24 February 2022
EMA/190956/2022
Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Imbruvica

ibrutinib

Procedure no: EMEA/H/C/003791/P46/036

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Steps taken for the assessment

Description	Date
Start of procedure	27 Dec 2021
CHMP Rapporteur Assessment Report	27 Jan 2022
CHMP adoption of conclusions	24 Feb 2022

Table of contents

1. Introduction 4

2. Scientific discussion 4

2.1. Information on the development program 4

2.2. Information on the pharmaceutical formulation used in the study<ies> 4

2.3. Clinical aspects 4

2.3.1. Introduction 4

2.3.2. Clinical study 5

3. Overall conclusion and recommendation 5

Annex. Line listing of all the studies included in the development program 6

1. Introduction

On 9th of December 2021, the MAH submitted a completed study, PYC1140, containing two paediatric/ adolescent patients, for Chronic Graft Versus Host Disease (cGVHD), in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

2. Scientific discussion

2.1. Information on the development program

Study PYC1140 has been submitted in accordance with Article 46 of Regulation (EC) No1901/2006. The study is part of the paediatric investigation plan (PIP) for Chronic Graft Versus Host Disease (cGVHD), which is not an authorized indication within the EU.

2.2. Information on the pharmaceutical formulation used in the study<ies>

Imbruvica (140mg capsule, 140-, 280-, 420- and 560 mg film-coated tablet)

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- Study PCYC-1140; A Randomized, Double-Blind Phase 3 Study of Ibrutinib in Combination With Corticosteroids versus Placebo in Combination With Corticosteroids in Subjects with New Onset Chronic Graft Versus Host Disease (cGVHD). The study includes two paediatric/adolescent patients aged ≥12-18 years.

Ibrutinib is an orally administered, covalently binding inhibitor of Bruton's tyrosine kinase (BTK). It was first approved in the EU in October 2014. It is currently approved for use in adult patients with the following blood cancers:

- Mantle cell lymphoma in patients whose disease does not respond to or has come back after previous treatment.
- Chronic lymphocytic leukaemia (CLL) in both previously treated and untreated patients.
- Waldenström's macroglobulinaemia (also known as lymphoplasmacytic lymphoma).

Study PCYC-1140 is part of the PIP for ibrutinib for cGvHD. The PIP includes one additional clinical study, Study PCYC-146-IM, with planned completion date Sep 2024. Graft Versus Host Disease (cGVHD) is not an authorized indication in the EU. Study PCYC-1140 includes only noninformative data from two paediatric/adolescent patients aged ≥12-18 with cGvHD.

No updates to the SmPC and package leaflet are proposed by the MAH in association with this final analysis of study PCYC-1140.

2.3.2. Clinical study

Study PCYC-1140 (study 1140):

A Randomized, Double-Blind Phase 3 Study of Ibrutinib in Combination With Corticosteroids versus Placebo in Combination With Corticosteroids in Subjects with New Onset Chronic Graft Versus Host Disease (cGVHD).

Description

Study 1140 was a Phase 3, multicenter, international, randomized, double-blind study designed to evaluate the safety and efficacy of oral ibrutinib in combination with prednisone vs. placebo in combination with prednisone in subjects with treatment-naive chronic graft vs. host disease (cGVHD). Study 1140 was conducted in subjects ≥12 years of age with cGVHD.

Study 1140 was initiated on 11 May 2017. The primary analysis was based on a data extract date of 30 March 2020 (approximately 1 year after the last subject was randomized) and the final analysis based on a data extract date of 12 July 2021, ie, with approximately 16 months of additional follow-up.

A total of 193 subjects (adult, ≥18 years: n=191; adolescent, ≥12 to <18 years: n=2) with treatment naive, moderate or severe cGVHD were randomized in a 1:1 ratio to receive either oral ibrutinib 420 mg daily (3 capsules) (Arm A) or matching placebo daily (3 capsules) (Arm B) both in combination with prednisone starting at 1 mg/kg/day.

Assessor's comment:
No conclusions on efficacy or safety of ibrutinib in paediatric patients with cGvHD can be drawn based on results of only two adolescent patients included in Study PYC1140. Furthermore, cGVHD is not an authorized indication in the EU. Hence, the submission of the final report of Study 1140 has no regulatory consequence.

3. Overall conclusion and recommendation

No conclusions on efficacy or safety of ibrutinib in paediatric patients with cGvHD can be drawn based on results of only two adolescent patients included in Study PYC1140. Graft Versus Host Disease (cGVHD) is not an authorized indication in the EU.

Accordingly, the data submitted does not change the risk benefit balance of ibrutinib and there is no regulatory consequence.

The PAM is considered

☒ **Fulfilled:**

No regulatory action required.

Annex. Line listing of all the studies included in the development program

The studies should be listed by chronological date of completion:

Non clinical studies

Not applicable

Clinical studies

Product Name: Imbruvica Active substance: Ibrutinib

Study title	Study number	Date of completion	Date of submission of final study report
A randomized, double-blind phase 3 study of ibrutinib in combination with corticosteroids versus placebo in combination with corticosteroids in subjects with new onset chronic Graft Versus Host Disease (cGVHD)	PCYC-1140-IM EudraCT Number: 2016-003286-26	12 Jul 2021	9 December 2021
Phase 1/2 dose finding, safety and efficacy study of ibrutinib in pediatric subjects with chronic Graft Versus Host Disease (cGVHD)	PCYC-146-IM EudraCT Number: 2017-004558-41	Sep 2024	-