Condine®

Lamivudine / Zidovudine

FORMS AND PRESENTATION

Condine®: Film coated tablets: Jar of 60 FCT.

COMPOSITION

Condine®: Each film coated tablet contains Lamivudine 150mg and Zidovudine 300mg.

Excipients: microcrystalline cellulose, sodium starch glycolate, colloidal silicon dioxide, magnesium stearate, hydroxypropyl methylcellulose, polyethylene glycol, titanium dioxide, polysorbate.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Therapeutic class: Antivirals for systemic use.

ATC code: J05AR01.

Lamivudine and Zidovudine are nucleoside analogues which have activity against HIV. Additionally, Lamivudine has activity against hepatitis B virus (HBV). Both medicinal products are metabolized intracellularly to their active moieties, Lamivudine 5'-Triphosphate (TP) and Zidovudine 5'-TP respectively. Their main modes of action are as chain terminators of viral reverse transcription. Lamivudine-TP and Zidovudine-TP have selective inhibitory activity against HIV-1 and HIV-2 replication in vitro; Lamivudine is also active against Zidovudine-resistant clinical isolates of HIV. Lamivudine in combination with Zidovudine exhibits synergistic anti-HIV activity against clinical isolates in cell culture.

Pharmacokinetic properties

Absorption

Lamivudine and Zidovudine are well absorbed from the gastrointestinal tract. The bioavailability of oral Lamivudine in adults is normally between 80–85% and for Zidovudine 60–70%.

Administration of crushed tablets with a small amount of semi-solid food or liquid would not be expected to have an impact on the pharmaceutical quality, and would therefore not be expected to alter the clinical effect. This conclusion is based on the physiochemical and pharmacokinetic data assuming that the patient crushes and transfers 100% of the tablet and ingests immediately.

Distribution

Intravenous studies with Lamivudine and Zidovudine showed that the mean apparent volume of distribution is 1.3 and 1.6 l/kg respectively. Lamivudine exhibits linear pharmacokinetics over the therapeutic dose range and displays limited binding to the major plasma protein albumin (<36% serum albumin in vitro). Zidovudine plasma protein binding is 34% to 38%. Interactions involving binding site displacement are not anticipated with Condine®.

Data show that Lamivudine and Zidovudine penetrate the central nervous system (CNS) and reach the cerebrospinal fluid (CSF). The mean ratios of CSF/serum Lamivudine and Zidovudine concentrations 2-4 hours after oral administration were approximately 0.12 and 0.5 respectively. The true extent of CNS penetration of Lamivudine and its relationship with any clinical efficacy is unknown.

Biotransformation

Metabolism of Lamivudine is a minor route of elimination. Lamivudine is predominately cleared unchanged by renal excretion. The likelihood of metabolic drug interactions with Lamivudine is low due to the small extent of hepatic metabolism (5-10%) and low plasma binding.

The 5'-glucuronide of Zidovudine is the major metabolite in both plasma and urine, accounting for approximately 50–80% of the administered dose eliminated by renal excretion. 3'-amino-3'-deoxythymidine (AMT) has been identified as a metabolite of Zidovudine following intravenous dosing.

Elimination

The observed Lamivudine half-life of elimination is 5 to 7 hours. The mean systemic clearance of Lamivudine is approximately 0.32 l/h/kg, with predominantly renal clearance (>70%) via the organic cationic transport system. Studies in patients with renal impairment show Lamivudine elimination is affected by renal dysfunction. Dose reduction is required for patients with creatinine clearance ≤50 ml/min.

From studies with intravenous Zidovudine, the mean terminal plasma half-life was 1.1 hours and the mean systemic clearance was 1.6 l/h/kg. Renal clearance of Zidovudine is estimated to be 0.34 l/h/kg, indicating glomerular filtration and active tubular secretion by the kidneys. Zidovudine concentrations are increased in patients with advanced renal failure.

INDICATIONS

Condine® is indicated in antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infection.

CONTRAINDICATIONS

- Hypersensitivity to the active substances or to any of the excipients.
- Zidovudine is contraindicated in patients with abnormally low neutrophil counts (<0.75 x 10^9/l), or abnormally low hemoglobin levels (<7.5 g/dl or 4.65 mmol/l). Condine® is therefore contra-indicated in these patients.

PRECAUTIONS

The special warnings and precautions relevant to both Lamivudine and Zidovudine are included in this section. There are no additional precautions and warnings relevant to the combination Condine®.

