20 May 2021
EMA/260697/2021
Human Medicines Division

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

Tivicay

dolutegravir

Procedure no: EMEA/H/C/002753/P46/014

Note

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

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1. Introduction

On 26th of February 2021, the MAH submitted the final Clinical Study Report for Study 204666 for dolutegravir (Tivicay), in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

These data are also submitted as a Post Authorisation Measure. Study 204666 is not part of any Paediatric Investigation Plan.

A short critical expert overview has also been provided.

No amendments to the Product Information are being submitted as part of this procedure.

2. Scientific discussion

2.1. Information on the development program

Study 204666 is not part of any Paediatric Investigation Plan.

2.2. Information on the pharmaceutical formulation used in the study

Tablets 50 mg.

2.2.1. Introduction

The MAH submitted a final report for:

Study: 204666: *An Open-Label, Multi-Centre, Post-Marketing Surveillance (PMS) to Monitor the Safety and Effectiveness of Tivicay Administered in Korean Subjects for Treatment of HIV-1 Infection in Real Life Practice*

2.2.2. Clinical study 204666

An Open-Label, Multi-Centre, Post-Marketing Surveillance (PMS) to Monitor the Safety and Effectiveness of Tivicay Administered in Korean Subjects for Treatment of HIV-1 Infection in Real Life Practice

The primary objectives: To identify the occurrence and frequency of adverse events, serious adverse events, adverse drug reactions, and unexpected (i.e. unlisted) adverse events and drug reactions and understand the factors affecting safety and effectiveness in the post-marketing context.

Participants: Adult and adolescent participants living with HIV-1 infection in South Korea and being treated with Tivicay 50mg tablets.

A total of 147 participants were identified via electronic case report forms for the re-examination period of 29 August 2014 to 28 August 2020. Of these, 8 were excluded from surveillance (5 had taken DTG prior to contract date; 1 had taken DTG prior to consent date; and 2 had required BID dosing due to apparent INSTI resistance but remained on once daily dosing). Thus, the final number of participants in the Safety Analysis set was 139, and the final number in the Effectiveness Analysis set was 75 (with 64 unable to be assessed by the Investigator).

Demographic and Baseline Data: Among 139 participants in the Safety Analysis, males accounted for 93% (129/139). The mean age was 47.63±14.36 years, ranging from a minimum of 17.00 years to a maximum of 80.00. In terms of age distribution, 50 to 59 years accounted for the largest proportion. There was a single adolescent (12 to <19 years) in the Safety Analysis, or 1/139. There were no participants who identified as pregnant or lactating.

Results: There were no AEs reported for the single adolescent participant enrolled in the study.

CHMP comment:

Only one adolescent patient (12 to <19 years), participated in the study. There was no AE reported for this patient and no individual patient data on efficacy was presented.

3. Rapporteur's overall conclusion and recommendation

This Article 46 submission concerns an open label study 204666 which is not part of any Paediatric Investigation Plan and is submitted as a PAM. No concerns are raised, the study does not significantly contribute to the safety and efficacy data of Tivicay considering only one adolescent patient participated in the study. In EU Tivicay is currently approved in children of at least 6 years of age or older and weighing at least 14 kg.

From a procedural point of view it is noted that on the the EMA website, the following definition is given to guide the industry to P46 submissions: "*Submission of final results of study involving paediatric patients submitted in fulfilment of Article 46 of the paediatric regulation*".

https://www.ema.europa.eu/en/human-regulatory/post-authorisation/post-authorisation-measures-questions-answers

"18.1. What is the "Article 46 paediatric study submission"? Article 46 of Regulation (EC) No 1901/2006 (The 'Paediatric Regulation') sets out the obligation for the Marketing Authorisation Holder to submit to the competent authority any MAH-sponsored studies involving the use in the paediatric population of an authorised medicinal product, whether or not they are part of a PIP. For centrally authorised medicinal products, the studies should be submitted to the European Medicines Agency. This includes clinical studies that are:

• completed or discontinued;

• published or not Studies should be submitted regardless of the region where they were performed, the aim, outcome, population studied and indication."

However, the definition is not considered distinct but rather too general. In Study 204666, included in the current P46 submission, only one adolescent was enrolled. The indication for Tivicay is already approved in children of at least 6 years of age, hence, the contribution or the value of reporting this single subject in the framework of the Art 46 procedures cannot be considered meaningful. Thus, the patient distribution for the data submitted does not justify the P46 framework.

☒ **Fulfilled:**

No regulatory action required.