48, 1% of subjects discontinued BIKTARVY due to adverse events, regardless of severity. Adverse Reactions: Adverse reactions (all Grades) reported in ≥2% of subjects receiving BIKTARVY through Week 48 in Trials 1489 and 1490, respectively were: diarrhea (6%, 3%), nausea (5%, 3%), headache (5%, 4%), fatigue (3%, 2%), abnormal dreams (3%, <1%), dizziness (2%, 2%), and insomnia (2%, 2%). Additional adverse reactions (all Grades) occurring in less than 2% of subjects administered BIKTARVY in Trials 1489 and 1490 included vomiting, flatulence, dyspepsia, abdominal pain, rash, and depression. Suicidal ideation, suicide attempt, and depression suicidal occurred in <1% of subjects administered BIKTARVY; all events were serious and primarily occurred in subjects with a pre-existing history of depression, prior suicide attempt, or psychiatric illness.

Laboratory Abnormalities: Laboratory abnormalities (Grades 3–4) occurring in ≥2% of subjects receiving BIKTARVY through Week 48 in Trials 1489 or 1490, respectively were: amylase >2.0 x ULN (2%, 2%), ALT >5.0 x ULN (1%, 2%), AST >5.0 x ULN (2%, 1%), Creatine Kinase >10.0 x ULN (4%, 4%), Neutrophils <750 mm3 (2%, 2%), and fasted LDL-cholesterol >190 mg/dL (2%, 3%). Changes in Serum Creatinine: Increases in serum creatinine occurred by Week 4 of treatment and remained stable through Week 48. In Trials 1489 and 1490, median serum creatinine increased by 0.10 mg/dL from baseline to Week 48 in the BIKTARVY group and was similar to the comparator groups.

Continued on next page.
Changes in Bilirubin: In Trials 1489 and 1490, total bilirubin increases were observed in 12% of subjects administered BIKTARVY through Week 48.

In Virologically Suppressed Adults: The safety of BIKTARVY in HIV-1 infected adults with virologically suppressed adults is based on Week 48 data from 282 subjects in a randomized, double-blind, active-controlled trial in which virologically suppressed subjects were switched from either DTG + ABC/3TC or ABC/DTG/3TC to BIKTARVY; and Week 48 data from 290 subjects in an open-label, active-controlled trial in which virologically suppressed subjects were switched from a regimen containing atazanavir (ATV) (given with cobicistat or ritonavir) or darunavir (DRV) (given with cobicistat or ritonavir) plus either FTC/TDF or ABC/3TC, to BIKTARVY.

Adverse Reactions: Overall, the safety profile in virologically suppressed adult subjects was similar to that in subjects with no antiretroviral treatment history.

Drug Interactions

Other Antiretroviral Medications: BIKTARVY is a complete regimen for the treatment of HIV-1 infection. BIKTARVY coadministration with other ARV medications for treatment of HIV-1 infection is not recommended. Complete information regarding potential drug interactions with other ARV medications is not provided.

Potential for BIKTARVY to Affect Other Drugs: BIC inhibits organic cation transporter 2 (OCT2) and multidrug and toxin extrusion transporters (MATE1) in vitro. Coadministration of BIKTARVY with drugs that are substrates of OCT2 and MATE1 (e.g., dofetilide) may increase their plasma concentrations.

Potential Effect of Other Drugs to Affect BIKTARVY: BIC is a substrate of CYP3A and UGT1A1. A drug that is a strong inducer of CYP3A and also an inducer of UGT1A1 may substantially decrease the plasma concentrations of BIC which may lead to loss of efficacy and development of resistance. The use of BIKTARVY with a drug that is a strong inhibitor of CYP3A and also an inhibitor of UGT1A1 may significantly increase the plasma concentrations of BIC. TAF is a substrate of P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP). Coadministration of drugs that inhibit P-gp and BCRP may increase the absorption and plasma concentrations of TAF. Coadministration of drugs that induce P-gp activity are expected to decrease the absorption of TAF, resulting in decreased plasma concentration of TAF, which may lead to loss of efficacy and development of resistance.

Drugs Affecting Renal Function: Because FTC and tenofovir are primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion, coadministration of BIKTARVY with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of FTC, tenofovir, and other renally eliminated drugs, which may increase the risk of adverse reactions.

Established and Potentially Significant Drug Interactions: The listing of established or potentially clinically significant drug interactions with recommended prevention or management strategies described are based on studies conducted with either BIKTARVY, the components of BIKTARVY (BIC, FTC, and TAF) as individual agents, or are drug interactions that may occur with BIKTARVY. An alteration in regimen may be recommended.

• Antiarhythmic: dofetilide. Coadministration is contraindicated due to potential for serious and/or life-threatening events.
• Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin. Coadministration with alternative anticonvulsants should be considered.
• Antimycobacterials: rifampin. Coadministration is contraindicated due to the effect on BIKTARVY. Rifabutin, rifapentine. Coadministration is not recommended.
• Herbal Products: St. John’s wort. Coadministration is not recommended.
• Medications/oral supplements containing polyvalent cations (e.g., Mg, Al, Ca, Fe): Antacids containing Al/Mg or Calcium: BIKTARVY can be taken under fasting conditions 2 hours before antacids containing Al/Mg or calcium. Routine administration of BIKTARVY simultaneously with or 2 hours after antacids containing Al/Mg or calcium is not recommended. Supplements containing Calcium or Iron: BIKTARVY and supplements containing calcium or iron can be taken together with food. Routine administration of BIKTARVY under fasting conditions simultaneously with, or 2 hours after, supplements containing calcium or iron is not recommended.
• Metformin: Refer to the prescribing information of metformin for assessing the benefit and risk of concomitant use of BIKTARVY and metformin.

Consult the full Prescribing Information prior to and during treatment with BIKTARVY for important drug interactions; this list is not all inclusive.

Use in Specific Populations

Also see Dosage and Administration, Warnings and Precautions, and Adverse Reactions.

Pregnancy: Pregnancy Exposure Registry: There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to BIKTARVY during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263. Risk Summary: There are insufficient human data on the use of BIKTARVY during pregnancy to inform a drug-associated risk of birth defects and miscarriage. BIC and TAF use in women during pregnancy has not been evaluated; however, FTC use during pregnancy has been evaluated in a limited number of women as reported to the APR. Available data from the APR show no difference in the overall risk of major birth defects for FTC compared with the background rate for major birth defects of 2.7% in a U.S. reference population of the Metropolitan Atlanta Congenital Defects Program (MACDP). The rate of miscarriage is not reported in the APR.

Lactation: The Centers for Disease Control and Prevention recommend that HIV-infected mothers not breastfeed their infants to avoid risking postnatal transmission of HIV. Based on published data, FTC has been detected in human milk; it is not known whether BIKTARVY or all of the components of BIKTARVY are present in human breast milk, affects human milk production, or has effects on the breastfed infant. BIC was detected in the plasma of nursing rat pups likely due to the presence of BIC in milk, and tenofovir has been shown to be present in the milk of lactating rats and rhesus monkeys after administration of TDF. It is unknown if TAF is present in animal milk. Because of the potential for HIV transmission in HIV-negative infants, developing viral resistance in HIV-positive infants, and adverse reactions in nursing infants, mothers should be instructed not to breastfeed.

Pediatric Use: Safety and effectiveness of BIKTARVY in pediatric patients less than 18 years of age have not been established.

Geriatric Use: Clinical studies of BIKTARVY did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

Renal Impairment: BIKTARVY is not recommended in patients with severe renal impairment (CrCl <30ml/min). No dosage adjustment of BIKTARVY is recommended in patients with CrCl >30ml/min.

Hepatic Impairment: No dosage adjustment of BIKTARVY is recommended in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. BIKTARVY is not recommended for use in patients with severe hepatic impairment (Child-Pugh Class C) as BIKTARVY has not been studied in these patients.

OVERDOSAGE:

If overdose occurs, monitor the patient for evidence of toxicity. Treatment consists of general supportive measures including monitoring of vital signs as well as observation of the clinical status of the patient.

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Top 10 Disruptive Trends to Watch For

Here are the things most likely to impact managed care

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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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Prepare for 2020 Disruptors

The factors that should be in your budget

It’s that time of the year when organizations begin developing their budgets for the coming year, by projecting membership growth, medical loss ratio, administrative expenses, as well as the investment in new initiatives. Most of these costs can, and will, be developed based on past trends that are adjusted incrementally for competitor, product, and market changes.

Beyond this, executives in the most successful organizations will also take a step back to think about what could go wrong and what could prevent their organization from reaching its goals. Aside from the inherent risk that all organizations have of unexpected staffing changes or poor sales performance, what are some of the biggest potential disruptors looming in 2020?

PERSONALIZED THERAPIES
As personalized approaches to cancer treatment like CAR T-cell therapy become more applicable to wider a range of malignancies, oncology centers will face significant pressure to incorporate these therapies in addition to surgery, chemotherapy, and radiation.

Because CAR T can in specific malignancies deliver such dramatic and rapid results, it has the potential to be a major disruptor, forcing providers and managed care organizations to include it as a first-line therapy. At a total cost ranging from $700,000 to well over $1 million, CAR T therapies could have a great impact on the cost of cancer treatment as well.

BLOCKCHAIN
The use of integrated, distributed systems of recording, storing, and viewing information critical to providers, payers, and regulators has the potential to address problems inherent in keeping provider directories up-to-date, tracking member prescription use from multiple pharmacies, integrating patient medical records in real time, and eliminating redundant diagnostic tests.

Many of the major managed care organizations have begun efforts to employ blockchain powered approaches to provider data management, including credentialing and directories.

ARTIFICIAL INTELLIGENCE
Applications for machine learning, or artificial intelligence (AI) in managed care organizations range from claims review for fraud or manipulative billing, to identification of high-risk members and the development of care plans, to viewing and approving authorizations, to data quality review and interface with electronic medical records.

In short, AI has the potential to change virtually every area of a healthcare organization and have a tremendous impact on staffing skillsets that managed care organizations require.

SOCIAL DETERMINANTS OF HEALTH
For most health plans, the SDoH conditions affecting their members are related to adequate housing, access to healthy food, and lack of transportation. Addressing these conditions on a member-by-member basis can have a dramatic impact on healthcare cost—but requires a new set of tools and employee skills and a transformation on how an organization defines itself and deploys its resources.

AMAZON-LIKE COMPETITORS
While Apple, Google, and Amazon have discussed their interest in the healthcare market, most of their activities have been relatively modest to date. That could change very rapidly.

These data-obsessed behemoths have the resources, technological capabilities, and loyal customers to be major disruptors when they enter the market in a larger way. Amazon’s purchase of PillPack is already raising significant concerns at large pharmacy chains and among PBM companies. Amazon’s Haven joint venture with Berkshire Hathaway and J.P. Morgan is starting to take form as a new intermediary focusing on outcomes-based reimbursement.

How much impact each of these or other potential disruptors will have in 2020 remains to be seen. But organizations that don’t take the time and effort to prepare for disruptors—do so at their own peril.

Don Hall, MPH, is principal of DeltaSigma LLC, a consulting practice specializing in strategic problem solving for managed care organizations. He most recently served as president and chief executive officer of a nonprofit, provider-sponsored health plan.
Reducing Hospital Readmission Rates for Heart Attack, CABG, and COPD

by NICHOLAS HAMM and KEITH LORIA

Last month, Managed Healthcare Executive brought you what you need to know about reducing heart failure readmissions. This month, in part 2 of our ongoing series, we’re taking a look at three other conditions tracked by the Hospital Readmissions Reduction Program (HRRP): acute myocardial infarction (AMI, or heart attack), coronary artery bypass grafting (CABG), and chronic obstructive pulmonary disease (COPD).

The final part will examine hospital readmissions caused by Elective Primary Total Hip Arthroplasty and/or Total Knee Arthroplasty (THA/TKA) and pneumonia.

Main causes of heart attack hospital readmissions
Andrew D. Boyd, MD, associate professor in the department of biomedical and health information sciences college at the University of Illinois at Chicago, led a recent study that looked at readmission trends for six diseases, including heart attacks, CABG, and COPD.

By examining data from 14,307 hospital reports from the HRRP from 2012–2015, the authors found that readmission rates for Medicare patients with these diseases were statistically higher among for-profit hospitals compared with nonprofit or government hospitals. In fact, the findings showed that those with heart attacks and COPD have the highest readmission rate, at 23% to 26%.

Stephen Sinatra, MD, a cardiologist in Manchester, Connecticut, notes the primary causes of re-hospitalization following heart attacks continues to be researched.

“For CABG, the main causes of hospital readmissions are complications such as wound infections, and pulmonary compromise like pleural effusions,” he says. “The method with which a CABG/CABS is performed is also important. When arteries are hooked up artery-to-artery, the prognosis is much better. Use of the internal mammary is superior to venous bypass grafts when the vessel is local to the artery needing bypassing, such as the left anterior descending artery (LAD).”

Still, he explains, a lot of these surgical outcomes depend on the individual (patient dependent) as well the experience of the surgeon, technical difficulty, what the surgeon finds once the heart is open, and operative time on bypass pump.

“When a surgeon bypasses vessels with major obstructions but leaves vessels that are only mildly ‘clogged,’ those un-bypassed vessels may still be prone to plaque rupture,” Sinatra says. “Bypassing more vessels, even those that are mildly obstructed, may help to reduce hospital readmissions.”

Main causes of COPD hospital readmissions
The major cause of hospital readmission is COPD because it’s a chronic illness.

“Pneumonia and other infections can also precipitate readmission, which is why antibiotics are used frequently to prevent infections and readmissions,” Sinatra says. “Unfortunately, that’s probably one of the many reasons we have antibiotic resistance today.”

Stephen Schimpff, MD, MACP, an internist in Baltimore, Maryland, and former CEO of the University of Maryland Medical Center, says the primary reason for unexpected 30-day readmission return is communication between hospitalist and primary care physicians.

“In times past, the PCP admitted their patients to the hospital, took care of them in the hospital, and discharged them so that the PCP had a clear understanding of the patient’s needs,” he says. “Today, two things have changed. PCPs rarely see their patients in the hospital and frequently don’t even know the patient has been
admitted. The patient is cared for by a hospitalist and at discharge, although a written record is sent to the PCP that may not arrive until sometime much later, there is rarely any verbal communication between the two at the time of discharge.

Furthermore, the patient is not instructed to obtain an appointment with the PCP or cardiologist within 48 to 72 hours, so the medications often aren’t reviewed in the context of the patient’s other issues and adjustments. The result is the patient has an exacerbation, goes to the ER, and is readmitted with recurrent heart failure.

For example, at the Charles-town Retirement Community in Catonsville, Maryland, a facility with 2,000 individuals with an average age of 82, the readmission rate has been brought down from the national average of over 25% to just under 10%.

“When a patient is admitted to the hospital, the PCP is aware and receives notification when the patient returns to the community and an appointment is set within 48 hours,” Schimpff says. “If the patient is sent back to the rehab unit, the doctor visits within the same time frame. That simple attention to communication and seeing the patient immediately is the key.”

**Reimbursement trends**

In a recent study conducted by Beth Israel Deaconess Medical and Harvard Medical School, which looked at heart attack readmissions, the findings revealed that although reductions in readmissions have been attributed to improvements in discharge planning and care transitions, these declines may instead be due to hospitals and clinicians intensifying efforts to treat patients who return to a hospital within 30 days of discharge in emergency departments and as observation stays.

The study suggested that financial penalties imposed by HRRP may have inadvertently pushed some physicians to avoid readmitting patients who needed hospital care, or potentially diverted hospital resources and efforts away from other quality improvement initiatives.

Based on the results of Boyd’s study, the authors recommend that policy makers may want to consider if readmission penalties are sufficient, examine how patient care can be improved, and make sure that type of ownership does not impact care quality.

Chetan Khamare, MD, cardiologist at the Premier Heart and Vascular Center in Zephyrhills, Florida, says the center is seeing a 2.9% net increase in 2019, compared to 2018, for heart attack and CABG. However, there is a 3% penalty for excess readmissions for CHF, acute MI, and CABG.

**Managing risk factors**

To drive down 30-day readmissions, the Premier Heart and Vascular Center has increased education around the importance of diet, exercise, and medication compliance at discharge; provided a follow-up appointment in the office prior to discharge; provided a home health RN to visit the patient after discharge; and called patients after discharge to ensure they have answers to any questions about medications and symptoms.

“We also assign a nurse navigator to follow up with the patient,” Khamare says. “And we have implemented immediate physician specialty consultation in the emergency department to determine if readmission is necessary.”

This strategy has helped drive down readmissions by as much as 5% this year.

“We have been effective in decreasing readmissions rates; however, more work needs to be done,” he says. “This is a work in progress.”

Sinatra’s biggest personal successes with patients with all these heart issues came with pairing conventional treatments with a “metabolic cardiology” protocol: CoQ10, D-ribose, L-carnitine, and magnesium, as well as omega-3s (fish oils). This combination of nutrients was instrumental in helping to prevent arterial reclosure and plaque rupture in his patients.

In an August 2019 study published in the *Annals of Internal Medicine*, researchers looked at 41 studies with a total of 134,034 participants to evaluate the effectiveness of omega-3 supplements. What they found is that omega-3 supplement use was correlated with an 8% reduction in heart attack risk and a 7% reduction in coronary artery disease when compared with the non-supplement group.

Another study conducted at Carnegie Mellon University showed that optimism is an extremely important healer. In their conclusion, they found that “Optimism predicts a lower rate of rehospitalization after coronary artery bypass graft surgery [and] fostering positive expectations may promote better recovery.”

“An often hidden risk factor in hospital readmissions is emotions—which can put patients into fight-or-flight mode and precipitate a cardiac event,” Sinatra says. “A lot of my patients needed to be counseled. I would tell them they needed to let the situation go—it’s not worth dying for.”

**Nicholas Hamm** is an editor with Managed Healthcare Executive.

**Keith Loria** is an award-winning journalist who has been writing for major newspapers and magazines for close to 20 years.
Leadership Tips
HELP YOUR ORGANIZATION SUCCEED

INDUSTRY ANALYSIS

How Healthcare Teams Inspire the C-Suite

Leadership doesn’t always come from the top by STEPHANIE STEPHENS

It’s usually the other way around, but teams really can motivate positivity from downstairs to upstairs. Here’s how.

Teams’ commitment, compassion, and curiosity go far

“I’m fortunate to lead a team of professionals who are fully committed to making a difference in the lives of the people they serve—our members,” says Managed Healthcare Executive Editorial Advisor Ginny Calega, MD, vice president of medical affairs at Independence Blue Cross. “They bring compassion and empathy to their jobs every day, whether it’s working closely with chronically ill members to better coordinate their care, or partnering with doctors in our network to help them deliver superior, affordable care.”

Calega’s staff realizes they have a responsibility. “At Independence Blue Cross, we interact with people when they are sick or hurt, often during some of the most difficult times in their lives,” she says. Kindness and understanding, shared with curiosity and ingenuity from staff, prompts positive letters from members.

“They continually look for new and better ways to serve our members and improve our company,” Calega says. “No one ever seems satisfied with the status quo, but they are always willing to go the extra mile to help a member or a fellow colleague.”

They ‘walk’ the healthcare talk

“Every month, I end monthly staff meetings with a ‘Why I Love HPSJ (Health Plan of San Joaquin)’ segment,” says Amy Shin, chief executive officer of HPSJ, in California’s Central Valley. “I have so much to love about what our staff does to support our community.”

She’s proud of HPSJ Walks for Health, which her staff avidly supports. “A third of employees participated at 2018 weekend events, generating almost $15,000 in HPSJ contributions for 18 local community causes,” Shin says. She credits her crew for keeping her moving with her own healthy “stepping.”

“Most staff takes the daily SonicBoom e-Challenge, an HPSJ wellness program,” Shin says. “One recent month, they hit 9.5 million steps.”

Her team never fails to “move her” in other ways. “HPSJ staff is local, they reflect the diversity of the Central Valley and are passionate about serving their community,” she says. “They positively impact our members and neighbors to stay active, healthy, and connected to each other and our community.”

When they really want to help, it shows

Currently president of TPG International Health Academy, Managed Healthcare Executive Editorial Advisor David Schmidt of Schmidt and Associates was CEO of Scan Health Plan, an HMO in California, for more than eight years.

“At SCAN, everyone came to work with a mortgage and a car payment, but they also came because they wanted to help elderly people, often frail, to navigate a critical part of their lives,” says Schmidt.

The company hired a third-party company to ask everyone, from staff to senior management, whether they “believed in the mission of the company,” and nearly 95% said they did.

“Employees were instructed to hold their boss and senior management accountable to fulfilling the mission,” Schmidt says.

The culture embraced unanimity. “Every employee had to go through a Trading Ages workshop, which uses simulations and education to reenact the aging process,” he says. “It had real importance in employees’ work lives and maybe more importantly, in their real lives.”

Stephanie Stephens, MA, is a journalist, producer, and host in Orange County, California.
As part of a combination regimen, provide your members with the only FDA-approved treatment for refractory MAC lung disease

In the United States, MAC is responsible for causing approximately 80% of pulmonary NTM infections.

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.

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.

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.
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% [65/224] vs 8.9% [10/112]) (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.

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 when administered to a pregnant woman, should be advised of the potential hazard to the fetus.


Please see the Brief Summary on the following pages.
ARIKAYCE® (amikacin liposome inhalation suspension)

BRIEF SUMMARY: For complete safety, please consult the full Prescribing 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, exacerbation of underlying pulmonary disease that have led to hospitalizations in some cases [see Warnings and Precautions (5.1, 5.2, 5.3, 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 antibiotic 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 [see Clinical Studier (14)]. 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.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions: ARIKAYCE is for oral inhalation use only. Administer by nebulization only with the Lamira® Nebulizer System. Refer to the Instructions for Use for all full administration information on use of ARIKAYCE with the Lamira Nebulizer System. Before first administration, instruct patients using a bronchodilator (“reliever”) to first use the bronchodilator following the bronchodilator lefriend for use information before using ARIKAYCE.

Pre-treatment with short-acting selective beta-2 agonists should be considered for patients with known hyperreactive airway disease, chronic obstructive pulmonary disease, asthma, or bronchospasm [see Warnings and Precautions (5.4)].

2.2 Recommended Dosage: The recommended dosage of ARIKAYCE in adults is once daily inhalation of the contents of one 510 mg/8 mL ARIKAYCE vial (510 mg of amikacin) using the Lamira Nebulizer System.

Administer ARIKAYCE with the Lamira Nebulizer System only. ARIKAYCE should be at room temperature before use. Prior to opening, shake the ARIKAYCE vial well for at least 10 to 15 seconds until the contents appear uniform and well mixed. The ARIKAYCE vial is opened by flipping up the plastic top of the vial then pulling downward to loosen the metal ring. The metal ring and the rubber stopper should be removed carefully. The contents of the ARIKAYCE vial can then be poured into the medication reservoir of the nebulizer handpiece.

If a daily dose of ARIKAYCE is missed, administer the next dose the next day. Do NOT double the dose to make up for the missed dose.

4 CONTRAINDICATIONS

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

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Pneumonitis: Hypersensitivity pneumonitis has been reported with the use of ARIKAYCE in the clinical trials. Hypersensitivity pneumonitis (reported as allergic bronchitis, pneumonitis, interstitial pneumonitis, anaphylaxis, or angioedema) was reported in patients treated with ARIKAYCE plus a background regimen (3.1%) compared to patients treated with a background regimen alone (0.8%). Most patients with hypersensitivity pneumonitis discontinued treatment with ARIKAYCE and received treatment with corticosteroids. [see Adverse Reactions (6.1)]. If hypersensitivity pneumonitis occurs, discontinue ARIKAYCE and manage the patient as medically appropriate.

5.2 Hemoptysis: 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 a background regimen (17.9%) compared to patients treated with a background regimen alone (12.5%) [see Adverse Reactions (6.1)]. If hemoptysis occurs, manage the patients as medically appropriate.

5.3 Bronchospasm: Bronchospasm has been reported with the use of ARIKAYCE in the clinical trials. Bronchospasm (reported as asthma, bronchial hyperreactivity, bronchospasm, dyspnea, dyspnea neuralgia, prolonged expiration, throat tightness, wheezing) was reported at a higher frequency in patients treated with ARIKAYCE plus a background regimen (28.7%) compared to patients treated with a background regimen alone (20.7%) [see Adverse Reactions (6.1)]. If bronchospasm occurs during the use of ARIKAYCE treat the patients as medically appropriate.

5.4 Exacerbation of Underlying Pulmonary Disease: 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, exacerbation of chronic obstructive pulmonary disease, infective exacerbation of bronchectasis) has been reported at a higher frequency in patients treated with ARIKAYCE plus a background regimen (14.8%) compared to patients treated with background regimen alone (9.8%) [see Adverse Reactions (6.1)]. If exacerbations of underlying pulmonary disease occurs during the use of ARIKAYCE, treat the patients as medically appropriate.

5.5 Ototoxicity: 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 a 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 5.9% in the background regimen alone arm) and dizziness (6.3% in ARIKAYCE plus background regimen vs 2.7% in the background regimen alone arm) [see Adverse Reactions (6.1)].

Close monitor patients with known or suspected auditory or vestibular dysfunction during treatment with ARIKAYCE. If ototoxicity occurs, manage the patient as medically appropriate, including potentially discontinuing ARIKAYCE.

5.6 Nephrotoxicity: Nephrotoxicity was observed during the clinical trials of ARIKAYCE in patients with MAC lung disease but not at a higher frequency than the background regimen alone [see Adverse Reactions (6.1)]. Nephrotoxicity has been associated with the aminoglycosides. Close monitoring of patients with known or suspected renal dysfunction may be needed when prescribing ARIKAYCE.

5.7 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.

5.8 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 pediﬁc patients exposed in utero. Patients who use ARIKAYCE during pregnancy, or become pregnant while taking ARIKAYCE should be apprised of the potential hazard to the fetus [see Use in Speciﬁc Populations (8.1)].

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described in greater detail in other sections of labeling:

- Hypersensitivity Pneumonitis [see Bowed Warning and Warnings and Precautions (5.1)]
- Hemoptysis [see Bowed Warning and Warnings and Precautions (5.2)]
- Bronchospasm [see Bowed Warning and Warnings and Precautions (5.3)]
- Exacerbation of Underlying Pulmonary Diseases [see Bowed Warning and Warnings and Precautions (5.4)]
- Ototoxicity [see Warnings and Precautions (5.5)]
- Nephrotoxicity [see Warnings and Precautions (5.6)]
- Neuromuscular Blockade [see Warnings and Precautions (5.7)]

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

Within the refractory NTM clinical program, 388 patients that participated in three clinical trials were treated with ARIKAYCE at the dose of 510 mg/day (median duration of exposure to ARIKAYCE was 169 days).

Trial 1 (NCT0234404) was an open-label, randomized (2:1), multi-center Phase 3 trial in patients with refractory Mycobacterium avium complex (MAC) lung disease. Patients were randomized to either 8 months of ARIKAYCE plus a background regimen (n=223) or background regimen alone (n=112).

Trial 2 (NCT01628600) was a single-arm extension of Trial 1 for refractory MAC lung disease patients that failed to achieve negative sputum cultures after 6 months of treatment or had a relapse or recurrence by Month 6 from either study arm of Trial 1. A total of 133 patients (n=74 from the prior background regimen arm alone of Trial 1, and n=59 from the prior ARIKAYCE plus background regimen arm in Trial 1) participated in the trial.

Trial 3 (NCT0131536) was a double-blind, randomized, placebo-controlled Phase 2 study in patients with refractory nontuberculous mycobacterial (NTM) lung disease caused by MAC and Mycobacterium abscessus. Patients were randomized to either ARIKAYCE plus background regimen or an inhaled diluted empty-liposomes placebo plus background regimen for 84 days.

Across all clinical trials of patients with and without refractory NTM lung infection, 802 patients were exposed to multiple doses of ARIKAYCE.

Serious Adverse Reactions Leading to Treatment Discontinuation

In the three NTM studies, there was a higher incidence of premature discontinuation of ARIKAYCE. In Trial 1, 33.1% discontinued ARIKAYCE prematurely, most were due to adverse reactions (17.4%) and withdrawal by subject (9.4%). In the comparator arm 8% of subjects discontinued their background regimen, with 0.9% due to adverse reactions and 5.4% due to withdrawal by subject. In Trial 2 (the single-arm extension of Trial 1), 20.3% of patients starting on ARIKAYCE discontinued prematurely with 14.9% discontinuing due to adverse reactions. In Trial 3, all 9 (29.6%) premature discontinuations occurred in the ARIKAYCE plus background regimen-treated patients and there were no premature discontinuations in the placebo plus background regimen arm.

Common Adverse Reactions

The incidence of adverse reactions in Trial 1 are displayed in Table 1. Only those adverse reactions with a rate of at least 5% in the ARIKAYCE plus background regimen group and greater than the background regimen alone group, are shown.

(continued on next page)
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 mice (up to 400 mg/kg/day) during organogenesis was not associated with fetal malformations. Ototoxicity 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 defects, 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
No animal reproductive toxicology studies have been conducted with ARIKAYCE or non-liposomal amikacin administered by inhalation.

Amikacin was subcutaneously administered to pregnant rats (Gestation Days 8-14) and mice (Gestation Days 7-13) at doses of 25, 100, or 400 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 (neurosperiticy and mortality were observed), precluding the evaluation of offspring at this dose. Fetuses of some dams were not observed at the low dose of 25 mg/kg. Clinical development of the rats and mice exposed to these doses of amikacin in utero did not differ significantly from control.

Ototoxicity was not adequately evaluated in offspring in animal developmental toxicology 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, systemic absorption of ARIKAYCE following inhaled 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.

8.3 Pediatric Use: Safety and effectiveness of ARIKAYCE in pediatric patients below 18 years of age have not been established.

8.5 Geriatric Use: In the NTM clinical trials, the total number of patients receiving ARIKAYCE, 196 (50.0%) were 65 years and 55 (14.2%) were ≥75 years. No overall differences in safety and effectiveness were observed between elderly subjects and younger subjects. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function (see Warnings and Precautions (5.6)).

8.6 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 hepatically 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. Hemodialysis may be helpful in removing amikacin from the body. In all cases of suspected overdose, physicians should consult the Regional Poison Control Center for information about effective treatment. In the case of any overdose, the possibility of drug interactions with alterations in drug disposition should be considered.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 2-year inhalation carcinogenicity study, rats were exposed to ARIKAYCE for 15-25, 50-70, or 155-170 minutes per day for 96-104 weeks. These provided approximate inhaled doses of 5, 15, and 45 mg/kg/day. Squamous cell carcinoma was observed in the lungs of 2 of 120 rats administered the highest dose tested. Maximum serum AUC levels of amikacin in the rats at steady state were approximately 1.3, 3.2, and 7.6 mcg·h/mL at the low, mid, and high doses, respectively, compared with 23.5 mcg·h/mL (8.0 to 46.5 mcg·h/mL) measured in humans. The squamous cell carcinomas may be the result of a high lung burden of particles from ARIKAYCE in the rat lung. The relevance of the lung tumor findings with regards to humans receiving ARIKAYCE is unknown.

No evidence of mutagenicity or genotoxicity was observed in a battery of in vitro and in vivo genotoxicity studies with a liposome-encapsulated amikacin formulation similar to ARIKAYCE in vitro microbial mutagenesis test, in vitro mouse lymphoma mutation assay, in vitro chromosomal aberration study, and an in vivo micronucleus study in rats.

No fertility studies were conducted with ARIKAYCE. Intraperitoneal administration of amikacin to male and female rats at doses up to 200 mg/kg/day prior to mating through Day 7 of gestation was not associated with impairment of fertility or adverse effects on early embryonic development.

13.2 Animal Toxicology and/or Pharmacology: To provide information about chronic dosing of ARIKAYCE to another animal species, a 9-month inhalation toxicology study was conducted in dogs. Foamy 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 hyperplasia, or the presence of pneumoelastic or neoplastic changes. Dogs were exposed to ARIKAYCE for up to 80 minutes per day, providing inhaled amikacin doses of approximately 5.10, and 30 mg/kg/day.
There is growing evidence that social determinants of health (SDoH) have a negative effect on health outcomes. SDoH are “the conditions in which people are born, grow, live, work, and age,” according to the CDC, and they play an important role in a patient’s overall health status. This is considered by many to be the top disruptive trend impacting the managed care space today.

Lindsey Morris, director of data science and analytics for Nashville, Tennessee-based axialHealthcare, a pain management and opioid data firm, says managed care is well-positioned to tackle SDoH by implementing population health risk management strategies that address social factors contributing to excess spending, unnecessary use of healthcare services, and worsened patient outcomes.
“However, barriers to MCO visibility into SDoH in healthcare claims, like lack of provider reimbursement for inquiring about SDoH, non-standardized SDoH screening tools across organizations, and limited evidence that SDoH screening improves outcomes, will need to be addressed,” she says.

Fortunately, a recent CMS decision allows Medicare Advantage plans to allocate their SDoH expenses as a medical cost. This means plans will be better positioned to help members overcome foundational barriers to care.

The 2019 Medicare Advantage and Part D Call Letter released by CMS also indicates how the federal government has shifted the regulatory calculation of medical loss ratio (MLR) from administrative to medical costs. “This new rule will enable managed care plans to be innovative in how they work with their consumer populations,” says Jason Rose, CEO of AdhereHealth, a Franklin, Tennessee, healthcare technology company. “In the year ahead, Medicare Advantage plans will augment an array of current programs and community outreach services to better address the most basic needs of their at-risk populations.”

For example, medication adherence is a predominant problem for consumers, however it is often SDoH that cause these barriers to better care in the first place. If a consumers doesn’t have food in their refrigerators, it is more challenging to engage them on the importance of medications for better health. If consumers don’t have access or funding for transportation to their doctors or pharmacies, how can they get the care needed?

“Medication adherence issues cause $300 billion dollars of annual unnecessary medical expense, about 10% of the nation’s healthcare spend,” says Rose. “With the SDoH rule change, health plans can improve their medication adherence strategies to capture value-based care reimbursement for Medicare Advantage Star Ratings and Medicaid Pay for Performance (P4P).”

Trey Sutten, CEO of Cardinal Innovations Healthcare, Charlotte, North Carolina, notes people’s living situations have a tremendous influence on their overall health and well-being, but it’s not something they typically or historically have connected with healthcare.

“Social determinants of health are taking a while to catch on with managed care leaders because supporting them is challenging due to cost and regulatory barriers,” he says. “However, that is changing because SDoH have such a significant impact on health outcomes, which makes social determinants a disruptive trend to watch.”

Cardinal Innovations Healthcare has leaned in on this trend, addressing housing in the community through its Transitions to Community Living Initiative.

“We’ve moved about 850 members from adult care facilities into independent housing and are piloting additional program elements based on the success we’ve seen,” Sutten says. “Members love this whole-person approach, and the numbers prove its positive impact: we’ve seen a 42% reduction in crisis service events, and a 71% reduction in crisis services costs.”

