DACLATA
(Daclatasvir)

Film Coated Tablets

COMPOSITION
Daclata 30mg Tablets: Each film coated tablet contains: Daclatasvir dihydrochloride equivalent to daclatasvir ..... 30mg.
Daclata 60mg Tablets: Each film coated tablet contains: Daclatasvir dihydrochloride equivalent to daclatasvir ..... 60mg.

DESCRIPTION
Daclata (Daclatasvir) is an inhibitor of HCV nonstructural protein 5A (NS5A). Daclatasvir is freely soluble in water (>700 mg/mL).

MECHANISM OF ACTION
Daclatasvir is a direct-acting antiviral agent (DAA) against the hepatitis C virus. Daclatasvir is an inhibitor of NS5A, a nonstructural protein encoded by HCV. Daclatasvir binds to the N-terminus of NS5A and inhibits both viral RNA replication and virion assembly. Characterization of daclatasvir-resistant viruses, biochemical studies, and computer modeling data indicate that daclatasvir interacts with the N-terminus within Domain 1 of the protein, which may cause structural distortions that interfere with NS5A functions.

PHARMACOKINETICS
Administration of daclatasvir tablets in HCV-infected subjects resulted in approximately dose-proportional increases in C_{max}, AUC, and C_{min} up to 60 mg once daily. The peak plasma concentrations occurred within 2 hours post dose. High fat meal food effect was observed with Daclatasvir. 88% of total radioactivity was recovered in feces (53% of the dose as unchanged daclatasvir) and 6.6% of the dose was excreted in the urine (primarily as unchanged daclatasvir). The terminal elimination half-life of daclatasvir ranged from approximately 12 to 15 hours. Daclatasvir is highly protein bound to plasma proteins and is unlikely to be removed by dialysis.

INDICATIONS AND USAGE
Daclata is indicated for use with sofosbuvir for the treatment of patients with chronic hepatitis C virus (HCV) genotype 3 infection. It's use is limited in: Sustained virologic response (SVR) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving daclatasvir in combination with sofosbuvir for 12 weeks.

DOSAGE AND ADMINISTRATION
The recommended dosage of Daclata is 60 mg, taken orally, once daily in combination with sofosbuvir for 12 weeks. Daclatasvir may be taken with or without food. The optimal duration of Daclatasvir and sofosbuvir for patients with cirrhosis has not been established. If sofosbuvir is permanently discontinued in a patient receiving Daclata with sofosbuvir, then Daclata should also be discontinued.

CONTRAINDICATIONS
- It is contraindicated in combination with drugs that strongly induce CYP3A and, thus, may lead to lower exposure and loss of efficacy of Daclatasvir.
- Contraindicated drugs include, Anticonvulsants drugs (phenytoin, carbamazepine, Antimycobacterial agents (rifampin), Herbal products St. John's wort (Hypericum perforatum).

Note: (This is not a comprehensive list of all drugs that strongly induce CYP3A).

WARNINGS AND PRECAUTIONS
- The concomitant use of Daclatasvir and other drugs may result in known or potentially significant drug interactions, some of which may lead to
  - Loss of therapeutic effect of Daclatasvir and possible development of resistance.
  - Dosage adjustments of concomitant medications or Daclatasvir.
  - Possible clinically significant adverse reactions from greater exposures of concomitant drugs or Daclatasvir.
- Consider the potential for drug interactions before and during Daclatasvir therapy, review concomitant medications during Daclatasvir therapy, and monitor for the adverse reactions associated with the concomitant drugs.
- The Serious Symptomatic Bradycardia when coadministered with Sofosbuvir and Amiodarone: The cases of symptomatic bradycardia and cases requiring pacemaker intervention have been reported when amiodarone is coadministered with sofosbuvir in combination with another HCV direct-acting antiviral, including Daclatasvir. A fatal cardiac arrest was reported in a patient receiving a sofosbuvir-containing regimen (ledipasvir/sofosbuvir). Bradycardia has generally occurred within hours to days, but cases have been observed up to 2 weeks after initiating HCV treatment. Patients also taking beta blockers or those with underlying cardiac comorbidities and/or advanced liver disease may be at increased risk for symptomatic bradycardia with coadministration of amiodarone. Bradycardia generally resolved after discontinuation of HCV treatment. The mechanism for this bradycardia effect is unknown.
- Coadministration of amiodarone with Daclatasvir in combination with sofosbuvir is not recommended. For patients taking amiodarone who have no alternative treatment options and who will be coadministered Daclatasvir and sofosbuvir:
  - Counsel patients about the risk of serious symptomatic bradycardia.
  - Cardiac monitoring in an inpatient 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 in combination with Daclatasvir who need to start amiodarone therapy due to no other alternative treatment options should undergo similar cardiac monitoring.
- Due to amiodarone's long elimination half-life, patients discontinuing amiodarone just prior to starting sofosbuvir in combination with Daclatasvir should also undergo similar cardiac monitoring.
- 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 pain, confusion, or memory problems.

