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Refusal of the marketing authorisation for Cabazitaxel Teva (cabazitaxel)

On 26 April 2019, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Cabazitaxel Teva, intended for the treatment of prostate cancer.

The company that applied for authorisation is Teva B.V. It may request a re-examination of the opinion within 15 days of receipt of notification of this negative opinion.

What is Cabazitaxel Teva?

Cabazitaxel Teva is a cancer medicine that contains the active substance cabazitaxel. It was to be available as a concentrate to be made into a solution for infusion (drip) into a vein.

Cabazitaxel Teva was developed as a 'hybrid medicine'. This means that Cabazitaxel Teva was intended to be similar to a 'reference medicine' containing the same active substance and already authorised in the European Union. The company made reference to two medicines, Jevtana (containing cabazitaxel) and Taxotere (containing docetaxel, see below for more details).

For more information on hybrid medicines, see the question-and-answer document here.

What was Cabazitaxel Teva expected to be used for?

Cabazitaxel Teva was expected to be used to treat men with prostate cancer, a cancer that affects the prostate gland (which produces the liquid in semen). Cabazitaxel Teva was to be used when the cancer had spread to other parts of the body (metastatic) despite treatments to prevent the production of testosterone or after surgical removal of the testes (castration). Cabazitaxel Teva was to be used in combination with prednisone or prednisolone (anti-inflammatory medicines) in patients who have previously been treated with docetaxel (another cancer medicine).

How does Cabazitaxel Teva work?

Cabazitaxel Teva is expected to work in the same way as the reference medicine, Jevtana. Cabazitaxel belongs to the group of cancer medicines known as 'taxanes'. Cabazitaxel works by blocking the ability

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of cancer cells to break down their internal 'skeleton' that allows them to divide and multiply. With their skeleton still in place, the cells cannot divide and they eventually die. Cabazitaxel also affects non-cancer cells, such as blood and nerve cells, which can cause side effects.

What did the company present to support its application?

Because Cabazitaxel Teva was developed as a hybrid medicine, the company presented data from the published literature to demonstrate that it is similar to Jevtana. There was no need for 'bioequivalence' studies to investigate whether Cabazitaxel Teva is absorbed similarly to Jevtana to produce the same level of the active substance in the blood. This is because Cabazitaxel Teva is given by infusion into a vein, so the active substance is delivered straight into the bloodstream.

The applicant also made reference to another medicine, Taxotere, which contains docetaxel. The company claimed that cabazitaxel is a derivative of docetaxel, and that the active substances do not differ significantly in their safety and effectiveness. To support this claim, the company referred to published data and provided an expert opinion.

What were the CHMP's main concerns that led to the refusal?

The CHMP did not agree that the data presented by the company were sufficient to support the claim that cabazitaxel and docetaxel should be considered the same active substance. Although cabazitaxel is a derivative of docetaxel, laboratory studies have shown that cabazitaxel and docetaxel have different properties, for example cabazitaxel can cross the blood-brain barrier while docetaxel cannot. Additionally, laboratory data suggest that cabazitaxel can be effective at treating cancer that is resistant to docetaxel. Data from clinical studies also showed differences in the safety profile of the two active substances. Furthermore, patients receiving cabazitaxel are exposed to the unchanged substance plus two active breakdown products, which are not formed when docetaxel is given.

Based on these findings, the CHMP was of the opinion that it cannot be concluded that cabazitaxel and docetaxel do not differ significantly with regard to safety and effectiveness. Thus Taxotere cannot be used to support the application for Cabazitaxel Teva and the CHMP recommended that Cabazitaxel Teva be refused marketing authorisation.

What consequences does this refusal have for patients in clinical trials?

The company informed the CHMP that there are no ongoing clinical trials with Cabazitaxel Teva in the EU.