Others:
Reduction of doses of lamivudine is recommended for patients with low body weight (less than 50 kg or 110 lb). Therefore patients with low body weight should not receive ***Duovir - D***.

SIDE EFFECTS
The most commonly observed side effects during clinical trials were headache, malaise and fatigue, nausea, vomiting, diarrhoea, anorexia, fever/ chills, neuropathy, insomnia, dizziness, nasal signs and symptoms, cough, musculoskeletal pain and neutropenia.

OVERDOSAGE
There is no known antidote for ***Duovir - D***.
Lamivudine : One case of an adult ingesting 6 gms of lamivudine has been reported. There were no clinical signs or symptoms noted and hematologic tests remained normal. It is not known whether lamivudine can be removed by peritoneal dialysis or hemodialysis.
Zidovudine : Acute overdoses of zidovudine have been reported in paediatric patients and adults. These involved exposures up to 50 grams. The only consistent findings were nausea and vomiting. Other reported occurrences included headache, dizziness, drowsiness, lethargy, confusion, and one report of a grand mal seizure. Hematologic changes were transient. All patients recovered. Hemodialysis and peritoneal dialysis appear to have a negligible effect on the removal of zidovudine while elimination of its primary metabolite is enhanced.

STORAGE
Store below 30°C

PRESENTATION
Duovir - D : Blister pack of 10 tablets and Container of 60 tablets

Cipla

DE37 A

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Lamivudine and Zidovudine Tablets 150 mg / 300 mg

Duovir - D

WARNING

ZIDOVUDINE, ONE OF THE TWO ACTIVE INGREDIENTS IN DUOVIR, HAS BEEN ASSOCIATED WITH HEMATOLOGIC TOXICITY INCLUDING NEUTROPENIA AND SEVERE ANEMIA, PARTICULARLY IN PATIENTS WITH ADVANCED HIV DISEASE (SEE WARNINGS AND PRECAUTIONS). PROLONGED USE OF ZIDOVUDINE HAS BEEN ASSOCIATED WITH SYMPTOMATIC MYOPATHY.

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, ZIDOVUDINE, AND OTHER ANTIRETROVIRALS (SEE WARNINGS AND PRECAUTIONS).

COMPOSITION
Each film-coated tablet contains
Lamivudine USP ..... 150 mg
Zidovudine USP..... 300 mg

DESCRIPTION
Duovir - D is a combination of two drugs commonly used in the management of Human Immuno-deficiency Virus (HIV) infection. Both lamivudine and zidovudine belong to the nucleoside analogue class of antiretroviral drugs. Both drugs act by inhibiting the reverse transcriptase enzyme of HIV, and by terminating the growth of the DNA chain. Lamivudine in combination with zidovudine has been shown to have synergistic antiretroviral activity.
Each tablet of ***Duovir - D*** contains half of the commonly prescribed daily doses of both lamivudine and zidovudine. With the availability of this combination tablet, patients may be better able to adhere to complex drug treatment regimens, thereby enhancing compliance.

INDICATION
Duovir - D is indicated for the treatment of HIV infection.

DOSAGE AND ADMINISTRATION

The recommended oral dose of ***Duovir - D*** for adults and adolescents (at least 12 years of age) is one tablet (containing 150 mg of lamivudine and 300 mg of zidovudine) twice daily with or without food.

Dose Adjustment

Because it is a fixed dose combination, ***Duovir - D*** should not be prescribed for patients requiring dosage adjustment, such as those with reduced renal function (creatinine clearance ≤ 50 mL/min), those with low body weight (<50 kg or 110 lb), or those experiencing dose-limiting adverse events.

CONTRAINDICATIONS

Duovir - D tablets are contraindicated in patients with previously demonstrated clinically significant hypersensitivity to any of the components of the product.

WARNINGS AND PRECAUTIONS

Since ***Duovir - D*** is a fixed–dose combination of lamivudine and zidovudine, it should ordinarily not be administered concomitantly with either lamivudine or zidovudine.

The complete prescribing information for all agents being considered for use with ***Duovir - D*** should be consulted before combination therapy with ***Duovir - D*** is initiated.

Bone Marrow Suppression: ***Duovir - D*** should be used with caution in patients who have bone marrow compromise evidenced by granulocyte count <1,000 cells/mm^3 or hemoglobin <9.5 g/dl (see side effects).

Frequent blood counts are strongly recommended in patients with advanced HIV disease who are treated with ***Duovir - D***. For HIV-infected individuals and patients with asymptomatic or early HIV disease, periodic blood counts are recommended.

Lactic Acidosis/Severe Hepatomegaly with steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination, including zidovudine and lamivudine. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Caution should be exercised when administering ***Duovir - D*** to any patient, and particularly to those with known risk factors for liver disease. Treatment with ***Duovir - D*** 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).

Prolonged Myopathy: Myopathy and myositis, with pathological changes similar to that produced by HIV disease, have been associated with prolonged use of zidovudine and therefore may occur with therapy with ***Duovir - D***.

Patients with HIV and Hepatitis B Virus Coinfection: In clinical trials and postmarketing experience, some patients with HIV infection who have chronic liver disease due to hepatitis B virus infection experienced clinical or laboratory evidence of recurrent hepatitis upon discontinuation of lamivudine. Consequences may be more severe in patients with decompensated liver disease.

Drug Interactions: Coadministration of ganciclovir, interferon-α , and other bone marrow suppressive or cytotoxic agents may increase the hematologic toxicity of zidovudine.

Impaired renal function: Reduction of the dosages of lamivudine and zidovudine is recommended for patients with impaired renal function. Patients with creatinine clearance ≤ 50 ml/min should not receive ***Duovir - D***.

Pregnancy: **Category C**. There are no adequate and well-controlled studies of this combination in pregnant women. ***Duovir - D*** should be used during pregnancy only if the potential benefits outweigh the risks.

Lactation: It is recommended that HIV-infected mothers not breast-feed their infants to avoid risking postnatal transmission of HIV infection.

Zidovudine is excreted in breast milk. No data are available on this combination or lamivudine. Therefore, there is a potential for adverse effects in nursing infants. Mothers should be instructed not to breast-feed if they are receiving ***Duovir - D***.

Paediatric use:

Duovir - D should not be administered to paediatric patients less than 12 years of age because it is a fixed-dose combination that cannot be adjusted for this patient population.