

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use lamivudine tablets (HBV) safely and effectively. See full prescribing information for lamivudine tablets (HBV).

LAMIVUDINE Tablets (HBV) for oral use Initial U.S. Approval: 1995

WARNING: RISK OF LACTIC ACIDOSIS, EXACERBATIONS OF HEPATITIS B UPON DISCONTINUATION OF LAMIVUDINE TABLETS (HBV), AND RISK OF HIV-1 RESISTANCE IF LAMIVUDINE TABLETS (HBV) IS USED IN PATIENTS WITH UNRECOGNIZED OR UNTREATED HIV-1 INFECTION

See full prescribing information for complete boxed warning

- Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues. Suspend treatment if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity occur. (5.1)
- Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued anti hepatitis B therapy (including lamivudine tablets (HBV)). Monitor hepatic function closely in these patients and, if appropriate, initiate anti-hepatitis B treatment. (5.2)
- Lamivudine tablets (HBV) contain a lower dose of the same active ingredient (lamivudine) as EPIVIR tablets and oral Solution used to treat HIV-1 infection. HIV-1 resistance may emerge in chronic hepatitis B patients with unrecognized or untreated HIV 1 infection because the lamivudine dosage in lamivudine tablets (HBV) is subtherapeutic and monotherapy is inappropriate for the treatment of HIV-1 infection HIV counseling and testing should be offered to all patients before beginning treatment with lamivudin tablets (HBV) and periodically during treatment. (5.3)

---INDICATIONS AND USAGE -

Lamivudine tablets (HBV) are a nucleoside analogue reverse transcriptase inhibitor indicated for the treatment of chronic hepatitis B virus infection associated with evidence of hepatitis B viral replication and active liver inflammation. (1)

-DOSAGE AND ADMINISTRATION-

- Adult patients: 100 mg, once daily. (2.2)
- Pediatric patients aged 2 to 17 years: 3 mg per kg once daily up to 100 mg once daily. Prescribe oral solution for pediatric patients requiring less than 100 mg daily. (2.3)Patients with renal impairment: Doses of lamivudine tablets (HBV) must be adjusted in accordance with renal function. (2.4)
- Lamivudine tablets (HBV) should not be used with other medications that contain lamivudine or emtricitabine
- -- DOSAGE FORMS AND STRENGTHS--

---CONTRAINDICATIONS--Patients with previously demonstrated clinically significant hypersensitivity (e.g., anaphylaxis) to any of the components of the products. (4)

- -WARNINGS AND PRECAUTIONS-Lamivudine tablets (HBV) should not be used with other medications that contain lamivudine or with medications that contain emtricitabine. (5.4)
- Emergence of Resistance-Associated HBV Substitutions: Monitor ALT and HBV DNA levels during lamivudine treatment to aid in treatment decisions if emergence of viral mutants or loss of therapeutic response is suspected. (2.6, 5.5)

---ADVERSE REACTIONS--The most common reported adverse reactions in those receiving lamivudine tablets (HBV) (incidence greater than or equal to 10% and reported at a rate greater than placebo) were ear, nose and throat infections, sore throat, and diarrhea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Hetero Labs Limited at 866-495-1995 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. See 17 for PATIENT COUNSELING INFORMATION and FDA- approved patient labeling.

Revised: 12/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: RISK OF LACTIC ACIDOSIS, EXACERBATIONS OF HEPATITIS B UPON DISCONTINUATION OF LAMIVUDINE TABLETS (HBV), AND RISK OF HIV-1 RESISTANCE IF LAMIVUDINE TABLETS (HBV) IS USED IN PATIENTS WITH UNRECOGNIZED OR UNTREATED HIV-1

- INDICATIONS AND USAGE
- DOSAGE AND ADMINISTRATION 2.1 HIV Counseling and Testing
- 2.2 Dosage in Adult Patients
- 2.3 Dosage in Pediatric Patients
- 2.4 Dosage Adjustment in Adult Patients With Renal Impairmen
- 2.5 Important Administration Instructions 2.6 Assessing Patients During Treatment
- 3 DOSAGE FORMS AND STRENGTHS
- 4 CONTRAINDICATIONS
- WARNINGS AND PRECAUTIONS
 - 5.1 Lactic Acidosis and Severe Hepatomegaly With Steatosis
 - 5.2 Exacerbation of Hepatitis After Discontinuation of Treatment
 - 5.3 Risk of HIV-1 Resistance if lamivudine Tablets (HBV) Is Used in Patients With Unrecognized or Untreated HIV-1 Infection
 - 5.4 Coadministration With Other Medications Containing Lamivudine or Emtricitabine
 - 5.5 Emergence of Resistance-Associated HBV Substitutions
- ADVERSE REACTIONS
- 6.1 Clinical Trials Experience 6.2 Postmarketing Experience

DRUG INTERACTIONS

Tablets: 100 mg (3)

- **USE IN SPECIFIC POPULATIONS**
- 8.1 Pregnancy 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Patients With Impaired Renal Function 8.7 Patients With Impaired Liver Function
- OVERDOSAGE
- DESCRIPTION 11
- 12 CLINICAL PHARMACOLOGY
 - 12.1 Mechanism of Action 12.3 Pharmacokinetics
- 12.4 Microbiology
- 13 NONCLINICAL TOXICOLOGY
- $13.1 \ \ Carcinogenesis, Mutagenesis, Impairment of Fertility$
- CLINICAL STUDIES
- 14.1 Clinical Studies of Lamivudine Tablets (HBV) in Adult Patients
- 14.2 Clinical Studies of Lamivudine Tablets (HBV) in Pediatric Subjects
- HOW SUPPLIED/STORAGE AND HANDLING 17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: RISK OF LACTIC ACIOOSIS, EXACERBATIONS OF HEPATITIS B UPON DISCONTINUATION OF LAMIVUDINE TABLETS (HBV), AND RISK OF HIV-1 RESISTANCE IF LAMIVUDINE TABLETS (HBV) IS USED IN PATIENTS WITH UNRECOGNIZED OR UNTREATED HIV-1

Lactic Acidosis and Severe Hepatomegaly

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination, including lamivudine tablets (HBV). Suspend treatment if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity occur [see Warnings and Precautions (5.1)].

 $\underline{\textbf{Exacerbations of Hepatitis B Upon Discontinuation of Lamivudine Tablets (HBV)}}$

Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued anti-hepatitis B therapy (including lamivudine tablets (HBVI)). Hepatic function should be monitored closely-with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy. If appropriate, initiation of anti-hepatitis B therapy may be warranted [see Warnings] and Precautions (5.2)]. Risk of HIV-1 Resistance if Lamivudine Tablets (HBV) Is Used in Patients With Unrecognized or Untreated HIV-1 Infection

Lamivudine tablets (HBV) are not approved for the treatment of HIV-1 infection because the lamivudine dosage in lamivudine tablets (HBV) is subtherapeutic and monotherapy is inappropriate for the treatment of HIV-1 infection. HIV-1 resistance may emerge in chronic hepatitis B-infected patients with unrecognized or untreated HIV-1 infection. Counseling and testing should be offered to all patients before beginning treatment with lamivudine tablets (HBV) and periodically during treatment [see Warnings and Precautions (5.3)].

