EMA/901090/2022

European Medicines Agency decision

P/0502/2022

of 1 December 2022

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for obinutuzumab (Gazyvaro), (EMEA-001207-PIP06-22) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

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 application submitted by Roche Registration GmbH on 4 August 2022 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 November 2022, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[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

A paediatric investigation plan for obinutuzumab (Gazyvaro), concentrate for solution for infusion, intravenous 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, is hereby agreed.

Article 2

A deferral for obinutuzumab (Gazyvaro), concentrate for solution for infusion, intravenous 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, is hereby granted.

Article 3

A waiver for obinutuzumab (Gazyvaro), concentrate for solution for infusion, intravenous 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, is hereby granted.

Article 4

This decision is addressed to Roche Registration GmbH, Emil-Barell Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/851947/2022 Corr[12]
Amsterdam, 11 November 2022

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001207-PIP06-22

Scope of the application

Active substance(s):

Obinutuzumab

Invented name and authorisation status:

See Annex II

Condition(s):

Prevention of cytokine release syndrome induced by anti CD20/CD3 antibodies

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Roche Registration GmbH

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted for agreement to the European Medicines Agency on 4 August 2022 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 12 September 2022.

[1] Correction as of 30 November 2022
[2] Corrigendum as of 16 December 2022

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

- to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
- to grant a deferral in accordance with Article 21 of said Regulation;
- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

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 are set out in the Annex I.

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:

Prevention of cytokine release syndrome induced by anti CD20/CD3 antibodies

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- concentrate for solution for infusion, intravenous use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition:

Prevention of cytokine release syndrome induced by anti CD20/CD3 antibodies

2.1.1. Indication(s) targeted by the PIP

As pretreatment to reduce the risk of cytokine release syndrome induced by glofitamab in children between 6 months and less than 18 years of age

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

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion

2.1.4. Measures

Area	**Description**
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**Study 1 - Paediatric Study CO43810** Open-label, single-arm, two-part trial to evaluate safety, tolerability, pharmacokinetics (PK), and antitumour activity of glofitamab in combination with chemotherapy in children from 6 months to less than 18 years of age with relapsed/refractory (R/R) mature B-cell non-Hodgkin lymphoma (B-NHL). Part 2 (cohort expansion) is gated on Part 1 results (safety, PK, and preliminary antitumor activity). All study participants must receive obinutuzumab pre-treatment 7 days prior to the first dose of glofitamab for

	the purpose of cytokine release syndrome (CRS) risk mitigation.
Modelling and simulation studies	**Study 2** Modelling and simulation study to determine the single pre-treatment intravenous dose of obinutuzumab in children from 6 months to less than 18 years of age with relapsed/refractory (R/R) mature B-cell non-Hodgkin lymphoma (B-NHL) who will be treated with glofitamab
Other studies	Not applicable
Extrapolation plan	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 March 2029
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 chronic lymphocytic leukaemia (CLL)

Authorised indication(s):

- Gazyvaro in combination with chlorambucil is indicated for the treatment of adult patients with previously untreated CLL and with comorbidities making them unsuitable for full-dose fludarabine based therapy.
  - Invented name(s): Gazyvaro
  - Authorised pharmaceutical form(s): concentrate for solution for infusion
  - Authorised route(s) of administration: intravenous use
  - Authorised via centralised procedure

2. Treatment of Follicular lymphoma (FL)

Authorised indication(s):

- Gazyvaro in combination with chemotherapy, followed by obinutuzumab maintenance therapy in patients achieving a response, is indicated for the treatment of patients with previously untreated advanced FL.
  - Invented name(s): Gazyvaro
  - Authorised pharmaceutical form(s): concentrate for solution for infusion
  - Authorised route(s) of administration: intravenous use
  - Authorised via centralised procedure
- Gazyvaro in combination with bendamustine followed by obinutuzumab maintenance is indicated for the treatment of patients with FL who did not respond or who progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen.
  - Invented name(s): Gazyvaro
  - Authorised pharmaceutical form(s): concentrate for solution for infusion
  - Authorised route(s) of administration: intravenous use
  - Authorised via centralised procedure