LIFE & ARTS

YOUR HEALTH | By Sumathi Reddy

A Cholesterol Drug Tug-of-War

Patients struggle for insurance approvals of PCSK9 inhibitors, powerful drugs that lower bad cholesterol when statins don't work

FROM LEFT: ROSS MANTLE FOR THE WALL STREET JOURNAL (2); EXCEL MEDICAL CLINICAL TRIALS, LLC

Carlyn Cirrincione, 22
Gibsonia, Pa.
Awaiting application approval

Nov. 2013: Gets cholesterol checked after 14-year-old brother had abnormally high cholesterol. Her results are high: 387 mg/dL total cholesterol and 297 mg/dL for LDL. She is diagnosed that year with familial hypercholesterolemia.

Dec. 2013: Goes on statin, Lipitor, for several months. Calves swell up. She is in pain. Goes off it two to three months later.

June 2014: Tries another statin, Pravachol. Experiences adverse side effects so stops using it.

Oct. 2014: Tries statin Crestor in combination with Zetia, another cholesterol-reducing medication.

Jan. 2015: Her pain is so debilitating she can't walk. She stops all statins but remains on Zetia. Her LDL remains high at more than 200 mg/dL. Later that year, her cardiologist tells her about PCSK9 inhibitor, Repatha. She begins taking samples. Cardiologist submits Carlyn's first application to insurer, UPCM Health.

Oct. 12, 2015: Application for Repatha denied.

April 2016: While taking the free samples of Repatha, her cholesterol is down to 129 mg/dL and her LDL is 82 mg/dL.

June 2016: Second application for Repatha is filed to her family's new insurance company, United Healthcare.

June 27, 2016: Request is denied.

April 2017: Third application for Repatha filed to UPMC Health plan after the family switches its insurance plan back to UPMC.

April 10, 2017: Request is denied.

ILLUSTRATION BY ROBERT HUNT

SLIM AND ATHLETIC, Carlyn Cirrincione doesn't look like someone who should be worried about having a heart attack.

But the 22-year-old CrossFit enthusiast and avid runner has to think about the health of her heart and cholesterol levels all the time. No bacon for her. No egg yolks. Ice cream, a once-loved treat, is on the blacklist.

What she does need, according to her doctor, is powerful new drugs known as PCSK9 inhibitors that can dramatically lower LDL, or bad cholesterol levels when other drugs, known as statins, can't do the job.

There is just one problem: the price tag. Nearly two years after the drugs were approved by the U.S. Food and Drug Administration, doctors and patients say getting insurance to pay for the drugs, which list for more than $14,000 a year before rebates or discounts, is a battle that requires countless hours, applications and appeals. Even then, the battle for insurance approval of PCSK9 inhibitors is successful less than half the time, according to several recent studies.

Carlyn Cirrincione, 22, and her mother Tracey, 45, above at their home in Gibsonia, Pa. Carlyn is hoping to be approved for Repatha, a PCSK9 inhibitor. Above, Dr. Seth Baum, president of the American Society for Preventive Cardiology, advocates for better access to PCSK9 inhibitors. Left, Repatha, made by Amgen Inc., is injected every two to four weeks.

Ms. Cirrincione hasn't yet been approved despite her and her doctor's numerous applications and efforts. She was diagnosed four years ago with familial hypercholesterolemia (FH), a genetic disorder that causes high cholesterol because the liver is unable to remove excess LDL. Her cholesterol at the time of her diagnosis was off the charts, with a total of 387 mg/dL and an LDL level more than four times what doctors recommend for FH patients, at 297 mg/dL.

High levels of cholesterol, a fat-like substance, can build up in the arteries and slow down or block blood flow to the heart, causing heart disease and heart attacks, and to the brain, causing strokes. Doctors typically recommend LDL levels no higher than 100 mg/dL for healthy individuals and less than 70 mg/dL for those with heart disease.

Most people with high cholesterol try to bring it down with a combination of healthy diet, exercise and drugs known as statins, such as atorvastatin (brand name Lipitor) and rosuvastatin (Crestor). But these drugs can't always get LDL levels low enough for FH patients. And for some, like Ms. Cirrincione, statins aren't an option because they cause severe muscular aches.

Some doctors believe PCSK9 inhibitors could be a lifesaving solution for millions of heart-disease patients and could transform treatment for the most difficult cases—patients with FH, as well as those with a history of heart disease or stroke for whom statins and other therapies are inadequate. Drug companies estimated the target population to be 11 million patients.

But other doctors say that until drug companies can prove PCSK9 inhibitors will reduce the number of deaths caused by heart disease, not just their ability to reduce heart attacks and strokes, the drugs aren't worth the high price.

