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 (MHRA-101094-PIP01-23) and to the deferral

MHRA-101094-PIP01-23-M01

Scope of the Application

Active Substance(s)

Givinostat

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 28/03/2024 14:46 GMT an application for a Modification

The procedure started on 04/06/2024 13:14 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-M01

Of 26/06/2024 08:22 BST

On the adopted decision for Givinostat (MHRA-101094-PIP01-23-M01) 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, 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.
Extrapolation, Modeling & Simulation Studies	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.
Other Studies	0	Not applicable.
Other Measures	0	Not applicable.

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

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	30/06/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes