Sofosbuvir (Sovaldi)

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Drug Summary

Sofosbuvir 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, 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.

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.

Manufacturer for United States

Sofosbuvir is manufactured as Sovaldi (soh-VAHL-dee) by Gilead Sciences (Figure 1) and (Figure 2). The drug sofosbuvir was previously known as GS-7977 and was originally developed by Pharmasset
as compound PSI-7977.

**Cost and Medication Access**

The wholesale acquisition cost (WAC) for sofosbuvir is $1,000 per 400 mg pill. Accordingly, the cost for the sofosbuvir component in a 12-week treatment course is $84,000 (and the total regimen cost depends on the other medications used in combination with sofosbuvir). For a 24-week course of sofosbuvir, the WAC is $168,000. 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 for Solvaldi and Harvoni web site and by contacting them directly by phone at 1-855-769-7284 (hours of operation Monday through Friday between 9:00 am and 8:00 pm Eastern Standard Time).

**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.

**Key Drug Interactions**

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