EMA/74599/2023

European Medicines Agency decision

P/0061/2023

of 24 February 2023

on the refusal of a modification of an agreed paediatric investigation plan for cariprazine (hydrochloride) (Reagila), (EMEA-001652-PIP01-14-M04) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0156/2015 issued on 10 July 2015, decision P/0076/2016 issued on 18 March 2016, decision P/0301/2018 issued on 12 September 2018 and the decision P/0105/2021 issued on 17 March 2021,

Having regard to the application submitted by Gedeon Richter Plc on 14 October 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 20 January 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the refusal of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the refusal of changes to the agreed paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for cariprazine (hydrochloride) (Reagila), capsule, hard, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, are hereby refused.

Article 2

This decision is addressed to Gedeon Richter Plc., Gyömrői út 19-21, 1103 - Budapest, Hungary.

EMA/853667/2022
Amsterdam, 20 January 2023

Opinion of the Paediatric Committee on the refusal of a modification of an agreed Paediatric Investigation Plan

EMEA-001652-PIP01-14-M04

Scope of the application

Active substance(s):

Cariprazine (hydrochloride)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of schizophrenia

Pharmaceutical form(s):

Capsule, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Gedeon Richter Plc

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Gedeon Richter Plc submitted to the European Medicines Agency on 14 October 2022 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0156/2015 issued on 10 July 2015, decision P/0076/2016 issued on 18 March 2016, decision P/0301/2018 issued on 12 September 2018 and the decision P/0105/2021 issued on 17 March 2021.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 21 November 2022.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to refuse the changes proposed by the applicant regarding the paediatric investigation plan.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver remain unchanged and are set out in the Annex I.

3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of schizophrenia

The waiver applies to:

- the paediatric population from birth to less than 13 years of age;
- capsule, hard, for oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric investigation plan

2.1. Condition:

Treatment of schizophrenia

2.1.1. Indication(s) targeted by the PIP

Treatment of schizophrenia

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 13 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1:** Stability and compatibility assessment of the content of opened cariprazine capsules sprinkled on food
Non-clinical studies	Study 2: *This study was deleted in procedure EMEA-001652-PIP01-14-M01.* Study 3: *This study was deleted in procedure EMEA-001652-PIP01-14-M01.*

Clinical studies	**Study 4:** Open-label, multicentre, multiple dose study to evaluate pharmacokinetics, safety and tolerability of cariprazine in adolescent subjects (and adults) with schizophrenia, schizoaffective disorder and schizophreniform disorder (RGH-188-201) **Study 5:** Randomised, 6 week, double blind, multicentre, placebo controlled, parallel group efficacy and safety study of cariprazine in adolescent subjects with schizophrenia (RGH-MD-20/RGH-188-202) **Study 6:** Open label, 2 year safety study of cariprazine in adolescents with schizophrenia (RGH-188-203)
Extrapolation, modelling and simulation studies	**Study 7**: Data extrapolation from the to be performed paediatric studies, adult cariprazine studies and literature to support assumptions about the maintenance of antipsychotic effect of cariprazine in adolescent schizophrenia (RGH-188-204)
Other studies	Not applicable.
Other measures	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By September 2025
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of schizophrenia

Authorised indication(s):

- Treatment of schizophrenia in adult patients
  - Invented name(s): Reagila
  - Authorised pharmaceutical form(s): Capsule, hard
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure