Sofosbuvir *(Sovaldi)*

Table of Contents

Drug Summary

Sofosbuvir (Figure 1) and (Figure 2) was a breakthrough new medication for the treatment of patients with chronic hepatitis C. Sofosbuvir has a number of ideal properties, including once-daily dosing, no meal restrictions, few adverse effects, minimal drug-drug interactions, a high genetic barrier to resistance, and relatively good safety and efficacy in patients with advanced liver disease. The use of sofosbuvir in combination with ribavirin was the first FDA-approved all oral therapy for hepatitis C. Of note, the activity against genotype 3 appears less than with genotype 2 and treatment of genotype 3 infection requires a longer all-oral course of treatment than with genotype 2. Sofosbuvir is primarily used now in fixed-dose combinations.

Adverse Effects

Sofosbuvir is generally well-tolerated. The most common adverse effects observed with sofosbuvir, when used in combination with ribavirin, have been fatigue and headache. Sofosbuvir is pregnancy category B. To report suspected adverse reactions, contact (1) Gilead Sciences, Inc. at 1-800-GILEAD-5 or (2) the FDA at 1-800-FDA-1088.

Class and Mechanism

Sofosbuvir is a nucleotide analog inhibitor of hepatitis C virus NS5B polymerase—the key enzyme mediating HCV RNA replication. Sofosbuvir is a prodrug and after ingestion it is rapidly converted to GS-331007, the

predominant circulating drug that accounts for greater than 90% of the systemically active drug. The compound GS-331007 is efficiently taken up by hepatocytes, whereby cellular kinases convert GS-331007 to its pharmacologically active uridine analog 5'-triphosphate form (GS-461203). This triphosphate compound mimics the natural cellular uridine nucleotide and is incorporated by the HCV RNA polymerase into the elongating RNA primer strand, resulting in chain termination. The active form GS-461203 targets the NS5B catalytic site and acts as a non-obligate chain terminator. The active compound (GS-461203) does not inhibit host DNA polymerases, RNA polymerases, or mitochondrial RNA polymerase.

Indications

The following indications for sofosbuvir relate to patients with chronic hepatitis C virus infection.

Sofosbuvir is indicated for treatment of patients with chronic HCV

- Genotype 1 or 4: sofosbuvir plus peginterferon-alfa plus ribavirin for 12 weeks
- Genotype 2: sofosbuvir plus ribavirin for 12 weeks
- Genotype 3: sofosbuvir plus ribavirin for 24 weeks

For the treatment of patients with HCV-HIV-1 coinfection: the recommendations are the same as listed above.

For patents with genotype 1 HCV who are not eligible to receive interferon: sofosbuvir plus ribavirin for 24 weeks can be considered.

For patients with HCV and hepatocellular carcinoma awaiting liver transplantation: sofosbuvir plus ribavirin for a duration of up to 48 weeks or until liver transplantation, whichever occurs first.

Simeprevir in Combination with Sofosbuvir for HCV Infection: for details see the Simeprevir Drug Summary page and Simeprevir Full Prescribing Information

Daclatasvir in Combination with Sofosbuvir for HCV Infection: for details see the Daclatasvir Drug Summary page and Daclatasvir Full Prescribing Information

Dosing

Sofosbuvir is available as a 400 mg tablet. The recommended dose of sofosbuvir is 400 mg taken orally once daily, with or without food. The 400 mg dose of sofosbuvir should be used, regardless of the patient's genotype and prior hepatitis C treatment experience. No dose adjustment is needed for mild-to-moderate renal impairment or with mild, moderate, or severe hepatic impairment. The prescribing information does not make a recommendation for dosing in patients who have severe renal impairment (eGFR less than 30 ml/min/1.73m^2) or end stage renal disease requiring dialysis. Sofosbuvir is also available as a fixed-dose combination pill (ledipasvir 90 mg and sofosbuvir 400 mg) taken once daily.

Cost and Medication Access

Gilead Sciences has an active sofosbuvir patient assistance program for eligible patients with hepatitis C who do not have insurance and are not covered by Medicaid or Medicare. Information regarding the Gilead Sciences sofosbuvir patient assistance program can be obtained at the Support Path website or by calling 1-855-769-7284.

Key Drug Interactions

For complete information on sofosbuvir-related drug interactions, see the Drug Interactions section in the Sofosbuvir (*Sovaldi*) Prescribing Information.

Full Prescribing Information

Sofosbuvir (*Sovaldi*) Full Prescribing Information

Figures

Figure 1. Sofosbuvir (*Sovaldi*) Pill Bottle

Photo: Andrew Karpenko, University of Washington

Figure 2. Sofosbuvir (*Sovaldi*) Pill

Photo: Andrew Karpenko, University of Washington