INDICATIONS AND USAGE

Lamivudine tablets (HBV) are indicated for the treatment of chronic hepatitis B virus (HBV) infection associated with evidence of hepatitis B viral replication and active liver inflammation [see Clinical Studies (14.1, The following points should be considered when initiating therapy with lamivudine tablets (HBV)

- Due to high rates of resistance development in treated patients, initiation of treatment with lamivudine tablets (HBV) should only be considered when the use of an alternative antiviral agent with a higher genetic
- barrier to resistance is not available or appropriate. Lamivudine tablets (HBV) have not been evaluated in patients co-infected with HIV, hepatitis C virus (HCV),
- Lamivudine tablets (HBV) have not been evaluated in liver transplant recipients or in patients with chronic hepatitis B virus infection with decompensated liver disease.
- Lamivudine tablets (HBV) have not been evaluated in pediatric patients younger than 2 years of age with chronic HBV infection.
- 2 DOSAGE AND ADMINISTRATION

2.1 HIV Counseling and Testing

HIV counseling and testing should be offered to all patients before beginning treatment with lamivudine tablets (HBV) and periodically during treatment because of the risk of emergence of resistant-HIV-1 and limitation of treatment options if lamivudine tablets (HBV) is prescribed to treat chronic hepatitis B infection in a patient who has unrecognized HIV-1 infection or acquires HIV-1 infection during treatment [see Warnings and Precautions (5.3)].

2.2 Dosage in Adult Patients

The recommended oral dosage of lamivudine tablets (HBV) is 100 mg once daily.

Table 1. Dosage of Lamivudine Tablets (HBV) in Adult Patients With Renal Impairment

2.3 Dosage in Pediatric Patients

Creatinine Clearance (mL/min)

The recommended oral dosage of lamivudine tablets (HBV) for pediatric patients aged 2 to 17 years is 3 mg per kg once daily up to a maximum daily dosage of 100 mg. The oral solution formulation should be prescribed for patients requiring a dosage less than 100 mg or if unable to swallow tablets. 2.4 Dosage Adjustment in Adult Patients With Renal Impairment

Recommended Dosage of Lamivudine Tablets (HBV)

Dosage recommendations for adult patients with reduced renal function are provided in Table 1 [see Clinical Pharmacology (12.3)].

≥50 100 mg once daily 30-49 100 mg first dose, then 50 mg once daily 15-29 100 mg first dose, then 25 mg once daily 5-14 35 mg first dose, then 15 mg once daily <5 35 mg first dose, then 10 mg once daily

Following correction of the dosage for renal impairment, no additional dosage modification of lamivudine tablets (HBV) is required after routine (4-hour) hemodialysis or peritoneal dialysis [see Clinical Pharmacology (12.3)1

There are insufficient data to recommend a specific dosage of lamivudine tablets (HBV) in pediatric patients with renal impairment

2.5 Important Administration Instructions

- Lamivudine tablets (HBV) may be administered with or without food.
- The tablets may be used interchangeably [see Clinical Pharmacology (12.3)]. The oral solution should be used for doses less than 100 mg.

PHARMACIST-DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

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feel very weak or tired unusual (not normal) muscle pain

Lamivudine tablets (HBV) should not be used with other medications that contain lamivudine or medications that contain emtricitabine [see Warnings and Precautions (5.4)].

2.6 Assessing Patients During Treatment

Patients should be monitored regularly during treatment by a physician experienced in the management of chronic hepatitis B. During treatment, combinations of such events such as return of persistently elevated ALT, increasing levels of HBV DNA over time after an initial decline below assay limit, progression of clinical signs or symptoms of hepatic disease, and/or worsening of hepatic necroinflammatory findings may be considered as potentially reflecting loss of therapeutic response. Such observations should be taken into consideration when determining the advisability of continuing therapy with lamivudine tablets (HBV).

The optimal duration of treatment, the durability of HBeAg seroconversions occurring during treatment and the relationship between treatment response and long-term outcomes such as hepatocellular carcinoma or decompensated cirrhosis are not known.

DOSAGE FORMS AND STRENGTHS

Lamivudine tablets (HBV): 100 mg are pink colored, capsule shaped, biconvex, film coated tablets, debossed

Lamivudine tablets (HBV) are contraindicated in patients who have experienced a previous hypersensitivity

reaction (e.g., anaphylaxis) to lamivudine or to any component of the tablets. WARNINGS AND PRECAUTIONS

Lactic Acidosis and Severe Hepatomegaly With Steatosis

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination, including lamivudine tablets (HBV) and other antiretrovirals A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Most of these reports have described patients receiving nucleoside analogues for treatment of HIV infection, but there have been reports of lactic acidosis in patients receiving lamivudine for hepatitis B. Particular caution should be exercised when administering lamivudine tablets (HBV) to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with lamivudine tablets (HBV) should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

5.2 Exacerbation of Hepatitis After Discontinuation of Treatment

Clinical and laboratory evidence of exacerbations of hepatitis have occurred after discontinuation of lamivudine tablets (HBV) (these have been primarily detected by serum ALT elevations, in addition to the reemergence of HBV DNA commonly observed after stopping treatment; see Table 4 for more information regarding frequency of posttreatment ALT elevations) *Isee Adverse Reactions* (6.1). Although most events appear to have been self-limited, fatalities have been reported in some cases. The causal relationship of hepatitis exacerbation after discontinuation of lamivudine tablets (HBV) has not been clearly established. Patients should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment with lamivudine tablets (HBV). There is insufficient evidence to determine whether re-initiation of lamivudine tablets (HBV) alters the course of posttreatment exacerbations of hepatitis.

5.3 Risk of HIV-1 Resistance if Lamivudine Tablets (HBV) Is Used in Patients With Unrecognized or Untreated

Lamivudine tablets (HBV) contain a lower lamivudine dose than the lamivudine dose in the following drugs used to treat HIV-1 infection:

- EPIVIR® tablets and oral solution,
- COMBIVIR® (lamivudine/zidovudine) tablets EPZICOM® (abacavir sulfate and lamivudine) tablets, and
- TRIZIVIR® (abacavir, lamivudine, and zidovudine) tablets

The formulation and dosage of lamivudine in lamivudine tablets (HBV) are not approved for patients co-infected with HBV and HIV. If a decision is made to administer lamivudine to such patients, the higher dosage indicated for HIV therapy should be used as part of an appropriate combination regimen, and the prescribing information for EPIVIR, COMBIVIR, EPZICOM, or TRIZIVIR, as well as for lamivudine tablets (HBV), should be consulted. HIV counseling and testing should be offered to all patients before beginning lamivudine tablets (HBV) and periodically during treatment because of the risk of rapid emergence of resistant HIV and limitation of treatment options if lamivudine tablets (HBV) is prescribed to treat chronic hepatitis B in a patient who has unrecognized or untreated HIV-1 infection or acquires HIV-1 infection during treatment.

5.4 Coadministration With Other Medications Containing Lamivudine or Emtricitabine

Do not coadminister lamivudine tablets (HBV) with other lamivudine-containing products including EPIVIF (lamivudine), COMBIVIR (lamivudine/zidovudine), EPZICOM (abacavir/lamivudine), or TRIZIVIR

Do not coadminister lamivudine tablets (HBV) with emtricitabine-containing products including ATRIPLA® (efavirenz/emtricitabine/tenofovir disoproxil fumarate), COMPLERA® (rilpivirine/emtricitabine/tenofovir disoproxil fumarate), EMTRIVA® (emtricitabine), STRIBILD® (elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate), or TRUVADA® (emtricitabine/tenofovir disoproxil fumarate).

5.5 Emergence of Resistance-Associated HBV Substitutions

In controlled clinical trials, YMDD-mutant HBV was detected in subjects with on-lamivudine tablets (HBV) re-In controlled clinical trials, YMDD-mutant HBV was detected in subjects with on-lamivudine tablets (HBV) reappearance of HBV DNA after an initial decline below the solution-hybridization assay limit [see Microbiology (12.4)]. Subjects treated with lamivudine tablets (HBV) (adults and children) with YMDD-mutant HBV at 52 weeks showed diminished treatment responses in comparison with subjects treated with lamivudine tablets (HBV) without evidence of YMDD substitutions, including the following: lower rates of HBeAg seroconversion and HBeAg loss (no greater than placebo recipients), more frequent return of positive HBV DNA, and more frequent ALT elevations. In the controlled trials, when subjects developed YMDD-mutant HBV, they had a rise in HBV DNA and ALT from their own previous on-treatment levels. Progression of hepatitis B, including death, has been constrained to come subjects with YMDD mutant HBV, vincluding wither from their progression of the patitis B, including death, has been reported in some subjects with YMDD-mutant HBV, including subjects from the liver transplant setting and from other clinical trials. In clinical practice, monitoring of ALT and HBV DNA levels during treatment with lamivuding tablets (HBV) may aid in treatment decisions if emergence of viral mutants is suspected.

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Lactic acidosis and severe hepatomegaly with steatosis [see Warnings and Precautions (5.1)]. Exacerbation of hepatitis B after discontinuation of treatment [see Warnings and Precautions (5.2)].
- Risk of emergence of resistant HIV-1 infection [see Warnings and Precautions (5.3)]
- Risk of emergence of resistant HBV infection [see Warnings and Precautions (5.4)].

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6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse Reactions in Clinical Trials of Adults With Chronic Hepatitis B Virus Infection: Clinical adverse reactions (regardless of investigator's causality assessment) reported in greater or equal to 10% of subjects who received lamivudine tablets (HBV) and reported at a rate greater than placebo are listed in Table 2.

Table 2. Clinical Adverse Reactions Reported in \geq 10% of Subjects who Received Lamivudine Tablets (HBV) for 52 to 68 Weeks and at an Incidence Greater than Placebo (Trials 1 to 3)

Adverse Event	Lamivudine Tablets (HBV) (n = 332)	Placebo (n = 200)
Ear, Nose, and Throat		
Ear, nose, and throat infections	25%	21%
Sore throat	13%	8%
Gastrointestinal		
Diarrhea	14%	12%

a Includes adverse events regardless of severity and causality assessment.

Specified laboratory abnormalities reported in subjects who received lamivudine tablets (HBV) and reported at a rate greater than in subjects who received placebo are listed in Table 3.

Table 3. Frequencies of Specified Laboratory Abnormalities Reported During Treatment at a Greater Frequency in Subjects Treated with Lamivudine Tablets (HBV)Than With Placebo (Trials 1 to 3)^a

Test (Abnormal Level)	Subjects With Abnormality/ Subjects With Observations		
	Lamivudine Tablets (HBV)	Placebo	
Serum Lipase ≥2.5 x ULN ^b	10%	7%	
CPK ≥7 x baseline	9%	5%	
Platelets <50,000/mm ³	4%	3%	

Includes subjects treated for 52 to 68 weeks.

Includes observations during and after treatment in the 2 placebo-controlled trials that collected this information

ULN = Upper limit of normal.

In subjects followed for up to 16 weeks after discontinuation of treatment, posttreatment ALT elevations were observed more frequently in subjects who had received lamivudine tablets (HBV) than in subjects who had received placebo. A comparison of ALT elevations between Weeks 52 and 68 in subjects who discontinued lamivudine tablets (HBV) at Week 52 and subjects in the same trials who received placebo throughout the treatment course is shown in Table 4.

Table 4. Posttreatment ALT Elevations With No-Active-Treatment Follow-up (Trials 1 and 3)

Abnormal Value	Subjects With ALT Elevation/ Subjects With Observations ^a		
	Lamivudine Tablets (HBV)b	Placebob	
ALT ≥2 x baseline value	27%	19%	
ALT ≥3 x baseline value ^c	21%	8%	
ALT ≥2 x baseline value and absolute ALT >500 IU/L	15%	7%	
ALT ≥2 x baseline value; and bilirubin >2 x ULN and ≥2 x baseline value	0.7%	0.9%	

^a Each subject may be represented in one or more category.

b During treatment phase

^c Comparable to a Grade 3 toxicity in accordance with modified WHO criteria

6.2 Postmarketing Experience

ULN = Upper limit of normal.

Adverse Reactions in Clinical Trials of Pediatric Subjects With Chronic Hepatitis B Virus Infection: Most commonly observed adverse reactions in the pediatric trials were similar to those in adult trials. Posttreatment transaminase elevations were observed in some subjects followed after cessation of lamivudine tablets (HBV).

In addition to adverse reactions reported from clinical trials, the following adverse reactions have been reported during postmarketing use of lamivudine tablets (HBV). Because these reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate the frequency or establish a causal relationship to drug exposure. These reactions have been chosen for inclusion due to a combination of

their seriousness, frequency of reporting, or potential causal connection to lamivudine. Blood and Lympatic System Disorders: Thrombocytopenia. **Digestive**: Stomatitis.

Endocrine and Metabolic: Hyperglycemia.

