21 September 2018
EMA/632431/2018
EMEA/H/C/004656

Withdrawal of the marketing authorisation application for Entolimod TMC (entolimod)

On 31 July 2018, TMC Pharma Services Ltd officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wished to withdraw its application for a marketing authorisation for Entolimod TMC, intended to be used to reduce the risk of death following exposure to potentially lethal amounts of radiation.

What is Entolimod TMC?

Entolimod TMC is a medicine that contains the active substance entolimod. It was to be available as a solution for injection into a muscle.

What was Entolimod TMC expected to be used for?

Entolimod TMC was expected to be used to reduce the risk of death in adults and children from 2 years of age exposed to a high amount of radiation following a disaster such as a nuclear accident. Exposure to high amounts of radiation can result in multiple organ failure and death.

Entolimod TMC was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 11 January 2016, for the treatment of acute radiation syndrome. Further information on the orphan designation can be found here.

How does Entolimod TMC work?

Entolimod TMC works by attaching to a protein on the surface of cells known as toll-like receptor 5 (TLR5). The attachment to TLR5 triggers production of substances whose effects are expected to reduce damage to the body caused by radiation.

What did the company present to support its application?

Because dangerous doses of radiation cannot be given to humans, the effects of Entolimod TMC against radiation were evaluated in a main study involving 179 macaque monkeys. The study looked at

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

how many of them survived high doses of radiation when given different doses of Entolimod TMC or placebo (a dummy treatment). The company also provided data from 2 studies in a total of 150 healthy participants. These studies examined the medicine's effects on humans and how the medicine was broken down and removed from the body.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn after the CHMP had evaluated the initial documentation provided by the company and formulated a list of questions.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?

Based on the review of the data, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Entolimod TMC could not have been approved to reduce the risk of death following exposure to potentially lethal amounts of radiation.

The CHMP's main concern was that there was insufficient evidence from studies, including the macaque study, to determine the effects of the medicine in humans and how it should be used. In addition, there were questions about whether the company had sufficient measures in place to ensure the manufacturing of Entolimod TMC was properly controlled. Therefore, at the time of the withdrawal, the CHMP was of the opinion that the benefits of Entolimod TMC did not outweigh its risks.

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 stated that they needed more time to generate the additional data required to address some of the points raised by the CHMP.

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 ongoing clinical trials or compassionate use programmes with the medicine.