European Medicines Agency

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Questions and answers on the withdrawal of the marketing application for Vorinostat MSD

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

On 13 February 2009 Merck Sharp & Dohme Limited officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Vorinostat MSD, for the treatment of adults with advanced cutaneous T-cell lymphoma. Vorinostat MSD was designated as an orphan medicinal product on 21 June 2004.

What is Vorinostat MSD?
Vorinostat MSD is a medicine that contains the active substance vorinostat. It was to be available as capsules.

What was Vorinostat MSD expected to be used for?
Vorinostat MSD was expected to be used to treat adults with advanced cutaneous T-cell lymphoma (CTCL). CTCL is a rare type of lymphoma (cancer of the lymph tissue) where some white blood cells (T-cells) grow in the skin. Vorinostat MSD was to be used in patients whose cancer was progressive (getting worse), persistent (not responding to treatment) or recurrent (kept on coming back), and had not responded to at least two other systemic (whole-body) treatments.

How is Vorinostat MSD expected to work?
The active substance in Vorinostat MSD, vorinostat, blocks the activity of proteins called histone deacetylases, which are involved in turning genes 'on' and 'off' within cells. In CTCL, Vorinostat MSD was expected to stop the genes that suppress the division and growth of the tumour cells from being turned off at the appropriate times. This was expected to lead to a reduction in the growth and division of the T-cells.

What documentation did the company present to support its application to the CHMP?
The effects of Vorinostat MSD were first tested in experimental models before being studied in humans.
The company presented the results of one main study in which 74 adults with advanced CTCL were given Vorinostat MSD. All of the patients had progressive, persistent or recurrent disease and had received two other systemic treatments. Vorinostat MSD was not compared with any other treatment. The main measure of effectiveness was based on the change in how much of the skin was affected by the disease and the severity of the skin lesions.

How far into the evaluation was the application when it was withdrawn?
The application was at day 206 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 Committee prepares a list of questions at day 120, which is sent to the company. Once the company has supplied responses to the questions, the Committee reviews them and may, before giving an opinion, ask any remaining questions at day 180. Following the Committee's opinion, it usually takes around two months for the European Commission to grant a licence.

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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 list of questions, at the time of the withdrawal, the Committee had some concerns and was of the provisional opinion that Vorinostat MSD could not have been approved for the treatment of advanced CTCL.

What were the main concerns of the CHMP?
The Committee was concerned over the way the main study was designed. Because Vorinostat MSD was not compared with any other treatment, its safety and effectiveness could not be adequately assessed. In addition, the study did not look at how long the patients survived. In particular, the CHMP was concerned about the risk of thromboembolic events (problems caused by the formation of clots in the blood vessels) in patients taking Vorinostat MSD.
Therefore, at the time of the withdrawal, the Committee's view was that a benefit of Vorinostat MSD 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 or compassionate use programmes with Vorinostat MSD?
The company informed the CHMP that there are no consequences on patients currently included in clinical trials, compassionate use programmes or named patient programmes with Vorinostat MSD.
If you are in a clinical trial, compassionate use programme or a named patient programme and need more information about your treatment, contact the doctor who is giving it to you.