Blood and Lymphatic: Anemia (including pure red cell aplasia and severe anemias progressing on therapy), lymphadenopathy, splenomegaly.

<u>Hepatic and Pancreatic:</u> Lactic acidosis and steatosis, posttreatment exacerbation of hepatitis [see Boxed Warning], pancreatitis.

Hypersensitivity: Anaphylaxis, urticaria <u>Musculoskeletal:</u> Cramps, rhabdomyolysis.

Nervous: Paresthesia, peripheral neuropathy <u>Respiratory:</u> Abnormal breath sounds/wheezing.

Skin: Alopecia, pruritus, rash. DRUG INTERACTIONS Lamivudine is predominantly eliminated in the urine by active organic cationic secretion. The possibility of interactions with other drugs administered concurrently should be considered, particularly when their main route of elimination is active renal secretion via the organic cationic transport system (e.g., trimethoprim). No data are available regarding interactions with other drugs that have renal clearance mechanisms similar to that of lamivudine

USE IN SPECIFIC POPULATIONS

8.1 Pregnancy: Teratogenic Effects:

Pregnancy Category C.

There are no adequate and well-controlled trials of lamivudine tablets (HBV) in pregnant women. Because animal reproduction studies are not always predictive of human response, lamivudine tablets (HBV) should be used during pregnancy only if the potential benefits outweigh the potential risks to the fetus. Antiretroviral Pregnancy Registry: To monitor maternal-fetal outcomes of pregnant women exposed to judine, a Pregnancy Registry has been established. Healthcare providers are encouraged to register patients

lamivudine, a Pregnancy Reg by calling 1-800-258-4263. Animal Data: Animal reproduction studies in rats and rabbits revealed no evidence of teratogenicity

Reproduction studies have been performed in rats and rabbits at orally administered doses up to 4,000 mg/kg/day and 1,000 mg/kg/day, respectively, producing plasma levels up to approximately 60 times that for the adult HBV dose. Evidence of early embryolethality was seen in the rabbit at exposure levels similar to hose observed in humans, but there was no indication of this effect in the rat at exposure levels up to 60 times those in humans. Studies in pregnant rats and rabbits showed that lamivudine is transferred to the fetus through the placenta

Lamivudine is excreted in human milk. Samples of breast milk obtained from 20 mothers receiving lamivudine monotherapy (300 mg twice daily, 6 times the recommended dosage for hepatitis B infection) or combination therapy (150 mg lamivudine twice daily [3 times the recommended dosage for hepatitis B infection] and 300 mg zidovudine twice daily) had measurable concentrations of lamivudine

Because of the potential for serious adverse reactions in nursing infants, a decision should be made to discontinue lamivudine tablets (HBV) taking into consideration the importance of continued hepatitis B therapy to the mother and the known benefits of breastfeeding.

8.5 Geriatric Use

11 DESCRIPTION

Lamivudine tablets (HBV) is indicated for the treatment of chronic hepatitis B virus infection in pediatric patients aged 2 to 17 years [see Indications and Usage (1), Clinical Pharmacology (12.3), Clinical Studies (14.2)]. The safety and efficacy of lamivudine tablets (HBV) in pediatric patients younger than 2 years have not been established.

Clinical trials of lamivudine tablets (HBV) did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. In particular, because lamivudine is substantially excreted by the kidney and elderly patients are more likely to have decreased renal function, renal function should be monitored and dosage adjustments should be made accordingly [see Dosage and Administration (2.4), Clinical Pharmacology (12.31)

8.6 Patients With Impaired Renal Function

Reduction of the dosage of lamivudine tablets (HBV) is recommended for patients with impaired renal function [see Dosage and Administration (2.4), Clinical Pharmacology (12.3)].

8.7 Patients With Impaired Liver Function

No dose adjustment for lamivudine is required for patients with impaired hepatic function 10 OVERDOSAGE

There is no known antidote for lamivudine tablets (HBV). If overdose occurs, the patient should be monitored and standard supportive treatment utilized, as required. Because a negligible amount of lamivudine was removed via (4-hour) hemodialysis, continuous ambulatory peritoneal dialysis, and automated peritoneal dialysis, it is not known if continuous hemodialysis would provide clinical benefit in a lamivudine overdose event.

Lamivudine tablets (HBV) is a synthetic nucleoside analogue with activity against HBV. The chemical name of lamivudine, USP is 2(1H) - Pyrimidinone, 4-amino-1- [2- (hydroxymethyl)-1,3-oxathio-lan-5-yl], (2R-cis)- It has a molecular formula of $C_8H_{11}N_3O_3S$ and a molecular weight of 229.26. It has the following structural formula of $C_8H_{11}N_3O_3S$ and a molecular weight of 229.26.

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Black Pharma Codes: Front 6282; Back 6283

feel cold, especially in your a feel dizzy or light-headed have a fast or irregular heartt

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What should I tell tablets (HBV)?

Lamivudine Tablets (HBV) are for oral administration. Each tablet contains 100 mg of lamivudine, USP and the inactive ingredients crospovidone, isomalt, isopropyl alcohol, magnesium stearate and methylene chloride. The tablets are coated with Opadry Pink containing hypromellose, iron oxide red, polyethylene glycol, polysorbate 80, titanium dioxide and yellow iron oxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Lamivudine is an antiviral agent [see Microbiology (12.4)].

Pharmacokinetics in Adults: The pharmacokinetic properties of lamivudine have been studied as single and multiple oral doses ranging from 5 mg to 600 mg per day administered to HBV-infected subjects.

Absorption and Bioavailability: Following single oral doses of 100 mg, the peak serum lamivudine Absorption and Bioavanability: Following Single oral coses of 100 mg, the peak serum immutation concentration (C_{max}) in HBV-infected patients (steady state) and healthy subjects (single dose) was 1.28 ± 0.56 mcg per mL and 1.05 ± 0.32 mcg per mL (mean \pm SD), respectively, which occurred between 0.5 and 2 hours after administration. The area under the plasma concentration versus time curve ($AUC_{101024h}$) following 100-mg lamivudine oral single and repeated daily doses to steady state was 4.3 ± 1.4 (mean \pm SD) and 4.7 ± 1.7 mcg+hour per mL, respectively. The relative bioavailability of the tablet and oral solution were demonstrated in healthy subjects. Although the solution demonstrated a slightly higher peak serum concentration (C_{max}), there was no significant difference in systemic exposure (AUC) between the oral solution and the tablet. Therefore, the oral solution and the tablet may be used interchangeably.

After oral administration of lamivudine once daily to HBV-infected adults, the AUC and C_{max} increased in proportion to dose over the range from 5 mg to 600 mg once daily.

