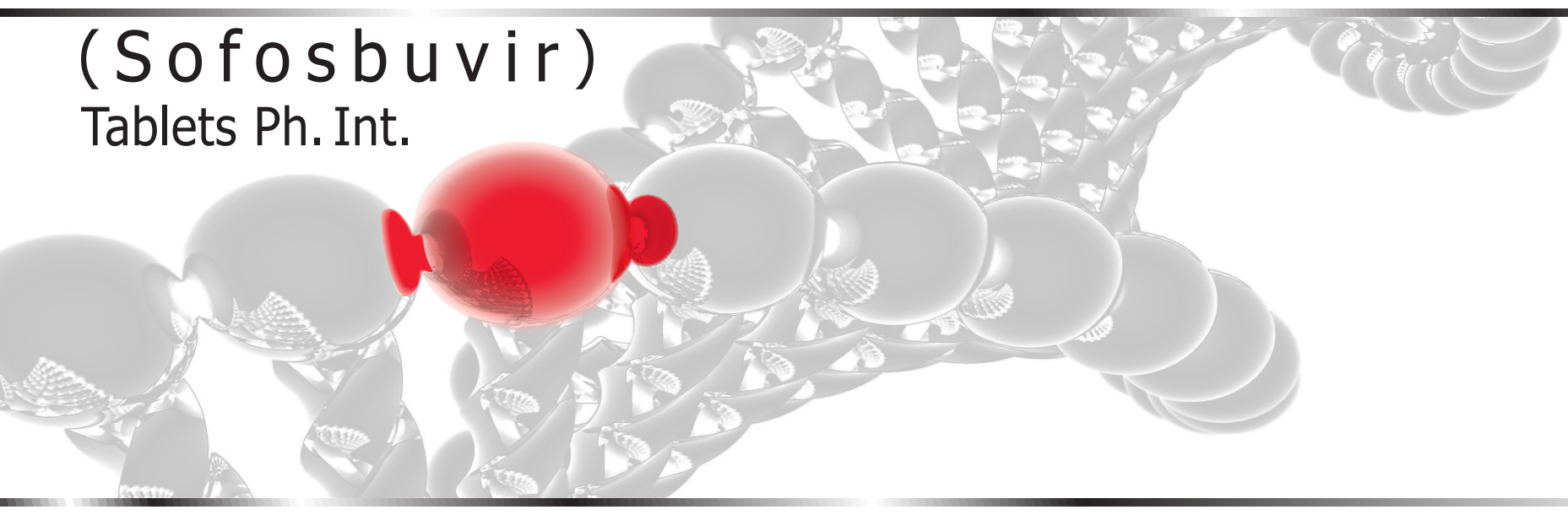
Sofos® 400mg

سوفوس ٤٠٠ ملی گرام ٹیبلٹس

انٹرنیشنل فارماکوپیا

(سوفوسبووِیر)

(Sofosbuvir)
Tablets Ph. Int.



DESCRIPTION

Sofosbuvir is a nucleotide analog inhibitor of HCV NS5B polymerase.

The IUPAC name for sofosbuvir is (S)-Isopropyl 2- ((S) - (2R,3R,4R,5R) - 5 - (2,4 - di-oxo-3,4 dihydropyrimidin-1 (2H) - yl)- 4-fluoro - 3-hydroxy-4- methyltetrahydrofu-ran-2-yl) methoxy) - (phenoxy) phosphorylamino) propanoate. It has a molecular for-mula of C22H29FN3O9P and a molecular weight of 529.45 g/mol.

MECHANISM OF ACTION

Sofosbuvir is a direct-acting antiviral agent against the hepatitis C virus. Sofosbuvir is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is essential for viral replication. Sofosbuvir is a nucleotide prodrug that undergoes intracellular me-tabolism to form the pharmacologically active uridine analog triphosphate (GS-461203), which can be incorporated into HCV RNA by the NS5B polymerase and acts as a chain terminator. In a biochemical assay, GS-461203 inhibited the poly-merase activity of the recombinant NS5B from HCV genotype 1b, 2a,3a and 4a with IC50 values ranging from 0.7 to 2.6 μM. GS-461203 is not an inhibitor of human DNA and RNA polymerases nor an inhibitor of mitochondrial RNA polymerase.

COMPOSITION

Each film-coated tablet contains:
Sofosbuvir.....400mg

Indications and Usage: Sofos contains the active substance sofosbuvir which is given to treat hepatitis C virus infection in adults of 18 years and older. Hepatitis C is a virus that infects the liver. This medicine works by lowering the amount of hepatitis C virus in your body and removing the virus from your blood over a period of time.