He believes adopting this type of approach industry-wide will impact how we structure managed care programs to lead with ways to support and address social determinants for members.

Here are nine other disruptive trends to keep an eye on:

**NEED FOR COST CONTROL**

DeWayne Wilson, chief financial officer for Arlington, Texas-based Texas Health Aetna, notes the continuing need for cost-control measures.

“These measures will require providers and payers to further explore and launch new collaboration models to address price transparency, as well as rate settings tied to outcomes and improvements distributed across all stakeholders,” he says. “This will include a significant focus on increased utilization of specialized networks, such as regional centers of excellence that have proven value for outcomes or spend, and greater integration of virtual primary care and telemedicine into health benefit design.”

Such digital platforms will continue to bridge the gap in current information exchange, patient navigation and price transparency. Consumerism as a guiding principle, he adds, will continue to influence where and from whom healthcare is purchased.

**PREDICTIVE ANALYTICS**

Morris says MCOs strive to find efficiencies—reducing spend by better managing utilization use of health services—and predictive analytics can help meet these goals by identifying high-risk patients and enabling provider intervention prior to high-cost, high-risk events.

Applying AI, or more specifically machine learning and predictive analytics, to population
health management has enormous potential to change the game for managed care organizations,” she says.

An example is the opioid epidemic. Although this crisis affects the entire nation, studies have shown it has an immense impact on the Medicaid population, driving up healthcare costs that the state has to shoulder.

“Through an assessment of claims data from one Medicaid population, we measured the difference in per member per month (PMPM) spend between two types of patients: those identified as in need of screening for opioid use disorder (OUD) and those diagnosed and placed in quality outpatient treatment,” Morris says.

The results were significant: $2,225 PMPM for patients recommended for OUD screening versus $500 PMPM for patients receiving treatment—an over $1,800 difference in PMPM spend.

MERGERS
Andrew Demetriou, managing director of Emeryville, California-based global consulting firm Berkeley Research Group, LLC, says the most disruptive factor that he sees for managed care is the restructuring of the managed care industry through mergers and integration with intermediaries and provider entities.

“As managed care companies extend into areas such a retail pharmacies (Aetna/CVS) and acquire physician provider networks, they are seeking a more comprehensive healthcare solution to employers and the public,” he says.

“However, the merger activity will trigger enhanced government scrutiny, with the FTC and Justice Department becoming more active in pre-merger review and litigation to block certain deals or to extract concessions in terms of mandatory divestiture or restrictions on expansion of acquired businesses.”

That was seen in the recent agreement concerning the merger of Optum and DaVita Medical Group. Because some of these transactions constitute horizontal expansion into new markets and changes in relationships among entities that have not historically been competitors, Demetriou notes traditional antitrust doctrines may not strictly apply, and yet federal and state antitrust regulators may feel political and public pressure to oppose transactions nonetheless.

DRUG PRICING TRANSPARENCY
Flaviu Simihaian, CEO of Troy Medicare, a Charlotte, North Carolina-based Medicare Advantage plan, notes there is already a proposal from the HHS to ban drug rebates from protection under the Anti-Kickback Safe Harbor rule as early as January 2020.

“What this means is that there will be more drug pricing transparency and less room for profiting by middlemen and PBMs,” he says. “On the other hand, current rebate savings may be passed to consumers in the form of higher drug prices, or managed care organizations will have to increase premiums to account for the difference. This has caused so much panic among managed care organizations and their PBM that after numerous complaints, CMS came out and assured payers that the government will pay 95% of any additional costs if the rule goes into effect.”

He also notes new high-cost therapies is something to keep an eye on. For instance, this summer, the FDA approved Novartis’ $2.1 million gene therapy for spinal muscular atrophy.

“As more and more new therapies are approved that cost several million dollars per treatment, the cost structure of managed care will change dramatically,” Simihaian says. “This will either trickle down to premiums and reinsurance, or it may create carve-outs as we have today with ESRD.”

MEDICATION ADHERENCE
AdhereHealth’s Rose says medication adherence will become a focal point for improving health outcomes in the years ahead.

“Whether it be Amazon’s acquisition of PillPack for multi-dose sorting packaging direct to consumer or outcomes-based contracting (OBC) for big pharma to take risks with health plans directly, medication adherence will be elevated as one of the top priorities for managed care organizations,” he says.

GOVERNMENT INTERVENTION
This is specifically for medication-assisted treatment (MAT) availability. Signed into law in October 2018, the SUPPORT (Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities) Act mandates state Medicaid programs to cover all three FDA-approved MAT drugs (buprenorphine, naltrexone, methadone), as well as behavioral therapy services from October 2020 to September 2025.

Elizabeth Ann Stringer, chief science officer for axialHealthcare, says managed care organi-
Organizations are making progress in expanding coverage, but many barriers still exist, including a lack of providers offering MAT, shortage of behavioral health coaches, an influx of cash-only clinics due to cumbersome reimbursement processes and low reimbursement rates, and even a lack of provider awareness and buy-in on MAT’s potential.

“To meet this mandate, MCOs will need to collaborate with organizations to develop innovative strategies that build quality MAT networks, advance universal clinical guidelines for MAT, and leverage technology to increase access in rural areas,” she says.

SHIFTING PROVIDERS

Another disrupter Texas Health Aetna’s Wilson sees is an increase in shifting hospital-based services to other types of providers. For example, online retailers like CVS are playing a bigger role to leverage community-based resources, access points and data (pharma, purchasing, etc.) to deliver more complex care, as well as provide ancillary services and products directly to consumers at lower costs.

“Also look for increased participation in virtual groups and practice support services,” he says. “Such services will enable independent practices to adopt and thrive in this dynamic and competitive healthcare market.”

PAYMENT INNOVATION

Paul Thompson, general manager for DXC Technology’s commercial healthcare payer segment, in Tyson, Virginia, says this is a topic that is impactful for any payer, be it government or commercial payer.

“Payment innovation is an encompassing trend already in the marketplace and is continuing to accelerate,” he says. “What you are going to see is payers and providers working much more collaboratively and that’s going to drive the need to share information, almost on a real-time basis.”

The most important part, he says, is to identify the business model that’s going to support it.

DATA-DRIVEN ENGAGEMENT

Donna Martin, senior vice president of global healthcare at Hinduja Global Solutions, a Lisle, Illinois-based company, which handles process management for healthcare companies, believes one of the most disruptive healthcare trends right now is the idea of moving toward more proactive, data-driven engagement with individuals.

“For years, we’ve seen reactive, symptomatic support, but today’s shift to proactive, insightful managed care support is driving more effective outcomes, success with at-home management and sustainable results,” she says. “We are beginning to recognize, because we now have the data to review with some insight, that SDoH is the disruptor to help both providers and payers move away from cost-determinations of care to a realistic, manageable environment where the patient’s wellness needs are more clearly understood.”

Soon, healthcare companies will have the ability to intervene, diagnose, treat disease, and prevent the more serious outcomes that have been the result of patient and provider negligence, as well as the artificial barriers set up by all parties to prevent abuse of the care system.

“This is something to watch because this is a big shift from how we’ve supported individuals requiring managed care in the past—and it requires top-down support for organizations to make these philosophical, technological, and operational changes,” Martin says.

Historically, the managed care system has been all about managed cost, in an attempt to control unnecessary outlays based on bad decisions by both patients and providers. But having the real and clean data that describes the patient’s home environment—their own genetics, their personal behavior (eating habits, substance abuse, and so on), their social situation (support groups, discrimination, gender bias), their physical environment (housing conditions, location), and availability of health services—allows the caregiver to build a realistic plan that accommodates each of these issues.

“Through the use of analytics and AI and by providing better individualized support, we can gain a better understanding of the motivation behind individual behavior,” Martin says. “Many individuals suffering from chronic conditions require data-driven coaching, knowledge, and community support resources in order to maintain an optimized lifestyle. This proactively engaged support, provided by professional support organizations working as a multi-faceted concierge extension of the managed care organizations, drives proven success in outcomes.”

Keith Loria is an award-winning journalist who has been writing for major newspapers and magazines for close to 20 years.
6 Most Valuable Skills Executives Want in Potential Hires

From technology skills to emotional intelligence, what you should be looking for in a candidate

by TRACEY WALKER

The market for pharma/life sciences talent is very tight and demand is projected to continue as hiring activity remains robust. In June 2019, the unemployment rate for science talent in the U.S. was 1.4% and the unemployment rate for healthcare talent was 1.5%, less than half of the overall U.S. unemployment rate of 3.7%, according to the U.S. Bureau of Labor Statistics.

“Tight job markets demand that organizations become more agile and nimble with talent,” says Allison Kerska, vice president, Life Sciences Integrated Operations, KellyOCG, a leading advisor of talent supply chain strategies and workforce solutions. “On top of that, individuals today continue to embrace a variety of different work styles geared to enhance flexibility and maximize their career potential.”

Over the past five years, employment in the U.S. pharma/life sciences industry grew by 11% and employment in the healthcare industry grew by 10%, faster than overall U.S. job growth of 9%, according to Emsi: Labor Market Analytics. Over the next five years, employment in the U.S. pharma/life sciences industry is projected to grow by 9% and employment in the healthcare industry is projected to grow by 11%, faster than projected overall U.S. job growth of 6%. Employment in the biotechnology space is projected to grow by 24% over the next five years.

To help meet the challenge of a changing workforce, we asked experts to share their opinions on the skills you should look for in a potential employee. Here’s what they said.

Emotional Intelligence (EQ)

“Look for someone who can recognize and understand the impact of their emotions and the emotions of those around them. Someone with a high EQ is able to think through a conflict before reacting and has the empathy and communication skills to elevate teams and make meaningful connections throughout the organization.” —Tyler Black, president of Global Medical Staffing, an international healthcare staffing company based in Salt Lake City
Soft skills
“While scientific and technical skills are critical, life sciences employers report that soft skills are also becoming increasingly important for successful candidates. With the rise of AI/automation, demand for skills that are essentially ‘human’ will continue to increase. Top/fast-growing in-demand soft skills for life sciences talent include decision making, teamwork, creativity, change management and negotiation skills.” —Sam Smith, vice president, Global Practice Lead, Life Sciences & Healthcare, KellyOCG

A team player
“Anyone can elevate themselves. The best hires are those who want to make everyone else around them better, whether or not they receive recognition for it. A team player gets along with their coworkers and wants the entire team to succeed. They help create a work environment that is collaborative, inclusive and focused on achieving team goals.” —Lynne Gross, president of RNnetwork, a travel nurse staffing company based in Boca Raton, Florida

Technology skills
“Skilled talent shortages persist throughout the life sciences sector, but advances in new technologies are expected to drive even greater demand for people who can leverage digital innovations in the industry. Life sciences companies are competing against numerous other companies for scarce tech talent, making attraction and retention strategies critical.

“Data science, machine learning, Python programming and Tableau are all some of the most in-demand skills.” —Kerska

Positive, can-do attitude
“There are people who look at the world and only see limitations, and then there are people who see the world as full of possibilities. Someone with the latter outlook is approachable, accepts feedback and helps bring up the morale of the team. They want to work through and overcome challenges rather than shy away from them. They’re not afraid of failure because they know it’s just another learning opportunity.” —Leslie Snavely, chief digital officer of CHG Healthcare, a healthcare staffing company based in Salt Lake City

Skills in emerging scientific fields
“With changing global population demographics, the profile of diseases continues to evolve, generating strong demand for innovation in the pharma/life sciences sector. Many life sciences companies’ R&D efforts are focused on attacking diseases at the molecular and sub-molecular level. Critical fields for R&D include molecular biology and genetics/genomics, biopharmaceuticals and biomechanics/biomedical engineering, including regenerative medicine and the Internet of Medical Things (IoMT). Pharma/life sciences employers are increasingly looking for candidates with skills in these emerging scientific fields. Cell biology, molecular biology, and immunology are always at the top of the list of in-demand skills.” —Smith
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Eight Ways to Reduce Healthcare Administrative Costs

BY KAREN APPOLD

As the healthcare industry grapples with tumultuous times, organizations are eager for strategies and solutions that will stabilize their business, reduce administrative costs, and guide their shift toward a new standard of care for patients as the industry transitions to a focus on population health.

