European Medicines Agency

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Questions and answers on the withdrawal of the marketing application for Orplatna

International non-proprietary name (INN): ***satraplatin***

On 1 August 2008, Pharmion Ltd. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Orplatna, for the treatment of patients with metastatic hormone-refractory prostate cancer who have failed prior chemotherapy.

What is Orplatna?
Orplatna is a medicine that contains satraplatin as the active substance. It was to be available as capsules to be taken by mouth containing 10 or 50 mg satraplatin.

What was Orplatna expected to be used for?
Orplatna was expected to be used to treat prostate cancer. This is cancer that affects the prostate gland, the gland below the bladder in men that produces the liquid in the semen. The medicine was to be used with prednisone or prednisolone (anti-inflammatory medicines) in patients who had failed to respond to other anti-cancer medicines, when their cancer had spread from the original site to other parts of the body (metastatic) and had been shown to be 'hormone-refractory'. This means that the cancer does not respond to hormonal treatment.

How is Orplatna expected to work?
The active substance in Orplatna, satraplatin, is a cytotoxic (a medicine that kills cells that are dividing, such as cancer cells) that belongs to the group 'platinum compounds'. These compounds are made from the metal platinum. In the body, satraplatin is expected to attach itself to the DNA within cells, stopping them reproducing. As a result, it is expected to stop the growth of tumour cells, which eventually die.

What documentation did the company present to support its application to the CHMP?
The effects of Orplatna were first tested in experimental models before being studied in humans. One main study compared the effectiveness of adding Orplatna or placebo (a dummy treatment) to prednisone in 950 patients with metastatic hormone-refractory prostate cancer in whom at least one previous treatment had failed. The main measure of effectiveness was 'progression-free survival' (the time taken for the disease to get worse) as well as overall survival time. Progression-free survival was measured using a 'composite' method, which means that there was more than one symptom that could be used as a measure. In this instance, progression could be measured as the appearance of new tumours as detected during a scan, the appearance of new bone problems, the progression of symptoms (such as pain, weight loss or problems with urination), or death.

How far into the evaluation was the application when it was withdrawn?
The application was at day 180 when the company withdrew. After the CHMP had assessed the responses from the company to a list of questions, there were still some unresolved issues outstanding. The CHMP normally takes up to 210 days to evaluate a new application. Based on the review of the initial documentation, the CHMP prepares a list of questions at day 120, which is sent to the company. Once the company has supplied responses to the questions, the CHMP reviews them and may, before

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giving an opinion, ask any remaining questions at day 180. Following the CHMP's opinion, it usually takes around two months for the European Commission to grant a licence.

What was the recommendation of the CHMP at that time?
Based on the review of the data and the company's response to the CHMP's list of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Orplatna could not have been approved for the treatment of metastatic hormone-refractory prostate cancer.

What were the main concerns of the CHMP?
The CHMP was concerned that the effectiveness of Orplatna had not been sufficiently shown. Compared with placebo, Orplatna did not increase overall survival time, and the small improvement seen in progression-free survival was not considered relevant in the absence of a benefit in terms of overall survival time. In addition, the CHMP had concerns over the composite measure of progression-free survival which the Committed noted had not been sufficiently justified.
The Committee also noted that docetaxel is the standard first-line treatment for hormone-refractory prostate cancer, and that it is likely that most patients who would benefit from Orplatna treatment would have failed docetaxel treatment. However, the Committee was concerned that the patients in the main study who had previously treated been with docetaxel had more side effects when taking Orplatna than the patients who had received other medicines for their cancer before the study.
Therefore, at the time of the withdrawal, the CHMP's view was that a benefit of Orplatna had not been sufficiently demonstrated and any benefits did not outweigh the identified risks.

What were the reasons given by the company to withdraw the application?
The letter from the company notifying the EMEA of the withdrawal of the application is available here.

What are the consequences of the withdrawal for patients undergoing clinical trials / compassionate use programmes with Orplatna?
The company informed the CHMP that Orplatna will continue to be made available for patients included in ongoing clinical trials.
If you are in a clinical trial or compassionate use programme and need more information about your treatment, contact the doctor who is giving it to you.