



European Medicines Agency

London, 19 March 2008
Doc. Ref. EMEA/CHMP/125421/2008

**QUESTIONS AND ANSWERS ON THE WITHDRAWAL OF THE MARKETING
APPLICATION
for
PRISTIQS**

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

On 10 March 2008, Wyeth Europe Ltd officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Pristiqs, for the treatment of vasomotor symptoms (hot flushes) associated with the menopause.

What is Pristiqs?

Pristiqs is a medicine containing the active substance desvenlafaxine. It was to be available as 50 and 100 mg tablets.

What was Pristiqs expected to be used for?

Pristiqs was expected to be used to treat hot flushes associated with the menopause in women.

How is Pristiqs expected to work?

The active substance in Pristiqs, desvenlafaxine, is a 'serotonin-noradrenaline re-uptake inhibitor' (SNRI). It works by preventing the neurotransmitters 5-hydroxytryptamine (also called serotonin) and noradrenaline from being taken back up into nerve cells in the brain.

Neurotransmitters are chemicals that allow certain nerve cells to communicate with one another. By blocking their re-uptake, desvenlafaxine increases the amount of these neurotransmitters in the spaces between these nerve cells, increasing the level of communication between the cells.

The reasons why menopausal women have hot flushes are unclear, but since 5-hydroxytryptamine and noradrenaline seem to be involved, desvenlafaxine was expected to help to reduce these symptoms.

What documentation did the company present to support its application to the CHMP?

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

The efficacy of Pristiqs was studied in three main studies involving a total of 1,510 women who were having at least seven moderate or severe hot flushes a day. Two of the studies (1,025 women) compared Pristiqs with placebo (a dummy treatment). The third study (485 women) compared Pristiqs with placebo and with tibolone (another type of medicine used to manage hot flushes). This study included women from Europe.

The main measures of efficacy were the change in the number of hot flushes per day and the change in their severity over the first 12 weeks of treatment.

How far into the evaluation was the application when it was withdrawn?

The application was at day 193 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 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 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 grant a licence.

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 Pristiqs could not have been approved for the treatment of vasomotor symptoms associated with the menopause.

What were the main concerns of the CHMP?

The CHMP was concerned that the results were not consistent across the three main studies: in particular, the study including European women did not confirm the benefits seen in the other two studies. The CHMP was concerned that a meaningful benefit of Pristiqs had not been demonstrated, when considered alongside the safety of the medicine in postmenopausal women, including side effects after stopping treatment.

Therefore, at the time of the withdrawal, the CHMP's view was that the benefit of Pristiqs had not been sufficiently demonstrated and any potential 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 Pristiqs?

The company informed the CHMP that there are no clinical trials or compassionate use programmes ongoing with Pristiqs in the treatment of hot flushes associated with the menopause.