- It is recommended that separate preparations of Lamivudine and Zidovudine should be administered in cases where dosage adjustment is necessary. In these cases the physician should refer to the individual prescribing information for these medicinal products.
- The concomitant use of stavudine with Zidovudine should be avoided.
- Opportunistic infections: Patients receiving Condine® or any other antiretroviral therapy may continue to develop opportunistic infections and other complications of HIV infection. Therefore patients should remain under close clinical observation by physicians experienced in the treatment of HIV infection.
- Transmission of HIV: Patients should be advised that current antiretroviral therapy, including Condine®, has not been proven to prevent the risk of transmission of HIV to others through sexual contact or contamination with blood. Appropriate precautions should continue to be taken.
- Hematological adverse reactions: Anemia, neutropenia and leucopenia (usually secondary to neutropenia) can be expected to occur in patients receiving Zidovudine. These occurred more frequently at higher Zidovudine dosages (1200-1500 mg/day) and in patients with poor bone marrow reserve prior to treatment, particularly with advanced HIV disease. Hematological parameters should therefore be carefully monitored in patients receiving Condine®. These hematological effects are not usually observed before four to six weeks therapy. For patients with advanced symptomatic HIV disease, it is generally recommended that blood tests are performed at least every two weeks for the first three months of therapy and at least monthly thereafter.

In patients with early HIV disease hematological adverse reactions are infrequent. Depending on the overall condition of the patient, blood tests may be performed less often, for example every one to three months. Additionally dosage adjustment of Zidovudine may be required if severe anemia or myelosuppression occurs during treatment with Condine®, or in patients with pre-existing bone marrow compromise e.g. hemoglobin <9 g/dl (5.59 mmol/l) or neutrophil count <1.0 x 10^9/l. As dosage adjustment of Condine® is not possible separate preparations of Zidovudine and Lamivudine should be used. Physicians should refer to the individual prescribing information for these medicinal products.

- Pancreatitis: Cases of pancreatitis have occurred rarely in patients treated with Lamivudine and Zidovudine. However it is not clear whether these cases were due to the antiretroviral treatment or to the underlying HIV disease. Treatment with Condine® should be stopped immediately if clinical signs, symptoms or laboratory abnormalities suggestive of pancreatitis occur.
- Lactic acidosis: Lactic acidosis usually associated with hepatomegaly and hepatic steatosis has been reported with the use of nucleoside analogues. Early symptoms (symptomatic hyperlactatemia) include benign digestive symptoms (nausea, vomiting and abdominal pain) non-specific malaise, loss of appetite, weight loss, respiratory symptoms (rapid and/or deep breathing) or neurological symptoms (including motor weakness).

Lactic acidosis has a high mortality and may be associated with pancreatitis, liver failure, or renal failure.

Lactic acidosis generally occurred after a few or several months of treatment.

Treatment with nucleoside analogues should be discontinued if there is symptomatic hyperlactatemia and metabolic/lactic acidosis, progressive hepatomegaly, or rapidly elevating aminotransferase levels.

Caution should be exercised when administering nucleoside analogues to any patient (particularly obese women) with hepatomegaly, hepatitis or other known risk factors for liver disease and hepatic steatosis (including certain medicinal products and alcohol). Patients co-infected with hepatitis C and treated with alpha interferon and ribavirin may constitute a special risk.

Patients at increased risk should be followed closely.

- Mitochondrial dysfunction: Nucleoside and nucleotide analogues have been demonstrated in vitro and in vivo to cause a variable degree of mitochondrial damage. There have been reports of mitochondrial dysfunction in HIV-negative infants exposed in utero and/or post-natally to nucleoside analogues. The main adverse events reported are hematological disorders (anemia, neutropenia), metabolic disorders (hyperlactatemia, hyperlipasemia). These events are often transitory. Some late-onset neurological disorders have been reported (hypertonia, convulsion, abnormal behavior). Whether the neurological disorders are transient or permanent is currently unknown. Any child exposed in utero to nucleoside and nucleotide analogues, even HIV-negative children, should have clinical and laboratory follow-up and should be fully investigated for possible mitochondrial dysfunction in case of relevant signs or symptoms. These findings do not affect current national recommendations to use antiretroviral therapy in pregnant women to prevent vertical transmission of HIV.
- Lipodystrophy: Combination antiretroviral therapy has been associated with the redistribution of body fat (lipodystrophy) in HIV patients. The long-term consequences of these events are currently unknown. Knowledge about the mechanism is incomplete. A connection between visceral lipomatosis and protease inhibitors (PIs) and lipoatrophy and nucleoside reverse transcriptase inhibitors (NRTIs) has been hypothesized. A higher risk of lipodystrophy has been associated with individual factors such as older age, and with drug related factors such as longer duration of antiretroviral treatment and associated metabolic disturbances. Clinical examination should include evaluation for physical signs of fat redistribution. Consideration should be given to the measurement of fasting serum lipids and blood glucose. Lipid disorders should be managed as clinically appropriate.
- Immune Reactivation Syndrome: In HIV-infected patients with severe immune deficiency at the time of institution of combination antiretroviral therapy (CART), an inflammatory reaction to asymptomatic or residual opportunistic pathogens may arise and cause serious clinical conditions, or aggravation of symptoms. Typically, such reactions have been observed within the first few weeks or months of initiation of CART. Relevant examples are cytomegalovirus retinitis, generalized and/or focal mycobacterium infections, and *Pneumocystis jiroveci* pneumonia (formerly known as *Pneumocystis carinii* pneumonia). Any inflammatory symptoms should be evaluated and treatment instituted when necessary.
- Liver disease: The safety and efficacy of Zidovudine has not been established in patients with significant underlying liver disorders.

Patients with chronic hepatitis B or C and treated with combination antiretroviral therapy are at an increased risk of severe and potentially fatal hepatic adverse events. In case of concomitant antiviral therapy for hepatitis B or C, please refer also to the relevant product information for these medicinal products.

If Condine® is discontinued in patients co-infected with hepatitis B virus, periodic monitoring of both liver function tests and markers of HBV replication for 4 months is recommended, as withdrawal of Lamivudine may result in an acute exacerbation of hepatitis.

Patients with pre-existing liver dysfunction, including chronic active hepatitis, have an increased frequency of liver function abnormalities during combination antiretroviral therapy, and should be monitored according to standard practice. If there is evidence of worsening liver disease in such patients, interruption or discontinuation of treatment must be considered.

- Patients co-infected with hepatitis C virus: The concomitant use of ribavirin with Zidovudine is not recommended due to an increased risk of anemia.
- Osteonecrosis: Although the etiology is considered to be multifactorial (including corticosteroid use, alcohol consumption, severe immunosuppression, higher body mass index), cases of osteonecrosis have been reported particularly in patients with advanced HIV-disease and/or long-term exposure to combination antiretroviral therapy (CART). Patients should be advised to seek medical advice if they experience joint aches and pain, joint stiffness or difficulty in movement.

Condine® should not be taken with any other medicinal products containing Lamivudine or medicinal products containing emtricitabine.

Ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

PREGNANCY AND LACTATION

As a general rule, when deciding to use antiretroviral agents for the treatment of HIV infection in pregnant women and consequently for reducing the risk of HIV vertical transmission to the newborn, the animal data as well as the clinical experience in pregnant women should be taken into account. In the present case, the use in pregnant women of Zidovudine, with subsequent treatment of the newborn infants, has been shown to reduce the rate of maternal-fetal transmission of HIV. A large amount of data on pregnant women taking Lamivudine or Zidovudine indicates no malformative toxicity.

For patients co-infected with hepatitis who are being treated with Lamivudine containing medicinal products such as Condine® and subsequently become pregnant, consideration should be given to the possibility of a recurrence of hepatitis on discontinuation of Lamivudine.

Nucleoside and nucleotide analogues have been demonstrated in vitro and in vivo to cause a variable degree of mitochondrial damage. There have been reports of mitochondrial dysfunction in HIV-negative infants exposed in utero and/or post-natally to nucleoside analogues.

Both Lamivudine and Zidovudine are excreted in breast milk at similar concentrations to those found in serum. As a general rule, it is recommended that mothers infected by HIV do not breast-feed their infants under any circumstances in order to avoid transmission of HIV.

There are no data on the affect of Zidovudine and Lamivudine on human female fertility.

In men Zidovudine has not been shown to affect sperm count, morphology or motility.

DRUG INTERACTIONS

Condine® contains Lamivudine and Zidovudine, therefore any interactions identified for these individually are relevant to Condine®. Clinical studies have shown that there are no clinically significant interactions between Lamivudine and Zidovudine.

