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Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Exelon and Prometax (rivastigmine)

On 14 March 2012, Novartis Europharm Ltd. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for an extension of indication for Exelon and Prometax, to add the use of the transdermal patch for the treatment of mild to moderately severe dementia in patients with Parkinson's disease.

What are Exelon and Prometax?

Exelon and Prometax are medicines containing the active substance rivastigmine. They are available as capsules, an oral solution and transdermal patches (patches that deliver the medicine across the skin).

Exelon and Prometax have been authorised in the EU since May 1998. All forms of the medicine can be used for the treatment of patients with mild to moderately severe Alzheimer's dementia, a progressive brain disorder that gradually affects memory, intellectual ability and behaviour.

The capsules and oral solution can also be used to treat mild to moderately severe dementia in patients with Parkinson's disease.

What were Exelon and Prometax expected to be used for?

The transdermal patches of Exelon and Prometax were also expected to be used to treat mild to moderately severe dementia associated with Parkinson's disease, which can already be treated using the capsules and oral solution.

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How are Exelon and Prometax expected to work?

The transdermal patches are expected to work in the same way as the capsules and oral solution. In patients with dementia associated with Parkinson's disease, certain nerve cells die in the brain, resulting in low levels of the neurotransmitter acetylcholine (a substance that allows nerve cells to communicate with each other). The active substance in Exelon and Prometax, rivastigmine, works by blocking the enzymes that break down acetylcholine: acetylcholinesterase and butyrylcholinesterase. By blocking these enzymes, rivastigmine allows levels of acetylcholine to be increased in the brain, helping to reduce the symptoms of dementia in patients with Parkinson's disease.

What did the company present to support its application?

The company presented the results of a study designed to assess the long-term effects of the capsule and transdermal patch in 583 patients with mild to moderately severe dementia associated with Parkinson's disease. About half of the patients took the capsule, and half were treated with the patch, for 76 weeks. This study was originally designed to assess the long-term safety of the capsules, but the company later extended its aim to include the assessment of the benefits and risks of the transdermal patch in the treatment of dementia associated with Parkinson's disease. The company also presented a 'pharmacokinetic' analysis of the way rivastigmine from the patch is handled in the body when given to patients with dementia associated with Parkinson's disease, compared with what is seen in patients with Alzheimer's dementia.

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

The application was withdrawn after 'day 90'. This means that the CHMP had evaluated the documentation provided by the company and formulated lists of questions. After the CHMP had assessed the company's responses to the questions, there were still some 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 the transdermal patch could not have been approved for the treatment of mild to moderately severe dementia associated with Parkinson's disease.

The Committee was concerned that the new study was not sufficient to conclude on the effectiveness of the patch in patients with dementia associated with Parkinson's disease. The company had presented pharmacokinetic data showing that, when using the patch, rivastigmine levels in patients with Parkinson's disease were similar to the levels seen in patients with Alzheimer's, but the CHMP noted that the dementia in the two diseases was different and could respond differently to treatment. The Committee therefore considered that the pharmacokinetic data were not sufficient to draw conclusions on the effectiveness of the patch and that additional data would be required.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Exelon/Prometax transdermal patch in the treatment of mild to moderately severe dementia associated with Parkinson's disease were uncertain and did not outweigh its risks.

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

In its official letter, the company stated that it decided to withdraw the application after the CHMP indicated that in order to conclude on a favourable approval additional data was required, which could not be generated within the allowed timeframe.

The withdrawal letter can be found here.

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

The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Exelon or Prometax.

If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening with Exelon and Prometax in their authorised indications?

There are no consequences on the use of Exelon and Prometax in their authorised indications.

The full European Public Assessment Report for Exelon can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.

The full European Public Assessment Report for Prometax can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.