21 July 2023

Dear Members of SMA Europe,

In response to your request to receive important updates about risdiplam, we are writing with the news that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has today adopted a positive opinion recommending the approval of an extension of the indication for risdiplam (Evrysdi) to include all ages, including infants with SMA from birth.[1] For more details, please see our press release here.

What happens next

In the European Union (EU), risdiplam is currently approved for use in patients from two months old with SMA Type 1, Type 2 or Type 3, or those who have up to four copies of a gene known as *SMN2*.[2]

The CHMP's recommendation has now been referred to the European Commission (EC) for review and a final decision, which is expected within two months. A positive EC decision will mean that risdiplam is approved for use in people with SMA from birth across all 27 European Union member states, as well as Iceland, Norway and Liechtenstein.

In SMA, intervention with disease-modifying therapy as early as possible is critical to counteract ongoing and irreversible loss of motor neurons.[3] In countries across the EU where age-related access restrictions to risdiplam have been imposed, Roche is actively engaged with reimbursement and assessment bodies to align on the requirements for reimbursement decision-making as quickly as possible. We are submitting reimbursement dossiers for extending reimbursement to babies less than two months in many countries in advance of the EC's expected decision to minimise any delay in patient access.

Evidence supporting the CHMP opinion

The CHMP's recommendation is based on the preliminary safety and pharmacokinetic data for 18 babies and efficacy data for 7 babies from the ongoing RAINBOWFISH study (NCT03779334), a multicenter, open-label, single-arm trial, designed to study risdiplam in babies from birth to six weeks with genetically diagnosed and pre-symptomatic Type 1 SMA.[4]

The preliminary efficacy data from RAINBOWFISH, presented at the Muscular Dystrophy Association (MDA) Clinical and Scientific Conference in March 2022, show that babies (n=7) treated with risdiplam for at least one year were able to sit, stand and walk within the timeframes of healthy babies.[5] Further, the safety profile of risdiplam in pre-symptomatic babies was consistent with the safety profile seen in previous trials with symptomatic SMA patients.

Enrolment for RAINBOWFISH completed with 26 newborns, who were aged 16 to 40 days at first risdiplam dose. Results from the primary analysis of the study will be shared with the community

at an upcoming scientific conference.

As we work to bring risdiplam to those who need it, we remain sincerely thankful for the SMA community's steadfast commitment to and participation in clinical trials like RAINBOWFISH that enable us to reach important milestones like this one today. None of this would be possible without your support, and we thank you for your continued partnership.

Below we have included some additional information for your members. Please do not hesitate to contact us with any questions.

Sincerely,

Louisa Danielle Townson

Louisa Townson, on behalf of the Roche Global SMA Team
Global Patient Partnerships Director, Rare Diseases

Frequently asked questions

- **Does the CHMP positive opinion mean that risdiplam is now approved in the EU for babies from birth?**
    - Not yet. The CHMP's recommendation has been referred to the European Commission (EC) for a final decision to authorise marketing approval for the label extension. A decision is typically made within 67 days.
    - Subject to the approval by the EC, health authorities in each EU and European Economic Area member state will then decide whether to reimburse risdiplam for use in their national health system.
    - In parallel, Roche is actively engaging with reimbursement and assessment bodies across Europe to minimise treatment delays

- **When will risdiplam become available in Europe for people with SMA from birth?**
    - Risdiplam is currently available in Europe for the treatment of SMA in patients 2 months of age and older, with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four *SMN2* copies.
    - Should the European Commission approve the label extension within 67 days (approximately 2 months), the indication will be updated accordingly.

- **When can the SMA community expect a full-data readout for RAINBOWFISH?**
    - Findings from the primary data analysis for RAINBOWFISH will be shared with the community at an upcoming scientific congress in 2023.

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References

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2. Evrysdi Summary of Product Characteristics 2021. Available at: https://www.ema.europa.eu/en/documents/product-information/evrysdi-epar-product-information_en.pdf. Last accessed: July 2023.
3. Day JW, et al. Advances and limitations for the treatment of spinal muscular atrophy. *BMC Pediatr*. 2022;22(1):632.
4. ClinicalTrials.gov: NCT03779334 (RAINBOWFISH). Available at: https:// clinicaltrials.gov/ct2/show/NCT03779334. Last accessed: July 2023.
5. Finkel RS, et al, on behalf of the RAINBOWFISH Study Group. RAINBOWFISH: Preliminary efficacy and safety data in risdiplam-treated infants with presymptomatic SMA. Poster presented at: Muscular Dystrophy Association Clinical and Scientific Conference. 2022; Nashville, TN.

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