Zidovudine is primarily metabolized by UGT enzymes; co-administration of inducers or inhibitors of UGT enzymes could alter Zidovudine exposure. Lamivudine is cleared renally. Active renal secretion of Lamivudine in the urine is mediated through organic cation transporters (OCTs); co-administration of Lamivudine with OCT inhibitors or

nephrotoxic drugs may increase Lamivudine exposure.
Lamivudine and Zidovudine are not significantly metabolized by cytochrome P_{450} enzymes (such as CYP 3A4, CYP 2C9 or CYP 2D6) nor do they inhibit or induce this enzyme system. Therefore, there is little potential for interactions with antiretroviral protease inhibitors, non-nucleosides and other medicinal products metabolized by major P_{450} enzymes.
Interaction studies have only been performed in adults.
- Antiretroviral medicinal products: In vitro antagonism of anti-HIV activity between stavudine and Zidovudine could result in decreased efficacy of both drugs. The combination of stavudine and Condine® is not recommended.
- Anti-infective products: The concomitant administration of clarithromycin 500mg twice daily and Zidovudine 100mg every 4 hours decreased Zidovudine AUC by 12%. Separate administration of Condine® and clarithromycin by at least 2 hours is recommended.
The concomitant administration of Trimethoprim/sulfamethoxazole (Co-trimoxazole) 160mg/800mg once daily for 5 days and Lamivudine 300mg single dose increased Lamivudine AUC by 40% due to organic cation transporter inhibition. No Condine® dosage adjustment is necessary, unless patient has renal impairment. When concomitant administration with co-trimoxazole is warranted, patients should be monitored clinically. High doses of trimethoprim/sulfamethoxazole for the treatment of *Pneumocystis jirovecii* pneumonia (PCP) and toxoplasmosis have not been studied and should be avoided.
- Antifungals: The concomitant administration of fluconazole 400mg once daily and Zidovudine 200mg thrice daily increased Zidovudine AUC by 74% due to UGT inhibition. As only limited data are available the clinical significance is not known. Monitor for signs of Zidovudine toxicity.
- Antimycobacterials: The concomitant administration of rifampicin 600mg once daily and Zidovudine 200mg thrice daily decreased Zidovudine AUC by 48% due to UGT inhibition. There is insufficient data to recommend dosage adjustment.
- Anticonvulsants: The concomitant administration of phenytoin and Zidovudine lead to an increase or decrease in phenytoin AUC. Monitoring of phenytoin concentrations is recommended.
The concomitant administration of valproic acid 250mg or 500mg thrice daily and Zidovudine 100mg thrice daily increased Zidovudine AUC by 80% due to UGT inhibition. As only limited data are available the clinical significance is not known. Monitor for signs of Zidovudine toxicity.
- Opioids: The concomitant administration of methadone 30 to 90mg once daily and Zidovudine 200mg every 4 hours increased Zidovudine AUC by 43%. As only limited data are available the clinical significance is not known. Monitor for signs of Zidovudine toxicity. Methadone dosage adjustment is unlikely in majority of patients; occasionally methadone re-titration may be required.
- Uricosuric: The concomitant administration of probenecid 500mg four times daily and Zidovudine 2mg/kg thrice daily increased Zidovudine AUC by 106% due to UGT inhibition. As only limited data are available the clinical significance is not known. Monitor for signs of Zidovudine toxicity.
- Exacerbation of anemia due to ribavirin has been reported when Zidovudine is part of the regimen used to treat HIV although the exact mechanism remains to be elucidated. The concomitant use of ribavirin with Zidovudine is not recommended due to an increased risk of anemia. Consideration should be given to replacing Zidovudine in a combination ART regimen if this is already established. This would be particularly important in patients with a known history of Zidovudine induced anemia.
- Concomitant treatment, especially acute therapy, with potentially nephrotoxic or myelosuppressive medicinal products (e.g. systemic pentamidine, dapsone, pyrimethamine, co-trimoxazole, amphotericin, flucytosine, ganciclovir, interferon, vincristine, vinblastine and doxorubicin) may also increase the risk of adverse reactions to Zidovudine. If concomitant therapy with Condine® and any of these medicinal products is necessary then extra care should be taken in monitoring renal function and hematological parameters and, if required, the dosage of one or more agents should be reduced.

