EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 April 2024
EMA/223194/2024
Human Medicines Division

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

Jakavi

Ruxolitinib

Procedure no: EMEA/H/C/002464/P46/021

Note

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

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1. Introduction

On 30 Jan 2024, the MAH submitted a completed paediatric study with Jakavi, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

Jakavi (ruxolitinib) was first granted marketing authorization in the EU/EEA via centralized procedure on 23-Aug-2012 for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post- polycythaemia vera (PV) myelofibrosis or post-essential thrombocythemia (ET) myelofibrosis. Since then, ruxolitinib has been granted approval in the EU for adult patients with PV and for patients aged 12 years and older with GvHD.

In Japan, ruxolitinib was approved for use in adult patients with myelofibrosis on 04Jul2014, for use in adult patients with PV on 24Sep2015, and for use in patients aged 12 years or older with GvHD on 23 Aug 2023.

Steps taken for the assessment	
Description	**Date**
Start of procedure	26 Feb 2024
CHMP Rapporteur Assessment Report	20 Mar 2024
CHMP members comments	n/a
Updated CHMP Rapporteur Assessment Report	n/a
CHMP adoption of conclusions:	25 Apr 2024

2. Scientific discussion

2.1. Information on the development program

The MAH stated that Study CINC424A1401 is a stand-alone study.

2.2. Clinical aspects

2.2.1. Introduction

The MAH submitted a final report for:

- Study CINC424A1401: Specified Drug-Use Survey of Jakavi Tablets in Japan

No changes to the current ruxolitinib Core Data Sheet or to the approved EU SmPC are proposed as a result of this study.

2.2.2. Clinical study CINC424A1401

Description

Study CINC424A1401 (hereafter referred to as Study A1401) was an observational, open label study to evaluate the safety and efficacy of long-term administration of Jakavi (ruxolitinib, INC424) in adult and paediatric patients with myelofibrosis in a real-world setting in Japan.

Due to the limited number of patients studied for ruxolitinib in Japan, an all-case surveillance on all patients treated with ruxolitinib was set as a condition for approval in Japan until post-marketing data had been accumulated for the specified number of patients. This study was conducted in all treated myelofibrosis patients from 04-Jul-2014, with an observation period of up to 3 years from the start of treatment.

The study completed at database lock on 31-Aug-2023.

Methods

Study participants

All patients, adult and paediatric, with MF who were treated with ruxolitinib on or after the approval date for MF (04-Jul-2014) were included in the study.

Objective(s)

Outcomes/endpoints

Safety endpoints

- Adverse events
- Adverse drug reactions
- Important investigational items (described in the final CSR)
- Laboratory values

Efficacy endpoints

- Proportion of spleen shrinkage
- Physician’s global assessment of improvement
- Response rate by patient background factor

Results

Participants

Study A1401 enrolled a total of two paediatric patients. One paediatric patient was <18 years old, the other paediatric patient was <18 years old.

At Baseline, the <18 year-old patient had myelofibrosis associated with leukemia since years.

At Baseline, the <18 year-old patient had primary myelofibrosis since years.

Efficacy results

For the <18 year-old patient, the global improvement assessment was: Improvement

For the <18 year-old patient the global improvement assessment was: Not evaluable.

Safety results

<18 year-old patient

The starting dose of ruxolitinib for this patient was 20 mg/day.

During the study, the following AEs that were suspected to be related to ruxolitinib were reported for this patient: CTCAE grade 4 platelet count decreased (Day 6, SAE, ruxolitinib dose changed; also suspected related to ganciclovir and valganciclovir), grade 3 anemia (Day 22, SAE), and grade 3 white blood cell count decreased (Day 54, SAE, ruxolitinib dose changed). All AEs were also suspected to be related to the underlying disease or complications.

SAEs reported for this patient that were not suspected to be related to ruxolitinib were grade 3 lymphocyte count decreased, grade 3 purpura, grade 3 CMV viremia (all on Day 32), grade 3 liver disorder (Day 43; also suspected related to cefepime, ganciclovir, voriconazole, and post-transfusion iron overload), grade 3 pneumonia fungal (Day 81), and grade 3 blast cell count increased and grade 5 acute biphenotypic leukemia (both on Day 83). All these AEs were also suspected to be related to the underlying disease or complications.

On Day 112, the patient died of leukemia. The death was not suspected to be related to ruxolitinib but was considered related to the underlying disease/complications.

<18 year-old patient

The starting dose of ruxolitinib for this patient was 50 mg/day.

During the study, the following AEs that were suspected to be related to ruxolitinib were reported for this patient: grade 4 myelosuppression (Day 16, SAE; also suspected related to vincristine), grade 2 pyrexia (Day 21, non-serious AE), grade 5 blast cell count increased (Day 56, SAE; ruxolitinib discontinued due to this AE), grade 3 herpes zoster (Day 80, SAE; also suspected related to vincristine and dexamethasone), grade 4 sepsis (Day 94, SAE; also suspected related to dexamethasone), grade 3 herpes zoster (second occurrence; Day 112, SAE; also suspected related to dexamethasone), grade 4 bronchopulmonary aspergillosis (Day 121, SAE; also suspected related to dexamethasone), grade 4 seizure (Day 135, SAE), and unknown grade respiratory disorder (Day 137, SAE; also suspected related to vincristine, dexamethasone, sepsis, and bronchopulmonary aspergillosis). Except for pyrexia, these AEs were also suspected to be related to the underlying disease or complications.

No additional SAEs not suspected to be related to ruxolitinib were reported for this patient.

On Day 141, the patient died due to leukemia, which was considered related to the SAEs of blast cell count increased and respiratory disorder. An additional factor other than ruxolitinib suspected to be related to the SAE of blast cell count increased was the underlying disease or complications, and additional factors other than ruxolitinib suspected to be related to the SAE of respiratory disorder were the underlying disease or complications, concomitant medications (dexamethasone and vincristine), and the concurrent SAEs of sepsis and bronchopulmonary aspergillosis.

2.2.3. Discussion on clinical aspects

Due to the very limited number of paediatric patients included in Study A1401, no new conclusions for paediatric patients can be drawn. No update of the SmPC is warranted.

3. CHMP’s overall conclusion and recommendation

The MAH has submitted the paediatric data from Study A1401 in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. No new conclusions are drawn.

The PAM is considered

☒ **Fulfilled:**

No regulatory action required.