25 September 2015
EMA/CHMP/628846/2015
Press Office

Press release

New medicine to treat heart failure recommended for approval

Entresto brings a new mechanism of action to the treatment of heart failure

The European Medicines Agency (EMA) has recommended granting a marketing authorisation for Entresto (sacubitril/valsartan) for the treatment of adults with symptomatic chronic heart failure with reduced ejection fraction, a condition where the heart muscle does not contract effectively and less oxygen-rich blood is pumped out to the body. Around half of people with heart failure will have reduced ejection fraction.

Heart failure is a common and serious condition often caused by coronary artery disease (when the blood vessels supplying the heart become narrow), a heart attack or high blood pressure. Heart failure generally worsens over time. Although currently recommended treatments have improved the prognosis for people with heart failure, it remains a life-threatening disease which results in frequent hospital visits, and seriously impairs a patient's ability to enjoy an active life.

Standard medicines used for patients with heart failure are angiotensin converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) if ACE inhibitors are not tolerated by the patient, in conjunction with beta-blockers and/or mineralocorticoid antagonists (MRAs). These medicines have been available for many years.

Entresto is a combination of valsartan (an ARB) and sacubitril. Sacubitril is the first in a new class of medicines called neprilysin inhibitors. Entresto works in two ways – valsartan blocks the angiotensin II type-1 receptor, suppressing the harmful effects of angiotensin II on the cardiovascular system while sacubitril blocks an enzyme known as neprilysin to enhance the protective neurohormonal systems of the heart. Because of its mechanism of action Entresto should not be given together with another ARB or with an ACE inhibitor.

The efficacy of Entresto compared with enalapril (an ACE inhibitor) was assessed in one randomised controlled trial including over 8,000 adults with heart failure with reduced ejection fraction. Patients also received other heart failure medicines. Patients were included in the trial if they were able to tolerate treatment with Entresto, i.e. they did not need to stop treatment with Entresto due to side effects during a run-in period before the start of the trial. The trial was stopped early when it was found that Entresto was more effective than enalapril in reducing deaths from cardiovascular disease. The patients were followed for a median of 27 months. During the follow-up period 13.3% of the

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 8427 **Facsimile** +44 (0)20 3660 5555
E-mail press@ema.europa.eu **Website** www.ema.europa.eu

patients treated with Entresto died from cardiovascular disease compared with 16.5% of the patients treated with enalapril. The trial also found that Entresto reduced the number of patients who had to be hospitalised for heart failure. Although the patients included in the trial were previously treated with ACE inhibitors or ARBs, the Committee for Medicinal Products for Human Use (CHMP) concluded that a similar benefit can be expected in patients not previously treated with these medicines.

The most common side effects reported with Entresto were hypotension (low blood pressure), hyperkalaemia (abnormally high levels of potassium in the blood) and kidney impairment. Therefore, CHMP recommended that treatment should not be started in patients with low blood pressure or high potassium levels. A follow-up plan to monitor the safety of Entresto, including the risk of angioedema (swelling of the lips and throat), was agreed by the CHMP.

The company received scientific advice from the CHMP on quality, non-clinical and clinical aspects of the application. This is one of the Agency's main tools to facilitate and stimulate research and development within the European Union (EU).

The opinion adopted by the CHMP at its September 2015 meeting is an intermediary step on Entresto's path to patient access. The CHMP opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation. Once a marketing authorisation has been granted, each Member State will take a decision on price and reimbursement based on the potential role/use of this medicine in the context of its national health system.

Notes

1. This press release, together with all related documents, is available on the Agency's website.
2. The applicant for Entresto is Novartis Europharm Ltd.
3. Valsartan is an angiotensin-receptor blocker, which is already available in most EU Member States.
4. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

Contact our press officer

Monika Benstetter

Tel. +44 (0)20 3660 8427

E-mail: press@ema.europa.eu

Follow us on Twitter @EMA_News