Sofopas 90mg/400mg

Ledipasvir / Sofosbuvir Tablets

DESCRIPTION:
Ledipasvir is hepatitis C virus (HCV) NS5A inhibitor, and sofosbuvir is a nucleotide analog inhibitor of HCV NS5B polymerase

Composition :
Each film-coated tablet contains :
Ledipasvir.....90mg
Sofosbuvir.....400mg
Genix Specs.

CLINICAL PHARMACOLOGY
Mechanism of Action: Sofopas is a fixed-dose combination of ledipasvir and sofosbuvir which are direct acting antiviral agents against the hepatitis C virus

PHARMACOKINETICS
Absorption. Following oral administration , ledipasvir median peak concentrations were observed 4 to 4.5 hours post-dose. Sofosbuvir was absorbed quickly and the peak median plasma concentration was observed ~0.8 to 1 .

Distribution: Ledipasvir is >99.8% bound to human plasma proteins. After a single 90 mg dose of [14C]-ledipasvir in healthy subjects, the blood to plasma ratio of 14C-radioactivity ranged between 0.51 and 0.66. Sofosbuvir is approximately 61–65% bound to human plasma proteins and the binding is independent of drug concentration over the range of 1 μg/mL to 20 μg/mL.
Metabolism In vitro, no detectable metabolism of ledipasvir was observed by human CYP1A2, CYP2C8, CYP2C9, CYP 2C19, CYP2D6, and CYP3A4.
Elimination Following a single 90 mg oral dose of [14C]-ledipasvir, mean total recovery of the [14C]-radioactivity in feces and urine was approximately 87%, with most of the radioactive dose recovered from feces (approximately 86%).

INDICATIONS:
It is indicated for the treatment of chronic hepatitis C (CHC) genotype 1,4,5 or 6 infection in adults (1)

DOSAGE :
The recommended dose of Sofopas is one tablet once daily with or without food. Recommended treatment duration for Sofopas and the recommended use of co-administered ribavirin for certain subgroups

Patient population*	Treatment	Duration
Patients with genotype 1 or genotype 4 CHC		
Patients without cirrhosis	Sofopas	12 weeks. - 8 weeks may be considered in previously untreated genotype 1-infected patients. - 24 weeks should be considered for previously treated patients with uncertain subsequent retreatment options.
Patients with compensated cirrhosis	Sofopas	24 weeks. - 12 weeks may be considered for patients deemed at low risk for clinical disease progression and who have subsequent retreatment options.
Patients with decompensated cirrhosis or who are pre-/post-liver transplant	Sofopas + ribavirin	24 weeks.
Patients with genotype 3 CHC		
Patients with cirrhosis and/or prior treatment failure	Sofopas + ribavirin	24 weeks.

* Includes patients co-infected with human immunodeficiency virus (HIV).
In patients without decompensated cirrhosis requiring the addition of ribavirin to their treatment regimen (see Table 1), the daily dose of ribavirin is weight based (< 75 kg = 1,000 mg and ≥ 75 kg = 1,200 mg) and administered orally in two divided doses with food.
In patients with decompensated cirrhosis, ribavirin should be administered at a starting dose of 600 mg given in a divided daily dose. If the starting dose is well-tolerated, the dose can be titrated up to a maximum of 1,000-1,200 mg daily (1,000 mg for patients weighing < 75 kg and 1,200 mg for patients weighing ≥ 75 kg). If the starting dose is not well-tolerated, the dose should be reduced as clinically indicated based on haemoglobin levels.
Dose modification of ribavirin in patients taking 1,000-1,200 mg daily
If Sofopas is used in combination with ribavirin and a patient has a serious adverse reaction potentially related to ribavirin, the ribavirin dose should be modified or discontinued, if appropriate, until the adverse reaction abates or decreases in severity.
Table 2 provides guidelines for dose modifications and discontinuation based on the patient's haemoglobin concentration and cardiac status.
Table 2: Ribavirin dose modification guideline for co-administration with Sofopas

Laboratory values	Reduce ribavirin dose to 600 mg/day if:	Discontinue ribavirin if:
Haemoglobin in patients with no cardiac disease	< 10 g/dL	< 8.5 g/dL
Haemoglobin in patients with history of stable cardiac disease	≥ 2 g/dL decrease in haemoglobin during any 4-week treatment period	< 12 g/dL despite 4 weeks at reduced dose

Once ribavirin has been withheld due to either a laboratory abnormality or clinical manifestation, an attempt may be made to restart ribavirin at 600 mg daily and further increase the dose to 800 mg daily. However, it is not recommended that ribavirin be increased to the originally assigned dose (1,000 mg to 1,200 mg daily).
Patients should be instructed that if vomiting occurs within 5 hours of dosing an additional tablet should be taken. If vomiting occurs more than 5 hours after dosing, no further dose is needed.
If a dose is missed and it is within 18 hours of the normal time, patients should be instructed to take the tablet as soon as possible and then patients should take the next dose at the usual time. If it is after 18 hours then patients should be instructed to wait and take the next dose at the usual time. Patients should be instructed not to take a double dose.
Elderly: dose adjustment is warranted for elderly patients
Renal impairment: No dose adjustment of Sofopas is required for patients with mild or moderate renal impairment. The safety of ledipasvir/sofosbuvir has not been assessed in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m2) or end stage renal disease (ESRD) requiring haemodialysis
Hepatic impairment: No dose adjustment of Sofopas is required for patients with mild, moderate or severe hepatic impairment (Child-Pugh-Turcotte [CPT] class A, B or C) (see section 5.2). Safety and efficacy of ledipasvir/sofosbuvir have been established in patients with decompensated cirrhosis (see section 5.1).
Paediatric population: The safety and efficacy of Sofopas in children and adolescents aged less than 18 years have not yet been established. No data are available.