“When healthcare organizations can achieve clinical and financial success, they are better able to influence and care for the communities they serve,” says Rhonda Medows, MD, CEO, Ayin Health Solutions, and president, population health management, Providence St. Joseph Health, Portland, Oregon. “The current state of the healthcare industry has a need for modernization, revenue diversification, and cost-efficient, total healthcare.” The healthcare industry currently spends 12 cents of every dollar on administrative costs—costs that could be better spent on patient care.

Here are eight ways that health insurers and hospitals can put the squeeze on administrative costs.

SIMPLIFY PROVIDER ENGAGEMENT

Given the complexity of the healthcare ecosystem and the unique needs of payers and providers in managing their businesses, payer and provider interactions can be confusing and frustrating—as well as result in unnecessary administrative costs. “For payers, simplifying how they engage with providers can reduce administrative costs and improve the provider relationship,” says Angie
Meoli, senior vice president of network strategy and provider experience at Aetna, a CVS Health company in Blue Bell, Pennsylvania.

For example, setting up a provider in a payer’s information system to process transactions and exchange data can take a significant amount of time and require many touchpoints between the provider and payer. This is often because they each use different systems without a standard format in terms of how data is shared. “Data integrity is critical for accurate implementation and execution of payment terms,” Meoli says.

“That’s why payers need to have processes and technology that can efficiently support their relationship with providers from start-up through later steps in the journey,” Meoli says. “Using dedicated service teams, streamlining escalation processes, and integrating tools are some of the ways payers can create a simple, transparent, and welcoming start-up experience.” Enhancing processes and tools for data management can also improve data accuracy, reduce rework, and ease administration costs.

RE-EVALUATE MAJOR EXPENSES

Push vendors and shippers for not only better prices, but also better service levels that will help reduce inventory. For instance, Keith Daniels, a partner at Carl Marks Advisors, an investment bank providing financial operational advisory services to middle-market companies, says he’s recently seen many companies renegotiate to achieve just-in-time-deliveries as well as return privileges in agreements that historically had neither. Part of this requires taking a vendor inventory to see if you can consolidate to achieve fewer—but stronger relationships.

Hospitals looking to reduce administrative costs should also look at payroll. “The strongest companies have successfully implemented strategies that reduce both overtime and turnover,” Daniels says. “In lieu of that, we’ve also seen some healthcare companies increase outsource labor strategies.”

Wendy Karsten, president of Care N’ Care Health Plan in Fort Worth, Texas, is also a proponent of outsourcing. “Forcing managers to periodically shop for a vendor to whom they can outsource some of a department’s tasks—or an entire department itself—is a valuable exercise,” she says. “It keeps innovation at its maximum, helps to keep internal costs from running out of control, and keeps every manager in the know of what else is available.”

DETERMINE IF HISTORICAL PROCESSES ARE OBSOLETE

“Take a fresh look at processes that may have become outdated and no longer serve a purpose, but are still being done simply out of habit,” Karsten says. “This often occurs whenever a vendor or system is changed—making it an ideal time to relook at all processes associated with that change. “We’ve found that some of the manual processes we’ve used for years to monitor vendors can be done more efficiently, cost effectively, and reliably through automation that has become an accepted part of vendor or client interaction. But far too often, staffs keep doing things the old way because that’s the way they’ve always been done.”

ADOPT COMMON TECHNOLOGY PLATFORMS

Payers and hospitals can work together to reduce costs by having common technology platforms. Otherwise, it’s difficult to effectively manage data between them. “Innovative technology plays an important role in reducing costs by ensuring that data is shared efficiently and effectively,” Meoli says. Blockchain, for example, can play a role by improving transparency and interoperability.

Some states have tried to address this challenge by using data exchange databases. However, they have limitations. For example, some state databases aren’t state wide or are limited to high-volume facilities.

Aetna is a founding member of two healthcare blockchain alliances, which focus on data quality for provider directories and reducing friction, cost, and integration complexity between the various parties within the healthcare ecosystem, Meoli says.

MEASURE PERFORMANCE AND IMPROVE QUALITY OUTCOMES

Providers can earn more from value-based arrangements and offset the administrative burden with technology-driven capabilities. For example, Aetna makes a population health and point-of-care platform that shows a complete view of a patient’s health available to

— ANGIE MEOLI, AETNA, A CVS HEALTH COMPANY
providers. This enables providers to be proactive and focus on patients who need care the most, such as those experiencing chronic conditions, quality gaps in care (such as the need for colorectal or breast cancer screenings), or ensuring a smooth transition when a patient moves from one care provider to another.

IMPLEMENT PREDICTIVE MODELING FOR PATIENT BILLING AND COLLECTIONS

Traditional consumer data points such as a credit score aren’t good predictors of patients’ true propensity to pay. “Without a better way to target their efforts, hospitals waste resources reaching out to patients who will never pay no matter what,” says David Grauer, MBA, MHSA, senior vice president at Health Catalyst.

Grauer’s company helped Minneapolis-based Allina Health, a not-for-profit health system, use predictive modeling of patients’ propensity to pay to help reduce administrative waste while also delivering stronger collections results. Allina stopped devoting any resources to contacting patients with a predictive high or low propensity to pay. Instead, they focused efforts on patients with medium-low to medium-high propensity to pay, and created workflows with targeted, automatically scheduled outreach actions to help further reduce waste in the collections process.

In the first year of implementation, Allina achieved a $2 million increase in overall collections, including more than $660,000 in additional patient payments collected by phone in the first two months. The propensity to pay machine learning model also improved Allina’s ability to engage with patients willing, able, and interested in paying their bill, which led to a 21% relative increase in the number of inbound calls from patients seeking to make a payment during the same first-year time period.

USE BUNDLED PAYMENTS

Under this model, multiple providers—a doctor and hospital—are paid a single payment for coordinating the total amount of services required for a pre-defined episode of care. In this system, the providers would be paid to manage a patient’s care, but they wouldn’t have to send the insurer a claim for each service rendered since they would have already been paid. They would only have to report the encounters. “Such a system would require developments in technology that aren’t available yet, and would require doctors and hospitals to have a business relationship that allowed for such coordination,” says John Baackes, CEO of L.A. Care Health Plan in Los Angeles, California.

“Of course, an insurer wouldn’t want to pay inaccurate claims, but if they were able to pre-pay hospitals for services based on knowing that an insured person will always use that institution, that could save both payers and providers a lot of administrative expenses,” Baackes says.

IMPROVE DATA SHARING

Health insurers and hospitals both have valuable data, and improved sharing of that data can help both entities reduce administrative costs. ‘This is one reason why many health plans and hospitals are pursuing an integration strategy, while others are exploring new partnership models focused on targeted cost-reduction efforts that benefit all sides, Grauer says.

As an example, one of Grauer’s insurer clients leveraged its data to help a large provider organization identify previously hidden high-risk chronic disease patients. “This enabled the health system to make targeted changes in its care management program that ultimately resulted in more efficient, lower cost care—a win-win for both organizations and a win-win-win when you consider the patients who benefited from getting (and staying) on the right care pathway,” Grauer says.

FINAL THOUGHTS

Administrative pressures can amplify quickly, and too often administrators wait to look for options until they’re in deep distress. “That’s not a good tactic,” Daniels says. “We’re living in a time of rapid, escalating change, and while we cannot be certain of the future, we know that financial pressures will continue to increase for the foreseeable future. This means that every healthcare organization should look at their options now.”

Karen Appold is a medical writer in Lehigh Valley, Pennsylvania.
Lower Patient Costs Don’t Have to Mean Lower Profits

How oncology practices can help reduce spending on cancer drugs—without compromising on patient care

by ANDREW SCHNEIDER, MD

As oncologists, we want to do what’s best for each patient—the most effective treatments with the fewest possible side effects. But treatment options with nearly identical clinical outcomes may have dramatically different costs.

Take, for instance, two medications that prevent bone fractures in patients with breast cancer, each with similar effectiveness and side effects: One costs Medicare about $2,300 a year, while the other costs about $550 a year.

In other cases, it’s an issue of providing treatment over more appropriate timeframes: Many patients receive medications to regrow their white blood cells and prevent infections. Often, the best choice is a short-acting growth factor that lasts a few days and costs $100 to $200. But physicians frequently still order a longer-acting, brand name drug that costs $3,000—providing treatment that goes beyond what patients need.

One reason oncologists don’t select less-expensive options is simply that it’s hard to keep up when innovation changes the value calculation. But in all honesty, oncologists focused on helping their patients live as well as and as long as they can aren’t always scrutinizing costs.

The challenge goes beyond education: Standard oncology practice business models don’t reward physicians for prioritizing value. For some practices, drug markups can account for a third of revenues, and choosing less-expensive medication may cause profitability to slip.

Look at treatment options for a type of breast cancer: If you’re not paying attention to value, you might select an evidence-based treatment regimen that costs more than $50,000. Of that, the practice’s drug margin would be about $3,000. But what happens when you select a value-based regimen—equally effective, similar side effects, but much less expensive? The overall costs would be under $10,000, but your practice’s drug margin would be about $600. In short, prioritizing value hurts your profits. Will you save the payer and patient $40,000 or get $2,400 less for your practice? Many doctors aren’t aware of these costs, but that’s the impact of those choices.

My practice faced this issue as an early adopter of value-based pathways. It didn’t take long to see that our profits would suffer. To overcome these barriers, we took part in alternative payment model (APM) that rewarded us for pursuing value. Instead of relying on the drug margin for revenue, we received a set rate per patient case. Now, when we select the less expensive of two equally effective regimens, it doesn’t impact our revenues. Our practice also gets a share of the plan’s drug savings. We protect our revenue, the plan saves money, and patients still receive top-of-the-line treatment.

This combination of value-informed care pathways and capitated payments reduced our average cancer treatment cost by nearly 15% per member, and our practice received about $200,000 in shared savings the first year.

Nearly half of oncologists surveyed in a recent report don’t use cancer treatment pathways. But as the pace of treatment innovation threatens the financial health of patients and oncology practices, it’s up to oncologists and their practices to take more responsibility for redefining their reimbursement models to care for patients’ financial outcomes, not just physical ones.

Andrew Schneider, MD, is an oncologist with South Florida Oncology and Hematology Consultants.
According to the Hepatitis B Foundation, hepatitis B is the most common serious liver infection in the world—with 80,000 Americans becoming newly infected with hepatitis B each year, and more than 2 million Americans are already chronically infected.

While many people infected with hepatitis B virus (HBV) may clear the virus in the acute phase (the first six months), some people are unable to clear the virus and it progresses to chronic hepatitis B.

“Treatment with one of the seven FDA-approved antivirals, intended to reduce liver damage and extend patient survival, may require lifelong medication therapy. Current antiviral therapy may be near $1,000 per month, therefore prevention strategies provide an effective way to significantly reduce spending,” says H. Kelley Riley, MD, chief medical officer, EnvisionRxOptions, a pharmacy benefits and services company in Twinsburg, Ohio.

“Since hepatitis B can be both acute and chronic, it has a significant impact on both pharmacy and medical spend,” says Managed Healthcare Executive Editorial Advisor David Calabrese, chief pharmacy officer at OptumRx. “Commonly used oral antiviral therapies often must be taken indefinitely in order to maintain suppression of the hepatitis B virus; and long-term complications associated with hepatitis B, including liver disease and impairment, the need for liver transplantation, and hepatocellular carcinoma, drive up healthcare costs.”

Cost and cures
Cost and cures are at the forefront of needs for new hepatitis B treatments.

