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Withdrawal of application for the marketing authorisation of Puldysa (idebenone)

Santhera Pharmaceuticals (Deutschland) GmbH withdrew its application for a marketing authorisation of Puldysa for the treatment of Duchenne muscular dystrophy.

The company withdrew the application on 28 October 2020.

What is Puldysa and what was it intended to be used for?

Puldysa was developed as a medicine to treat worsening of breathing in patients with Duchenne muscular dystrophy who are not receiving corticosteroids.

The medicine contains the active substance idebenone and was to be available as film-coated tablets to be taken by mouth.

It was developed as a 'hybrid medicine'. This means that it was intended to be similar to a 'reference medicine' containing the same active substance and already authorised in the European Union. The reference medicine is Mnesis, which is authorised in Italy for the treatment of glaucoma.

Puldysa was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 20 March 2007 for Duchenne muscular dystrophy. Further information on the orphan designation can be found here.

How does Puldysa work?

The active substance in Puldysa, idebenone, is an antoxidant that acts on mitochondria (the structures inside cells that produce the energy necessary for cells to work). In patients with Duchenne muscular dystrophy, mitochondria do not work properly and produce toxic forms of oxygen that damage muscle cells. Idebenone is thought to help improve production of energy by restoring mitochondrial function, thereby preventing cell damage and loss of muscular function including that of breathing muscles.

Idebenone is also authorised in the EU for the treatment of cognitive and behavioural deficits, Friedreich's ataxia and Leber's hereditary optic neuropathy.

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What did the company present to support its application?

The company provided results from three main studies involving patients with Duchenne muscular dystrophy who were not being treated with corticosteroids. In two studies Puldysa was compared with placebo (a dummy treatment) and effectiveness was measured by improvement in lung function or change in PEF (peak expiratory flow, an indicator of breathing function) after one year of treatment. In the third study patients treated with Puldysa were followed up longer to see if the effects on breathing were maintained.

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

The application was withdrawn after the European Medicines Agency had evaluated the information from the company and prepared questions for the company. After the Agency had assessed the company's responses to the last round of questions, there were still some unresolved issues.

What did the Agency recommend at that time?

Based on the review of the data and the company's response to the Agency's questions, at the time of the withdrawal, the Agency had some concerns and its provisional opinion was that Puldysa could not have been authorised for the treatment of worsening breathing function in patients with Duchenne muscular dystrophy who are not using corticosteroids.

The Agency considered that beneficial effects on lung function were not consistent across studies and it was unclear if they could be maintained long-term.

Therefore, at the time of the withdrawal, the Agency's opinion was that the benefits of Puldysa 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 it is withdrawing its application after an ongoing main study which was expected to provide further evidence for Puldysa in Duchenne muscular dystrophy was stopped because it was unable to achieve its objectives.

Does this withdrawal affect patients in clinical trials or compassionate use programmes?

The company informed the Agency that all clinical trials and compassionate use programmes for Puldysa in Duchenne muscular dystrophy are being discontinued. Clinical trial doctors will contact patients to organise final follow-up visits.

If you are in a clinical trial or compassionate use programme and need more information, speak with your clinical trial doctor.