Amsterdam, 19 May 2022
EMA/CHMP/241590/2022
Committee for Medicinal Products for Human Use (CHMP)

Assessment report for paediatric studies submitted in accordance with article 46 of regulation (EC) No 1901/2006, as amended

IMBRUVICA

International non-proprietary name: ibrutinib

Procedure no.: EMEA/H/C/003791/P46/037

Marketing authorisation holder (MAH): Janssen-Cilag International NV

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Steps taken for the assessment	
Description	**Date**
Start of procedure	21 Mar 2022
CHMP Rapporteur Assessment Report	22 Apr 2022
CHMP adoption of conclusions:	19 May 2022

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1. Introduction

On 21 Feb 2022, the MAH submitted data from an ongoing study for Imbruvica, in accordance with Article 46 of Regulation (EC) No1901/2006.

These data are NOT submitted as part of a post-authorisation measure or specific obligation.

Article 46 requires marketing-authorisation holders to submit information on studies conducted in children of authorised medicines that have been completed since the Paediatric Regulation came into force on 26 January 2007 and are sponsored by the marketing-authorisation holder. Information must be submitted within six months of completion of each study¨.

The study of ibrutinib monotherapy in 19 Japanese patients with steroid dependent/refractory chronic GvHD s currently ongoing and included 1 (one) pediatric patient, who died during participation in study. No other pediatric patients will be enrolled, which prompted the MAH to submit the procedure ahead of time (i.e. no CSR).

2. Scientific discussion

2.1. Information on the development program

The MAH stated that study GVH3001, a Phase 3 Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor Ibrutinib in Subjects with Steroid Dependent/Refractory Chronic Graft Versus Host Disease (cGVHD) is a stand-alone study.

2.2. Information on the pharmaceutical formulation used in the study

Ibrutinib monotherapy 420 mg qd.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a summary of findings from ongoing study GVH3001, a Phase 3 Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor Ibrutinib in Subjects with Steroid Dependent/Refractory Chronic Graft Versus Host Disease (cGVHD).

2.3.2. Clinical study

Study GVH3001 is an open-label, single arm study that was conducted in Japan only, to evaluate the efficacy, safety, and PK of single-agent ibrutinib 420 mg in Japanese subjects, ≥12 years of age with steroid dependent/refractory cGVHD.

A total of 19 subjects including 18 adult subjects aged ≥18 years and 1 adolescent subject aged 13 years with steroid dependent/refractory cGVHD were enrolled in this study.

Subjects received a maximum of 420 mg of ibrutinib once daily unless they had intervening unacceptable toxicity or met other criteria for subject discontinuation.

The primary endpoint of this study is overall response rate (complete response [CR]+partial response [PR]).

Although Study GVH3001 is ongoing, no new pediatric data will become available during the remainder of the study, as the 1 adolescent subject (13 yo) enrolled in the study died of multiple organ dysfunction syndrome possibly ibrutinib-related before the reported data cut-off in 2020.

2.3.3. Clinical Pharmacology

Venous blood samples were collected to determine plasma concentration of ibrutinib and the metabolite PCI-45227. The plasma concentration data of ibrutinib and PCI-45227 were used to determine PK parameters by noncompartmental method based on actual sampling times. Only one adolescent subject was included in the study. Due to the limited data in children, no conclusions on the paediatric population can be drawn.

3. CHMP overall conclusion and recommendation

☒ **Fulfilled:**

No regulatory action required. No changes in labelling.