ADVERSE EFFECTS

Adverse reactions have been reported during therapy for HIV disease with Lamivudine and Zidovudine separately or in combination. For many of these events, it is unclear whether they are related to Lamivudine, Zidovudine, the wide range of medicinal products used in the management of HIV disease, or as a result of the underlying disease process.
As Condine® contains Lamivudine and Zidovudine, the type and severity of adverse reactions associated with each of the compounds may be expected. There is no evidence of added toxicity following concurrent administration of the two compounds.
Cases of lactic acidosis, sometimes fatal, usually associated with severe hepatomegaly and hepatic steatosis, have been reported with the use of nucleoside analogues.
Combination antiretroviral therapy has been associated with redistribution of body fat (lipodystrophy) in HIV patients including the loss of peripheral and facial subcutaneous fat, increased intra-abdominal and visceral fat, breast hypertrophy and dorsocervical fat accumulation (buffalo hump).
Combination antiretroviral therapy has been associated with metabolic abnormalities such as hypertriglyceridemia, hypercholesterolemia, insulin resistance, hyperglycemia and hyperlactatemia.
In HIV-infected patients with severe immune deficiency at the time of initiation of combination antiretroviral therapy (CART), an inflammatory reaction to asymptomatic or residual opportunistic infections may arise.
Cases of osteonecrosis have been reported, particularly in patients with generally acknowledged risk factors, advanced HIV disease or long-term exposure to combination antiretroviral therapy (CART). The frequency of this is unknown.
The adverse reactions considered at least possibly related to the treatment are listed below by body system, organ class and absolute frequency.
Frequencies are defined as very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1000 to <1/100), rare (≥ 1/10,000 to <1/1000), very rare (<1/10,000). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.
Lamivudine
- Blood and lymphatic systems disorders: Neutropenia and anemia (both occasionally severe), thrombocytopenia (uncommon); pure red cell aplasia (very rare).
- Nervous system disorders: Headache, insomnia (common); peripheral neuropathy (or paresthesia) (very rare).
- Respiratory, thoracic and mediastinal disorders: Cough, nasal symptoms (common).
- Gastrointestinal disorders: Nausea, vomiting, abdominal pain or cramps, diarrhea (common); pancreatitis, rises in serum amylase (rare).
- Hepatobiliary disorders: Transient rises in liver enzymes (uncommon); hepatitis (rare).
- Skin and subcutaneous tissue disorders: Rash, alopecia (common); angioedema (rare).
- Musculoskeletal and connective tissue disorders: Arthralgia, muscle disorders (common); rhabdomyolysis (rare).
- General disorders and administration site conditions: Fatigue, malaise, fever (common).
Zidovudine
The adverse reactions profile appears similar for adults and adolescents. The most serious adverse reactions include anemia (which may require transfusions), neutropenia and leucopenia. These occurred more frequently at higher dosages (1200-1500 mg/day) and in patients with advanced HIV disease (especially when there is poor bone marrow reserve prior to treatment), and particularly in patients with CD4 cell counts less than 100/mm³.
The incidence of neutropenia was also increased in those patients whose neutrophil counts, hemoglobin levels and serum vitamin B_{12} levels were low at the start of Zidovudine therapy.
- Blood and lymphatic system disorders: Anemia, neutropenia and leucopenia (common); thrombocyopenia and pancytopenia (with marrow hypoplasia) (uncommon); pure red cell aplasia (rare); aplastic anemia (very rare).
- Metabolism and nutrition disorders: Lactic acidosis in the absence of hypoxemia, anorexia (rare).
- Psychiatric disorders: Anxiety and depression (rare).
- Nervous system disorders: Headache (very common); dizziness (common); insomnia, paresthesia, somnolence, loss of mental acuity, convulsions (rare).
- Cardiac disorders: Cardiomyopathy (rare).
- Respiratory, thoracic and mediastinal disorders: Dyspnea (uncommon); cough (rare).
- Gastrointestinal disorders: Nausea (very common); vomiting, abdominal pain and diarrhea (common); flatulence (uncommon); oral mucosa pigmentation, taste perversion and dyspepsia, pancreatitis (rare).
- Hepatobiliary disorders: Raised blood levels of liver enzymes and bilirubin (common); liver disorders such as severe hepatomegaly with steatosis (rare).
- Skin and subcutaneous tissue disorders: Rash and pruritus (uncommon); nail and skin pigmentation, urticaria and sweating (rare).
- Musculoskeletal and connective tissue disorders: Myalgia (common); myopathy (uncommon).
- Renal and urinary disorders: Urinary frequency (rare).
- Reproductive system and breast disorders: Gynecomastia (rare).
- General disorders and administration site conditions: Malaise (common); fever, generalized pain and asthenia (uncommon); chills, chest pain and influenza-like syndrome (rare).

