

Injectables for high blood pressure are in the works. Could they mean no more daily pills?

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About <u>one-third</u> of adults have high blood pressure. Two-thirds of these have uncontrolled high blood pressure.

A key driver of poor blood pressure control is people not taking their tablets as prescribed. Tablets have been used to treat high blood pressure



for decades. But about <u>one in two</u> people prescribed them stop taking them in the first year. Others don't take their tablets reliably.

Tablets for high blood pressure, or <u>hypertension</u>, are short-acting. So they need to be taken at least once a day. But in recent clinical trials, injectable treatments have reduced blood pressure for up to <u>six months</u>.

If approved, these injectables would be the first new drug class for high blood pressure <u>in decades</u>.

By potentially making it easier for people to stick with their treatment, these injectables could help achieve a long-lasting reduction in blood pressure.

Lowering blood pressure by even <u>just 5mmHg</u> (millimeters of mercury, a measurement used to record blood pressure) can dramatically <u>lower the chance</u> of developing heart disease or stroke.

Are these injections like vaccines?

These injectables are not "vaccines" in the conventional sense. Instead, they are similar to already-approved injectables, such as the diabetes and weight-loss drugs Ozempic and Trulicity. But unlike these medicines which are self-administered, the ones for high blood pressure would be delivered by a doctor or nurse under the skin.

Two <u>drug candidates</u> in recent clinical trials target a liver protein called angiotensinogen. This is a crucial part of your body's hormone system that regulates blood pressure and fluid balance.

The injectables work by a process called "RNA interference," which interferes with synthesis of the angiotensinogen protein. This disrupts the cascade of events that would otherwise lead to high blood pressure.



Blood pressure tablets also target the angiotensinogen system, but their effect only lasts a maximum 24 hours.

Do they work?

Two promising candidates in clinical trials are IONIS-AGT-LRx from Ionis Pharmaceuticals and zilebesiran from Alnylam Pharmaceuticals.

IONIS-AGT-LRx is injected under the skin weekly. It was found to be safe in <u>very small trials</u> of healthy volunteers or those with mild-to-moderate high blood pressure. But larger trials are needed to confirm blood pressure lowering benefits.

In comparison, zilebesiran is injected under the skin every six months. Studies in recent months show a significant blood pressure lowering effect and good safety profile in younger and middle-aged people, even when taken with traditional blood pressure tablets.

Zilebesiran's blood pressure lowering effect appears to be equivalent to what you'd acheive if you took one type of blood pressure <u>tablet</u> (about a 10–15 mmHg reduction), but clearly with a much longer lasting action. Most people would need to use it with another blood pressure lowering pill.

Are they safe?

<u>Early evidenceis promising</u>. Studies show good tolerance in younger and middle-aged people with limited other health problems. The most common side effects are minor reactions such as redness or swelling at the injection site in about one in six people.

A small proportion of people had mildly raised blood potassium levels



and mild changes in kidney function, but this seemed to be short term. We also see these changes with other classes of high blood pressure treatments.

How can I access these new treatments?

These injectables are not available to the public. Clinical trials are under way around the world to provide more evidence about:

- their long-term safety, especially in high-risk people with multiple health conditions
- any interactions with other drugs
- their ability to reduce rates of heart disease and stroke.

One such trial, running in 2024, is of <u>zilebesiran</u>. This will be conducted at sites including Sydney's Concord Repatriation General Hospital.

If large-scale trials are successful, the <u>drug companies</u> would then need to apply for regulatory approval. So it would likely be at least five years before these drugs were on the market.

Will they replace tablets?

Although such long-acting injections could make it easier for people to stick with their treatment, they're unlikely to replace tablets any time soon.

Even if approved, initially at least these are likely to be prescribed for people at high risk or whose blood pressure is not adequately controlled by tablets.

Many people need more than one medicine to lower their blood pressure.



So it is likely these medicines would be used in addition to current therapies.

In a nutshell

Injectables are potentially the first new drug class for high blood pressure in decades. They would be administered every few weeks or months via regular injections rather than taking tablets every day or even several times a day.

If these progress successfully through <u>clinical trials</u> and receive regulatory approval, these injectables could be a game-changer in how we treat high blood pressure.

More information on <u>high blood pressure</u> is available from <u>Hypertension</u> <u>Australia</u>.

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