We can serve

9 million co-infected
with **HCV+HIV**

170 million
HCV Infected individual

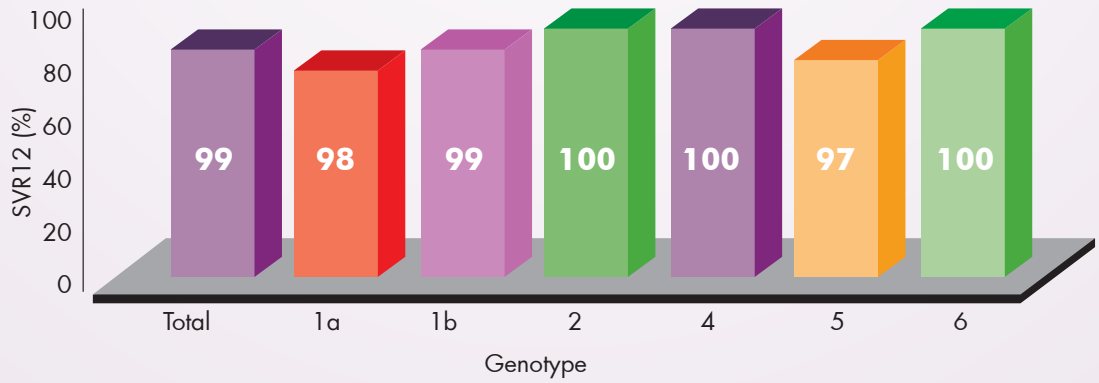
Sofosvel

Sofosbuvir + Velpatasvir

The First Global Generic for Hepatitis C Patients

- **A** single tablet regimen for all genotypes
- **E**nsures high SVR12 for patients with Child-Pugh B (Decompensated) cirrhosis
- **H**ighly effective and well tolerable
- **N**o need for expensive genotype testing

Ensures high cure rate to HCV genotype 1,2,4,5,6

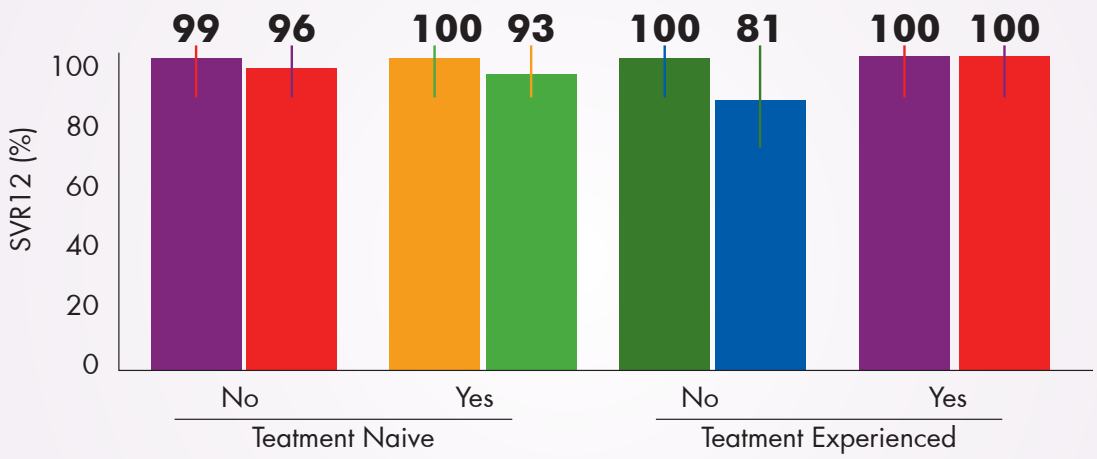


Sofosvel

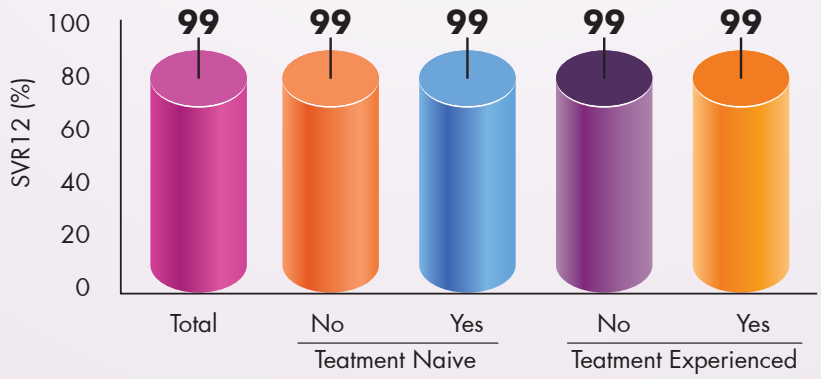
Sofosbuvir + Velpatasvir

The First Global Generic for Hepatitis C Patients

Ensures sustained virologic response to HCV genotype 2 or 3 with or without previous treatment, including with compensated cirrhosis.



Provides superior sustained SVR12 among both treatment experienced and untreated patients infected with HCV.



