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Questions and answers

Withdrawal of the application for a change to the marketing authorisation for Eviplera (emtricitabine / rilpivirine / tenofovir disoproxil)

On 16 July 2013, Gilead Sciences International Limited officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wished to withdraw its application to extend the use of the anti-HIV medicine Eviplera from the treatment of patients with a viral load of 100,000 copies/ml or less to include patients with a viral load of up to 500,000 copies/ml.

What is Eviplera?

Eviplera is an anti-HIV medicine that contains the active substances emtricitabine (200 mg), rilpivirine (25 mg) and tenofovir disoproxil (245 mg). It is available as tablets.

Eviplera has been authorised since November 2011 and is used to treat HIV-1 in previously untreated adult patients who have a viral load of 100,000 copies/ml or less. HIV-1 virus is the most common type of HIV, the virus that causes acquired immune deficiency syndrome (AIDS).

What was Eviplera expected to be used for?

Eviplera was also expected to be used to treat HIV-1 in previously untreated patients with a viral load of between 100,000 and 500,000 copies/ml.

How is Eviplera expected to work?

Eviplera contains three active substances: emtricitabine, which is a nucleoside reverse-transcriptase inhibitor; rilpivirine, which is a non-nucleoside reverse-transcriptase inhibitor (NNRTI); and tenofovir disoproxil, which is a 'prodrug' of tenofovir, meaning that it is converted into the active substance

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tenofovir in the body. Tenofovir is a nucleotide reverse-transcriptase inhibitor. Both nucleoside and nucleotide reverse-transcriptase inhibitors are commonly known as NRTIs.

All three active substances block the activity of reverse transcriptase, an enzyme produced by HIV that allows the HIV virus to infect cells and multiply. By blocking this enzyme, Eviplera reduces the amount of HIV in the blood and keeps it at a low level. Eviplera does not cure HIV infection or AIDS, but it may slow down the damage to the immune system and the development of infections and diseases associated with AIDS.

All three active substances are already available in separate medicines in the European Union (EU).

What did the company present to support its application?

The applicant presented data from a main study in 799 patients with HIV-1 which compared Eviplera with another anti-HIV medicine, Atripla. Around 25% of patients had a viral load between 100,000 and 500,000 copies/ml at the beginning of the study. The main measure of effectiveness was based on the number of patients whose viral load reduced to less than 50 copies/ml after 48 weeks of treatment.

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 a list of questions. The company had not yet responded to the questions at the time of the withdrawal.

What was the recommendation of the CHMP at that time?

At the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Eviplera could not be approved for use in patients with viral loads between 100,000 and 500,000 copies/ml. The results of the main study confirmed what had been shown in previous studies submitted during the medicine's initial authorisation: that in patients with viral loads higher than 100,000 copies/ml there was a greater risk of treatment failure with Eviplera, which could increase the risk of resistance to Eviplera and similar treatments. Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Eviplera did not outweigh its risks in the extended indication.

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

In its letter notifying the Agency of the withdrawal of the application, the company gave as its reason the CHMP's provisional opinion that the data provided were not sufficient to recommend an extension of the indication.

The withdrawal letter is available here.

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

The company informed the CHMP that there are no consequences of the withdrawal on ongoing Gilead-sponsored clinical trials or compassionate use programmes.

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