DOSAGE AND ADMINISTRATION

Therapy should be initiated by a physician experienced in the management of HIV infection.
Condine® may be administered with or without food.
To ensure administration of the entire dose, the tablet(s) should ideally be swallowed without crushing. For patients who are unable to swallow tablets, tablets may be crushed and added to a small amount of semi-solid food or liquid, all of which should be consumed immediately.
Adults and adolescents weighing at least 30 kg
The recommended dose of Condine® is one tablet twice daily.
Children weighing between 21 kg and 30 kg
The recommended oral dose of Condine® is one-half tablet taken in the morning and one whole tablet taken in the evening.
Children weighing from 14 kg to 21 kg
The recommended oral dose of Condine® is one-half tablet taken twice daily.
The dosing regimen for pediatric patients weighing 14-30 kg is based primarily on pharmacokinetic modelling and supported by data from clinical studies using the individual components Lamivudine and Zidovudine. A pharmacokinetic overexposure of Zidovudine can occur, therefore close safety monitoring is warranted in these patients. If gastrointestinal intolerance occurs in patients weighing 21-30 kg, an alternative dosing schedule with one-half tablet taken thrice daily can be applied in attempt to improve tolerability.
Condine® tablets should not be used for children weighing less than 14 kg, since doses can not be appropriately adjusted for the weight of the child. In these patients, Lamivudine and Zidovudine should be taken as separate formulations according to the prescribed dosing recommendations for these products.
For situations where discontinuation of therapy with one of the active substances of Condine®, or dose reduction is necessary separate preparations of Lamivudine and Zidovudine are available.
Renal impairment
Lamivudine and Zidovudine concentrations are increased in patients with renal impairment due to decreased clearance. Therefore as dosage adjustment of these may be necessary it is recommended that separate preparations of Lamivudine and Zidovudine be administered to patients with reduced renal function (creatinine clearance ≤50 ml/min). Physicians should refer to the individual prescribing information for these medicinal products.
Hepatic impairment
Limited data in patients with cirrhosis suggest that accumulation of Zidovudine may occur in patients with hepatic impairment because of decreased glucuronidation. Data obtained in patients with moderate to severe hepatic impairment show that Lamivudine pharmacokinetics are not significantly affected by hepatic dysfunction. However, as dosage adjustments for Zidovudine may be necessary, it is recommended that separate preparations of Lamivudine and Zidovudine be administered to patients with severe hepatic impairment. Physicians should refer to the individual prescribing information for these medicinal products.
Dosage adjustments in patients with hematological adverse reactions
Dosage adjustment of Zidovudine may be necessary if the hemoglobin level falls below 9 g/dl or 5.59 mmol/l or the neutrophil count falls below 1.0 x 109/l. As dosage adjustment of Condine® is not possible, separate preparations of Zidovudine and Lamivudine should be used. Physicians should refer to the individual prescribing information for these medicinal products.
Dosage in the elderly
No specific data are available, however special care is advised in this age group due to age associated changes such as the decrease in renal function and alteration of hematological parameters.

OVERDOSAGE

There is limited experience of overdosage with Condine®. No specific symptoms or signs have been identified following acute overdose with Zidovudine or Lamivudine apart from those listed as undesirable effects. No fatalities occurred, and all patients recovered.
If overdosage occurs the patient should be monitored for evidence of toxicity, and standard supportive treatment applied as necessary. Since Lamivudine is dialyzable, continuous hemodialysis could be used in the treatment of overdosage, although this has not been studied. Hemodialysis and peritoneal dialysis appear to have a limited effect on elimination of Zidovudine, but enhance the elimination of the glucuronide metabolite. For more details physicians should refer to the individual prescribing information for Lamivudine and Zidovudine.

STORAGE CONDITIONS

Store below 30°C.
Keep in original pack in intact conditions.
Date of revision: June 2015.

This is a medicament
- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you
- Follow strictly the doctor's prescription, the method of use, and the instructions of the pharmacist who sold the medicament
- The doctor and the pharmacist are experts in medicine, its benefits and risks
- Do not by yourself interrupt the period of treatment prescribed for you
- Do not repeat the same prescription without consulting your doctor
- Medicament: keep out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists

PI138/3

Benta S.A.L.,
Dbayeh - Lebanon