Method of administration
For oral use.
Patients should be instructed to swallow the tablet whole with or without food. Due to the bitter taste, it is recommended that the film-coated tablet is not chewed or crushed.

USE IN SPECIFIC POPULATIONS
Pregnancy: Pregnancy Category B: It should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Nursing Mothers: The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SOFOPAS .

CONTRAINDICATIONS:
Hypersensitivity to the active substances or to any of the excipients .
Co-administration with rosuvastatin or St. John's wort (Hypericum perforatum)

PRECAUTION:
Bradycardia with amiodarone coadministration: Serious symptomatic bradycardia may occur in patients taking amiodarone, particularly in patients also receiving beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease. Coadministration of amiodarone with SOFOPAS is not recommended. In patients without alternative, viable treatment options, cardiac monitoring is recommended.
Sofopas should not be administered concomitantly with other medicinal products containing sofosbuvir.
Treatment of patients with prior exposure to HCV direct-acting antivirals
In patients who fail treatment with ledipasvir/sofosbuvir, selection of NS5A resistance mutations that substantially reduce the susceptibility to ledipasvir is seen in the majority of cases . Limited data indicate that such NS5A mutations do not revert on long-term follow-up. There are presently no data to support the effectiveness of retreatment of patients who have failed ledipasvir/sofosbuvir with a subsequent regimen that contains an NS5A inhibitor. Similarly, there are presently no data to support the effectiveness of NS3/4A protease inhibitors in patients who previously failed prior therapy that included an NS3/4A protease inhibitor. Such patients may therefore be dependent on other drug classes for clearance of HCV infection. Consequently, consideration should be given to longer treatment for patients with uncertain subsequent retreatment options.
Renal impairment: No dose adjustment of Sofopas is required for patients with mild or moderate renal impairment.
Patients with decompensated cirrhosis and/or who are awaiting liver transplant or post-liver transplant: The relative efficacy of 12 and 24 weeks of therapy has not been established. Therefore, 24 weeks of therapy is recommended . Treatment with Sofopas should be guided by an assessment of the potential benefits and risks for the individual patient.
Use with potent P-gp inducers: Medicinal products that are potent P-glycoprotein (P-gp) inducers (e.g. rifampicin, carbamazepine and phenytoin) may significantly decrease ledipasvir and sofosbuvir plasma concentration which may lead to reduced therapeutic effect of Sofopas. Such medicinal products should not be used with Sofopas.
Use with certain HIV antiretroviral regimens: Sofopas has been shown to increase tenofovir exposure, especially when used together with an HIV regimen containing tenofovir disoproxil fumarate and a pharmacokinetic enhancer (ritonavir or cobicistat). The potential risks and benefits associated with co-administration of Sofopas with the fixed-dose combination tablet containing elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate or tenofovir disoproxil fumarate given in conjunction with a boosted HIV protease inhibitor (e.g. atazanavir or darunavir) should be considered, particularly in patients at increased risk of renal dysfunction. Patients receiving Sofopas concomitantly with elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate or with tenofovir disoproxil fumarate and a boosted HIV protease inhibitor should be monitored for tenofovir-associated adverse reactions.
Use with HMG-CoA reductase inhibitors: Co-administration of Sofopas and HMG-CoA reductase inhibitors (statins) can significantly increase the concentration of the statin, which increases the risk of myopathy and rhabdomyolysis .
HCV/HBV (hepatitis B virus) co-infection: There are no data on the use of Sofopas in patients with HCV/HBV co-infection.
Paediatric population: Sofopas is not recommended for use in children and adolescents under 18 years of age because the safety and efficacy have not been established in this population.

ADVERSE EFFECTS:
The most common adverse reactions (incidence greater than or equal to 10%, all grades) observed with treatment with SOFOPAS for 8, 12, or 24 weeks are fatigue and headache

INTERACTIONS:
- Coadministration with amiodarone may result in serious symptomatic bradycardia. Use of SOFOPAS with amiodarone is not recommended .
- P-gp inducers (e.g., rifampin, St. John's wort): May alter concentrations of ledipasvir and sofosbuvir. Use of SOFOPAS with P-gp inducers is not recommended.
- Coadministration with rosuvastatin may result in increase its concentration & risk of mayopathy including rhabdomyolysis. Use of SOFOPAS with rosuvastatin is not recommended.
- Consult the full prescribing information prior to use for potential drug interactions.

STORAGE:
Store below 30°C.
Protect from heat, light & moisture.

INSTRUCTION:
To be sold on the prescription of a registered medical practitioner only.
Keep all medicines out of the reach of children.

PRESENTATION:
Sofopas (Ledipasvir/Sofosbuvir) tablets 90mg/400mg are available in HDPE bottle containing 7 tablets.
Sofopas (Ledipasvir/Sofosbuvir) tablets 90mg/400mg are available in HDPE bottle containing 14 tablets.
Sofopas (Ledipasvir/Sofosbuvir) tablets 90mg/400mg are available in HDPE bottle containing 28 tablets.

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