24 March 2017
EMA/188385/2017
EMEA/H/C/004100

Questions and answers

Withdrawal of the marketing authorisation application for Blectifor (caffeine citrate)

On 9 March 2017, Viridian Pharma Ltd officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Blectifor, for the prevention of bronchopulmonary dysplasia.

What is Blectifor?

Blectifor is a medicine that contains the active substance caffeine citrate. It was to be available as a solution for injection, which can also be given by mouth.

What was Blectifor expected to be used for?

Blectifor was expected to be used to prevent bronchopulmonary dysplasia, a lung disease affecting premature babies who have been on prolonged mechanical ventilation (using a machine that supplies oxygen to support breathing). In these babies, the continuous high pressure and high concentration of the oxygen supplied through mechanical ventilation may cause inflammation and injury to the lungs and prevent normal development of the alveoli (air sacs in the lungs). This leads to difficulty breathing and poor growth, and later in life can result in frequent infections of the airways and long-term lung problems.

Blectifor was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 11 April 2014 for the prevention of bronchopulmonary dysplasia. Further information on the orphan designation can be found here.

How does Blectifor work?

The active substance in Blectifor, caffeine citrate, is a stimulant of the nervous system and is currently authorised in the EU as Peyona for the treatment of a breathing disorder called primary apnoea in

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

premature babies. In the prevention of bronchopulmonary dysplasia, caffeine citrate is expected to act mainly by stimulating the part of the brain that controls breathing, which is thought to help babies breathe on their own and reduce the time spent on mechanical ventilation. In addition, caffeine citrate may also have other effects in the lungs, such as reducing inflammation, which are expected to prevent the damage that leads to bronchopulmonary dysplasia.

What did the company present to support its application?

The company presented data from the published scientific literature mainly on the use of caffeine citrate for the treatment of primary apnoea in premature babies; several articles also provided data on the development of bronchopulmonary dysplasia in these patients.

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 several concerns and was of the provisional opinion that, based on the data submitted by the company, Blectifor could not have been approved for the prevention of bronchopulmonary dysplasia.

The Committee considered that the role of caffeine citrate in the prevention of the disease had not been sufficiently demonstrated, and no definite conclusion on the effect of caffeine citrate for the prevention of bronchopulmonary dysplasia could be drawn. Furthermore, the proposed indication was not supported by the provided literature, and the target population was considered not sufficiently characterised.

Another concern was that the applicant did not demonstrate the so-called well-established use (systematic and documented use in the EU for more than 10 years) of caffeine citrate for the prevention of bronchopulmonary dysplasia. Additionally, the facility designated to test the stability of Blectifor was not certified to comply with good manufacturing practices (GMP).

Therefore, at the time of the withdrawal, the CHMP was of the opinion that the company had not provided enough data to support the application for Blectifor.

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 it was doing so for commercial reasons.

The withdrawal letter is available here.