

**MHRA**  
10 South Colonnade  
Canary Wharf  
London  
E14 4PU  
United Kingdom

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## **Decision Cover Letter**

### **Decision of the licensing authority to:**

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-101094-PIP01-23-M03

### **Scope of the Application**

#### **Active Substance(s)**

GIVINOSTAT HYDROCHLORIDE MONOHYDRATE

#### **Condition(s)**

Treatment of Duchenne muscular dystrophy

#### **Pharmaceutical Form(s)**

Oral suspension

#### **Route(s) of Administration**

ORAL USE

#### **Name / Corporate name of the PIP applicant**

Italfarmaco S.p.A

#### **Basis for the Decision**

Pursuant to the Human Medicines Regulations 2012, Italfarmaco S.p.A submitted to the licensing authority on 24/04/2026 12:54 BST an application for a Modification

The procedure started on 29/04/2026 19:12 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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## Final Decision Letter

MHRA-101094-PIP01-23-M03

Of 01/06/2026 11:51 BST

On the adopted decision for GIVINOSTAT HYDROCHLORIDE MONOHYDRATE (MHRA-101094-PIP01-23-M03) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for GIVINOSTAT HYDROCHLORIDE MONOHYDRATE, Oral suspension , ORAL USE .

This decision is addressed to Italfarmaco S.p.A, Viale Fulvio Testi 330, Milan, ITALY, 20126

## ANNEX I

### 1. Waiver

#### 1.1 Condition:

Treatment of Duchenne muscular dystrophy The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age. Pharmaceutical form(s): Oral suspension Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

### 2. Paediatric Investigation Plan:

#### 2.1 Condition(s):

Treatment of Duchenne muscular dystrophy.

## 2.2 Indication(s) targeted by the PIP:

Treatment of Duchenne muscular dystrophy.

## 2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 2 years to less than 18 years of age.

## 2.4 Pharmaceutical Form(s):

Oral suspension.

## 2.5 Studies:

| Study Type           | Number of Studies | Study Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|----------------------|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Quality Measures     | 1                 | Study 1 Assessment of the suitability of the oral suspension formulation, of intragastric administration via feeding tubes.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Non-Clinical Studies | 1                 | Study 2 Safety study of givinostat in juvenile rats from post-natal day (PND)7.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Clinical Studies     | 5                 | Study 3 (DSC/11/2357/43) 2-part open-label study to assess the safety, tolerability, pharmacokinetics (PK), effects on histology and clinical parameters of givinostat in ambulant paediatric patients from 7 years to less than 11 years of age with DMD. Study 4 (DSC/14/2357/48) Randomised, double-blind safety and efficacy study of givinostat versus placebo in ambulant paediatric patients from 6 years to less than 18 years of age with DMD. Study 5 (DSC/14/2357/50) Randomised, double-blind safety and efficacy study of givinostat versus placebo in non-ambulant paediatric patients from 9 years to less than 18 years of age with DMD. Study 6 (DSC/14/2357/51) Open-label, long term safety study of givinostat in paediatric patients from 6 years to less than 18 years of age with DMD. Study 7 (DSC/14/2357/52) Open-label, safety and pharmacokinetic study of givinostat in paediatric |

|                                                         |   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|---------------------------------------------------------|---|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                         |   | patients from 2 years to less than 6 years of age with DMD.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <b>Extrapolation, Modeling &amp; Simulation Studies</b> | 5 | Study 8 Population pharmacokinetic (PK) model to support dose rationale of givinostat in paediatric patients with DMD. Study 9 Population pharmacokinetic (PK)-pharmacodynamic (PD) model to estimate the risk of experiencing a reduction in platelets in DMD patients treated with givinostat. Study 10 Population pharmacokinetic (PK)-pharmacodynamic (PD) model to correlate clinical parameters with PK data in DMD patients treated with givinostat. Study 11 Analysis of existing in-house pharmacokinetic (PK) /pharmacodynamic (PD) data and literature data on givinostat in the treatment of DMD to support extrapolation of efficacy data in patients with DMD younger than 6 years of age. Study 12 Population pharmacokinetic (PK)-pharmacodynamic (PD) model to correlate clinical parameters with PK data in DMD patients treated with givinostat. |
| <b>Other Studies</b>                                    | 0 | Not applicable                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>Other Measures</b>                                   | 0 | Not applicable                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |

### 3. Follow-up, completion and deferral of a PIP:

|                                                                                                  |            |
|--------------------------------------------------------------------------------------------------|------------|
| <b>Concerns on potential long term safety and efficacy issues in relation to paediatric use:</b> | Yes        |
| <b>Date of completion of the paediatric investigation plan:</b>                                  | 30/06/2028 |
| <b>Deferral of one or more studies contained in the paediatric investigation plan:</b>           | Yes        |

