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APPLICATION NUMBER:

214187Orig1s000

OTHER REVIEW(S)

Division of Antivirals

REGULATORY PROJECT MANAGER LABELING REVIEW

Applications:

NDA 214187
NDA 208341/S-17

Name of Drug:

Epclusa (sofosbuvir and velpatasvir), tablets, 400 mg/100 mg and 200 mg/50 mg

Epclusa (sofosbuvir and velpatasvir), oral pellets, 200 mg/50 mg and 150 mg/37.5 mg

Applicant: Gilead Sciences, Inc.

Labeling Reviewed

Submission Dates: Prescribing Information (PI) (May 7, 2021)
Patient Package Insert (PPI) (May 17, 2021)
Instructions for Use (IFU), oral pellet only (May 17, 2021)

Background and Summary Description:

On December 15, 2020, Gilead Sciences, Inc., submitted original NDA 214187, for Epclusa (sofosbuvir and velpatasvir) oral pellets and an efficacy supplement, NDA 208341/S-17, for Epclusa (sofosbuvir and velpatasvir) tablets that proposed updating the labeling with dosing recommendations for the Epclusa pellets in patients 3 years and older. The submissions included data from study GS-US-342-1143, "A Phase 2, Open-Label, Multicenter, Multi-cohort Study to Investigate the Safety and Efficacy of Sofosbuvir/Velpatasvir in Adolescents and Children with Chronic HCV Infection", cohort 3, which enrolled patients 3 to less than 6 years of age. In addition, the sponsor conducted a BE/BA study that showed the pellets are bioequivalent to the tablet formulation. The submissions were submitted to fulfill the requirements of the Written Request. In addition, the submissions were submitted to fulfill the following PREA PMR that was included in the June 28, 2016 Approval letter for NDA 208341/0:

3092-2 Conduct a study to evaluate the pharmacokinetics, safety and treatment response (using sustained virologic response) of sofosbuvir and velpatasvir in pediatric subjects 3 through less than 12 years of age with chronic hepatitis C virus infection.

Review

For the purposes of this review, the last approved PI and PPI (NDA 208341/S-15, approved on July 14, 2020) was compared to the draft PI received on May 7, 2021, and the draft PPI received on May 17, 2021.

GLOBAL EDITORIAL CHANGES

- Minor editorial and formatting revisions were made throughout the PI and PPI.
- Subsections were renumbered throughout the PI as an additional subsection was added to the label.
- Revised date will be updated to reflect Month and Year the action is taken in the PI and PPI.

HIGHLIGHTS OF PRESCRIBING INFORMATION

PRODUCT TITLE

- New dosage form was added

RECENT MAJOR CHANGES

The following sections were added under this heading

- Indications and Usage
- Dosage and Administration
    - Recommended Treatment Regimen and Duration in Patients 3 years of Age and Older (2.2).
    - Recommended Dosage in Pediatric Patients 3 Years of Age and Older (2.4)
    - Preparation and Administration of Oral Pellets (2.5).

INDICATIONS AND USAGE

- Expanded the patient population to include pediatric patients 3 years of age and removed the minimum patient weight requirement of 17 kg.

DOSAGE AND ADMINISTRATION

- Updated subsections 2.2, 2.3, and 2.4 with Epclusa oral pellets dosing information for patients 3 years of age and older and removed the minimum weight requirement of 17 kg.
- Added new subsection, 2.5 “Preparation and Administration of Oral Pellets”.

DOSAGE FORMS AND STRENGTHS

- Added information for Epclusa oral pellets: 200mg of sofosbuvir and 50 mg of velpatasvir; 150 mg of sofosbuvir and 37.5 mg of velpatasvir.

ADVERSE REACTIONS

- Adverse reactions updated to list the adverse reactions specific to the age group in which they were observed.

- Adverse reaction listed for adults and pediatric subjects 6 years of age and older as headache and fatigue
- The most common adverse reactions in pediatric subjects less than 6 years of age has been added and listed as vomiting and product use issue (spitting up the drug)

FULL PRESCRIBING INFORMATION: CONTENTS*

DOSAGE AND ADMINISTRATION

- Updated subsection 2.2 to remove the minimum weight limit for the patient and to update the minimum patient age to 3 years of age
- Updated subsection 2.4 to revise the minimum pediatric patient age from 6 to 3 years of age.
- Added subsection 2.5: Preparation and Administration of Oral Pellets

CLINICAL STUDIES

- Specified the subjects for the clinical trial summarized in subsection 14.5 were adults.

FULL PRESCRIBING INFORMATION (FPI)

1 INDICATIONS AND USAGE

- Revised the minimum patient age from 6 to 3 years of age.
- Removed the minimum patient body weight requirement.

2 DOSAGE AND ADMINISTRATION

- 2.2 Recommended Treatment Regimen and Duration in Patients 3 Years of Age and Older
  - Revised the minimum patient age from 6 to 3 years of age.
  - Removed the requirement of a minimum patient body weight.
  - Updated Table 1 to capture the above two revisions (e.g., age and body weight).

- 2.4 Recommended Dosage in Pediatric Patients 3 Years of Age and Older
  - Revised the minimum patient age from 6 to 3 years of age.
  - Removed the requirement of a minimum patient body weight.
  - Specified that in pediatric patients less than 6 years of age, to administer the oral pellets with food to increase the tolerability related to palatability.
  - Two columns added to Table 2 to
    - specify the EPCLUSA daily dose, and
    - list dosing via the oral pellet.
- Addition of subsection 2.5, entitled, “Preparation and Administration of Oral Pellets”.

3 DOSAGE FORMS AND STRENGTHS

- Added information for the Epclusa, oral pellets

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience

- Adverse Reactions in Pediatric Subjects
  - Added adverse reaction data for pediatric subjects 3 to less than 6 years of age.

8 USE IN SPECIFIC POPULATIONS

- 8.4 Pediatric use
  - Updated with data from pediatric patients 3 years of age and older, with no minimum weight limit.

11 DESCRIPTION

- Added header for the description of Epclusa tablets.
- Added a new header and section describing the Epclusa pellet.

12 CLINICAL PHARMACOLOGY

- 12.3 Pharmacokinetics
  - Under Specific Populations: Pediatric Patients subsection, added the PK data from patients 3 to 6 years of age and older.
- 12.4 Microbiology
  - Under the Pediatric subsection, added data from patients 3 to less than 6 years of age.

14 CLINICAL STUDIES

- 14.1 Description of Clinical Trials
  - Updated Table 12 to include information from the trial (NCT03022981) in pediatric subjects 3 to less than 6 years of age.
  - Added a footnote to Table 12 to define treatment-experience (TE) subjects as those who have failed an interferon-based regimen with or without ribavirin and with or without an HCV protease inhibitor (boceprevir, simeprevir, or telaprevir).
- 14.7 Clinical Trials in Pediatric Subjects
  - Updated to include data from pediatric subjects 3 to less than 6 years of age.

16 HOW SUPPLIED/STORAGE AND HANDLING

- Added a header to identify the tablet specific information.
- Added a new section to provide for the supplied/storage and handling information for the new oral pellet formulation.

17 PATIENT COUNSELLING INFORMATION

- Added new text to refer the patient to the new Instructions for Use, which is a new component of the FDA-approved patient labeling.

PATIENT INFORMATION

- Updated header to add the oral pellets.
- Under the description, “What is EPCLUSA”, updated to provide for information regarding the oral pellet.
  - The minimum patient age has been revised from 6 years to 3 years of age.

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