Rotigaptide

Also called: ZP-123; GAP-486; Rotigaptida

What it is

Rotigaptide (ZP-123, GAP-486) is a stable all-D-amino-acid antiarrhythmic hexapeptide that enhances connexin-43 gap-junction coupling (PMID 16415913). It prevented reentrant ventricular tachycardia in ischaemic dogs (PMID 12776869) and reduced infarct size in pigs (PMID 26750458), but had no effect on forearm blood flow in 27 healthy volunteers (PMID 18789901); its maker's phase 2 trials (NCT00124891) were terminated and it was never approved.

Approval status

Discontinued. Never approved anywhere. Developed by Zealand Pharma (as ZP-123) and licensed to Wyeth (as GAP-486), its three phase 2 trials in ventricular arrhythmia (NCT00124891, NCT00137293, NCT00137332) were all terminated in 2005-2006 with no results posted, and the programme did not advance; Wyeth instead took the oral follow-on danegaptide (GAP-134) forward. Later human work is limited to small academic forearm studies at the University of Edinburgh (NCT00901563, NCT07192744). ChEMBL records a highest clinical phase of 2. Drugs@FDA holds no application (searched November 4, 2026).

Dosing, as printed in the page's Recommended Dosing box

Used in human trials

No manufacturer dose exists for this use: these are amounts given in published trials, not recommendations.

Protocol and source	Dose	Frequency	Duration	Route
Forearm mechanistic study: healthy volunteers **[Human study]** PMID 18789901	0.25-25 nmol/min	Continuous infusion	During the study session	Intra-brachial (intra-arterial)

Educational information, not medical advice. Each dose above is tagged with its source: an approved label, a published human study, animal data, or amounts reported by users. None is a recommendation for you. An unapproved compound has no established safe or effective human dose, and products sold for "research use only" are not made or tested for people. Talk to a doctor before acting on anything on this site, including before you start, stop or change any medicine or dose.

Key human evidence

The 2 human studies carded on the page (28 study cards in all):

• **Protection of heart and artery from ischaemia-reperfusion injury** (Human, 2016). A two-part randomised, double-blind study. In pigs, a left-anterior-descending artery was blocked to cause a heart attack and rotigaptide (n = 9) or placebo (n = 10) was given into a vein before and during two hours of reperfusion; the treated pigs had a much smaller infarct, 18.7% of the area at risk against 43.6% (P = 0.006). In the human part, a short period of forearm ischaemia and reperfusion blunted the arteries' response to acetylcholine in people given placebo but not in those given rotigaptide into the artery, while the response to sodium nitroprusside was unchanged in both. The authors read this as protection of the artery lining. **PMID 26750458**

• **No effect on healthy forearm blood vessels in 27 volunteers** (Human, 2008). Forearm blood flow was measured in 27 healthy men during infusion of rotigaptide into the brachial artery at 0.25 to 25 nmol/min, given alone and together with vessel-dilating agents (acetylcholine, bradykinin, sodium nitroprusside), with and without aspirin and a technique that clamps nitric oxide. Rotigaptide did not change resting blood flow and did not alter the response to any of the dilators, nor did it change the release of the clot-dissolving factor t-PA that bradykinin triggers. The authors concluded that opening connexin-43 coupling does nothing to normal forearm vessels and left open whether it helps in vascular disease. **PMID 18789901**

Interactions

A PubMed search for interaction studies of this compound with any drug (November 4, 2026, 0 records) found none in people. That is not evidence that it is safe to combine with anything.

Side effects and cautions

Reported side effects	Contraindications and cautions
• No drug-related side effects reported in phase 1 trials that gave it intravenously to about 200 healthy people (PMID 17845503) • No effect on resting forearm blood flow or on the vessels' responses in 27 healthy volunteers (PMID 18789901) • In animals it did not change heart rate, blood pressure, the QT interval or left-ventricular pressure at antiarrhythmic doses (PMIDs 16344331, 12776869) • No binding of note across a panel of 80 receptors and ion channels, and no effect on the hERG channel at active concentrations (PMID 15877626) • A developer review reported no drug-related toxicity at plasma levels up to 77,000 times the active concentration (PMID 17845503) (1 more on the page)	• Investigational and discontinued: never approved anywhere, and its maker's phase 2 trials were terminated without results • No trial has tested whether it prevents arrhythmias, or is safe, in people with heart disease; human data are limited to small mechanistic studies • Its benefit in animals depended on the disease model and sometimes failed entirely (PMIDs 17224477, 15650154, 21493965) • It is not danegaptide (GAP-134), its oral follow-on, nor its parent peptide AAP10; results for those do not transfer • As an injectable research peptide it has no established dosing, formulation or purity standard for human use

Five questions to ask

1. Rotigaptide is listed here as "Discontinued". What does the evidence on this sheet mean for someone in my situation, and is there an approved treatment I should consider instead?
2. Here are the medicines and supplements I take. Do any of them interact with Rotigaptide? This sheet records none published, which does not mean none exist.
3. Which side effects should make me stop and call you, for example no drug-related side effects reported in phase 1 trials that gave it intravenously to about 200 healthy people?
4. Do any of the cautions on this sheet apply to me, such as: Investigational and discontinued: never approved anywhere, and its maker's phase 2 trials were terminated without results?

5. What should we check before I start and while I am on it (blood tests, blood pressure, weight), and how often?

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