(11-28) 11:59 PST SAN FRANCISCO -- A new generation of blood thinners offers potentially millions of people alternatives to warfarin, a 60-year-old anticlotting drug derived from rat poison that can be difficult for patients to manage and requires frequent monitoring.

While these new drugs have great promise, they come with a potentially fatal flaw: If a patient starts bleeding seriously, there's no simple way to stop it.

"It's groundbreaking and it's exciting. We're thrilled to have these medications available to us," said Dr. Matthew DeVane, a Walnut Creek cardiologist who serves as board director for the American Heart Association's East Bay region. "The downside of the new ones is we don't have an antidote to reverse the blood thinning effects."

A South San Francisco biotechnology company is working on that.

Portola Pharmaceuticals Inc. earlier this month received an undisclosed sum of money from large drug manufacturers Bristol-Myers Squibb and Pfizer Inc. to test an agent that could reverse the effects of these new anticoagulants in the event of bleeding from injury, surgery or some other cause.

"It's a very unique and creative deal," said Mardi Dier, chief financial officer of Portola, which at the same time is developing its own anticoagulant. "This is a way for them (the big drug companies) to have some input in how their drugs will work with the antidote. It really validates the importance of the antidote."

Tames swelling, clots

Anticoagulants have long been prescribed to heart attack and stroke patients to prevent swelling and blood clots. While often referred to as blood thinners, they don't really thin the blood. They decrease the blood's ability to clot, which prevents harmful clots from blocking blood vessels and causing heart attacks or stroke.

The most widely prescribed anticoagulant, warfarin, sold under the brand name Coumadin, was originally developed as a rat poison, and is now one of the most frequently prescribed medications in the United States, with nearly 18 million prescriptions dispensed annually.

Despite its popularity, the drug isn't for some patients because it has numerous drug and food interactions and requires frequent blood tests to monitor its levels.

"Once you get to a steady state on Coumadin, you only have to check once a month. The problem is that patients don't always go to the lab every month," DeVane said.

But it has advantages in that it's effective and cheap, and has an antidote. The antidote, vitamin K, allows the blood to clot if administered promptly by injection or orally.

The new generation of blood thinners in recent years is expected to grab a share of a market that is estimated at around $5 billion a year worldwide and is expected to reach $20 billion by 2020.

Pradaxa approved

Pradaxa, a twice-daily pill from Boehringer Ingelheim, received approval from the U.S. Food and Drug Administration in October 2010 for prevention of strokes in patients with atrial fibrillation, the most common type of irregular heartbeat.

In November 2011, the FDA approved another drug for atrial fibrillation called Xarelto, which Johnson & Johnson developed with Bayer.

It can be taken just once a day. The drug has since received approval to treat additional conditions, including deep vein thrombosis, which develops when clots form in deep veins, most commonly in the leg.

Bristol-Myers Squibb and Pfizer are awaiting FDA approval for their jointly developed drug, Eliquis, which works much like Xarelto.

Portola is also developing its own version of an anticoagulant directed at seriously ill patients who have difficulty moving.

While none of these new drugs has a reversal agent, most of the concern has been directed at Pradaxa. The drug has been around the longest and has been the target of a number of lawsuits from the families of patients who have died from uncontrolled bleeding.

All anticoagulants carry a risk of bleeding, but the newer drugs are drawing attention to the problem even though some of the latest studies have shown that the risk of bleeding while on these drugs is no higher than for patients on warfarin.

The number of serious adverse drug events reported to the FDA - those causing injury, disability or death - has increased 90 percent over the past four years, according to the nonprofit Institute for Safe Medication Practices. The group attributed part of those increases to the new anticoagulants.

In its 2011 report, the nonprofit said 542 reports of deaths associated with Pradaxa were reported to the FDA last year. The number of deaths topped all other medicines, including warfarin, the second most frequently reported drug for serious adverse effects, but with 72 deaths.

Information for Xarelto was not yet available in 2011, but the nonprofit's October report found the new drug accounted for 158 serious adverse events in the first quarter of the year. In addition, the report points out that these new-generation coagulants cost about 15 times as much as Coumadin. Xarelto and Pradaxa cost about $3,000 a year, versus about $200 for the generic version of Coumadin.

Hope with antidote

Portola hopes to prevent such problems with its antidote, which will be designed to work for Xarelto, Eliquis and the company's own investigative anticoagulant. The antidote won't work on Pradaxa because that drug works slightly differently. Portola's Dier said the collaboration with the big drug manufacturers will start before the end of the year.

Doctors say that an antidote would offer peace of mind, but some are not ready to replace their faithful standby with these newcomers.

Dr. Junaid Khan, director of cardiovascular services at Alta Bates Summit Medical Center in Oakland and Berkeley, said he's concerned that these newer drugs are eliminated through the kidneys, which could cause problems in an older patient population prone to kidney disease.

"The medical world is still learning how to deal with these drugs," Khan said. "I still truly do not know where they fit in, and we definitely try to use them on patients who have a problem with Coumadin, but I'm not convinced it's the first line to replace Coumadin."

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