Sofosvel

Sofosbuvir + Velpatasvir

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Prescribing Information

COMPOSITION: Sofosvel Tablet: Each film coated tablet contains Sofosbuvir INN 400 mg and Velpatasvir INN 100 mg. **PHARMACOLOGICAL INFORMATION: Therapeutic class:** Antiviral agent. **PHARMACOLOGICAL ACTION:** *Mechanism of Action:* Sofosbuvir is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is required for viral replication. Sofosbuvir is a nucleotide prodrug that undergoes intracellular metabolism 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 polymerase activity of the recombinant NS5B from HCV genotype 1b, 2a, 3a and 4a with an IC50 value ranging from 0.36 to 3.3 micromolar. GS-461203 is neither an inhibitor of human DNA and RNA polymerases nor an inhibitor of mitochondrial RNA polymerase. Velpatasvir is an inhibitor of the HCV NS5A protein, which is required for viral replication. Resistance selection in cell culture and cross-resistance studies indicate Velpatasvir targets NS5A as its mode of action. **Pharmacodynamics:** *Cardiac Electrophysiology:* The effect of Sofosbuvir 400 mg (recommended dosage) and 1200 mg (three times the recommended dosage) on QTc interval was evaluated in an active-controlled (Moxifloxacin 400 mg) thorough QT trial. At a dose three times the recommended dose, Sofosbuvir does not prolong QTc to any clinically relevant extent. The effect of Velpatasvir 500 mg (five times the recommended dosage) was evaluated in an active-controlled (Moxifloxacin 400 mg) thorough QT trial. At a dose five times the recommended dose, Velpatasvir does not prolong QTc interval to any clinically relevant extent. **Pharmacokinetics:** Absorption: Sofosbuvir: Tmax=0.5-1 hrs. Cmax=567ng/mL, 898ng/mL (GS-331007). AUC=1268ng•hr/mL, 14,372ng•hr/mL (GS-331007). Velpatasvir: Tmax=3 hrs. Cmax=259ng/mL. AUC=2980ng•hr/mL. Distribution: Sofosbuvir: Plasma protein binding (61-65% sofosbuvir). Velpatasvir: Plasma protein binding (>99.5% velpatasvir). Metabolism: Sofosbuvir: Via Cathepsin A, CES1, and HINT1. Prodrug that undergoes intracellular metabolism to form GS-461203. GS-331007 is the primary circulating metabolite. Velpatasvir: Via CYP2B6, CYP2C8, CYP3A4. Elimination: Sofosbuvir: Urine (80%, predominantly as GS-331007), feces (14%); T1/2=0.5 hrs, 25 hrs (GS-331007) (median). Velpatasvir: Urine (0.4%), feces (94%); T1/2=15 hrs (median). **THERAPEUTIC INDICATIONS:** Sofosvel is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection: ◗ without cirrhosis or with compensated cirrhosis. ◗ with decompensated cirrhosis for use in combination with Ribavirin. **DOSAGE AND ADMINISTRATION:** The recommended dosage of Sofosvel is one tablet taken orally once daily with or without food. Table 2 shows the recommended treatment regimen and duration based on patient population. Table 2: Recommended treatment regimen in patients with genotype 1, 2, 3, 4, 5 or 6 HCV

Patient Population	Treatment Regimen and Duration
Patients without cirrhosis and patients with compensated cirrhosis (Child-Pugh A)	Sofosbuvir/Velpatasvir 12 weeks
Patients with decompensated cirrhosis (Child-Pugh B or C)	Sofosbuvir/Velpatasvir + Ribavirin[a] 12 weeks

