26 July 2013
EMA/447220/2013
EMEA/H/C/000833/II/18

Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Effentora (fentanyl)

On 11 July 2013, Teva Pharma B.V. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a new indication for Effentora, to extend the treatment for breakthrough pain to adult patients with chronic (long-term) persistent pain from causes other than cancer.

What is Effentora?

Effentora is a medicine that contains the active substance fentanyl. It is already used to treat 'breakthrough' pain in adults with cancer who are using opioid painkillers to control long-term cancer pain. Breakthrough pain is when a patient experiences additional, sudden pain in spite of ongoing treatment with painkillers.

Effentora is available as 'buccal tablets' (tablets that dissolve in the mouth). It has been authorised in the European Union since 4 April 2008.

What was Effentora expected to be used for?

Effentora was also expected to be used to treat breakthrough pain in adults with long-term persistent pain from causes other than cancer, who were already receiving regular treatment with opioids to control their persistent pain.

How was Effentora expected to work?

In adults with long-term pain due to causes other than cancer, Effentora was expected to work in the same way as it does in adults with cancer pain.

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The active substance in Effentora, fentanyl, is an opioid. It is a well-known substance, which has been used to control pain for many years. In Effentora, it is given as a buccal tablet, so that fentanyl is absorbed through the lining of the mouth. Once absorbed, fentanyl acts on receptors in the brain and spinal cord to control pain.

What did the company present to support its application?

The applicant presented data from 3 main studies in adults with breakthrough pain already using opioids. The effects of Effentora were compared with those of placebo (a dummy treatment) in 79 patients with neuropathic pain (pain due to nerve damage) in one study, and in 77 patients with low-back pain in a second study. The duration of treatment was determined by the time needed by each patient to control 9 episodes of breakthrough pain within a 21-day period. The third study, which lasted for 12 weeks, looked at the effects of Effentora in 148 patients with non-cancer-related long-term pain. In all of the studies, the main measure of effectiveness was the change in pain intensity in the 60 minutes after taking the tablet. Each patient ranked their pain intensity on a scale of 0 to 10.

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

The application was withdrawn after 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 concerns and was of the provisional opinion that Effentora could not have been approved for the treatment of breakthrough pain in adults with long-term pain other than cancer pain.

The CHMP considered that, although the use of Effentora is accepted in cancer patients who have limited survival, further data were needed to support its safe use in adults with non-cancer-related pain, who have normal life expectancy and may need long-term treatment. The Committee noted that several cases of misuse or abuse of the medicine had been reported in the studies, and was concerned about the risk of addiction in non-cancer patients when using Effentora in the long term. The Committee also had concerns that the patients in the studies had high levels of background pain and might not have been representative of the intended treatment group, which consists of patients with breakthrough pain but whose background pain is otherwise well controlled by regular opioid treatment.

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Effentora in patients with non-cancer-related long-term pain 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 the data submitted were not sufficient to address the Committee's concerns.

The withdrawal letter is available 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 Effentora.

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 Effentora for the treatment 'breakthrough' pain in adults with cancer?

There are no consequences on the use of Effentora in its authorised indication.

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