21 June 2024

Dear members of the World Duchenne Organization,

Following your request for regular updates, it is a great pleasure to share with you that the European Medicines Agency (EMA) has validated and initiated review of the marketing authorisation application (MAA) for delandistrogene moxeparvovec, a gene therapy submitted for the treatment of ambulatory patients aged 3-7 years old with Duchenne muscular dystrophy (DMD).

The MAA has been submitted to the EMA and is based on results from the pivotal Phase 3 EMBARK study (NCT05096221), a global, randomised, double-blind, placebo-controlled study in patients with DMD aged 4 through 7 years. The MAA is also supported by data from ENDEAVOR (NCT04626674), an open- label Phase 1b study in patients with DMD, that is enrolling ambulatory and non-ambulatory patients of various ages and across a broad range of *DMD* mutations, along with Phase 1 and 2 studies which provide longer term efficacy, safety and biological data to support the benefit-risk assessment.

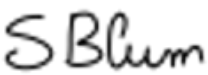
Approval for delandistrogene moxeparvovec has already been granted in five countries that can accept applications for marketing authorisation based on Phase 1 and Phase 2 data: UAE, Qatar, Kuwait, Bahrain and Oman.

Regulatory reviews in other countries and further submissions are underway.

Additionally, on 20 June, 2024 the U.S. Food & Drug Administration (FDA) converted the accelerated approval of delandistrogene moxeparvovec for ambulatory boys with DMD to a traditional approval and expanded the label to include individuals with a confirmed mutation in the *DMD* gene who are aged 4 and older. The FDA also issued an accelerated approval for non-ambulatory boys aged 4 and older.

We appreciate the contributions of so many families to help advance this DMD gene therapy. We are working with speed on regulatory submissions in a number of countries and look forward to providing additional updates in the future. We are so grateful for your partnership as we continue this journey.

Sincerely,



Sandra Blum
Global Patient Partnership Leader

FAQs

What is delandistrogene moxeparvovec?

- Duchenne is characterised by mutations in the dystrophin gene that result in the lack of dystrophin protein. In the absence of dystrophin, which is required to strengthen and protect muscles, muscles become weakened and damaged.[1] Delandistrogene moxeparvovec addresses the root genetic cause of the disease by delivering a gene that codes for a functional shortened form of the dystrophin protein to muscle cells known as micro-dystrophin. Delandistrogene moxeparvovec is given as a one-time intravenous (IV) infusion.

What is the difference between traditional approval and accelerated approval?

- The FDA's Accelerated Approval programme allows earlier approval of medicines for serious conditions based on surrogate endpoints like biomarkers, rather than confirmed clinical benefit. This shortens the time to medicines availability to patients.
- In the case of delandistrogene moxeparvovec, accelerated approval was based on expression of delandistrogene moxeparvovec micro-dystrophin in skeletal muscle observed in patients treated with the medicine.
- Confirmatory trials must be conducted demonstrating actual clinical benefit post-approval and to convert the accelerated approval into standard approval. The confirmatory trial for delandistrogene moxeparvovec was EMBARK.

What clinical trial data was the traditional approval based on?

- The expanded delandistrogene moxeparvovec label is based on data from the pivotal Phase 3 EMBARK study, a global, randomised, double-blind, placebo-controlled study in patients with Duchenne between the ages of 4 through 7 years and data from ENDEAVOR, an open label, Phase 1b study in patients with Duchenne, that is enrolling ambulant and non-ambulant participants who are aged 2 years and older.

Does this approval change access to delandistrogene moxeparvovec in countries where it is approved?

- No, the approval does not change access pathways to delandistrogene moxeparvovec where it has been approved. In countries where delandistrogene moxeparvovec is approved or under review, we are pursuing a broader label in line with the FDA to ensure we are reaching as many eligible patients as possible.

[1] Duan D, et al. Duchenne muscular dystrophy. Nat Rev Dis Primers. 2021;7(1):13.