17 October 2019
EMA/595138/2019
Human Medicines Evaluation Division

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

Harvoni

ledipasvir / sofosbuvir

Procedure no: EMEA/H/C/003850/P46/022

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

Table of contents

1. Introduction 3

2. Scientific discussion 3

2.1. Information on the development program 3

2.2. Information on the pharmaceutical formulation used in the study 3

2.3. Clinical aspects 3

3. CHMP overall conclusion and recommendation 4

☒ Fulfilled: 4

1. Introduction

Gilead Sciences Ireland UC (Gilead) has submitted a final clinical study report the Gilead study GS-US-337-1904, in accordance with Article 46 of Regulation (EC) No 1901/2006. Gilead confirms that there are no regulatory consequences identified.

2. Scientific discussion

2.1. Information on the development program

This is a standalone study.

2.2. Information on the pharmaceutical formulation used in the study

Subjects were assigned to receive LDV/SOF 90/400 mg (1 x 90/400−mg tablet, i.e. adult tablet, or 4 x 22.5/100 mg tablets) once daily based on a swallowability assessment performed during screening period. All subjects were able to swallow the 90/400 mg tablet, the lower dose tablet was not used.

This is the approved dose for adolescents.

2.3. Clinical aspects

Background

Chronic hepatitis C is highly prevalent in Egyptian pediatric patients receiving cancer chemotherapy or following allogeneic bone-marrow transplantation (El-Sayed 2011 and 2004). The progression of HCV-related liver disease in this population may be rapid and a main cause of death in Egyptian patients with allogeneic bone marrow transplantation.

The study

Study GS-US-337-1904 [study period August 2016 to Feb 2019] was conducted at 1 study center in Egypt, in adolescents (12-18 years of age) with chronic hepatitis C infection of genotypes 1 or 4, who were receiving maintenance cancer chemotherapy for a hematologic malignancy. A total of 19 subjects were enrolled out of 24 screened.

Of those 19 enrolled, 16 were males, and 13/19 aged 12 to 15. All had genotype 4-infection, none had cirrhosis.

All 19 completed the 12 weeks of treatment, and SVR12 was achieved in 19/19.

There were no specific safety issues identified. Serious adverse events were reported in 3 subjects, non-related to the hep C therapy (but to underlying condition/cancer therapy). None of the chemotherapy interruptions or discontinuations was due to a study drug-related AE. Laboratory abnormalities were frequent, and deemed most likely caused by underlying treatment.

None experienced an HCV flare (defined in the protocol as ≥ 3**-**fold increase in aALT combined with ≥ 1 $\log_{10}$ increase in HCV RNA from Day 1 of the study).

3. CHMP overall conclusion and recommendation

In this phase 2 study of limited size the efficacy and safety of sof/ldv in adolescents with chronic hepatitis C who were receiving a maintenance cancer chemotherapy regimen was without remarks. The outcome is rather expected; sof/ldv has been studied in fairly large number of patients with a prior liver transplant, i.e. and subsequent immunosuppressive therapy, with favourable efficacy and safety outcomes.

The company does not propose any labelling changes. This is endorsed.

☒ Fulfilled:

No regulatory action required.