Absolute bioavailability in 12 adult subjects was $86\% \pm 16\%$ (mean \pm SD) for the 150-mg tablet and 87%± 13% for the 10-mg per mL oral solution.

Effects of Food on Oral Absorption: The 100-mg tablet was administered orally to 24 healthy subjects on 2 occasions, once in the fasted state and once with food (standard meal: 967 kcal; 67 grams fat, 33 grams protein, 58 grams carbohydrate). There was no significant difference in systemic exposure (AUC) in the fed and

Distribution: The apparent volume of distribution after IV administration of lamivudine to 20 asymptomatic HIV-1-infected subjects was 1.3 ± 0.4 L per kg, suggesting that lamivudine distributes into extravascular spaces. Volume of distribution was independent of dose and did not correlate with body weight.

Binding of lamivudine to human plasma proteins is less than 36% and independent of dose, In vitro studies showed that over the concentration range of 0.1 to 100 mcg per mL, the amount of lamivudine as erythrocytes ranged from 53% to 57% and was independent of concentration.

Metabolism: Metabolism of lamivudine is a minor route of elimination. In humans, the only known metabolite of lamivudine is the trans-sulfoxide metabolite. In 9 healthy subjects receiving 300 mg of lamivudine as single oral doses, a total of 4.2% (range: 1.5% to 7.5%) of the dose was excreted as the trans-sulfoxide metabolite in the urine, the majority of which was excreted in the first 12 hours. Serum concentrations of the trans-sulfoxide metabolite have not been determined

Elimination: The majority of lamivudine is eliminated unchanged in urine by active organic cationic secretion. In 9 healthy subjects given a single 300-mg oral dose of lamivudine, renal clearance was 199.7 \pm 56.9 mL per min (mean \pm SD). In 20 HIV-1-infected subjects given a single IV dose, renal clearance was 280.4 \pm 75.2 mL per min (mean \pm SD), representing 71% \pm 16% (mean \pm SD) of total clearance of lamivudine.

In most single-dose trials in HIV-1-infected subjects, HBV-infected subjects, or healthy subjects with serum sampling for 24 hours after dosing, the observed mean elimination half-life $(t_{\rm kp})$ ranged from 5 to 7 hours. In HIV-1-infected subjects, total clearance was 398.5 \pm 69.1 mL per min (mean \pm SD). Oral clearance and elimination half-life were independent of dose and body weight over an oral dosing range of 0.25 to 10 mg per kg.

<u>Special Populations:</u> Adults With Renal Impairment: The pharmacokinetic properties of lamivudine have been determined in healthy subjects and in subjects with impaired renal function, with and without hemodialysis

Table 5. Pharmacokinetic Parameters (Mean ± SD) Dose-Normalized to a Single 100-mg Oral Dose of Lamivudine in Subjects With Varying Degrees of Renal Function

	Creatinine Clearance Criterion (Number of Subjects)				
Parameter	≥80 mL/min (n = 9)	20-59 mL/min (n = 8)	<20 mL/min (n = 6)		
Creatinine clearance (mL/min)	97 (range 82-117)	39 (range 25-49)	15 (range 13-19)		
Cmax (mcg/mL)	1.31 ± 0.35	1.85 ± 0.40	1.55 ± 0.31		
AUC (mcg•h/mL)	5.28 ± 1.01	14.67 ± 3.74	27.33 ± 6.56		
CI/F (mL/min)	326.4 ± 63.8	120.1 ± 29.5	64.5 ± 18.3		

Exposure (AUC), C_{max} , and half-life increased with diminishing renal function (as expressed by creatinine clearance). Apparent total oral clearance (CI/F) of lamivudine decreased as creatinine clearance decreased. T_{max} was not significantly affected by renal function. Based on these observations, it is recommended that the dosage of lamivudine be modified in patients with renal impairment [see Dosage and Administration (2.4)].

Hemodialysis increases lamivudine clearance from a mean of 64 to 88 mL per min; however, the length of time of hemodialysis (4 hours) was insufficient to significantly alter mean lamivudine exposure after a single-dose administration. Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis have negligible effects on lamivudine clearance. Therefore, it is recommended, following correction of dose for creatinine clearance, that no additional dose modification be made after routine hemodialysis or peritoneal dialysis.

It is not known whether lamivudine can be removed by continuous (24-hour) hemodialysis Pediatric Patients With Renal Impairment: The effect of renal impairment on lamivudine pharmacokinetics

in pediatric patients with chronic hepatitis B is not known.

Adults With Hepatic Impairment: The pharmacokinetic properties of lamivudine in adults with hepatic impairment are shown in Table 6). Subjects were stratified by severity of hepatic impairm

Table 6. Pharmacokinetic Parameters (Mean \pm SD) Dose-Normalized to a Single 100-mg Dose of Lamivudine in Subjects With Normal or Impaired Hepatic Function

	Normal	Impairment ^a		
Parameter	(n = 8)	Moderate (n = 8)	Severe (n = 8)	
C _{max} (mcg/mL)	0.92 ± 0.31	1.06 ± 0.58	1.08 ± 0.27	
AUC (mcg•h/mL)	3.96 ± 0.58	3.97 ± 1.36	4.30 ± 0.63	
T _{max} (h)	1.3 ± 0.8	1.4 ± 0.8	1.4 ± 1.2	
CI/F (mL/min)	424.7 ± 61.9	456.9 ± 129.8	395.2 ± 51.8	
Clr (mL/min)	279.2 ± 79.2	323.5 ± 100.9	216.1 ± 58.0	

Pharmacokinetic parameters were not altered by diminishing hepatic impairment. Therefore, no dose adjustment for lamivudine is required for patients with impaired hepatic function. Safety and efficacy of lamivudine tablets (HBV) have not been established in the presence of decompensated liver disease [see Indications and Usage (1)1.

Adults Post-Hepatic Transplant: Fourteen HBV-infected subjects received liver transplant following lamivudine Adults Post-repair. I railsplant routeen HBV-Illiected subjects received liver transplant rollowing faintwolline therapy and completed pharmacokinetic assessments at enrollment, 2 weeks after 100-mg once-daily dosing (pre-transplant), and 3 months following transplant; there were no significant differences in pharmacokinetic parameters. The overall exposure of lamivudine is primarily affected by renal impairment; consequently, transplant patients with renal impairment had generally higher exposure than patients with normal renal function. Safety and efficacy of lamivudine tablets (HBV) have not been established in this population [see Indications and Usage

Pediatric Subjects: Lamiyudine pharmacokinetics were evaluated in a 28-day dose-ranging trial in 53 Peolatric Subjects: Lamivudine pharmacokinetics were evaluated in a 28-day dose-ranging frail in 53 pediatric subjects with chronic hepatitis B. Subjects aged 2 to 12 years were randomized to receive lamivudine 0.35 mg per kg twice daily, 3 mg per kg once daily, 1.5 mg per kg twice daily, or 4 mg per kg twice daily. Subjects aged 13 to 17 years received lamivudine 100 mg once daily. Lamivudine T_{max} was 0.5 to 1 hour. In general, both C_{max} and exposure (AUC) showed dose proportionality in the dosing range studied. Weight-corrected oral clearance was highest at age 2 and declined from 2 to 12 years, where values were then similar to those seen in adults. A dose of 3 mg per kg given once daily produced a steady-state lamivudine AUC (mean 5,953 ng•hour per mL ± 1,562 SD) similar to that associated with a dose of 100 mg per day in adults.

