

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205834Orig1s007, s008, s009

CHEMISTRY REVIEW(S)

**ONDP Division of New Drug Products-I
Quality Assessment for Efficacy or Labeling Supplement**

**HARVONI (ledipasvir and sofosbuvir) Tablets
90mg/400mg**

Gilead

NDA 205-834

S-007:	EDR-082	SD-194	August 26, 2015
S-008:	EDR-083	SD-195	August 26, 2015
S-009:	EDR-084	SD-196	August 26, 2015

Submission Date:	as above
GRMP Date:	Feb 2, 2016
PDUFA Date:	Feb 26, 2016

Summary:

These three efficacy supplements expand the indication to include these subpopulations:

- S-007: Liver Transplant Recipients with Genotype 1 HCV Infection
- S-008: Liver Transplant Recipients with Genotype 4 HCV Infection
- S-009: Patients with Decompensated Cirrhosis with Genotype 1 HCV Infection

No CMC information is included in Module 2, and there is no Module 3.

There are no changes to the Description or How Supplied sections of the Prescribing Information, and no CMC-related edits to the Patient Information and Patient Counseling Information sections. No container labels are provided. This was verified in the three labeling amendments submitted on Sept 2, 2015.

This is all consistent with the use of the currently approved products, without any change to the dosage form, container/closure or CMC-related labeling.

In Section 1.12, the applicant requests a categorical exclusion from the requirements to prepare an Environmental Assessment. Although some increase in use of the drug may result from the change in labeling, the supplement meets the requirements of a categorical exclusion under:

- 21 CFR §25.31(b) because the estimated concentration of the active drug substance at the point of entry, referred to as the Expected Introduction Concentration (EIC), into the aquatic environment will be below 1 part per billion (ppb). Calculations are supplied. The applicant states that to the best of their knowledge, no extraordinary circumstances exist.

Conclusions:

These supplements are recommended for filing and for approval from the Product Quality perspective. The only CMC issue is the categorical exclusion from the requirement to perform an environmental assessment. This should be granted, since the applicant has provided an appropriate claim per 21 CFR §25.31.

**Stephen
Miller -S**

Digitally signed by Stephen Miller -S
DN: c=US, o=U.S. Government, ou=HHS,
ou=FDA, ou=People, cn=Stephen Miller
-S,
0.9.2342.19200300.100.1.1=1300087013
Date: 2015.09.25 13:52:17 -04'00'

Stephen P. Miller, Ph.D.

CMC-Lead

**Balajee
Shanmugam
-S**

Digitally signed by Balajee
Shanmugam -S
DN: c=US, o=U.S. Government,
ou=HHS, ou=FDA, ou=People,
0.9.2342.19200300.100.1.1=130021
7143, cn=Balajee Shanmugam -S
Date: 2015.09.25 15:38:36 -04'00'

Balajee Shanmugam, Ph.D.

Acting Branch Chief

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBYN S JORDON
02/24/2016