21 March 2024
EMA/CHMP/68942/2024
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Agilus

dantrolene sodium / hemiheptahydrate

On 21 March 2024, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Agilus[2], intended for the treatment of malignant hyperthermia in combination with adequate support measures.

The applicant for this medicinal product is Norgine B.V.

Agilus will be available as 120 mg powder for solution for injection. The active substance of Agilus is dantrolene sodium, hemiheptahydrate, a directly acting muscle relaxant (ATC code: M03CA01). Dantrolene is a skeletal muscle relaxant that binds to the ryanodine receptor-1 (RYR1), preventing the release of calcium from the sarcoplasmic reticulum.

The benefit of Agilus is reducing the mortality and morbidity of malignant hyperthermia as shown in the bridging study to the reference product, results from preclinical studies, clinical experience in case series, and consensus guidelines. Compared to the formulation of the reference medicine, mannitol and sodium hydroxide have been replaced with hydroxypropyl-beta-cyclodextrin (HP-β-CD) and Macrogol 3350, which shortened the time for preparation and decreased the volume of water needed to dissolve each vial. Fast and ease of use are important clinical advantages for the treatment of an acute and life-threatening condition. The most common side effect of Agilus is muscle weakness.

Agilus is a hybrid medicine[3] of Dantrolen IV 20 mg which has been authorised in the European Union since 1984. Agilus contains the same active substances as Dantrolen IV 20 mg but will be available in a higher 120 mg strength. In the formulation of Agilus, the mannitol and sodium hydroxide have been replaced with HP-β-CD and Macrogol 3350 to shorten the preparation time and improve the ease of use. Studies have demonstrated the satisfactory quality of Agilus, and its bioequivalence to the reference product Dantrolen IV 20 mg.

[1] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued 67 days from adoption of the opinion
[2] This product was designated as an orphan medicine during its development. EMA will now review the information available to date to determine if the orphan designation can be maintained
[3] Hybrid applications rely in part on the results of pre-clinical tests and clinical trials for a reference product and in part on new data.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

The full indication is:

In combination with adequate support measures, Agilus is indicated for the treatment of malignant hyperthermia in adults and children of all ages.

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and made available in all official European Union languages after the marketing authorisation has been granted by the European Commission.