ADVERSE REACTIONS
The reported adverse events are; Serious symptomatic bradycardia, headache and fatigue, nausea and diarrhea. The laboratory abnormalities which includes transient, asymptomatic lipase elevations of greater than 3 times the upper limit of normal (ULN).

DRUG INTERACTIONS
- Daclatasvir is a substrate of CYP3A. Therefore, moderate or strong inducers of CYP3A (bosentan, dexamethasone, efavirenz, etravirine, modafinil, nafcillin, rifapentine) may decrease the plasma levels and therapeutic effect of daclatasvir. The strong inhibitors of CYP3A (atazanavir/ritonavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, posaconazole, saquinavir, telithromycin, voriconazoleeg) may increase the plasma levels of daclatasvir. The moderate inhibitors of CYP3A (atazanavir, ciprofloxacin, darunavir/ritonavir, diltiazem, erythromycin, fluconazole, fosamprenavir, verapamil) may increase the plasma levels of daclatasvir.
- The use of Daclatasvir with anticoagulants (dabigatran etexilate) is not recommended in specific renal impairment groups, depending on the indication.
- The coadministration of antiarrhythmic agents (amiodarone) with Daclatasvir in combination with sofosbuvir is not recommended because it may result in serious symptomatic bradycardia. The mechanism of this effect is unknown. If coadministration is required, cardiac monitoring is recommended.
- Patients already receiving daclatasvir initiating digoxin: Initiate treatment using the lowest appropriate digoxin dosage. Monitor digoxin concentrations; adjust digoxin doses if necessary and continue monitoring. Measure serum digoxin concentrations before initiating daclatasvir, if patient already receiving digoxin prior to initiating daclatasvir.
- Monitor for HMG-CoA reductase inhibitors (Atorvastatin, Fluvastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin) associated adverse events such as myopathy.
- Daclatasvir is an inhibitor of P-glycoprotein transporter (P-gp), organic anion transporting polypeptide (OATP) 1B1 and 1B3, and breast cancer resistance protein (BCRP). Administration of Daclatasvir may increase systemic exposure to medicinal products that are substrates of P-gp, OATP 1B1 or 1B3, or BCRP, which could increase or prolong their therapeutic effect.

USE IN SPECIFIC POPULATIONS
Pregnancy
No data with Daclatasvir in pregnant women are available to inform a drug-associated risk.
Lactation
No information regarding the presence of daclatasvir in human milk, the effects on the breastfed infant, or the effects on milk production is available. Daclatasvir is present in the milk of lactating rats. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for Daclatasvir and any potential adverse effects on the breastfed infant from Daclatasvir or from the underlying maternal condition.
Pediatric Use
Safety and effectiveness of Daclatasvir in pediatric patients younger than 18 years of age have not been established.
Geriatric Use
Safety was similar across older and younger subjects and there were no safety findings unique to subjects 65 years and older. No dosage adjustment of Daclatasvir is required for elderly patients.
Renal Impairment
No dosage adjustment of Daclatasvir is required for patients with any degree of renal Impairment.
Hepatic Impairment
No dosage adjustment of Daclatasvir is required for patients with mild (Child-Pugh A), moderate (Child-Pugh B), or severe (Child-Pugh C) hepatic impairment. Safety and efficacy of Daclatasvir have not been established in patients with decompensated cirrhosis.
Liver Transplant Patients
The safety and efficacy of Daclatasvir combination therapy have not been established in liver transplant patients.

OVERDOSAGE
There is no known antidote for overdose of Daclatasvir. Treatment of overdose with Daclatasvir should consist of general supportive measures, including monitoring of vital signs and observation of the patient's clinical status. Because daclatasvir is highly protein bound (>99%), dialysis is unlikely to significantly reduce plasma concentrations of the drug.

DOSAGE & INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of the reach of children. Store below 30°C in a dry place. Protect from light.

PRESENTATION
Daclata 30mg tablets: Alu. Alu. blister pack of 4 x 7's.
Daclata 60mg tablets: Alu. Alu. blister pack of 4 x 7's.

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(ڈیکلاٹس ویر)
فلم کوٹڈ گولیاں

5130290

خوراک وہدایات
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔
30°C سے کم درجہ حرارت میں خشک جگہ پر رکھیں۔
روشنی سے بچائیں۔

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