Harvoni® (ledipasvir/sofosbuvir) – Expanded orphan indication, new formulation approval

- On August 28, 2019, the FDA approved Gilead's Harvoni (ledipasvir/sofosbuvir), for the treatment of adults and 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 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, for use in combination with ribavirin.
- Harvoni was previously approved in adult patients for the same indications and was also approved in pediatric patients 12 years of age and older or weighing at least 35 kg with HCV genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis.
- Along with the expanded indication, the FDA also approved a new oral pellet formulation of Harvoni and a new strength (45 mg/200 mg) of the oral tablet formulation. Previously, Harvoni was only available as a 90 mg/400 mg tablet.
- The efficacy of Harvoni was evaluated in 90 patients 6 years to < 12 years of age with HCV genotype 1 or 4 infection. The sustained virologic response (SVR12) or cure rate was 99% (86/87) in patients with genotype 1 HCV infection, and 100% (2/2) in patients with genotype 4 HCV infection.
- The efficacy of Harvoni was also evaluated in 34 patients 3 years to < 6 years of age with HCV genotype 1 or genotype 4 infection. The SVR12 rate was 97% (32/33) in patients with genotype 1 HCV infection, and the one patient with genotype 4 HCV infection also achieved SVR12. One patient prematurely discontinued study treatment due to an adverse event.
- Harvoni carries a boxed warning for risk of hepatitis B virus reactivation in patients coinfected with HCV and hepatitis B virus.
- When used in combination with ribavirin, all contraindications to ribavirin also apply to Harvoni combination therapy.
- Additional warnings and precautions for Harvoni include serious symptomatic bradycardia when coadministered with amiodarone, risk of reduced therapeutic effect due to use with P-gp inducers, and risks associated with combination treatment.
- The recommended treatment regimen, duration, and dosage for Harvoni combination therapy in pediatric patients 3 years of age and older are provided in the tables below.
    - Harvoni pellets should not be chewed. If Harvoni pellets are administered with food, the pellets should be sprinkled on one or more spoonfuls of non-acidic soft food at or below room temperature.
    - Refer to the Harvoni label for additional dosing and administration recommendations, including dosing in adult patients.

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Genotype	Patient population	Treatment regimen and duration
Genotype 1	Treatment-naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni 12 weeks†
	Treatment-experienced* without cirrhosis	Harvoni 12 weeks
	Treatment-experienced* with compensated cirrhosis (Child-Pugh A)	Harvoni 24 weeks‡
	Treatment-naïve and treatment-experienced* with decompensated cirrhosis (Child-Pugh B or C)	Harvoni + ribavirin 12 weeks
Genotype 1 or 4	Treatment-naïve and treatment-experienced* liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Pugh A)	Harvoni + ribavirin 12 weeks
Genotype 4, 5, or 6	Treatment-naïve and treatment-experienced*, without cirrhosis or with compensated cirrhosis (Child-Pugh A)	Harvoni 12 weeks

* Treatment-experienced adult and pediatric patients have failed a peginterferon alfa +/- ribavirin based regimen with or without an HCV protease inhibitor.
† Harvoni for 8 weeks can be considered in treatment-naïve genotype 1 patients without cirrhosis who have pretreatment HCV RNA less than 6 million IU/mL.
‡ Harvoni + ribavirin for 12 weeks can be considered in treatment-experienced genotype 1 patients with cirrhosis who are eligible for ribavirin

Body weight	Dosing of Harvoni	Harvoni daily dose
At least 35 kg	one 90 mg/400 mg tablet once daily or two 45 mg/200 mg tablets once daily or two 45 mg/200 mg packets of pellets once daily	90 mg/400 mg
17 kg to less than 35 kg	one 45 mg/200 mg tablet once daily or one 45 mg/200 mg packet of pellets once daily	45 mg/200 mg
Less than 17 kg	one 33.75 mg/150 mg packet of pellets once daily	33.75 mg/150 mg

- Gilead's launch plans for Harvoni oral pellets and the new oral tablet strength (45 mg/200 mg) are pending. Harvoni oral pellets will be available in 33.75 mg/150 mg and 45 mg/200 mg strengths.