Ledipasvir-Sofosbuvir *(Harvoni)*

Table of Contents

Drug Summary

The fixed-dose combination of ledipasvir-sofosbuvir (Figure 1) and (Figure 2) provides an effective and well-tolerated one-pill once-a-day option for treatment of genotypes 1, 4, 5, and 6 chronic hepatitis C (HCV) infection. This direct-acting antiviral regimen was the first FDA-approved interferon- and ribavirin free regimen to treat hepatitis C. Ledipasvir-sofosbuvir can be used without ribavirin in most patients with genotype 1A, except those who are cirrhotic and treatment-experienced. In addition, persons with HCV genotype 1 may be eligible for an 8-week duration if they are treatment-naïve, without cirrhosis, and have a pretreatment HCV RNA level less than 6 million. Similar to sofosbuvir-velpatasvir, the other NS5B-NS5A inhibitor combination, ledipasvir-sofosbuvir has been shown to be safe and effective for the treatment of HCV in persons with decompensated cirrhosis.

Adverse Effects

Available data from clinical trials has demonstrated the combination of ledipasvir-sofosbuvir has been very well tolerated. The most common reported adverse effects are fatigue and headache.

Class and Mechanism

Ledipasvir is a potent inhibitor of HCV NS5A, a viral phosphoprotein that plays an important role in viral replication, assembly, and secretion. Sofosbuvir is a nucleotide analog inhibitor of hepatitis C virus NS5B polymerase—the key enzyme mediating HCV RNA replication. The triphosphate form of sofosbuvir

(GS-461203) mimics the natural cellular uridine nucleotide and is incorporated by the HCV RNA polymerase into the elongating RNA primer strand, resulting in viral chain termination.

Indications

The fixed dose combination ledipasvir-sofosbuvir (90 mg/400 mg) is indicated for treatment, with or without ribavirin, for the treatment of patients with chronic hepatitis C genotypes 1, 4, 5, and 6. The detailed indications are listed below. When treating patients coinfected with HCV and HIV, the recommendations are the same as listed below.

Genotype 1

- Treatment-naïve patients without cirrhosis or with compensated cirrhosis (Child-Pugh A) : ledipasvir-sofosbuvir x 12 weeks*
- Treatment-experienced** patients without cirrhosis: ledipasvir-sofosbuvir x 12 weeks
- Treatment-experienced** patients with compensated cirrhosis (Child-Pugh A): ledipasvir-sofosbuvir x 24 weeks[†]
- Treatment-naïve and treatment-experienced** patients with decompensated cirrhosis (Child-Pugh B or C): ledipasvir-sofosbuvir plus ribavirin[‡] x 12 weeks

Genotype 1 or 4

- Treatment-naïve and treatment-experienced ** liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Pugh A): ledipasvir-sofosbuvir plus ribavirin[§] x 12 weeks

Genotype 4, 5, or 6

- Treatment-naïve and treatment-experienced ** patients without cirrhosis or with compensated cirrhosis (Child-Pugh A): ledipasvir-sofosbuvir plus ribavirin x 12 weeks

Footnotes
*Based on a subset analysis from the ION-3 trial, ledipasvir-sofosbuvir for 8 weeks can be considered in treatment-naïve genotype 1 patients without cirrhosis who have pre-treatment HCV RNA less than 6 million IU/mL.

**Treatment-experienced patients include those who have failed a peginterferon alfa plus ribavirin based regimen, with or without an HCV protease inhibitor.

[†]Ledipasvir-sofosbuvir for 12 weeks can be considered in treatment-experienced genotype 1 patients with cirrhosis who are eligible for ribavirin (see footnote[§] for ribavirin dosage recommendations).

[‡]In patients with decompensated cirrhosis, the starting dosage of ribavirin is 600 mg and can be titrated up to

Figure 1. Tablets - Ledipasvir-sofosbuvir (*Harvoni*)

Photo: Andrew Karpenko, University of Washington

Figure 2. Bottle - Ledipasvir-sofosbuvir (*Harvoni*)

Photo: Andrew Karpenko, University of Washington