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Refusal of the marketing authorisation for Daybu (trofinetide)

The European Medicines Agency has recommended the refusal of the marketing authorisation for Daybu, a medicine intended for the treatment of Rett syndrome, a rare inherited condition that affects the brain and nervous system.

The Agency issued its opinion on 26 February 2026. The company that applied for authorisation, Acadia Pharmaceuticals, may ask for re-examination of the opinion within 15 days of receiving the opinion.

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

Daybu was developed as a medicine for treating Rett syndrome in adults and children aged 2 years and older. Rett syndrome affects mainly girls and women and leads to intellectual disability as well as loss of speech and previously learned skills between 6 and 18 months of age. Other symptoms include difficulty breathing, irregular heartbeat, a gradual loss of the ability to move, feeding difficulties such as chewing and swallowing problems, sleeping problems, constipation, repetitive hand movements and seizures.

Daybu contains the active substance trofinetide and was to be available as a solution to be drunk twice a day.

Daybu was designated an 'orphan medicine' (a medicine used in rare diseases) on 10 August 2015 for the treatment of Rett syndrome. Further information on the orphan designation can be found on the Agency's website: ema.europa.eu/en/medicines/human/orphan-designations/eu-3-15-1534.

How does Daybu work?

In Rett syndrome, levels of insulin-like growth factor 1 (IGF-1) in the brain are lower than normal, which is thought to affect nerve function. IGF-1 is a hormone that is important for the normal development and functioning of the nervous system.

The active substance in Daybu, trofinetide, is made up of a molecule derived from IGF-1. Trofinetide is thought to help improve brain cell structure and how brain cells communicate with each other, although the way it works in the treatment of Rett syndrome is unclear.

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What did the company present to support its application?

The company presented the results from a main study in 187 girls and women with Rett syndrome who received either Daybu or placebo (a dummy treatment) every day for 12 weeks. The main measures of effectiveness were changes in patients' scores on two standard scales: the Rett Syndrome Behaviour Questionnaire (RSBQ) scale, which measures patients' behavioural, emotional and physical symptoms, and the Clinical Global Impression of Improvement (CGI-I) scale, which measures patients' overall health improvement as observed by their clinician.

What were the main reasons for refusing the marketing authorisation?

The European Medicine Agency considered that the size of Daybu's effects observed after 12 weeks of treatment are too small and are therefore not expected to be clinically meaningful for patients. The Agency also noted that the study did not assess several key symptoms of Rett syndrome and that the conclusion on the long-term effectiveness data was complicated by the large number of patients who withdrew from the study.

The Agency also considered that the proposed use for Daybu — treatment of Rett syndrome — was not representative of the patients included in the main study, as the latter did not involve patients across the different disease stages.

Therefore, the Agency's opinion was that the benefits of Daybu in the treatment of Rett syndrome have not been demonstrated 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 Daybu.

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