“The ultimate goal is to identify drugs or a combination of drugs that will substantially increase the functional cure rate for the infection and potentially reduce the duration of time needed for therapy,” says Calabrese. “Several novel therapies in the pipeline for the treatment of hepatitis B show promise in early-stage data.”

- JNJ-3989 (formerly ARO-HBV, Arrowhead Pharmaceuticals/Janssen) is a third-generation subcutaneously administered RNA interference therapy in phase 1/2 studies as a curative treatment for patients with chronic HBV.
- Inarigivir soproxil (Spring Bank Pharmaceuticals) is an oral treatment designed to selectively act within cells infected with HBV to inhibit viral replication and induce the cell’s antiviral defense. Inarigivir is also in phase 2 studies for treatment of HBV, as a combination therapy with Vemlidy (tenofovir alafenamide, Gilead) compared to Vemlidy monotherapy.
- Myrcludex B (bulevirtide, MYR Pharmaceuticals) is a first-in-class subcutaneously administered treatment in phase 2b studies for chronic HBV and hepatitis D virus (HDV) coinfection. HDV only occurs in people coinfected with HBV, and current therapy options are limited.

“In keeping with the trend of specialty medications, pharmaceutical manufacturers will likely set high prices for these drugs; and for payers, it becomes even more complex when multiple drugs from different brand manufacturers are used in combination to increase the likelihood of a functional cure of hepatitis B,” says Calabrese.

“Payers should be cognizant of preventive guidance; there may be increased encouragement to screen for HBV and administer preventive vaccination to a broader scope of individuals,” says Riley. “Treatments for those with chronic hepatitis B are still long-term and costly; and future pipeline treatments may be curative, which as seen in hepatitis C, could come with a high cost for a short amount of time. The future will most likely be a continued push for screening and prevention. Due to the global need to treat chronic hepatitis B, manufacturers are likely to continue research and conduct development to pursue a cure for hepatitis B.”

Erin Johanek, PharmD, RPh is a staff pharmacist at Southwest General Health Center, Middleburg Heights, Ohio.
Value-Based Arrangement Will Change the Way Cancer Care is Paid For

A look at a risk-based oncology arrangement in Minnesota

by Tracey Walker

Blue Cross and Blue Shield of Minnesota will be jointly accountable with Minnesota Oncology, a practice in The US Oncology Network, for the overall cost of cancer care provided to Blue Cross members through a value-based risk arrangement.

The five-year collaboration, which began September 1, 2019, will include an agreed-upon set of quality metrics based on the latest scientific research and proven clinical guidelines. Minnesota Oncology will be responsible for ensuring continued alignment with evidence-based best practices and, as a result, will no longer be required to secure prior authorization from Blue Cross for coverage of selected services that are typically associated with high rates of overutilization.

The terms of the arrangement are based on the principle that effective outcomes for patients are determined by the quality of care provided—not the quantity. The agreement is competitive and proprietary; therefore, the specific terms of the agreement are confidential.

“The top issue across the industry is the sustainability of healthcare,” says Karen Amezcua, senior director of contracting, Blue Cross and Blue Shield of Minnesota. “We know that if healthcare is not affordable, access becomes limited, which leads to long-term impacts to population health. For more than a decade, value-based care has been seen as a potential solution to the unsustainable rise in healthcare costs.”

Comprehensive care

According to Amezcua, making the shift to paying for quality instead of quantity is important in all types of care, but it’s especially useful for complex conditions like cancer. “It allows providers to focus on the patients’ holistic needs and not be limited to services covered by the traditional fee-for-service payment model,” she says. “Paying for value in oncology is especially important, as it supports a comprehensive care model that provides individualized care coordination for patients with complex care needs. It also ensures that the best possible outcomes are occurring through medically necessary care at the right time and place.”

This program adds value by using value-based payment to move resources in a manner that improves the patient’s experience while maintaining physician independence. In the long run, this will be rewarding to healthcare executives and the community, according to John Schwerkoske, MD, president and medical oncologist at Minnesota Oncology.

“The program structure reinforces the delivery of high-value care close to home in a community-based setting,” Schwerkoske says. Amezcua expects to see high-quality cancer care provided with an improved patient experience at a lower overall cost—as a result of fewer hospital admissions and ER visits.

With an enhanced focus on patient-centric healthcare, clinical staff at Minnesota Oncology will offer care coordination services on an individualized basis for Blue Cross members. Minnesota Oncology has a comprehensive care model: In addition to providers and nurses, social workers, dietitians, genetic counselors, and experienced oncology pharmacists who educate and monitor patients on IV and oral chemotherapy, the model also includes important patient care factors like remote symptoms monitoring, advance care planning, palliative care, sexual health, and survivorship, according to Schwerkoske.
Some stress is a healthy, normal part of life, especially if you are a CEO at a healthcare organization. 

“However, chronic stress is linked to a myriad of diseases and negatively affects every system of the body,” says Stevyn Guinnip MSEd, corporate kinesiologist, Furniture For Life, a Boulder, Colorado-based maker and distributor of health and wellness furnishings.

Alexis Guy Brandon, MMS, PA-C, senior staff physician assistant for Grand Rounds, a company that provides medical expertise and personalized navigation, agrees. “The work that healthcare executives do every day is so important to the communities they serve,” Brandon says. “But to do it effectively, it is important that you are also prioritizing self-care.”

Here are 12 stress-busters that can help you relax and unwind.

**GET PLENTY OF SLEEP**

“Everyone knows the body and brain require a minimum of seven hours of sleep each night, but most people struggle to prioritize it as such,” says Heidi Hanna, PhD, chief energy officer at Synergy Brain Fitness, a training company based in San Diego, and director of education at the American Institute of Stress. 

“Build in three to five minutes every hour to rest your mind by focusing on breathing, moving, or playing,” Hanna says. Before bed use relaxation techniques like meditation or a warm bath, she adds.

**TAKE A VIRTUAL VACATION**

“While taking a vacation is the ultimate stress reducer, planning one can also be a great stress-buster,” says Lindsay Resnick, executive vice president of Wunderman Thompson Health. “The distraction from day-to-day pressures combined with the mental ‘vacation’ you get from exploring options—where to stay, what to see, what to do, etc. can be cathartic.”

**GET A MASSAGE**

According to the Mayo Clinic, massage can be an effective treatment for reducing stress, pain, and muscle tension. “Considering how many executives sit at their desks for long hours, suffering from neck and back pain, a massage may be just what they need to feel better, think clearer, and be more productive,” says Guinnip.

**MAKE EXERCISE AND HEALTHY EATING A PRIORITY**

“Studies show that a minimum of 30 minutes each day is required to lift low-energy states like fatigue and depression,” Hanna says, “and a minimum of 45 minutes is needed to lower overactive states like ADD and anxiety.”

It’s also important to demonstrate to your colleagues that they too should make it a priority, says Brandon. “This can come in the form of converting some meetings into ‘walking meetings,’ bringing yoga to the office, having a ‘meditation break,’ or creating team-bonding opportunities via making healthy lunch fun with a ‘salad party’ or participating in an afternoon plank challenge,” she says.

**CONNECT WITH OTHERS**

According to Hanna, studies show that feeling isolated is worse for your health than smoking cigarettes—“which is not a pro-smoking pitch by any means,” she says. “Being part of a tribe strengthens our ability to cope with demands on our energy, especially when times are tough. Social support is life support, and no matter how busy we may be,
it’s important to invest in meaningful relationships. Just keep in mind that when it comes to connection, quality is more important than quantity, so don’t spread yourself too thin trying to keep up with all of your social media networks.”

CONNECT MIND & BODY
“When it comes to stress, the most important thing to understand is that our body and mind are connected,” says Kristin M. Jordal, vice president, health engagement, Cigna. “With all of life’s responsibilities, we often neglect our personal health. I make a point of putting my health and well-being at the forefront by:

- Exercising at least 15 minutes a day and striving to eat healthy food.
- Practicing mindfulness using the Happify app that Cigna provides to employees.
- Dedicating time to focus on financial health so that I can have peace of mind.
- Creating a workspace that allows me to stay focused and productive.
- Making the time to build and maintain strong relationships with my colleagues, family and friends.”

LAUGH A LITTLE
It turns out that laughter really is the best medicine. Research shows that finding something funny, whether you laugh out loud or not, helps to reduce stress hormones and inflammation in the brain and body, while improving immune function, memory, and more. “With all this evidence, it’s a great idea to plan some humor interventions throughout the day, like watching a funny YouTube video, creating a funny folder of images that make you laugh, and having a humor buddy who you share funny things with throughout the day,” Hanna says.

FIND A CONFIDANT
“We all experience stress and keeping it bottled up doesn’t help anyone,” says Leslie Snavely, chief digital officer, CHG Healthcare, a national healthcare staffing company in Salt Lake City. “Find someone you can talk to, whether that’s your leader, a peer, or a counselor.”

GIVE BACK
“Positive psychologists have shown that one of the most significant ways to boost happiness is to do something nice for someone else, or share words of appreciation or gratitude,” Hanna says. According to the Cleveland Clinic, the brain and body benefit from giving through a decrease in blood pressure, increased self-esteem, elevated mood, lower levels of stress, longevity, and happiness.

“Whn we feel overwhelmed by stress, one of the quickest ways to mobilize stress hormones to take action is to focus on ways to serve others,” she says.

PRACTICE WHAT YOU PREACH
We stress the importance of work/life balance to our teams, but we sometimes forget to follow our own advice, according to Tyler Black, president, Global Medical Staffing, an international physician staffing company in Salt Lake City. “Taking time for yourself is important part of maintaining a healthy lifestyle, so make it a priority to leave work on time, use your vacation time, avoid emailing after work hours, and make time to have some fun at work. Plus, by embracing work/life balance yourself, you’re also showing your team that it’s important they do the same.”

DEVELOP YOUR SPIRITUAL MUSCLE
“By far, the greatest stress reduction advice I can offer is to develop your spiritual muscle by spending time thinking about your meaning and purpose in life,” Hanna says. “Initially the questions around faith and trust can be stressful because there is so much debate and discourse around religion these days, but studies are quite clear that those who believe in something greater than themselves have a much more resilient brain. And this doesn’t mean you need to believe in anything in particular but having belief and trusting the process is the best way to let go of the stress and tension that results from realizing we are not in control.”

JUST BREATHE
Research shows that breathing at a rate of about 5.5 to 6 breaths per minute (inhale to a count of 5 and exhale to a count of 5) at an even 1:1 ratio is ideal for building resilience based on correlation with heart rate variability.

“Some practitioners recommend a slightly extended exhalation to encourage an even greater sense of calm due to the role of the exhalation phase encouraging the parasympathetic, or relaxation, response,” Hanna says. “However, it’s important that you experiment with different techniques and variations until you find the breathing style that is ideal for you, and never force deep breathing as it can actually cause more stress.”
Authorized Generics

What you need to know  by MARI EDLIN

Authorized generics might just be the answer for drug manufacturers whose patents for their branded drugs have expired. Instead of risking the loss of market share when other drug companies enter the generics marketplace, brand name manufacturers could develop their own generics.

An authorized generic is exactly the same product as an approved branded drug, but is marketed without the brand name on the label. Usually sold at a lower price, it can be marketed by a branded drug company or by another company with the brand company’s permission.

"By making an authorized generic, a brand manufacturer gets a jump start on the competition as generics start to appear," says Karen Berger, PharmD, a staff pharmacist at Plymouth Park Pharmacy in Fair Lawn, New Jersey.

"Authorized generics, which are identical to the brand, should not be confused with a branded generic that has gone through the abbreviated new drug application (ANDA) process and is assigned a name other than its chemical name," she says.