No Dosage Recommendations in Severe Renal Impairment and End Stage Renal Disease No dosage recommendation can be given for patients with severe renal impairment (estimated Glomerular Filtration Rate [eGFR] less than 30 mL/min/1.73 m^2) or with end stage renal disease (ESRD), due to higher exposures (up to 20-fold) of the predominant Sofosbuvir metabolite. **ADVERSE REACTIONS** The most common side effects observed with Sofosbuvir and Velpatasvir combination were Fatigue, Nausea, Headache, Anemia, Diarrhea, Insomnia, Pruritus, Muscle spasm, Dyspnea and Cough. There are some rare adverse events including reduced hemoglobin level, reduced lymphocyte count, reduced neutrophil count and reduced platelet count. Serious Symptomatic Bradycardia developed when Sofosbuvir is coadministered with Amiodarone and another HCV Direct Acting Antiviral. **CONTRAINDICATIONS:** Sofosvel and Ribavirin combination regimen is contraindicated in patients for whom Ribavirin is contraindicated. Refer to the Ribavirin prescribing information for a list of contraindications for Ribavirin. **DRUG INTERACTIONS:** *Potential for Other Drugs to Affect Sofosbuvir/Velpatasvir:* Sofosbuvir and Velpatasvir are substrates of drug transporters P-gp and BCRP while GS-331007 (the predominant circulating metabolite of Sofosbuvir) is not. In vitro, slow metabolic turnover of Velpatasvir by CYP2B6, CYP2C8, and CYP3A4 was observed. Drugs that are inducers of P-gp and/or moderate to potent inducers of CYP2B6, CYP2C8, or CYP3A4 (e.g., Rifampin, St. John's wort, Carbamazepine) may decrease plasma concentrations of Sofosbuvir and/or Velpatasvir, leading to reduced therapeutic effect of Sofosbuvir/Velpatasvir. The use of these agents with Sofosbuvir/Velpatasvir is not recommended. Sofosbuvir/Velpatasvir may be coadministered with P-gp, BCRP, and CYP inhibitors. *Potential for Sofosbuvir/Velpatasvir to Affect Other Drugs* Velpatasvir is an inhibitor of drug transporters P-gp, breast cancer resistance protein (BCRP), OATP1B1, OATP1B3, and OATP2B1. Coadministration of Sofosbuvir/Velpatasvir with drugs that are substrates of these transporters may increase the exposure of such drugs. *Established and Potentially Significant Drug Interactions:* Table 3 provides a listing of established or potentially clinically significant drug interactions. The drug interactions described are based on studies conducted with either Sofosbuvir/Velpatasvir, the components of Sofosbuvir/Velpatasvir as individual agents, or are predicted drug interactions that may occur with Sofosbuvir/Velpatasvir. Drugs without Clinically Significant Interactions with Sofosbuvir/Velpatasvir Based on drug interaction studies conducted with the components of Sofosbuvir or Velpatasvir, no clinically significant drug interactions have been observed with the following drugs Sofosbuvir/Velpatasvir: Atazanavir/Ritonavir, Cyclosporine, Darunavir/Ritonavir, Dolutegravir, Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide, Emtricitabine, Raltegravir or Rilpivirine Sofosbuvir: Ethinyl Estradiol/Norgestimate, Methadone, or Tacrolimus Velpatasvir: Ethinyl Estradiol/Norgestimate, Ketoconazole, or Pravastatin. See Table 3 for use of Sofosbuvir/Velpatasvir with certain HIV antiretroviral regimens **WARNINGS AND PRECAUTIONS:** *Serious Symptomatic Bradycardia When Sofosbuvir Is Coadministered with Amiodarone and another HCV Direct Acting Antiviral* Coadministration of Amiodarone with Sofosbuvir/Velpatasvir is not recommended. For patients taking Amiodarone who have no other alternative viable treatment options and who will be coadministered Sofosbuvir/Velpatasvir: ◗ Counsel patients about the risk of symptomatic bradycardia. ◗ Cardiac monitoring in an in-patient setting for the first 48 hours of coadministration is recommended, after which outpatient or self-monitoring of the heart rate should occur on a daily basis through at least the first 2 weeks of treatment. Patients who are taking Sofosbuvir/Velpatasvir who need to start Amiodarone therapy due to no other alternative viable treatment options should undergo similar cardiac monitoring as outlined above. Due to Amiodarone's long half-life, patients discontinuing Amiodarone just prior to starting Sofosbuvir/Velpatasvir should also undergo similar cardiac monitoring as outlined above. Patients who develop signs or symptoms of bradycardia should seek medical evaluation immediately. Symptoms may include near-fainting or fainting, dizziness or lightheadedness, malaise, weakness, excessive tiredness, shortness of breath, chest pains, confusion, or memory problems. *Risk of Reduced Therapeutic Effect Due to Concomitant Use of Sofosbuvir/Velpatasvir with Inducers of P-gp and/or Moderate to Potent Inducers of CYP.* Drugs that are inducers of P-gp and/or moderate to potent inducers of CYP2B6, CYP2C8, or CYP3A4 (e.g., Rifampin, St. John's wort, Carbamazepine) may significantly decrease plasma concentrations of Sofosbuvir and/or Velpatasvir, leading to potentially reduced therapeutic effect of Sofosbuvir/Velpatasvir. The use of these agents with Sofosbuvir/Velpatasvir is not recommended. *Risks Associated with Ribavirin and Sofosbuvir/Velpatasvir Combination Treatment:* If Sofosbuvir/Velpatasvir is administered with Ribavirin, the warnings and precautions for Ribavirin apply to this combination regimen. Refer to the Ribavirin prescribing information for a full list of the warnings and precautions for Ribavirin. **OVERDOSAGE:** No specific antidote is available for overdose with Sofosbuvir/Velpatasvir. If overdose occurs the patient must be monitored for evidence of toxicity. Treatment of overdose with Sofosbuvir/Velpatasvir consists of general supportive measures including monitoring of vital signs as well as observation of the clinical status of the patient. Hemodialysis can efficiently remove the predominant circulating metabolite of Sofosbuvir, GS-331007, with an extraction ratio of 53%. Hemodialysis is unlikely to result in significant removal of Velpatasvir since Velpatasvir is highly bound to plasma protein. **PHARMACEUTICAL INFORMATION: Storage Conditions:** Store in cool and dry place, away from light. Keep out of the reach of children. **Presentation & Packaging: Sofosvel Tablet:** Each commercial box contains 6's tablets in Alu-Alu blister pack.**COMPOSITION: Sofosvel Tablet:** Each film coated tablet contains Sofosbuvir INN 400 mg and Velpatasvir INN 100 mg.

BEACON® Pharmaceuticals Limited
Light for life

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