Gender: There are no significant gender differences in lamivudine pharmacokinetics. Race: There are no significant racial differences in lamivudine pharmacokinetics.

<u>Drug Interactions:</u> Interferon Alfa: Multiple doses of lamivudine and a single dose of interferon were coadministered to 19 healthy male subjects in a pharmacokinetics trial. Results indicated a 10% reduction in lamivudine AUC, but no change in interferon pharmacokinetic parameters when the 2 drugs were given in combination. All other pharmacokinetic parameters (C_{max}, T_{max} and 1_{1/2}) were unchanged. There was no significant pharmacokinetic interaction between lamivudine and interferon alfa in this trial.

Ribavirin: In vitro data indicate ribavirin reduces phosphorylation of lamivudine, stavudine, and zidovudine. However, no pharmacokinetic (e.g., plasma concentrations or intracellular triphosphorylated active metabolite concentrations) or pharmacodynamic (e.g., loss of HIV-1/HCV virologic suppression) interaction was observed when ribavirin and lamivudine (n = 18), stavudine (n = 10), or zidovudine (n = 6) were coadministered as part of a multi-drug regimen to HIV-1/HCV co-infected subjects.

Trimethoprim/Sulfamethoxazole: Lamivudine and trimethoprim/sulfamethoxazole (TMP/SMX) were coadministered to 14 HIV-positive subjects in a single-center, open-label, randomized, crossover trial. Each subject received treatment with a single 300-mg dose of lamivudine and TMP 160 mg/SMX 800 mg once a day for 5 days with concomitant administration of lamivudine 300 mg with the fifth dose in a crossover design. coadministration of TMP/SMX with lamivudine resulted in an increase of 44% ± 23% (mean ± SD) in lamivudine ALIC a decrease of 29% + 13% in lamiyudine oral clearance, and a decrease of 30% + 36% in lamiyudine renal clearance. The pharmacokinetic properties of TMP and SMX were not altered by coadministration with lamivudine

Zidovudine: Lamivudine and zidovudine were coadministered to 12 asymptomatic HIV-positive adult subjects in a single-center, open-label, randomized, crossover trial. No significant differences were observed in AUC or total clearance for lamivudine or zidovudine when the 2 drugs were administered together. Coadministration of lamivudine with zidovudine resulted in an increase of $39\% \pm 62\%$ (mean \pm SD) in C_{max} of zidovudine.

Mechanism of Action: Lamivudine is a synthetic nucleoside analogue. Intracellularly, lamivudine is phosphorylated to its active 5'-triphosphate metabolite, lamivudine triphosphate, 3TC-TP. The principal mode of action of 3TC-TP is the inhibition of the RNA- and DNA- dependent polymerase activities of HBV reverse transcriptase (rt) via DNA chain termination after incorporation of the nucleotide analogue into viral DNA. 3TC-TP is a weak inhibitor of mammalian α , β , and γ -DNA polymerases.

Antiviral Activity: Activity of lamivudine against HBV in cell culture was assessed in HBV DNA-transfected 2.2.15 cells, HB611 cells, and infected human primary hepatocytes. EC_{50} values (the concentration of drug needed to reduce the level of extracellular HBV DNA by 50%) varied from 0.01 μ M (2.3 ng per mL) to 5.6 μ M (1.3 mcg per mL) depending upon the duration of exposure of cells to lamivudine, the cell model system, and the protoco used. See the EPIVIR prescribing information for information regarding activity of lamivudine against HIV.

Resistance: Lamivudine-resistant isolates were identified in subjects with virologic breakthrough, defined when using solution hybridization assay as the detection of HBV DNA in serum on 2 or more occasions after failing to detect HBV DNA on 2 or more occasions and defined when using PCR assay as a greater than 1 \log_{10} (10-fold) increase in serum HBV DNA from nadir during treatment in a subject who had an initial virologic

December 2013

Lamivudine-resistant HBV isolates develop rtM204V/l substitutions in the YMDD motif of the catalytic domain of the viral reverse transcriptase. rtM204V/l substitutions are frequently accompanied by other substitutions (rtV173L, rtL180M) which enhance the level of lamivudine resistance or act as compensatory substitution: replication efficiency. Other substitutions detected in lamivudine-resistant HBV isolates include rtL801

In 4 controlled clinical trials in adults with HBeAg-positive chronic hepatitis B virus infection (CHB), YMDD-mutant HBV was detected in 81 of 335 subjects receiving lamivudine tablets (HBV) 100 mg once daily for 52 weeks. The prevalence of YMDD substitutions was less than 10% in each of these trials for subjects studied at 24 weeks and increased to an average of 24% (range in 4 trials: 16% to 32%) at 52 weeks. In limited data from a long-term follow-up trial in subjects who continued 100 mg per day lamivudine tablets (HBV) after one of these trials, YMDD substitutions further increased from 18% (10 of 57) at 1 year to 41% (20 of 49), 53% (27 of 51), and 69% (31 of 45) after 2, 3, and 4 years of treatment, respectively. Over the 5-year treatment period, the proportion of subjects who developed YMDD-mutant HBV at any time was 69% (40 of 58).

In a controlled trial, treatment-naive subjects with HBeAg-positive CHB were treated with lam (HBV) or lamivudine tablets (HBV) plus adefovir dipivoxil combination therapy. Following 104 weeks of therapy, YMDD-mutant HBV was detected in 7 of 40 (18%) subjects receiving combination therapy compared with 15 of 35 (43%) subjects receiving therapy with only lamivudine tablets (HBV). In another controlled trial, combination therapy was evaluated in adult subjects with HBeAg-positive CHB who had YMDD-mutant HBV and diminished clinical and virologic response to lamivudine tablets (HBV). Following 52 weeks of lamivudine tablets (HBV) plus adefovir dipivoxil combination therapy (n = 46) or therapy with only lamivudine tablets (HBV) (n = 49), YMDDmutant HBV was detected less frequently in subjects receiving combination therapy, 62% versus 96%

A published trial suggested that the rates of lamivudine resistance in subjects treated for HBeAq-negative CHB appear to be more variable (0% to 27% at 1 year and 10% to 56% at 2 years).

