



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Positive opinion on the marketing authorisation for Nerlynx (neratinib)

Outcome of re-examination

On 28 June 2018 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending marketing authorisation for the medicinal product Nerlynx for the treatment of patients with a type of breast cancer called early-stage hormone-receptor positive, HER2-positive breast cancer. The company that applied for authorisation is Puma Biotechnology Ltd.

On 22 February 2018, the CHMP had originally adopted a negative opinion for Nerlynx for broader use in HER2-positive early breast cancer. At the request of the applicant, the CHMP started a re-examination of its opinion. Following the re-examination, the CHMP adopted a final positive opinion on 28 June 2018, but in a restricted patient population.

What is Nerlynx?

Nerlynx is a medicine that contains the active substance neratinib. It is to be available as tablets.

What is Nerlynx expected to be used for?

Nerlynx is expected to be used to treat adults with early breast cancer who have undergone surgery, to reduce the risk of their cancer coming back. Nerlynx is expected to be given for one year, following treatment with another medicine, trastuzumab, for the same purpose. It is intended for use only in breast cancers that produce high levels of a protein called HER2, which helps cells to divide and grow (HER2-positive breast cancer), and that also have receptors (targets) for the female sex hormones (hormone-receptor positive breast cancer).

How does Nerlynx work?

The active substance in Nerlynx, neratinib, is a type of cancer medicine called a tyrosine kinase inhibitor. It attaches to the HER2 protein on the cancer cells, and so blocks its action. Because HER2 helps cancer cells to grow and divide, blocking it helps to stop them growing and prevent the cancer coming back.



What did the company present to support its application?

The company provided the results from one main study involving 2,840 women with early breast cancer with high levels of HER2 who had already received treatment that included trastuzumab. In these women, daily treatment with Nerlynx for a year was compared with placebo (a dummy treatment). The main measure of effectiveness was the proportion of women who had lived without the cancer coming back at the end of the 2-year study.

What were the CHMP's main concerns that led to the initial negative opinion?

The CHMP noted that a greater proportion of women given Nerlynx in the study lived for 2 years without their disease coming back than women given placebo (around 94% versus 92% respectively). However, it was uncertain that this difference in benefit would be seen in clinical practice. Furthermore, Nerlynx causes side effects in the digestive system, particularly diarrhoea, which affected most patients and might be severe and difficult to manage. The Committee therefore concluded that the benefits were not enough to outweigh the risk of side effects and recommended that Nerlynx be refused marketing authorisation.

What happened during the re-examination?

During the re-examination the CHMP looked again at all the data and considered whether there would be a group of patients where the benefits outweighed the risks.

What were the conclusions of the CHMP following the re-examination?

Following its review of the data and discussion within the Committee, the CHMP noted that benefits seemed to be largely confined to patients whose cancer was hormone-receptor positive.

The Committee therefore concluded that the benefits of the medicine would outweigh its risks if the medicine's use were restricted to treatment of early breast cancer that not only had high levels of HER2 but was also hormone-receptor positive. Measures would need to be put in place to manage Nerlynx' side effects.

The summary of the positive opinion of the CHMP is available on the Agency's website: [ema.europa.eu/Find medicine/Human medicines/Pending EC decisions](http://ema.europa.eu/Find%20medicine/Human%20medicines/Pending%20EC%20decisions).