Leaving nothing to chance

"While a separate NDA is not required for marketing an authorized generic, the FDA requires that the NDA holder notify the FDA if it markets an authorized generic. The NDA holder may market both an authorized generic and its brand name product..."
at the same time,” says Charlie Kohler, spokesperson for the FDA. That’s exactly what PDL BioPharma did this year to protect its expensive blood pressure medicine Tekturna (aliskiren tablets) under threat of a generic competitor and the end of its patent last year. It produced its own authorized generic of the drug that sells for less than its branded version but more than competing generics.

Those are just a few examples of the nearly 1,200 authorized generics tracked by the FDA.

Why authorized generics? One of the primary goals for pharmaceutical brand teams that undertake an approved generics strategy is to slow the pace of market share decline after market exclusivity loss, according to a 2015 study from Cutting Edge Information.

In essence, PDL is competing against itself and maximizing profits, suggests an article in KHN. According to the Pharmaceutical Research and Manufacturers of America (PhRMA), authorized generics increase competition through lower prices and cost savings.

Eli Lilly used a similar strategy, making authorized generics before its patents for Humalog (insulin lispro) expired. Eli Lilly recently made its authorized generic of insulin lispro injection available at half the cost.

Mylan did the same for its EpiPen, and anticipates that 85% of prescriptions will shift to its new authorized EpiPen generic.

2. Manufacturers can maintain market share of product through authorized generics.

“Prime takes a ‘lowest net cost’ approach to managing drugs with our clients, which in some cases means encouraging the use of originator brands over authorized generics when the net cost (with rebate) is lower than the authorized generic price,” he says.

“In doing so, the objective is to help ensure members aren’t penalized by higher out-of-pocket costs. For those members with coinsurance and high-deductible plans, we override benefits to help ensure the member isn’t penalized,” Lassen says.

Pfizer, which has the broadest portfolio of authorized generics in the United States, stated its position on authorized generics in an August 2018 report. The company believes that authorized generics “help advance public health and the broader healthcare system by increasing competition, improving access, and helping patients adhere to high quality, affordable medicines.”

Pfizer attributes increased adherence to more ease in switching from a branded product to an authorized generic that looks similar to the original drug: As reported in a 2018 issue of BMJ, in an FDA-sponsored study of 210,000 patients, switching from a brand to an authorized generic was associated with lower “switchback” rates compared to switching from a brand to a regular generic.

“By making an authorized generic, a brand manufacturer gets a jump start on the competition as generics start to appear.”

—KAREN BERGER, PHARMD, PLYMOUTH PARK PHARMACY

1. Recent market pressures around high drug costs have prompted them to provide cost relief, and

2. Manufacturers can maintain market share of product through authorized generics.
Increased competition

“For generic drug companies, there is a strong incentive to be the first to file a Paragraph IV certification under Hatch-Waxman and market their products during the 180-day exclusivity period, even if there is shared generic exclusivity, because competition with other generic products is more limited during that period,” says Andrew Powaleny, director, public affairs, PhRMA.

The Hatch-Waxman Act of 1984 allows the first manufacturer that comes out with an ANDA to have 180 days of exclusivity, at which time the FDA can’t approve another generic, often resulting in lawsuits and counter suits. However, if an authorized generic avoids a lawsuit while holding tight in its 180-day exclusivity period, the manufacturer will make money on both the brand and authorized generic, Berger says.

After the 180-day period, other generics might start to hit the market at a lower price, urging large chains and buying groups to send these to their stores from wholesalers.

Cost savings

According to the Federal Trade Commission, consumers and the healthcare system could benefit from an authorized generic on the market during an 180-day exclusivity period because of increased competition that reduces generic prices and results in significant cost savings.

An FTC report notes that “competition from an authorized generic during the 180-day exclusivity period is associated with retail generic prices that are 4% to 8% lower and wholesale generic prices that are 7% to 14% lower than prices without authorized generic competition.”

In addition, the FTC found that, following the 180-day exclusivity period, the presence of an authorized generic “tended to be associated with lower prices in markets where an exclusivity period had expired” as retail prices post-exclusivity were found to be 10% to 11% lower and wholesale prices were 6% to 13% less.

“As such, Congress should reject attempts to delay, restrict or prohibit authorized generics,” Powaleny says.

Berger says a patient’s insurance determines if authorized generics could save money. “Usually generics should have a lower copay so technically an authorized generic should have a lower copay for the patient than a brand would. Because every insurance has different structures and rebates and different technicalities, it is hard to generalize, but I would venture to say that most generics—whether it is a regular old generic, branded generic, or authorized one—should be less expensive than a brand,” she says.

Both Berger and Powaleny agree that drug rebates could influence the true cost of a drug. Berger says rebates play a role in price savings from authorized generics that can be more profitable than a brand name drug because they usually aren’t subject to rebates that flow from a drugmaker to PBMs and lower a brand’s revenue.

“If an authorized generic is not more cost effective than a brand discount [cost] minus the rebate, the plan [employer] may be better off with the brand; however, the member would likely pay less with the authorized generic as it has a deeper discount (cost), and the member pays a generic copayment or a lower cost in the deductible phase,” she says.

Medicaid, however, requires manufacturers to calculate and pay mandatory Medicaid rebates on authorized generics taken by Medicaid patients, Powaleny says.

Preventing drug shortages

Berger and Lassen agree that authorized generics have not filled the void during drug shortages. “It seems that when a drug is unavailable, it’s unavailable from every manufacturer whether it is a regular generic, authorized, or branded,” Berger says.

“To date, we have not seen the use of authorized generics play a significant role in helping to eliminate drug shortages,” Lassen says.

Sanofi, however, says that in 2015, it developed an authorized generic version of leflunomide for rheumatoid arthritis—17 years after the launch of Arava, its branded version—to meet demand left by a drug shortage from generic makers of leflunomide.

Berger predicts that the next big step for authorized generics will occur when companies that make biologics, such as AbbVie’s Humira (adalimumab), try to extend their profitability by making an authorized generic when their patents expire.

Mari Edlin, a frequent contributor to Managed Healthcare Executive, is based in Sonoma, California.
CMS has approved a costly and life-saving cancer treatment that immobilizes patients’ own immune system.

The novel FDA-approved therapy targets chimeric antigen receptors (CAR) of T-cells to battle some types of non-Hodgkin lymphoma (NHL) and B-cell precursor acute lymphoblastic leukemia for which chemotherapy and other treatments have failed.

“Medicare approval is a big deal, as a large percentage of those needing CAR T for a relapse of NHL are over age 65,” says James Essell, MD, chair of cellular therapy at the US Oncology Network in Cincinnati, Ohio. “CAR T offers a potential cure for those who’ve not responded to chemotherapy.”

Here are three takeaways on the intersection of Medicare and CAR T-cell therapy:

Don’t view CAR T as a drug, but as a therapy.
Genetically modifying patients’ immune cells requires a series of steps: collecting patients’ cells, modifying T-cells in the lab to attack cancer, then infusing them back into the body.

Once insurance is in place, cells are gathered, then shipped to the manufacturer to be modified, a two-to-three-week process. Chemotherapy then trims unmodified T-cells prior to infusion. “Once cells are infused, patients need at least 30 days of close monitoring for potentially life-threatening side effects,” Essell says. “That’s why CAR T is not so much a drug as a therapy, says Mariana Socal, MD, PhD, MPP, MS, assistant scientist in health policy and management at Johns Hopkins Bloomberg School of Public Health in Baltimore. “CAR T is a whole new territory pioneering the next generation of therapies,” she says. “When you look at its clinical benefits and how it’s administered, it’s a less costly intervention than bone marrow and organ transplants.”

Medicare approval is not automatic.
Medicare coverage of CAR T is limited to clinical conditions where the therapy has been proven to be highly beneficial, Socal says. Coverage is also limited to facilities enrolled in the FDAs program called Risk Evaluation and Mitigation Strategies (REMS). “This makes sure these therapies will be covered for the right patients in the right places that can handle toxicity and other complications that unfortunately are frequent,” she says.

Thus, only major academic medical centers in urban settings and with the capacity to do extensive, high-level research offer CAR T, Essell says. “Since one has to be referred to an academic center, patients may end up excluded from this potentially life-saving therapy. They [may not] have the resources to travel out of town with a caregiver for a month or longer,” he says.

Essell believes the Medicare ruling eventually will lead to top-tier private practice oncology clinics offering the therapy in conjunction with local hospitals.

Speed of access depends on more than insurance approval.
CAR T tends to be a last resort for seriously ill patients who have not responded to other available therapies. “This is a living therapy that cannot be pulled off the shelf, like chemotherapy,” Essell says. “It takes a highly skilled, coordinated team to control patients’ disease from the evaluation for CAR T through the waiting period during the CAR T manufacturing process.”

“Timing is critical,” he says. “Some cancers, such as large-cell lymphoma, can grow very rapidly, doubling in a matter of days.”

Delays aren’t due to Medicare approval and reimbursement so much as drug procurement mechanisms: the supply chain from the manufacturer to wholesalers to specialty pharmacies, Socal says.

Michele Meyer is a freelance writer from Houston.
Five Attributes of the Perfect Healthcare Analytics Team

Building the perfect analytics team can be a constant evolution

by MATT TURNER

Healthcare organizations across the country are under increasing pressure to grow and develop their internal analytical capabilities. The “Moneyball Effect” has hit the healthcare industry—an industry that has trailed others in the depth and breadth of data used for making business decisions.

Companies are recruiting new types of executives (e.g., chief analytics officers, chief data officers) charged with leading digital transformation activities and building teams of analytical rock stars. These leaders must draw from a diverse set of disparate educational backgrounds to forge a new generation of analytics teams. While the traditional skillsets of analysis remain important, the democratization of cloud-based machine learning and artificial intelligence systems will require new talent to realize better outcomes.

Without strong talent development programs, many first-generation analytics programs will fail to realize their promise. This can have the unintended effect of creating “analytical backlash” within an organization. Progressive healthcare executives will provide guidance, development, and support to maximize their analytics investments.

How do you build these new teams? How do we develop the next generation of healthcare analytics experts? I believe there are five key attributes that we should be searching for:

1. **CURIOSITY**

   The best analytics experts are infinitely curious (they ask “why” a lot). They see the industry without constraints. Rather than becoming overwhelmed by the complexity of healthcare, they are fascinated and driven by the possibilities. A savvy analyst or data scientist will be driven by intrinsic motivation to answer challenging questions. They will not wait for the C-Suite to knock but will be knocking with ideas, questions, and insights they have discovered. I believe this is the most foundational skill necessary for exploring the healthcare data landscape.

2. **PASSION**

   Experienced healthcare leaders know that it can feel more like a “calling” and less like a career. This extends to the analytics professions—the most successful team members will harbor a natural passion or connection to improving healthcare. This may stem from a personal story or experience, be motivated by a family connection or a fascination stoked in education. Some of the finest analytics experts may be biology majors or other “pre-med dropouts” who are striving to improve healthcare from a different angle. When recruiting analytics professionals, have a very open mind and look for these interesting backgrounds; passionate employees are typically proactive learners and will collaborate with clinical and financial experts to make things better. They drive the change we want to see in our organizations.

3. **CREATIVITY**

   Analytics is a beautiful alchemy of technical skill, quantitative ability, and open-ended creativity. The most impactful insights typically emerge from this manner of thinking. Analytics professionals who show high creativity will find unique perspectives to visualize data, model features previously missed, and present their findings...
in novel, impactful ways. These types of insights are motivating to the analytics team and resonate with leaders—a win-win! Humans are visual creatures who best consume insights through strong visual methods. Look for analytics professionals with an artistic flair who are motivated by beautiful visualizations.