The following points should be considered when initiating treatment with Sofosbuvir:

- Monotherapy of Sofosbuvir is not recommended for treatment of CHC.
- Treatment regimen and duration are dependent on both viral genotype and patient population .
- Treatment response varies based on baseline

PHARMACOKINETICS

Absorption:

- Peak plasma time: 0.5-2 hr (sofosbuvir); 2-4 hr (metabolite GS-331007)
- AUC when coadministered with ribavirin (with or without peg-interferon): 828 ng
- hr/mL (sofosbuvir); 6790 ng•hr/mL (metabolite GS-331007)

Distribution: Plasma bound: 61-65% (sofosbuvir); minimal for metabolite GS-331007

Metabolism:

- Liver
- Substrate: P-gp transporter and breast cancer resistance protein (substrate for so-fosbuvir but not metabolite GS-331007)

Elimination:

- Excretion: Urine (78% metabolite GS-331007; 3.5% sofosbuvir)
- Half-life: 0.4hr (sofosbuvir); 27 hr (metabolite GS-331007)

Patients with Renal Impairment: No dose adjustment is required for patients with mild or moderate renal impairment. The safety and efficacy of Sofosbuvir have not been established in patients with severe renal impairment or ESRD. No dose recommendation can be given for patients with severe renal impairment .

Patients with Hepatic Impairment: No dose adjustment of Sofosbuvir is recommended for patients with mild, moderate and severe hepatic impairment.

Dosage & Administration: The recommended dose of Sofosbuvir is one 400 mg tablet, taken orally, once daily with or without food. Sofosbuvir should be used in combination with ribavirin or in combination with pegylated interferon and ribavirin for the treatment of CHC in adults.

Table-1 Recommended Regimens and Treatment Duration for Sofosbuvir Combination Therapy.

	TREATMENT	DURATION
Patients with genotype 3 CHC	Sofosbuvir + ribavirin[b]	24 weeks
Patients with genotype 2 CHC	Sofosbuvir + ribavirin[b]	12 weeks
Patients with genotype 1 or 4 CHC	Sofosbuvir+ peginterferon alfa[a] + ribavirin	12 weeks

a. See peginterferon alfa prescribing information for dosing recommendation for patients with genotype 1 or 4 CHC.
b. Dose of ribavirin is weight-based (<75 kg = 1000 mg and ≥75 kg = 1200 mg). The daily dose of ribavirin is administered orally in two divided doses with food. Patients with renal impairment (CrCl ≤ 50 mL/min) require ribavirin dose reduction; refer to ribavirin prescribing information.

TREATMENT DURATION

Patients with genotype 1or4 CHC Sofosbuvir+Peginterferon alfa+Ribavirin 12 weeks.
Patients with genotype 2 CHC Sofosbuvir+ribavirin 12 weeks.
Patients with genotype 3 CHC Sofosbuvir+ribavirin 24 weeks.

Sofosbuvir in combination with ribavirin for 24 weeks can be considered as a therapeutic option for CHC patients with genotype 1 infection who are ineligible to receive an interferon-based regimen.

Sofosbuvir in combination with ribavirin is recommended for up to 48 weeks or until the time of liver transplantation, whichever occurs first, to prevent post-transplant HCV reinfection.

CONTRAINDICATIONS

When Sofosbuvir is used in combination with ribavirin or peginterferon alfa/ribavirin, the contraindications applicable to those agents are applicable to combination therapies. Refer to the prescribing information of peg interferon alfa and ribavirin for a list of their contraindications. Sofosbuvir combination treatment with ribavirin or peginterferon alfa/ribavirin is contraindicated in women who are pregnant or may become pregnant and men whose female partners are pregnant because of the risks for birth defects and fetal death associated with ribavirin.

WARNINGS AND PRECAUTIONS

Pregnancy: Use of Ribavirin or Peginterferon Alfa/Ribavirin may cause birth defects and/or death of the exposed fetus and animal studies have shown that interferons have abortifacient effects. Ribavirin therapy should not be started unless a report of a

negative pregnancy test has been obtained immediately prior to initiation of therapy.

Nursing Mothers: It is not known whether Sofosbuvir and its metabolites are present in human breast milk. Because of the potential for adverse reactions from the drug in nursing infants, a decision must be made whether to discontinue nursing or discontinue treatment with ribavirin-containing regimens, taking into account the importance of the therapy to the mother.

Pediatric Use : Safety and effectiveness of Sofosbuvir in children less than 18 years of age have not been established.

Adverse Reactions: The most common adverse events (incidence greater than or equal to 20%, all grades) observed with Sofosbuvir in combination with ribavirin were fatigue and headache. The most common adverse events observed with Sofosbuvir in combination with peginterferon alfa and ribavirin were fatigue, headache, nausea, insomnia and anemia. Very common side effects (may affect more than 1 in 10 people) •fever, chills, flu-like symptoms •diarrhoea, feeling sick (nausea), being sick (vomiting) •trouble sleeping (insomnia) •feeling tired and irritable •headache •rash, itchy skin •loss of appetite •feeling dizzy •muscle aches and pains, pain in the joints •shortness of breath, cough

Drug Interactions: Drugs that are potent intestinal P-gp inducers (e.g., rifampin, St. John's wort) may alter the concentrations of sofosbuvir.

INSTRUCTIONS

Keep all medicines out of the reach of children.
Store below 30°C, Protect from heat, light & moisture.

PRESENTATION

SOFOS (Sofosbuvir) Tablets 400mg are available in Alu-Alu blister pack of 28's.

خوراک : معالج کی ہدایت کے مطابق استعمال کریں۔
ہدایات : ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، روشنی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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