Pediatric Subjects: In a controlled trial in pediatric subjects, YMDD-mutant HBV was detected in 31 of 166 (19%) subjects receiving lamivudine tablets (HBV) for 52 weeks. For a subgroup that remained on therapy with lamivudine tablets (HBV) in a follow-up trial, YMDD substitutions increased from 24% (29 of 121) at 12 months to 59% (68 of 115) at 24 months and 64% (66 of 103) at 36 months of treatment with lamivudine tablets (HBV).

<u>Cross-Resistance:</u> HBV containing lamivudine resistance-associated substitutions (rtL180M, rtM204I, rtM204V, rtL180M and rtM204V, rtV173L and rtL180M and rtM204V) retain susceptibility to adefovir dipivoxil but have reduced susceptibility to entecavir (30 fold) and telbivudine (greater than 100 fold). The lamivudine resistance-associated substitution rtA181T results in diminished response to adefovir and telbivudine. Similarly, HBV with entecavir resistance-associated substitutions (I169T/M250V and T184G/S202I) have greater than 1,000fold reductions in susceptibility to lamivudine.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility Carcinogenesis: Long-term carcinogenicity studies with lamivudine in mice and rats showed no evidence

of car<mark>cinogenic potential</mark> at exposures up to 34 times (mice) and 200 times (rats) those observed in humans at the recommended therapeutic dose for chronic hepatitis B.

Mutagenesis: Lamivudine was not active in a microbial mutagenicity screen or an *in vitro* cell transformation assay, but showed weak *in vitro* mutagenic activity in a cytogenetic assay using cultured human lymphocytes and in the mouse lymphoma assay. However, lamivudine showed no evidence of *in vivo* genotoxic activity in the rat at oral doses of up to 2,000 mg per kg producing plasma levels of 60 to 70 times those in humans at the recommended dose for chronic hepatitis B.

 $\underline{Impairment\ of\ Fertility:}\ In\ a\ study\ of\ reproductive\ performance,\ lamivudine\ administered\ to\ rats\ at\ doses\ up\ to\ 4,000\ mg\ per\ kg\ per\ day,\ producing\ plasma\ levels\ 80\ to\ 120\ times\ those\ in\ humans,\ revealed\ no\ evidence\ of\ impaired\ fertility\ and\ no\ effect\ on\ the\ survival,\ growth,\ and\ development\ to\ weaning\ of\ the\ offspring.$ 14 CLINICAL STUDIES

14.1 Clinical Studies of Lamivudine Tablets (HBV) in Adult Patients

The safety and efficacy of lamivudine tablets (HBV) 100 mg once daily versus placebo were evaluated in 3 controlled trials in subjects with compensated chronic hepatitis B virus infection. All subjects were aged 16 years or older and had chronic hepatitis B virus infection. Bla subjects were aged 16 years or older and had chronic hepatitis B virus infection (serum HBsAg-positive for at least 6 months) accompanied by evidence of HBV replication (serum HBeAg-positive and positive for serum HBV DNA) and persistently elevated ALT levels and/or chronic inflammation on liver biopsy compatible with a diagnosis of chronic viral hepatitis. The results of these trials are summarized below.

Trial 1 was a randomized, double-blind trial of lamivudine tablets (HBV) 100 mg once daily versus placebo for 52 weeks followed by a 16-week no-treatment period in 141 treatment-naive US subjects. Trial 2 was a randomized, double-blind, 3-arm trial that compared lamiyudine tablets (HBV) 25 mg once

daily versus lamivudine tablets (HBV) 100 mg once daily versus placebo for 52 weeks in 358 Asian subjects Trial 3 was a randomized, partially-blind trial conducted primarily in North America and Europe in 238 subjects who had ongoing evidence of active chronic hepatitis B despite previous treatment with interferon alfa. The trial compared lamivudine tablets (HBV) 100 mg once daily for 52 weeks, followed by either lamivudine tablets (HBV) 100 mg or matching placebo once daily for 16 weeks (Arm 1), versus placebo once daily for 68 weeks (Arm 2).

Principal endpoint comparisons for the histologic and serologic outcomes in subjects receiving lamivudine tablets (HBV) (100 mg daily) or placebo in these trials are shown in the following tables.

Table 7. Histologic Response at Week 52 Among Adult Subjects Receiving Lamivudine Tablets (HBV) 100 mg Once Daily or Placebo

	Tria	Trial 1		Trial 2		Trial 3	
Assessment	Lamivudine Tablets (HBV) (n = 62)	Placebo (n = 63)	Lamivudine Tablets (HBV) (n = 131)	Placebo (n = 68)	Lamivudine Tablets (HBV) (n = 110)	Placebo (n = 54)	
Improvement ^a	55%	25%	56%	26%	56%	26%	
No Improvement	27%	59%	36%	62%	25%	54%	
Missing Data	18%	16%	8%	12%	19%	20%	

Improvement was defined as a greater than or equal to 2-point decrease in the Knodell Histologic Activity Index (HAI) at Week 52 compared with pretreatment HAI. Subjects with missing data at baseline were excluded.

Table 8. HBeAg Seroconverters^a at Week 52 Among Adult Subjects Receiving Lamivudine Tablets (HBV)

	Tria	al 1	Tria	ıl 2	Tria	ıl 3
Seroconversion	Lamivudine Tablets (HBV) (n = 63)	Placebo (n = 69)	Lamivudine Tablets (HBV) (n = 140)	Placebo (n = 70)	Lamivudine Tablets (HBV) (n = 108)	Placebo (n = 53)
Seroconverters	17%	6%	16%	4%	15%	13%

Three-component seroconversion was defined as Week 52 values showing loss of HBeAg, gain of HBeAb, and reduction of HBV DNA to below the solution-hybridization assay limit. Subjects with negative baseline HBeAg or HBV DNA assay were excluded from the analysis.

