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Refusal of the marketing authorisation for Meplyffa (arimoclomol)

The European Medicines Agency has recommended the refusal of the marketing authorisation for Meplyffa[1], a medicine intended for the treatment of Niemann-Pick disease type C.

The Agency issued its opinion on 23 July 2026. The company that applied for authorisation, Zevra Denmark A/S, may ask for re-examination of the opinion within 15 days of receiving the opinion.

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

Meplyffa was intended to be used together with miglustat, another medicine to treat symptoms of Niemann-Pick disease type C, in patients aged two years and older with the condition. Niemann-Pick disease type C is a progressive and fatal genetic disease that affects the body's ability to transport fats inside cells. Over time, these fats build up in cells of the brain and other organs, causing the cells to stop working properly and eventually die. This leads to symptoms such as problems with balance, movement and swallowing, as well as behavioural problems and learning disabilities.

Meplyffa contains the active substance arimoclomol and was to be available as capsules to be taken by mouth.

Niemann-Pick disease type C is rare and Meplyffa was designated an 'orphan medicine' (a medicine used in rare diseases) on 19 November 2014.

How does Meplyffa work?

Niemann-Pick disease type C is caused by mutations (changes) in genes that provide instructions for making proteins called NPC1 and NPC2. These proteins are normally involved in transporting fats within the cell. In people with Niemann-Pick disease type C, NPC1 or NPC2 do not function properly, leading to a harmful build-up of fat in cells.

The active substance in Meplyffa, arimoclomol, increases the activation of proteins in the cell called TFEB and TFE3. These proteins stimulate the production of functioning NPC proteins, as well as other proteins that help cells clear fats. This is expected to prevent the build-up of fats in organs such as the

[1] A previous application for this medicine (under the name Miplyffa) was withdrawn in March 2022.

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brain and help reduce the symptoms of the disease.

What did the company present to support its application?

The company provided results of a main study that looked at the effectiveness of Meplyffa at slowing the progression of Niemann-Pick disease type C over time. The study involved 50 children and adolescents aged from 2 to 18 years who received either Meplyffa or placebo (a dummy treatment) for 1 year in addition to the standard care they were already receiving, which included miglustat in most cases. The main measure of effectiveness was a change in the disease severity score measured using a scale called the 5-domain NPCCSS. This scale rates disease severity based on ambulation (ability to walk), swallowing ability, cognition (intellectual function), speech and fine motor (movement) skills.

What were the main reasons for refusing the marketing authorisation?

Based on the submitted data, the Agency concluded that the efficacy of Meplyffa had not been sufficiently demonstrated. Due to the way the data had been handled and the results analysed, there were uncertainties about the reliability and robustness of the results. Moreover, no benefit was seen in terms of ambulation and cognition.

Although data for the subgroup of patients who were also taking miglustat showed a treatment effect favouring Meplyffa, this finding was not considered robust since effectiveness had not been demonstrated in the overall population.

Therefore, the Agency's opinion was that the benefits of Meplyffa were not sufficient to establish a positive benefit-risk balance of the medicine in the treatment of Niemann-Pick disease type C, and it recommended refusing marketing authorisation.

During the assessment, the Agency considered interventions from patient organisations and caregivers representing patients with Niemann-Pick disease and acknowledged the patient perspective and the important unmet medical need in Niemann-Pick disease.

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

The company informed the Agency that it will continue with its ongoing compassionate use programmes pending discussions with national authorities that have granted approval for compassionate use.

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