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Update as of 9 February 2024:

The company for Nezglyal has requested a re-examination of EMA's January 2024 opinion. Upon receipt of the grounds of this request, the Agency will re-examine its opinion and issue a final recommendation.

Refusal of the marketing authorisation for Nezglyal (leriglitazone)

The European Medicines Agency has recommended the refusal of the marketing authorisation for Nezglyal, a medicine intended for the treatment of cerebral adrenoleukodystrophy. Cerebral adrenoleukodystrophy is a form of an inherited disease called adrenoleukodystrophy in which fatty substances known as 'very long chain fatty acids' build up in tissues around the body, mainly in the brain, spinal cord and adrenal glands (two glands situated above the kidneys). In cerebral adrenoleukodystrophy, a build-up of these substances in the brain causes inflammation and destruction of the protective sheath (myelin) that insulates and helps signalling by nerve cells.

The Agency issued its opinion on 25 January 2024. The company that applied for authorisation, Minoryx Therapeutics S.L., may ask for re-examination of the opinion within 15 days of receiving the opinion.

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

Nezglyal was developed as a medicine for treating male adults and children aged 2 years and older with cerebral adrenoleukodystrophy.

Nezglyal contains the active substance leriglitazone and was to be available as a suspension to be taken by mouth.

How does Nezglyal work?

The active substance in Nezglyal, leriglitazone, works by attaching to and activating receptors (targets) called 'PPAR gamma receptors', which are found inside cells, including nerve cells. PPAR gamma receptors play a role in regulating the function of mitochondria (energy-producing structures in cells), how cells respond to oxidative stress (damage caused by toxic oxygen-containing molecules known as free radicals) and inflammation. Leriglitazone is therefore expected to protect nerve cells from damage

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by reducing inflammation, improving the function of mitochondria and protecting against damage from free radicals.

What did the company present to support its application?

The company presented results from a main study involving 116 male adults with adrenoleukodystrophy who either took leriglitazone or placebo. The study looked at the change in the distance patients could walk in six minutes after 96 weeks of treatment.

What were the main reasons for refusing the marketing authorisation?

The study did not show a difference between the medicine and placebo in terms of the distance patients could walk in six minutes. The study included patients with adrenoleukodystrophy and not cerebral adrenoleukodystrophy in whom the effects of the medicine could be different as it would need to cross the blood brain barrier to have an effect. The blood brain barrier is a membrane barrier that prevents substances from the blood entering the brain. In addition, children for whom Nezglyal was also intended were not included in the study. In terms of safety there were concerns about weight gain and oedema (fluid retention), the clinical consequences of which were unclear. Moreover, no measures could be identified to manage or reduce these risks. Therefore, the Agency's opinion was that the benefits of Nezglyal did not outweigh its risks and it recommended refusing marketing authorisation.

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

The company informed the Agency that there are no consequences for patients in clinical trials or in compassionate use programmes with Nezglyal.

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