

MEDIA RELEASE • MEDIA RELEASE • MEDIA RELEASE**New heart failure medicine LCZ696 (sacubitril valsartan) to be available to the NHS under the Early Access to Medicines Scheme (EAMS)**

- *Novartis's LCZ696 (sacubitril valsartan) is the first non-oncology drug to gain EAMS status under the Medicines and Healthcare products Regulatory Agency's (MHRA) programme for innovative medicines*
- *Novartis will provide LCZ696 (sacubitril valsartan) to the NHS for eligible patients enrolled in EAMS*

Frimley, September 1, 2015 – Novartis today announced that its investigational heart failure treatment LCZ696 (sacubitril valsartan) has been given a positive scientific opinion under the Medicines and Healthcare products Regulatory Agency (MHRA) Early Access to Medicines Scheme (EAMS) for patients with significant unmet medical need. This allows LCZ696 (sacubitril valsartan) to be made available to eligible patients before a final European licensing decision is made.

It is the first time a drug not intended to treat cancer has been recognised under EAMS.

Heart failure affects around 550,000 people in the UK and costs the NHS about £2.3bn a year^{1,2}. Heart failure has a poor prognosis: around 60% of patients diagnosed with heart failure die within five years³ and survival rates are worse than certain cancers, such as breast and prostate⁴.

"This is great news for patients with heart failure. The EAMS positive scientific opinion ensures patients with this debilitating condition can access sacubitril valsartan earlier than expected," said Prof Iain Squire, Professor of Cardiovascular Medicine, University of Leicester and Honorary Consultant Physician, University Hospitals of Leicester NHS Trust. "Based on what we've seen in clinical trials, access to this new medicine will help patients live longer and keep them out of hospital, compared to currently available treatment."

The MHRA has given LCZ696 (sacubitril valsartan) a positive scientific opinion based on the high level of unmet need in heart failure and data from the PARADIGM-HF study that showed LCZ696 (sacubitril valsartan) significantly improved patient outcomes compared to the current gold standard treatment, including a reduction both in cardiovascular deaths and hospitalisations due to heart failure⁵.

Hugh O'Dowd, General Manager at Novartis UK & Ireland, said: "Despite widespread use of available treatments and implementation of NICE guidelines, outcomes remain poor for those diagnosed with heart failure. So it's very encouraging that LCZ696 (sacubitril valsartan) will be available via the EAMS, allowing patients in the UK with this debilitating condition to gain benefit. We are working closely with the NHS to ensure eligible patients have rapid access under the scheme while we await the final European licensing decision."

Life Sciences Minister George Freeman said: "Heart failure is a devastating condition that affects hundreds of thousands of people in the UK, so I am delighted that patients will now be able to access this life-enhancing treatment. The UK's Early Access to Medicines Scheme is making a real difference in speeding up access to drugs and almost 300 patients with complex conditions have already received innovative treatments earlier than they otherwise would have thanks to the scheme."

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About LCZ696 (sacubitril valsartan) in heart failure

LCZ696 (sacubitril valsartan) is an ARNI (angiotensin receptor neprilysin inhibitor) and has a unique mode of action, which is thought to reduce the strain on the failing heart⁶. It harnesses the body's natural defences against heart failure, simultaneously acting to enhance the levels of natriuretic and other endogenous vasoactive peptides, while also inhibiting the renin-angiotensin-aldosterone system (RAAS)⁶.

In the Phase III trial, PARADIGM-HF, in patients with heart failure with a reduced ejection fraction, patients on LCZ696 (sacubitril valsartan) were significantly less likely to die from cardiovascular causes than those on the comparator, ACE-inhibitor enalapril⁵.

In PARADIGM-HF, LCZ696 (sacubitril valsartan)⁵:

- Reduced the risk of dying from a cardiovascular cause by 20% ($p=0.00004$) vs enalapril
- Reduced heart failure hospitalisations by 21% ($p=0.00004$) vs enalapril
- Reduced the risk of dying from any cause by 16% ($p=0.0005$) vs enalapril
- Overall there was a 20% risk reduction on the primary endpoint, a composite measure of CV death or heart failure hospitalisation ($p=0.0000002$).

Patients' reports of how they felt and doctors' assessments of disease severity were also significantly better with LCZ696 (sacubitril valsartan) than enalapril⁷.

