Risdiplam Comment: Tablet Formulation and New Clinical Evidence

This comment builds upon the submission for the addition of risdiplam to the World Health Organization's (WHO) Model List of Essential Medicines (EML) by presenting two key developments since the application's publication in November 2024. First, the approval of a tablet formulation of risdiplam offers a more convenient and accessible treatment option, particularly in resource-limited settings. Second, new clinical evidence from a case study demonstrates the potential of prenatal risdiplam administration in altering the disease course of spinal muscular atrophy (SMA).

Tablet Formulation Approval

On February 11, 2025, the U.S. FDA announced the approval of a tablet formulation of risdiplam for individuals living with spinal muscular atrophy (SMA). The following month, the Japanese Ministry of Health, Labour and Welfare similarly announced the approval of risdiplam's tablet formulation.[1] This new 5mg tablet provides for a more convenient option for SMA patients aged two and older who can take a tablet instead of the oral solution. Key benefits of this oral formulation include:

- **Refrigeration-free storage:** unlike the risdiplam's traditional liquid formulation, the table does not require refrigeration, which can offer improved accessibility in resource-limited settings.
- **Flexible oral administration:** the table can be swallowed whole with water or dispersed in drinking water.
- **Simplified dosing:** each tablet contains a fixed dose of 5mg, eliminating the need for syringe-based measurement and potentially improving adherence.

Roche has published a graphic that provides an overview of the key differences between risdiplam's liquid versus tablet formulation.

Image 1: Liquid versus tablet risdiplam[2]

	Liquid For illustrative purposes only.	Tablet
Eligibility	**No age or weight** requirements	Patient must be **≥2 years of age and weigh ≥20 kg (44 lb)**
Administration	Taken via **oral syringe**	Can be **swallowed whole with water** or **dispersed with bottled water**
Storage	**Refrigerate** 36°F to 46°F (2°C to 8°C)	**Room temperature** 68°F to 77°F (20°C to 25°C)
G- or NG-tube	**Can** be used with G- or NG-tube	**Cannot** be used with G- or NG-tube
Dosing	Once daily **based on patient's age and weight**	**5-mg dose** once daily
Obtaining Evrysdi	Shipped **directly to your patient's door** through a specialty pharmacy	

[1] Chugai, 2025. *Chugai obtains regulatory approval for first table for SMA, Evrysdi.* Available at: https://www.chugai-pharm.co.jp/english/news/detail/20250327160001_1140.html
[2] Roche, 2025. *Evrysdi tablet overview.* Available at https://www.evrysdi-hcp.com/content/dam/gene/evrysdi-hcp/pdf/evrysdi-tablet-overview.pdf

The approval of the risdiplam tablet was based on a bioavailability and bioequivalence study (NCT04718181). The study results confirmed that the 5mg tablet - whether swallowed whole or dispersed in non-chlorinated drinking water - was bioequivalent to the oral solution of risdiplam.[3]

Patent Status

The patents listed in the FDA Orange Book under the tablet formulation of risdiplam correspond to the same patents listed for risdiplam's oral formulation. Table 1 highlights the patents covered in the Orange Book for risdiplam and whether they are listed for risdiplam's oral formulation, tablet formulation, or both.

Table 1: Orange Book Patents Risdiplam

Patent Number	Patent Expiration	Oral Formulation	Tablet Formulation
9586955	02/08/2033	Yes	Yes
9969754	05/11/2035	Yes	Yes
11534444	10/04/2038	Yes	Yes
11827646	01/25/2036	Yes	Yes
11938136	11/08/2036	Yes	No
12122789	04/15/2041	Yes	Yes

A package of 30 risdiplam 5mg tablets is listed at the price of $33,140 to $37,147 on GoodRX.[4] That is a price range from $1,105 to $1,238 per day. In contrast, the same source lists the price of 160ml (0.75ml/mg) of risdiplam at a retail price of $31,882 (special drug coupons can apply to reduce this price). At 5mg a day (24 days), the solution is priced at $1,328 per day.

New Clinical Evidence

In February 2025, a case study was published in *The New England Journal of Medicine,* reporting the first documented use of prenatal risdiplam treatment.[5] In this case study, risdiplam was administered orally to a mother pregnant with a fetus at risk of the severe form of SMA (type 1).

This case study provides the first reported evidence of prenatal treatment with risdiplam for SMA, demonstrating its transplacental passage and biological activity. Administered orally to a mother carrying a fetus with genetically confirmed type 1 SMA, risdiplam led to increased SMN protein levels and the absence of SMA symptoms in the child at 30 months of age. While congenital abnormalities were present, they were attributed to early fetal development rather than drug exposure.

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[3] Kletzl H, Heinig K, Jaber B, et al. 2024. Bioequivalence and food effect assessment for a room-temperature stable risdiplam tablet formulation in healthy volunteers. Presented at: *Muscular Dystrophy Association (MDA) Clinical & Scientific Conference*; March 3-6, Orlando, FL.

[4] GoodRx. *Evrysdi (risdiplam) prices, coupons, and patient assistance programs.* Available at: https://www.goodrx.com/evrysdi?label_override=evrysdi&form=tablet&dosage=5mg&quantity=30&drugId=101084

[5] Finkel, R.S., Hughes, S.H., Parker, J., Civitello, M., Lavado, A., Mefford, H.C., Mueller, L. and Kletzl, H., 2025. Risdiplam for Prenatal Therapy of Spinal Muscular Atrophy. *New England Journal of Medicine*.

Pharmacokinetic and pharmacodynamic data confirmed target engagement, supporting the potential of prenatal intervention to alter disease progression.

While this is a single case and cannot be generalized, it suggests that even earlier intervention—before birth—may further improve outcomes. Given the severe and often fatal course of untreated type 1 SMA, ensuring timely access to risdiplam is critical.

Five Year Data from SUNFISH Trial

In mid-March, Roche shared five year safety and efficacy data from SUNFISH (NCT02908685, n=231) for SMA Types 2 and 3.[6] While the poster presentation is not yet publicly available, the results show that motor function improvements in the first year of treatment with risdiplam were maintained over five years. In contrast, untreated patients experienced significant decline in motor function over the same five-year period.

Patients aged 12 and older, along with caregivers, reported stabilization or improvement in independence for daily activities, as assessed by the SMA Independence Scale (SMAIS-ULM). Adverse events (AEs) and serious adverse events (SAEs) were consistent with the underlying disease, with low rates aligning with previous data cut-offs. Treatment adherence exceeded 99%.

Generic Manufacturing in India

On March 24th, the Delhi High Court denied Roche's petition for an injunction against Natco Pharma. The court ruled that given Roche's high pricing of Evrysdi (risdiplam), public interest outweighed the need for an injunction. This legal development has opened the door for access to generic versions of risdiplam in India - effectively, generic manufacturers like Natco can produce generic versions of risdiplam. In the case, Natco held that they intend on making the product available at a price nearly 80-90% lower than Roche's price. This further empowers KEI's arguments in our application that risdiplam can be made for drastically lower prices, paving the way for greater access.

Concluding Comment

The recent approval by the FDA of the tablet formulation and the emerging evidence on prenatal treatment strengthen the case for risdiplam's inclusion in the EML. As research continues to advance and early screening becomes more widespread, ensuring availability and access to risdiplam remains an imminent priority.

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[6] Roche, 2025. *Roche to share latest scientific advancements from its neuromuscular portfolio at Muscular Dystrophy Association (MDA) 2025 conference*. Available at: https://www.roche.com/media/releases/med-cor-2025-03-17