European Medicines Agency

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Questions and answers on the withdrawal of the marketing authorisation application for Zunrisa
casopitant

On 25 September 2009, Glaxo Group Ltd officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Zunrisa, for the prevention of nausea and vomiting in patients undergoing surgery or receiving chemotherapy.

What is Zunrisa?
Zunrisa is a medicine that contains the active substance casopitant. It was expected to be available as tablets (50 and 150 mg).

What was Zunrisa expected to be used for?
Zunrisa was expected to be used in combination with other medicines to prevent nausea and vomiting in patients receiving chemotherapy treatments (medicines to treat cancer) that are moderate or strong triggers of nausea and vomiting.
Zunrisa was also expected to be used with other medicines to prevent nausea and vomiting in patients undergoing surgery.

How is Zunrisa expected to work?
The active substance in Zunrisa, casopitant, is a 'neurokinin 1 (NK1) receptor antagonist'. It blocks a chemical in the body called substance P from attaching to the NK1 receptors. When substance P attaches to these receptors, it can cause nausea and vomiting. By blocking the receptors, casopitant was expected to prevent nausea and vomiting which often happens during chemotherapy or as a complication of surgery.

What documentation did the company present to support its application to the CHMP?
The effects of Zunrisa were first tested in experimental models before being studied in humans. The company presented data from large studies in cancer patients receiving chemotherapy. The patients were given a combination of Zunrisa with two other medicines (dexamethasone and ondansetron) or the combination without Zunrisa. The main measure of effectiveness was the number of patients who did not vomit or needed to be given rescue medication for vomiting in the first five days following the start of a cycle of chemotherapy.
The company also presented data from studies in patients at a high risk of having nausea and vomiting after surgery. The patients received Zunrisa with ondansetron or ondansetron alone. The main measure of effectiveness for the study was the number of patients who did not vomit or needed to be given any rescue medication in the first 24 hours after surgery.

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.
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 issue a decision on this opinion.

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 CHMP had some concerns and was of the provisional opinion that Zunrisa could not have been approved for use with other medicines in the prevention of nausea and vomiting in patients receiving chemotherapy or in those undergoing surgery.

What were the main concerns of the CHMP?
After looking at the results of the main studies, the CHMP noted that, while the studies showed that Zunrisa was effective in some cancer patients receiving chemotherapy, its use in patients receiving chemotherapy treatments that are moderate triggers of nausea and vomiting was not fully supported by the results. The Committee also asked the company to reconsider the target population for patients having surgery to ensure it adequately reflected the kind of patients who were involved in the studies.

What were the reasons given by the company for withdrawing the application?
The letter from the company notifying the CHMP of the withdrawal of the application is available here.

What are the consequences of the withdrawal for patients in clinical trials or compassionate use programmes using Zunrisa?
The company informed the CHMP that at the time of the withdrawal one clinical trial with Zunrisa was ongoing. However that trial was being stopped. If you are a patient in this trial and need more information about your treatment, contact the doctor who is treating you.