4. CRITICAL THINKING
Although creativity is important, analytics remains grounded in stone-cold quantitative and rational thinking. The most beautiful dashboards must be driven by highly accurate data coupled with well-applied algorithms and statistical methods. “You can’t beat bad math,” the saying goes, and business leaders who rely on these analytics shops must develop trust that these teams are well steeped in critical-thinking approaches. The very term “analytics” emerges from the discipline of “analysis” and without exception analytics professionals must be skilled analysts. This means that they are open minded, form strong hypotheses, and test them with rigor. Good analysts deeply immerse themselves in the data and become subject matter experts in their given domain. A clinical analytics expert in our academic health system will become deeply skilled in understanding data on nursing documentation, laboratory results, diagnosis patterns, and other relevant healthcare data assets. This foundational knowledge of data cannot be overlooked—you must “know thy data” before attempting to draw insights or correlations.

5. SMART
Analytics experts may not have to max out the math section of graduate exams but they certainly must be well skilled in their relevant domains. This may mean deep expertise in mathematical and statistical modeling, technical skill in programming languages such as SQL, R, or Python, and educational training in the latest visualization packages. Most analytics professionals will be highly proficient in both quantitative disciplines such as mathematics, statistics, or economics and in technical disciplines such as engineering and computer science. Many of our most talented professionals have interesting blends of these backgrounds such as an undergraduate degree in computer science coupled with graduate training in math or statistics. Others have more traditional business analyst skillsets such as finance, but have developed their skills in programming and data visualization best practices. Many universities are now offering formal programs in analytics and data science, which are producing graduates ready to hit the ground running. Online educational opportunities (Coursera, Udemy, among others) are leveling the playing field by allowing smart, young (or old!) learners the opportunity to build their skillsets in the latest data visualization or machine learning methods. The amount of content online for developing skills has proliferated in the past few years (another reason screening for passion and curiosity is so critical). Healthcare organizations that are looking to find this talent should start with local educational facilities. Developing talent pipelines through internships, part-time opportunities, and other related programs are a cost-effective way to find talent and provide meaningful learning opportunities for students. These current students make the best future employees. The digitization of the American educational system is rendering students who are now digital natives and are learning the latest tools and methods. This will prepare them to make a quick impact in your organization.

Ultimately, the discipline of analytics is a team sport that requires a variety of backgrounds, experiences, and various technical disciplines. The “perfect” analytics team will consist of talent gleaned from these different backgrounds and united together through rigorous analytical inquiry, strong data tools, and refined methods.

Different healthcare organizations will need to tailor the exact ratios of expertise based on their unique needs. Managed care organizations, value-based payment arrangements, and population health experts may need to attract more actuarial or risk-based backgrounds. Financial institutions may need more forecasting and quantitative modeling expertise. Clinical units may need talent with additional subject matter expertise in biomedical informatics. Although the specific disciplines will be highly dependent on the problems being solved, these principles for selecting talent should be widely applicable across organization types. Analytics involves significant investment in new processes and breakthrough technologies—but the most important ingredient is the people who make these insights attainable.

Matt Turner, is chief data officer at the Medical University of South Carolina (MUSC).
For decades, generic drugs were an effective and less costly option for patients, but new changes in the market are making it more difficult than ever for generics and biosimilars to successfully compete on formularies.

"Generics are a threatened species right now and that goes double for biosimilars," says Louis Tharp, executive director and co-founder of the Global Healthy Living Foundation and CreakyJoints.

Experts note a significant shift in the marketplace that has led to more generic drugs getting placed on higher formulary tiers—significantly increasing copay amounts for patients. Branded manufacturers also deploy a series of strategies, such as the use of rebates, to try to limit the reach of new generic products.

"Generally, what we have been observing and hearing from members are increasing challenges in terms of formulary access, both with respect to older commoditized generics and newer generic launches," says Craig Burton, vice president of policy for the Association for Accessible Medicines.

Research has shown a significant drop in the number of generic medications being placed on the lowest formulary tiers in recent years. Some believe the trend is driving up patient costs and making it increasingly difficult for generics to compete.

According to a recent Avalere survey examining Medicare Part D trends of generic drugs, researchers found that in 2011, 71% of generic drugs were placed on tier 1; but by 2015, only 19% of covered generic drugs were placed on tier 1. It was much more likely in 2015...
that generic drugs would be placed on tier 2 (46%) or tier three or higher (35%). This 53% drop in the number of drugs placed on the lowest tier also translated to a $6.2 billion increase in the total patient cost sharing for the same drugs.

One potential reason for the significant jump in patient cost-sharing could have been attributed to increased utilization; however, Avalere found that during this time period utilization only increased by about 20%. In addition, the price of generic drugs assessed only increased by 1% during the same period.

“The result was pretty clear—this is simply plans shifting generic drugs to tiers with higher copays, mixing them in on branded drug tiers with higher copays and seniors not receiving the full value of those generics,” Burton says.

Just this year, Avalere released a new analysis of Medicare Part D generic trends and found that between 2016 and 2019, generic drugs were placed on the lowest tier 14% of the time.

Burton says since research seems to indicate that the trend of placing generic drugs on branded tiers with higher copays does not appear to be driven by the price of generics, the association has had to consider other possibilities for the change in practices.

The emerging assumption is that higher brand drug costs are driving greater co-pays across the board, he says.

A 2019 Johns Hopkins University study published in *JAMA Internal Medicine,* analyzed 57 Medicare Part D formularies and found that 72% placed at least one branded drug in a lower cost-sharing tier than its generic product. In addition, 30% of the formularies adopted fewer utilization controls on the branded product compared to its generic counterpart.

“That should be economically impossible,” Tharp says.

**Entrance challenges**

Older generics aren’t the only ones finding it difficult to compete in today’s marketplace. New generic or biosimilar launches are also finding it difficult to gain a share of the market—often due to brand rebates that drive down the overall cost of a branded competitor.

“*We have to sit down and seriously change the structure, and in the process, we cannot kill insurance companies, drug companies, PBMs, hospitals, [or] doctors.*”

—LOUIS THARP, GLOBAL HEALTHY LIVING FOUNDATION AND CREAKYJOINTS

“A number of new generic launches are seeing significant challenges to even being available to patients because they are being excluded from formularies presumably as a result of brand drug rebate agreements that are conditioned on the exclusion of the generic competitor,” Burton says.

In general, he says one of the problems is the lack of transparency about what happens to rebate money or what effect these rebates really have on formularies.

Lack of access may be hindering medication affordability—a problem for high-cost conditions, such as diabetes. According to the American Diabetes Association, three follow-on biologic insulins have been approved by the FDA, and two are available for sale in the United States. These drugs are priced about 15% lower than their original version; however, none of the follow-on biologic insulins have been approved as substitutable or interchangeable, making their use more difficult.

“The ADA recommends the FDA continue its efforts to encourage additional competition within the insulin landscape, including fostering biosimilar competition,” they wrote in a public policy statement addressing the rising costs of insulin and strategies to lower insulin costs.

**Increasing competition**

The FDA announced steps to encourage biosimilars and more affordable brand insulin starting in 2020, but according to a white paper released by the Biosimilars Council, several barriers need to be addressed that could limit patient access to biosimilar insulin forms.

To improve biosimilar access to formularies, the council recommends that policymaking by the FDA, CMS, and Congress should ensure that rebates and “formulary gamesmanship” don’t prevent patient access to biosimilar insulin forms.

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“The ADA recommends the FDA continue its efforts to encourage additional competition within the insulin landscape, including fostering biosimilar competition,” they wrote in a public policy statement addressing the rising costs of insulin and strategies to lower insulin costs.
Pharmacy Best Practices

Burton says the Association for Accessible Medicines has proposed several possible steps to CMS that could improve generics access to formularies. For instance, the association believes that generics should automatically be placed on generic tiers when they are launched and should no longer be co-mingled on tiers with branded drugs.

Tharp says it’s important to remember that PBMs are simply trying to succeed in the capitalist system the country has created. "There aren’t any solutions to this," he says. "We have to sit down and seriously change the structure, and in the process, we cannot kill insurance companies, drug companies, PBMs, hospitals, [or] doctors.”

Tharp believes policy efforts that make sweeping moves to eliminate rebates entirely—like the proposal by President Trump to eliminate drug rebates in Medicare and Medicaid—fail to take into consideration the complexity of the current system.

"You can’t just say the rebate rule is gone because that’s a major profit center for PBMs. In the current system we need PBMs, and they are only doing what the system allows them to do," he says.

Trump’s proposal was withdrawn in July after receiving significant backlash from insurers and hospitals. Although it may not be easy, Tharp says he remains optimistic that if the country as a whole reconsiders its current healthcare philosophy, it may be possible to reverse current trends and appreciate the value that generics can play in the market.

Jill Sederstrom is a freelance writer based in Kansas City.

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<td>E. Total Non-requested Distribution</td>
<td>31,733 31,663</td>
</tr>
<tr>
<td>(Sum of 15c and e)</td>
<td></td>
</tr>
<tr>
<td>F. Total Distribution</td>
<td>31,733 31,663</td>
</tr>
<tr>
<td>(Sum of 15c and g)</td>
<td></td>
</tr>
<tr>
<td>G. Copies not Distributed</td>
<td>31,733 31,663</td>
</tr>
<tr>
<td>5. Consumers</td>
<td>31,733 31,663</td>
</tr>
<tr>
<td>H. Total</td>
<td>31,733 31,663</td>
</tr>
<tr>
<td>(Sum of 15f and i)</td>
<td></td>
</tr>
<tr>
<td>I. Percent Paid and/or Requested Circulation</td>
<td>45.49% 50.33%</td>
</tr>
<tr>
<td>16. Electronic Copy Circulation</td>
<td></td>
</tr>
<tr>
<td><em>If you are not claiming electronic copies, skip to line 17</em></td>
<td></td>
</tr>
<tr>
<td>a. Total Number of Electronic Copies</td>
<td>13,245 11,345</td>
</tr>
<tr>
<td>b. Total Requested and Paid Print Copies (Line 15C)</td>
<td>9,280</td>
</tr>
<tr>
<td>Requested/Paid Electronic Copies</td>
<td></td>
</tr>
<tr>
<td>c. Total Requested Copy Distribution (Line 15F) +</td>
<td>25,217</td>
</tr>
<tr>
<td>Requested/Paid Electronic Copies</td>
<td></td>
</tr>
<tr>
<td>d. Percent Paid and/or Requested Circulation</td>
<td>40,943</td>
</tr>
<tr>
<td>(Both Print &amp; Electronic Copies)</td>
<td>40,943</td>
</tr>
</tbody>
</table>
| 17. Publication of Statement of Ownership for a Requester Publication is required and will be printed in the October issue of this publication.

Name and Title of Editor, Publisher, Business Manager, or Owner: Christine Shappell, Audience Development Research Director
Signature:

Christine Shappell, Audience Development Research Director

Date: 9/30/19

I certify that the statements made by me above are correct and complete.
“In all honesty, oncologists focused on helping their patients live as well and as long as they can aren’t always scrutinizing costs.”
—Andrew Schneider, MD, South Florida Oncology and Hematology Consultants. Read more on page 23.

**HIV linked to cancer mortality**
Mortality after diagnosis in patients with nonadvanced cancers who received stage-appropriate treatment and survived 1 year or more after diagnosis:

<table>
<thead>
<tr>
<th>Cancer</th>
<th>HIV infected</th>
<th>HIV uninfected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>37%</td>
<td>20%</td>
</tr>
<tr>
<td>Prostate</td>
<td>22%</td>
<td>25%</td>
</tr>
<tr>
<td>Breast</td>
<td>37%</td>
<td>25%</td>
</tr>
</tbody>
</table>

**The economic burden of cancer**

- **Pancreatic**: $6.1 billion
- **Breast**: $6.2 billion
- **Colorectal**: $9.4 billion
- **Lung**: $21.3 billion

Total annual cost of lost earnings due to cancer deaths: **$94.4 billion**

Source: JAMA Oncology

**Size of global immuno-oncology assays market by 2025**

$6.63 billion

Source: Zion Market Research

**THE BOTTOM LINE**

*BY NICHOLAS HAMM*