FDA clears first daily pill that could change bad cholesterol treatment

The USFDA has approved Lipfendra, the first oral PCSK9 inhibitor, for lowering LDL cholesterol. The once-daily pill could improve long-term adherence, though Indian access will depend on approval and cost.

For years, one of the most powerful treatments for lowering "bad" cholesterol – a leading factor behind heart attacks and strokes – has remained out of reach for many patients and not because it did not work, but because it came as an injection.

That could now be changing.

The US Food and Drug Administration (USFDA) has approved Lipfendra, which has enlicitide as the active ingredient, developed by Merck, making it the world's first oral drug in the PCSK9 inhibitor class, a new and powerful medicine for stubborn cholesterol in the arteries.

The once-daily pill promises to make one of the most effective cholesterol-lowering therapies easier to use, potentially transforming care for millions of people who struggle to bring their cholesterol under control.

"I wouldn't call this exciting in the sense of a breakthrough discovery. I'd call it exciting in the sense that it makes a therapy we already trust usable for a lot more people who actually need it. Those are two different kinds of excitement," Mumbai-based senior cardiologist Dr S A Merchant told India Today.

The approval has generated global excitement because it tackles one of the biggest barriers to treatment – patients' reluctance or inability to take regular injections.

While the science behind the medicine is familiar, the convenience of swallowing a daily pill instead of injecting oneself every few weeks could significantly improve adherence, doctors say.

For India, where cholesterol disorders have reached alarming levels, the development carries particular significance, even though the drug may take some time to arrive anytime soon.

INDIA'S CHOLESTEROL CRISIS

India is quietly battling an enormous cholesterol epidemic.

A landmark survey by the Indian Council of Medical Research (ICMR) and the Madras Diabetes Research Foundation, published in The Lancet in 2023, found that more than 81 per cent of Indians have dyslipidaemia, an umbrella term for unhealthy blood fat levels. Around 20.9 per cent – roughly 185 million people-elevated LDL cholesterol, commonly known as "bad" cholesterol.

LDL cholesterol is dangerous because it gradually accumulates inside blood vessels, narrowing arteries over years without causing symptoms. Often, the first sign of trouble is a heart attack or stroke.

Recognising the growing burden, the Cardiological Society of India released its first lipid management guidelines in July 2024, recommending that people at high cardiovascular risk – including those with diabetes or hypertension – maintain LDL cholesterol below 70 mg/dL.

Yet many patients fail to achieve these targets despite treatment.

Statins remain the cornerstone of cholesterol management and have saved millions of lives.

However, around one in five patients does not reach recommended LDL levels even on maximum tolerated doses. Others develop muscle pain or weakness that limits how much statin they can take.

That is where PCSK9 inhibitors come in.

WHAT CHANGES NOW

PCSK9 inhibitors represent one of the biggest advances in cholesterol treatment over the past decade.

The medicines work by blocking a protein called PCSK9, which interferes with the liver's ability to remove LDL cholesterol from the bloodstream. When PCSK9 is blocked, the liver clears much more LDL, dramatically lowering cholesterol levels.

Until now, every drug in this class – including evolocumab, alirocumab and inclisiran – has required injections.

Enlicitide changes only one aspect of that equation: it turns a needle into a pill.

Clinical trials showed the medicine lowered LDL cholesterol by about 56 per cent overall and by 58.2 per cent in adults with familial hypercholesterolaemia, a genetic condition that causes extremely high cholesterol from birth.

The effectiveness is broadly comparable to injectable PCSK9 medicines.

"The recent US FDA approval of the first oral PCSK9 inhibitor is an exciting and clinically meaningful development," said Dr Anshul Kumar Jain, director of cardiology at CK Birla Hospital in Delhi.

"An effective oral option has the potential to improve patient acceptance, convenience and long-term adherence, enabling more individuals to achieve their LDL cholesterol goals."

The approval is especially important because high cholesterol is often called a "silent killer."

"High cholesterol is a silent condition; it causes no symptoms until it manifests as a heart attack or stroke," Dr Jain said.

Doctors believe that many patients discontinue injectable therapies – not because they are ineffective, but because regular injections become difficult to sustain over years.

According to Dr Merchant, that practical challenge has limited the widespread use of an otherwise highly effective treatment.

A daily tablet removes one of the biggest psychological and logistical barriers associated with long-term injectable therapy.

NOT A MIRACLE CURE

Despite the excitement, cardiologists caution that the new approval should not be mistaken for a cure or a replacement for existing treatments.

Statins will remain the first-line therapy for most patients.

"Statins are still our backbone, and they'll stay that way," pointed out Dr Merchant.

PCSK9 inhibitors are primarily meant for people who continue to have dangerously high LDL despite taking the highest tolerable doses of statins, those who cannot tolerate statins adequately, or patients with inherited disorders such as familial hypercholesterolaemia.

There are other important caveats too.

The FDA approval is based on the drug's impressive ability to lower LDL cholesterol, a well-established marker linked to cardiovascular risk.

However, the large clinical trial designed to prove that enlicitide directly reduces heart attacks, strokes and cardiovascular deaths is still underway.

"Patients should know the difference between 'lowers your numbers' and 'proven to cut your heart attack risk,' even if the two are closely linked," Dr Merchant explained.

Doctors stress that this distinction is important because while decades of evidence show that lowering LDL generally reduces cardiovascular events, every new medicine must independently demonstrate long-term outcome benefits.

Lifestyle also remains indispensable.

Experts emphasise that no cholesterol-lowering medicine can replace healthy eating, regular exercise, maintaining a healthy weight and avoiding tobacco.

As Dr Jain points out, medicines should be viewed as an important addition, not an alternative, to comprehensive cardiovascular prevention.

WHAT IT MEANS FOR INDIA

Although the FDA approval marks an important global milestone, Indian patients are unlikely to benefit immediately.

The medicine still needs regulatory approval in India before becoming commercially available. Even after approval, questions around pricing, insurance coverage and inclusion in Indian treatment guidelines will determine how widely it is used.

Cost has long been one of the biggest hurdles for PCSK9 inhibitors in India so far.

Current injectable therapies, particularly inclisiran that needs to be taken once every six months, can cost more than Rs 1 lakh annually.

No insurance coverage, patent restrictions, has meant that these highly effective medicines remain restricted to a relatively small group of patients. Whether an oral formulation becomes more affordable remains to be seen.

News Source:

https://www.indiatoday.in/health/story/oral-pcsk9-inhibitor-lipfendra-approved-by-usfda-for-lowering-ldl-cholesterol-2949856-2026-07-17