

# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

### *APPLICATION NUMBER:*

**212477Orig1s000**

*Trade Name:* HARVONI oral pellets, 33.75mg/150mg and 45mg/200mg

*Generic or Proper Name:* ledipasvir and sofosbuvir

*Sponsor:* Gilead Sciences, Inc.

*Approval Date:* August 28, 2019

*Indication:* for the treatment of chronic hepatitis C virus (HCV) in adults and pediatric patients 3 years of age and older:

- Genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
- Genotype 1 infection with decompensated cirrhosis, in combination with ribavirin
- Genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin

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## 212477Orig1s000

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*APPLICATION NUMBER:*

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**APPROVAL LETTER**

NDA 212477

**NDA APPROVAL**

Gilead Sciences, Inc.  
Attention: Xiaoping Qi, MS, RAC  
Associate Director, Regulatory Affairs  
333 Lakeside Drive  
Foster City, CA 94404

Dear Ms. Qi:

Please refer to your new drug application (NDA) dated February 28, 2019, received February 28, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for HARVONI<sup>®</sup> (ledipasvir and sofosbuvir) oral pellets, 33.75 mg/150 mg and 45 mg/200 mg.

This new drug application provides for the following:

- The use of HARVONI<sup>®</sup> (ledipasvir and sofosbuvir) oral pellets, 33.75 mg/150 mg, 45 mg/200 mg, for the treatment of pediatric patients 3 years of age and older with chronic hepatitis C virus (HCV):
  - genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
  - genotype 1 infection with decompensated cirrhosis, for use in combination with ribavirin
  - genotype 1 or 4 liver transplant recipients without cirrhosis or with compensated cirrhosis, for use in combination with ribavirin
- To make corresponding changes to the Patient Information

### **APPROVAL & LABELING**

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

### **WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at [FDA.gov](http://FDA.gov).<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible via publicly available labeling repositories.

## **CARTON AND CONTAINER LABELING**

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 212477.**” Approval of this submission by FDA is not required before the labeling is used.

## **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for age 0 to 3 years because studies are impossible or highly impracticable due to spontaneous HCV clearance resulting in very few patients requiring treatment in this age group.

This product is appropriately labeled for the use in ages 12 to 17 years of age for this indication. Therefore, no additional studies are needed in this pediatric group.

We note that you have fulfilled the pediatric study requirement for ages 3 to less than 12 years for this application.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

## **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the Prescribing Information, Medication Guide, and Patient Package Insert (as applicable) to:

OPDP Regulatory Project Manager  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.<sup>3</sup>

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.<sup>4</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>5</sup> For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.<sup>6</sup>

## **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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<sup>3</sup> When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

<sup>4</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

<sup>6</sup> <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>

If you have any questions, contact Philip Villasurda, Regulatory Project Manager, at Philip.Villasurda@fda.hhs.gov or call at (301) 796-2586 or (301) 796-1500.

Sincerely,

*{See appended electronic signature page}*

Debra Birnkrant, MD  
Director  
Division of Antiviral Products  
Office of Antimicrobial Products  
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Container Labeling

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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