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Questions and answers

Withdrawal of the marketing authorisation application for Zenhale (mometasone furoate/formoterol fumarate)

On 5 November, Schering-Plough Europe officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Zenhale, for the maintenance treatment of asthma.

What is Zenhale?

Zenhale is a medicine that contains the active substances mometasone furoate and formoterol fumarate. It was to be available as a suspension for inhalation in a metered-dose inhaler.

What was Zenhale expected to be used for?

Zenhale was expected to be used in adults and adolescents aged 12 years and older as a maintenance treatment for asthma, including for reducing exacerbations (where asthma gets worse, requiring rescue treatment with other medicines).

It was developed for use in patients whose asthma was not adequately controlled by an inhaled corticosteroid used, when needed, with an inhaled short-acting 'beta-2 agonist' (a bronchodilator, a medicine that widens the airways in the lungs). It was also expected to be used in patients whose asthma was already controlled with both an inhaled corticosteroid and a long-acting beta-2 agonist.

How is Zenhale expected to work?

Both formoterol and mometasone have been available in the European Union for the maintenance treatment of asthma for a number of years.

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Mometasone is a corticosteroid with anti-inflammatory effects. When inhaled, it relieves the symptoms of asthma by blocking the release from white blood cells of substances that are involved in inflammatory reactions in the airways.

Formoterol is a long-acting beta-2 agonist. It works by attaching to beta-2 receptors that are found in the muscle cells of many organs and that cause the muscles to relax. When inhaled, it causes the muscles of the airways to relax, helping to keep the airways open and allowing the patient to breathe more easily.

What did the company present to support its application?

The effects of Zenhale were first tested in experimental models before being studied in humans.

There were four main studies involving a total of 2,977 adults and adolescents who had been receiving treatment with inhaled corticosteroids or a combination of inhaled corticosteroid and a long-acting beta-2 agonist.

The patients were treated with one of the following: Zenhale, mometasone furoate alone, formoterol fumarate alone, an asthma medicine containing fluticasone propionate and salmeterol (another combination of a steroid and a long-acting bronchodilator used in asthma), or placebo (a dummy treatment).

The main measures of effectiveness in the studies were based on the change in FEV_1 after 12 weeks. FEV_1 is the most air a person can breathe out in one second. Two studies also looked at the how long it took before the patients had their first severe exacerbation.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after ‘day 181’. This means that the CHMP had evaluated the documentation provided by the company and formulated a list of questions. After the CHMP had assessed the company’s responses to the last round of questions, there were still unresolved issues.

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 lists of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Zenhale could not have been approved for the maintenance treatment of asthma.

Following a routine inspection of study sites, the CHMP had concerns over the way the studies were conducted in some sites, which cast doubt on the reliability of the results. The CHMP also had concerns with one of the comparator medicines, mometasone furoate, which was not in an approved formulation. The company was asked to provide further data to justify the use of that comparator, specifically to show how mometasone furoate in the comparator was released in the body compared with the approved mometasone furoate.

What were the reasons given by the company for withdrawing the application?

The letter from the company notifying the Agency of the withdrawal of the application is available under the tab ‘All documents’.

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

The company informed the CHMP that this withdrawal does not have any consequences for patients in ongoing trials or on compassionate use programmes.