The two PCSK9 inhibitors currently on the market were approved in 2015. Amgen Inc. makes the drug Repatha (evolocumab), which has a list price of about $14,536 a year. Sanofi SA and Regeneron Pharmaceuticals Inc. makes Praluent (alirocumab), which has a list price of $14,600 a year. The medicines are new entrants in a group of extremely costly drugs that have cropped up in recent years.

Doctors, consumers and lawmakers have spoken out against escalating drug prices. The criticism has triggered hearings in Congress. A public furor over the high cost of EpiPen allergic-reaction treatments also led manufacturer, Mylan NV, to began selling a generic version of the devices that sells for half the $609 list price.

Doctors and researchers say part of the reason PCSK9 inhibitors are priced so high is because they are a fully human monoclonal antibody, which is harder to manufacture than a normal pill. Patients inject them into their bodies every two to four weeks.

Sanofi and Regeneron remain concerned about restrictive access to PCSK9 inhibitors but are starting to see more approvals for Praluent and more confidence from prescribers in preparing the necessary documentation, said Ashleigh Koss, a Sanofi spokeswoman. Kristen Neese, a spokeswoman for Amgen, said while Repatha isn't a replacement for statins, "many patients are not adequately treated by statins and are at high risk for cardiovascular events like heart attack or stroke." She noted that payers don't pay the list price for the drug, and the price is supported by "robust" data from its clinical trial. The company is offering support, such as a $5 copay card for eligible patients.

For people who are approved by their insurers, high copays can pose an additional barrier to obtaining the drugs. One recent analysis of all PCSK9 inhibitor prescription claims in the first year the drugs were approved found that 27% of claims had a monthly copay of more than $400. The mean copay amount was $107 for patients with commercial insurance plans and $213 for those with government-funded Medicare. Another recent analysis from Duke researchers found that 35% of approved patients never picked up the medication.

"We've been waiting for this kind of advance for quite a long time," said Seth Baum, president of the American Society for Preventive Cardiology. "We finally have it, and now we need to be able to use it."

Health insurers and their consultants say PCSK9 inhibitors have less-expensive alternatives in statin drugs. They also say that the PCSK9 drugs are a lifelong prescription at a high cost.

Insurance companies are also mindful of setting a precedent, said Helen Leis, a partner in the health and life sciences practice of consulting firm Oliver Wyman, a division of Marsh & McLennan Cos. Approving one set of pricey drugs could set a precedent when it comes to other expensive drugs that treat a larger population, such as cancer drugs.

In 2016, 88.4% of patients with a commercial insurance plan were rejected when trying to get a new prescription for a PCSK9 inhibitor, according to data from Symphony Health Solutions. That number declined to 72.8% after 14 days, likely due to patient appeals.

Doctors have had mixed reactions to results of Amgen's clinical trial for its drug, Repatha, announced in March. The study followed 27,564 patients over 2.2 years and found that Repatha reduced the risk of heart attacks and strokes by 20% compared with the standard treatment with statins.

For Dr. Baum, the trial was proof that that PCSK9 inhibitors are very effective, showing they could lower LDL by 60%. "We do know unequivocally that a lower LDL equals a lower risk of heart attack, stroke and death," said Dr. Baum, who has been paid as a consultant and scientific board member for Amgen and Sanofi/Regeneron.

But some doctors say the study would have been more convincing if the drug had lowered the heart attack risk more and caused a decline in deaths. The lower LDL "didn't translate into a mortality benefit," said Sanjay Kaul, a cardiologist at **Cedars-Sinai** Medical Center in Los Angeles.

Some health plans have entered into "value-based" contracts with drug companies, in which the drug

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What Is Familial Hypercholesterolemia (FH)?

FH is a genetic disorder that causes high cholesterol from birth because the liver is unable to remove excess LDL, which is known as bad cholesterol from the blood stream. High levels of cholesterol lead to heart disease and stroke, among other health problems.

FH is usually inherited from one parent with a dominant gene. It is estimated that about one in 250 people have FH which translates into 1.3 million patients in the U.S. and 30 million world-wide.

Experts say only about 10% of patients in the U.S. that have FH have been diagnosed. Most doctors view it as a rare disorder, and even though the American Academy of Pediatrics recommends universal cholesterol screening for children between the ages of nine and 11 it isn't always done.

FH patients have a 50% chance of passing on the disorder to each of their children.

LDL levels of 190 mg/dL or more in adults, or over 160 mg/dL in children, and a family history of early heart disease are red flags for doctors to consider FH may be present. Untreated, FH patients have a 2.5- to 10-fold increased risk of having heart disease.

Men who aren't treated have a 50% risk of having a heart attack by age 50, while untreated women have a 30% risk for having one by age 60.

FH is diagnosed using a series of clinical criteria based on personal and family history, blood cholesterol, and potentially genetic testing although genetic testing is rarely done in the U.S.

Sources: FH Foundation; Joshua Knowles, Stanford Center for Inherited Cardiovascular Disease; Seth Baum, American Society for Preventive Cardiology.