**INDICATIONS AND USAGE**

Entecavir is a Hepatitis B virus nucleoside analog reverse transcriptase inhibitor indicated for the treatment of chronic hepatitis B in adults with evidence of active viral replication and who have not responded to, or have developed resistance to, prior nucleoside analog therapy.

**CONTRAINDICATIONS**

Entecavir is contraindicated in patients with active liver disease with fulminant or decompensated decompensatedChild-Pugh Class C liver disease. Patients with Child-Pugh Class C liver disease should be observed closely for evidence of disease progression.

**WARNINGS AND PRECAUTIONS**

1. **Severe Acute Exacerbations of Hepatitis B**

   Patients coinfected with HIV and HBV, and Lactic Acidosis and Hepatomegaly

   The potential for severe acute exacerbation of hepatitis B with loss of hepatitis B e antigen (HBeAg) in patients treated with entecavir has been well-studied. The frequency and rate of severe acute exacerbations vary between populations, with the highest rates observed in Asian populations and the lowest rates in the US Hispanic population. Following entecavir discontinuation, the rate of post-treatment flares could be higher in Asian populations with a history of severe acute exacerbations.

2. **Drug Interactions**

   Entecavir is a potent inhibitor of HIV reverse transcriptase and should be used with caution in patients infected with HIV who are also receiving antiretroviral therapy. In patients receiving concomitant therapy with entecavir and other antiretrovirals, the frequency and nature of adverse events were consistent with those expected in patients receiving antiretroviral therapy alone. Patients receiving entecavir in combination with other antiretrovirals should be monitored closely for evidence of hepatotoxicity.

3. **Hepatic Impairment**

   The pharmacokinetics of entecavir following a single 0.5 mg dose were assessed in a single-arm, open-label trial of HBeAg-positive or -negative, lamivudine-refractory subjects with hepatic impairment ranging from 62% to 73% of the administered dose. Renal clearance is independent of dose and ranges from 62% to 73% of the administered dose. The pharmacokinetics of entecavir following a single 0.5 mg dose were assessed in a single-arm, open-label trial of HBeAg-positive or -negative, lamivudine-refractory subjects with hepatic impairment ranging from 62% to 73% of the administered dose. Renal clearance is independent of dose and ranges from 62% to 73% of the administered dose.

4. **Adverse Reactions**

   Adverse reactions reported in clinical trials included: headache, fatigue, dizziness, and nausea. One percent of patients treated with entecavir discontinued treatment due to adverse reactions.

5. **Nuclear Acid Interactions**

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6. **Clinical Pharmacology**

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**DOSAGE AND ADMINISTRATION**

1. **Severe Acute Exacerbations of Hepatitis B**

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Antiviral Activity

HIV type 1 (HIV-1) isolates using a variety of cells and assay conditions yielded EC50 values ranging from

Triphosphate is a weak inhibitor of cellular DNA polymerases α, β, and δ and mitochondrial DNA polymerase

than those observed in humans, entecavir did not induce the human CYP450 enzymes 1A2, 2C9, 2C19, 2D6, 3A4, 2B6, and 2E1. At concentrations up to approximately 340-fold higher

the 22 subjects, 3 subjects experienced virologic rebound with the emergence of rtM204I/V and rtL180M,

:  Genotypic evaluations were performed on evaluable samples (>300

DNA and HBeAg loss and, for HBeAg-negative was <0.7 MEq/mL HBV DNA and ALT normalization.

fibromas were induced in females at exposures 4 times those in humans.

hepatocellular adenomas were increased in females at exposures 24 times those in humans; combined

vascular tumors in female mice (hemangiomas of ovaries and

proliferation in the lung, which was not observed in rats, dogs, or monkeys administered entecavir,

isolates from lamivudine-refractory subjects failing entecavir therapy were susceptible in cell culture to

resistance, also confer decreased phenotypic susceptibility to entecavir. The efficacy of entecavir against

Subjects with evaluable baseline histology (baseline Knodell Necroinflammatory Score ≥2).

increase from baseline.

Physicians should inform their patients of the following important points when initiating entecavir treatment:

• You have unusual (not normal) muscle pain.

Entecavir is a prescription medicine used to treat chronic hepatitis B virus (HBV) in adults who have active

You may be more likely to get lactic acidosis or serious liver problems if you are female, very overweight, or

virus may develop resistance to certain HIV medicines and become harder to treat.

Antiretroviral Pregnancy Registry.

• You have kidney problems. Your entecavir dose or schedule may need to be changed.

Entecavir will not cure HBV.

• You have unusual (not normal) liver test results.

You should not take entecavir with any other hepatitis B medicine.

• Your liver is too large.

Tell your healthcare provider if you have any skin rash or fever while taking entecavir.

entecavir. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-888-FDA-1088.

The most common side effects of entecavir include:

• Diarrhea

• Rash

• Nausea

• Headache

Tell your healthcare provider if you have any side effect that bothers you that lasts for more than a few days.

Tell your healthcare provider if you have any skin rash or fever while taking entecavir. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-888-FDA-1088.

How should I take Entecavir?

• Take one 10 mg tablet, once a day, with or without food

• Take entecavir at the same time each day

• Take entecavir every day unless your doctor tells you to stop.

You should not take entecavir with any other hepatitis B medicine.

You should not take entecavir with other medicines unless your doctor tells you to do so.

• You have kidney problems. Your entecavir dose or schedule may need to be changed.

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