



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/782147/2015
EMA/H/C/004062

EPAR summary for the public

Entresto

sacubitril / valsartan

This is a summary of the European public assessment report (EPAR) for Entresto. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Entresto.

For practical information about using Entresto, patients should read the package leaflet or contact their doctor or pharmacist.

What is Entresto and what is it used for?

Entresto is a heart medicine that contains the active substances sacubitril and valsartan. It is used in adults with long-term heart failure who have symptoms of the disease. Heart failure is the inability of the heart to pump enough blood around the body.

How is Entresto used?

Entresto is available as tablets (24 mg sacubitril / 26 mg valsartan, 49 mg sacubitril / 51 mg valsartan, and 97 mg sacubitril / 103 mg valsartan). Entresto can only be obtained with a prescription.

Entresto tablets are taken twice a day. The recommended starting dose is one tablet of Entresto 49 mg / 51 mg twice a day and the dose is then doubled after 2 to 4 weeks to 97 mg / 103 mg twice a day. The doctor may choose lower doses for certain patients. For further information, see the summary of product characteristic (also part of the EPAR).

How does Entresto work?

The two active substances in Entresto, sacubitril and valsartan, work in different ways. Sacubitril blocks the breakdown of natriuretic peptides produced in the body. Natriuretic peptides cause sodium and water to pass into the urine thereby reducing the strain on the heart. Natriuretic peptides also reduce blood pressure and protect the heart from developing fibrosis (scar tissues) that occurs in heart failure.



Valsartan is an 'angiotensin-II-receptor antagonist', which means that it blocks the action of a hormone called angiotensin II. The effects of angiotensin II can be harmful in patients with heart failure. By blocking the receptors to which angiotensin II normally attaches, valsartan stops the hormone's harmful effects on the heart and it also reduces blood pressure by allowing blood vessels to widen.

What benefits of Entresto have been shown in studies?

In the main study, Entresto was compared to enalapril, another medicine used for heart failure. Patients in the study had long-term heart failure with symptoms of the disease and reduced ejection fraction (the proportion of blood leaving the heart). In the group treated with Entresto, 21.8% (914 of 4,187) patients either died as a result of heart and circulation problems or were admitted to hospital with heart failure compared to 26.5% (1,117 of 4,212) patients treated with enalapril. In general, patients were monitored for about 27 months, during which they took the medicine for about 24 months on average. The study was stopped early because there was compelling evidence that Entresto was more effective than enalapril.

What are the risks associated with Entresto?

The most common side effects with Entresto (which may affect more than 1 in 10 people) are high blood potassium levels, low blood pressure and the kidneys working less well. A potentially severe side effect, angioedema (rapid swelling of deeper skin tissues as well as the tissues around the throat, causing breathing difficulty), can occur uncommonly (affecting fewer than 1 in 100 people). For the full list of all side effects reported with Entresto, see the package leaflet.

Entresto must not be taken with medicines known as ACE inhibitors (which are used to treat heart failure and high blood pressure). It must not be taken by patients who have suffered angioedema, those who have severe liver disease or by women who are pregnant. For the full list of restrictions see the package leaflet.

Why is Entresto approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Entresto's benefits are greater than its risks and recommended that it be approved for use in the EU. The main study found that Entresto reduced deaths from heart and circulation problems or hospital admissions for heart failure.

Entresto's serious side effects in the main study were similar to those of enalapril, which is already authorised for use in heart failure. Valsartan, one of the active substances in the medicine, is well established for the treatment of high blood pressure and heart failure; its side effects are well known.

What measures are being taken to ensure the safe and effective use of Entresto?

A risk management plan has been developed to ensure that Entresto is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Entresto, including the appropriate precautions to be followed by healthcare professionals and patients.

Further information can be found in the [summary of the risk management plan](#).

Other information about Entresto

The European Commission granted a marketing authorisation valid throughout the European Union for Entresto on 19 November 2015.

The full EPAR and risk management plan summary for Entresto can be found on the Agency's website: [ema.europa.eu/Find medicine/Human medicines/European public assessment reports](http://ema.europa.eu/Find%20medicine/Human%20medicines/European%20public%20assessment%20reports). For more information about treatment with Entresto, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 11-2015.