26 September 2014
EMA/587197/2014
EMEA/H/C/000983/II/11

Questions and answers

Refusal of a change to the marketing authorisation for Javlor (vinflunine)

On 25 September 2014, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of a change to the marketing authorisation for the medicinal product Javlor. The change concerned an extension of indication to add treatment of breast cancer.

The company that applied for the change to the authorisation is Pierre Fabre Médicament. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Javlor?

Javlor is a cancer medicine that has been authorised in the EU since September 2009. It is already used to treat adults with advanced or metastatic 'transitional-cell carcinoma of the urothelial tract' (a cancer that affects the lining of the bladder and the rest of the urinary tract). 'Metastatic' means that the cancer has spread to other parts of the body.

Javlor contains the active substance vinflunine and is available as a concentrate for solution for infusion (drip) into a vein.

What was Javlor expected to be used for?

Javlor was also expected to be used in combination with the cancer medicine capecitabine for the treatment of adult patients with locally advanced or metastatic breast cancer. It was to be used in patients previously treated with, or resistant to, another type of cancer medicine called an anthracycline and who are also resistant to a third type of cancer medicines called taxanes.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

How is Javlor expected to work?

The active substance in Javlor, vinflunine, belongs to the group of cancer medicines known as 'vinca alkaloids'. It attaches to a cell protein called tubulin, which is important in the formation of the internal 'skeleton' that cells need to allow them to divide. By attaching to tubulin in cancer cells, vinflunine stops the formation of the skeleton, preventing the division and spread of the cancer cells.

What did the company present to support its application?

The company presented the results of a main study involving 770 patients with advanced breast cancer previously treated with or resistant to an anthracycline and who are taxane resistant. In the study, Javlor given together with capecitabine was compared with capecitabine alone. The main measure of effectiveness was progression-free survival (how long patients lived without their disease getting worse).

What were the CHMP's main concerns that led to the refusal of the change to the marketing authorisation?

The CHMP noted that the effectiveness of Javlor in combination with capecitabine had not been sufficiently demonstrated. Although there was an improvement in progression-free survival, this was considered to be small. In addition, there was no benefit in terms of other important measures of effectiveness, including overall survival (how long patients lived). Compared with patients given capecitabine alone, more patients receiving Javlor plus capecitabine experienced side effects including neutropenia (abnormally low blood levels of white blood cells), gastrointestinal events such as constipation, nausea and vomiting and stomach ache, fatigue and nervous system disorders such as damage to the nerves in the extremities.

Therefore, at that point in time, the CHMP was of the opinion that the modest effect of Javlor in the treatment of breast cancer did not outweigh the additional risks observed. Hence, the CHMP recommended that the change to the marketing authorisation be refused.

What consequences does this refusal have for patients in clinical trials or compassionate use programmes?

The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Javlor.

If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening with Javlor for the treatment of transitional-cell carcinoma of the urothelial tract?

There are no consequences on the use of Javlor in its authorised indication.

The full European Public Assessment Report for Javlor can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.