Normalization of serum ALT levels was more frequent with lamivudine tablets (HBV) treatment compared

The majority of subjects treated with lamivudine tablets (HBV) showed a decrease of HBV DNA to below the assay limit early in the course of therapy. However, reappearance of assay-detectable HBV DNA during treatment with lamivudine tablets (HBV) was observed in approximately one-third of subjects after this initial

14.2 Clinical Studies of Lamiyudine Tablets (HRV) in Pediatric Subjects

The safety and efficacy of lamiyudine tablets (HBV) were evaluated in a double-blind clinical trial in 286 The safety and efficacy of infilintuoline tablets (HBV) were evaluated in a utourie-fullint clinical trial in 200 subjects aged from 2 to 17 years, who were randomized (2:1) for receive 52 weeks of laminudine tablets (HBV) (3 mg per kg once daily to a maximum of 100 mg once daily) or placebo. All subjects had compensated chronic hepatitis B accompanied by evidence of hepatitis B virus replication (positive serum HBAG) and positive for serum HBV DNA by a research branched-chain DNA assay) and persistently elevated serum ALT levels. The combination of loss of HBeAg and reduction of HBV DNA to below the assay limit of the research assay, evaluated combination of loss of riberg and reduction of riby DNA to below the assay limit of the research assay, evaluated at Week 52, was observed in 23% of subjects treated with lamivudine tablets (HBV) and 13% of placebo-treated subjects. Normalization of serum ALT was achieved and maintained to Week 52 more frequently in subjects treated with lamivudine tablets (HBV) compared with placebo (55% versus 13%). As in the adult controlled trials, most subjects treated with lamivudine tablets (HBV) had decreases in HBV DNA below the assay limit early in treatment, but about one-third of subjects with this initial response had reappearance of assay-detectable HBV DNA during treatment. Adolescents (aged 13 to 17 years) showed less evidence of treatment effect than younger

16 HOW SUPPLIED/STORAGE AND HANDLING

Lamivudine tablets (HBV), 100 mg are pink colored, capsule shaped, biconvex, film coated tablets, debossed with '37' on one side and '1' on the other side.

if one side and it on the other side.	
Bottle of 60 tablets	NDC 31722-752-60
Bottle of 600 tablets	NDC 31722-752-06
Blister card of 10 Unit-dose tablets	NDC 31722-752-31
Blister pack of 100 (10x10) Unit-dose tablets	NDC 31722-752-32

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Preserve in well-closed, light-

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information). Advice for the Patient

- Advise patients to remain under the care of a physician while taking lamivudine tablets (HBV) and discuss any new symptoms or concurrent medications with their physician
- Advise patients that lamivudine tablets (HBV) is not a cure for hepatitis B, that the long-term treatment benefits of lamivudine tablets (HBV) are unknown at this time, and, in particular, that the relationship of initial treatment response to outcomes such as hepatocellular carcinoma and decompensated cirrhosis is unknown [see Dosage and Administration (2.6)].
- Inform patients that deterioration of liver disease has occurred in some cases when treatment v discontinued. Instruct patients to discuss any changes in regimen with their physician [see Warnings and Precautions (5.2)].
- Inform patients that emergence of resistant hepatitis B virus and worsening of disease can occur during reatment, and they should promptly report any new symptoms to their physician [see Warnings and Precautions (5.5)].
- Counsel patients on the importance of testing for HIV to avoid inappropriate therapy and development of resistant HIV. HIV counseling and testing should be offered before starting lamivudine tablets (HBV) and
- periodically during therapy. Advise patients that lamivudine tablets (HBV) contain a lower dose of the same active ingredient (lamivudine)
- as EPIVIR tablets, EPIVIR oral solution, COMBIVIR tablets, EPZICOM tablets, and TRIZIVIR tablets. Lamivudine tablets (HBV) should not be taken concurrently with EPIVIR, COMBIVIR, EPZICOM, or TRIZIVIR [see Dosage and Administration (2.1), Warnings and Precautions (5.3, 5.4)].
- Advise patients not to take lamivudine tablets (HBV) with emtricitabine-containing medicines, such as ATRIPLA, COMPLERA, EMTRIVA, STRIBILD, or TRUVADA [see Warnings and Precautions (5.4)]. Advise patients that treatment with lamivudine tablets (HBV) has not been shown to reduce the risk of
- transmission of HBV to others through sexual contact or blood contamination [see Use in Specific Populations

- Instruct patients to avoid doing things that can spread HBV infection to others.
- Do not share needles or other injection equipment
- Do not share personal items that can have blood or body fluids on them, like toothbrushes and razor
- **Do not have any kind of sex without protection.** Always practice safe sex by using a latex or polyurethane condom to lower the chance of sexual contact with semen, vaginal secretions, or blood.

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Manufactured for: Camber Pharmaceuticals, Inc. Piscataway, NJ 08854 By: HETERO™ Hetero Labs Limited, Unit V, Polepally, Jadcherla, Mahaboob Nagar - 509 301, India.

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CAMBER

By: HETERO™ Hetero Labs Limited, Unit V, Polepally, Jadcherla, Mahaboob Nagar - 509 301 AMBER nufactured for: nber Pharmaceuticals, cataway, NJ 08854

Inactive ingredients:
Lamivudine tablets (
magnesium stearate au
Opadry Pink containing
polysorbate 80, titaniu , and TRIZIVIR ; f companies. their r The n Hetero are registered

ablets (HBV): crospovidone, is earate and methylene chloride. T ontaining hypromellose, iron oxid 0, titanium dioxide and yellow irr nformation has been approved t isom .. The xide r riron id by the U.S. Food and Drug

you would like more informati u can as your pharmacist or hu nivudine tablets (HBV) that is v talk with your thcare provider itten for health p ır healthcare r for informat professional

What are the

USP

Keep lamivudine tablets children. ŧ scribed for purposes other than those list et. Do not use lamivudine tablets (HBV) f t prescribed. Do not give lamivudine tablet if they have the same symptoms that y and

General information tablets (HBV)

How should I store lamivudine to Store lamivudine tablets (H to 77°F (20°C to 25°C). tablets (HBV) at room 25°C). (HBV) and : all medicines out of the reach

your doctor for medical advice about side effects to FDA at 1-800-FDA-1088.
v should I store lamivudine tablets (HBV)? possible on, ask y if you e side effects of lamivudine tablets your healthcare provider or phan have any side effect effects.

These are For more Call your of side effects

e not all the p information

ear, nose, ar sore throat diarrhea most s (HBV) s side e

t important i V)?" information I should know

If you take too much lamivudine tablets (HBV), call your healthcare provider or go to the nearest hospital emergency room right away.
 It is important to stay under your healthcare provider's care while taking lamivudine tablets (HBV), Tell your healthcare provider about any new symptoms that you have.
 What are the possible side effects of lamivudine tablets (HBV)?
 Lamivudine tablets (HBV) may cause serious side effects, including:

Take lamivudine tablets (HBV) by mouth, Tell your healthcare provider if you have to 17 years of age, your healthcare provider t dose of lamivudine tablets (HBV) based on trouble sw

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Tell suppre

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Pregnancy Registry. There is a pregnancy registry for w take antiviral medicines during pregnancy. The purporegistry is to collect information about the health of you baby. Talk to your healthcare provider about how you can in this registry.

Talk to your healthcare provider about how you can in this registry.

The present milk and may harm your baby. You and your preast milk and may harm your baby. You and your provider should decide if you will take lamivudine tabletheastfeed.

Tell your healthcare provider about all the medicines you take prescription and over-the-counter medicines, vitamins, a supplements. n pass into healthcare s (HBV) or

of y r women irpose of you and you take