About the Early Access to Medicines Scheme

The Early Access to Medicines Scheme (EAMS), which is run by the Medicines and Healthcare products Regulatory Agency (MHRA), aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation when there is a clear unmet medical need.

Under the scheme, the MHRA gives a scientific opinion on the benefit/risk balance of the medicine, based on the data available when the EAMS submission is made. The opinion lasts for a year and can be renewed. The scheme is voluntary and the opinion from MHRA does not replace the normal licensing procedures for medicines.

The scientific opinion is provided after a two-step evaluation process: the promising innovative medicine (PIM) designation and then the early access to medicines scientific opinion. LCZ696 (sacubitril valsartan) was awarded the PIM designation in April 2015, based on the results of the PARADIGM-HF trial. More information is available on the MHRA website at <https://www.gov.uk/apply-for-the-early-access-to-medicines-scheme-eams>.

About heart failure

Around 550,000 people in the UK have heart failure¹; both the incidence and prevalence of heart failure increase with age⁴. The risk of heart failure is higher in men than in women but there are more women than men with heart failure due to population demographics⁴. The most common cause of heart failure in the UK is coronary artery disease⁴. Heart failure has a poor prognosis: 60% of patients diagnosed with heart failure die within five years³. Survival rates are similar to those for cancer of the colon, and worse than those from cancer of the breast or prostate⁴. Heart failure has a major impact on quality of life and is associated with mood disorders⁴.

On average, a general practitioner looks after 30 patients with heart failure and will diagnose ten new heart failure patients annually⁴. Heart failure accounts for a total of 1 million inpatient bed days – 2% of all NHS inpatient bed-days – and 5% of all emergency medical admissions to hospital⁴. It is estimated that the total annual cost of heart failure to the NHS is around 2% of the total NHS budget: approximately 70% of this total is due to the costs of hospitalisation⁴. As well as NHS costs, heart failure also places a burden on other agencies such as social services and the benefits system, and of course on the patients with heart failure and their families and caregivers⁴.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as “being investigated,” “thought,” “plans,” “growing,” or similar terms, or by express or implied discussions regarding potential marketing approvals for LCZ696 (sacubitril valsartan), or regarding potential future revenues from LCZ696 (sacubitril valsartan). You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialise, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that LCZ696 (sacubitril valsartan) will be approved for sale in any market, or submitted for approval in any additional markets, or at any particular time. Neither can there be any guarantee that LCZ696 (sacubitril valsartan) will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that LCZ696 (sacubitril valsartan) will be commercially successful in the future. In particular, management’s expectations regarding LCZ696 (sacubitril valsartan) could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company’s ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected manufacturing issues, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2014, the Group achieved net sales of USD 58.0 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 120,000 full-

time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit <http://www.novartis.com>.

¹ British Heart Foundation. At-home treatment for heart failure patients eases burden for families and for NHS. 9 June 2015. Available at: <https://www.bhf.org.uk/news-from-the-bhf/news-archive/2015/june/at-home-treatment-for-heart-failure-patients-eases-burden-for-families-and-for-nhs> Last accessed August 2015

² NHS Choices. The NHS in England. About the National Health Service (NHS). January 2015. Available at <http://www.nhs.uk/NHSEngland/thenhs/about/Pages/overview.aspx> Last accessed August 2015.

³ Sutherland K. Bridging the quality gap: heart failure. 2010. London. Health Foundation. Available from: http://www.health.org.uk/sites/default/files/BridgingTheQualityGapHeartFailure_0.pdf Last accessed August 2015

⁴ National Clinical Guideline Centre. Chronic heart failure: the management of chronic heart failure in adults in primary and secondary care. 2010. London: National Clinical Guideline Centre. Available from: <http://guidance.nice.org.uk/CG108/Guidance/pdf/English> Last accessed August 2015

⁵ McMurray JJV, *et al.* Angiotensin-Neprilysin Inhibition versus Enalapril in Heart Failure. *N Engl J Med.* 2014;371:993-1004

⁶ Langenickel TH and Dole WP. Angiotensin receptor-neprilysin inhibition with LCZ696: a novel approach for the treatment of heart failure. *Drug Discov Today Ther Strateg.* 2012;9:e131-e139

⁷ Packer M, *et al.* Angiotensin-Neprilysin Inhibition and Clinical Progression in Surviving Patients with Heart Failure *Circulation.* 2015;131:54-61