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Approval of the marketing authorisation for Daybu (trofinetide)

Re-examination leads to recommendation to approve

After re-examining its initial opinion, the European Medicines Agency has recommended approving the marketing authorisation for the medicine Daybu for the treatment of neurobehavioural symptoms of Rett syndrome in adults and children aged 5 years and older. Neurobehavioural symptoms include repetitive hand movements, restlessness, general mood problems, anxiety, sleep and communication problems.

The Agency had initially refused the application on 26 February 2026 for Daybu in the treatment of Rett syndrome. After re-examination on 25 June 2026, the Agency recommended that marketing authorisation could be granted, but for a restricted indication.

The company that applied for authorisation is Acadia Pharmaceuticals B.V.

What is Daybu and what is it 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 is a disorder that affects the way the brain develops. It 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, repetitive hand movements, constipation and seizures.

Daybu contains the active substance trofinetide and is to be available as a solution to be drunk or administered via gastric tube 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.

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The active substance in Daybu, trofinetide, is made up of a molecule derived from IGF-1. The way that trofinetide works in Rett syndrome is unclear.

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 a patient's behavioural, emotional and physical symptoms based on their caregiver's responses, and the clinical global impression of improvement (CGI-I) scale, which measures a patient's overall health improvement as observed by their clinician.

What were the main reasons for initially refusing the marketing authorisation?

The European Medicine Agency considered that the size of Daybu's effects observed after 12 weeks of treatment were too small and were therefore not expected to be clinically meaningful for the treatment of Rett syndrome. The Agency noted that the study did not assess several key symptoms of Rett syndrome, such as seizures, 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 in patients aged 2 years and older — was not representative of the patients included in the main study, as the latter did not involve patients across the different stages of the disease.

Therefore, the Agency's opinion was that the benefits of Daybu in the treatment of Rett syndrome were not demonstrated and it recommended refusing marketing authorisation.

What happened during the re-examination?

The company proposed to restrict the use of Daybu to the treatment of neurobehavioural symptoms of Rett syndrome, which include repetitive hand movements, restlessness, general mood problems, anxiety, and sleep and communication problems, in adults and children aged 5 years and older.

During the re-examination, as in the initial assessment, the Agency consulted a group of external experts, including specialists in neurology and parents of children with Rett syndrome. The Agency also considered contributions from patient organisations, learned societies, clinicians and families participating in a compassionate use programme.

What were the conclusions of the re-examination?

During the initial evaluation, the Agency considered that the data provided on Daybu did not provide evidence on some of the key symptoms of Rett syndrome, such as seizures. However, the data showed some improvement in neurobehavioral symptoms, as assessed by the RSBQ and CGI-I scales. The Agency considered that although these improvements were small, they were relevant in the context of a rare and serious disorder such as Rett syndrome in the proposed restricted use.

The age range proposed during the re-examination was better aligned with the patients involved in the main study, who were aged 5 years or more.

Therefore, the Agency concluded that the benefits of Daybu in the treatment of neurobehavioural symptoms of Rett syndrome in adults and children aged 5 years and older are greater than its risks, and recommended granting a marketing authorisation for Daybu.