PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

LODIZ (Tablet)

Lamivudine / Zidovudine.

Read all of this leaflet carefully before you start taking LODIZ

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **LODIZ** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

1. WHAT LODIZ CONTAINS

- The active substances are Lamivudine and Zidovudine. Each film-coated tablet contains Lamivudine 150 mg and Zidovudine 300 mg.
- The other ingredients are: colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, Opadry 13B58802 IH, sodium starch glycolate.

2. WHAT LODIZ IS USED FOR

LODIZ tablets are indicated as part of an antiretroviral combination therapy for the treatment of HIV infected adults and children over 12 years of age, with progressive immunodeficiency (CD4 Count ≤ 500 cells/mm^1).

3. BEFORE YOU TAKE LODIZ

Do not take LODIZ:

- If you are hypersensitive (allergic) to Lamivudine or Zidovudine or any of the other ingredients of **LODIZ** tablets.
- Not recommended for use in children below 12 years of age. Insufficient data available.
- If you have abnormally low neutrophil counts (<0,75 x 10^9/l), or abnormally low haemoglobin levels (<7,5 g/dl).
- The combination of zidovudine with either ribavirin or stavudine is antagonistic *in vitro*. The concomitant use of either ribavirin or stavudine with **LODIZ** should be avoided.

Take special care with LODIZ:

- You may develop a potentially fatal condition known as lactic acidosis while taking **LODIZ**. Inform your doctor or other healthcare professional immediately if you develop nausea, vomiting, abdominal pain, dyspnoea, fatigue and weight loss. Your doctor will perform blood tests and treat you accordingly.
- If you became pregnant while taking **LODIZ** your baby may develop blood and nervous system disorders. Your doctor will monitor your baby's condition.
- Pancreatitis (inflammation of the pancreas) has been observed in some patients receiving **LODIZ**. Inform your doctor or other healthcare professional immediately if you develop abdominal pain, nausea or vomiting. Your doctor will discontinue treatment with **LODIZ** until the diagnosis of pancreatitis is excluded.
- If you have kidney problems your doctor or healthcare professional will need to adjust the dosage of **LODIZ**.
- You may develop liver problems when taking **LODIZ**. Inform your doctor or healthcare professional if you have any pre-existing liver disease including Hepatitis B or C.
  Do not stop taking **LODIZ** if you are co-infected with HIV and Hepatitis as this may cause the Hepatitis to worsen.
- You may develop a condition known as lipodystrophy while taking **LODIZ**. Inform your doctor or healthcare professional if you notice a change in the distribution of your body fat (e.g. accumulation of fat around the waist/stomach area, on the back of the neck and between the shoulders (buffalo hump), breast enlargement), wasting of the arms, legs and facial muscles, and increased blood glucose and lipid values.

- If you are taking **LODIZ** for the first time you may develop a condition known as Immune Reconstitution Inflammatory Syndrome (IRIS), within the first few months of treatment. This condition can cause opportunistic infections that are being treated to become worse or opportunistic diseases that were asymptomatic to be unmasked. Tell your doctor or healthcare professional if your general health worsens or if you think you may have an infection. You should not stop taking **LODIZ**, Your doctor will treat the infections appropriately.
- You may develop a condition known as osteonecrosis while taking **LODIZ**. Seek medical advice if you experience joint aches and pain, joint stiffness or difficulty in movement.
- You may continue to develop opportunistic infections and other complications of HIV infection while taking **LODIZ**. You should remain under close observation by healthcare professionals experienced in the treatment of patients with associated HIV disease. Regular monitoring of viral load and CD4 counts needs to be done.
- You are still at risk of transmitting HIV to others through sexual contact or blood contamination while taking current antiretroviral therapy including **LODIZ**. Appropriate precautions should continue to be employed.

Taking LODIZ with food and drink:

LODIZ tablets can be taken with or without food.

Pregnancy and Breastfeeding:

The safety of lamivudine in human pregnancy has not been established thus treatment during the first trimester of pregnancy is not advised.

The use of zidovudine in pregnant women, with subsequent treatment of the newborn infants, has been shown to reduce the rate of maternal-foetal transmission of HIV. This has however not been established for lamivudine. Consequently the administration of **LODIZ** during pregnancy will only be considered if expected benefits outweigh any possible risks.

Studies in lactating rats showed that, following oral administration, lamivudine and zidovudine were excreted in the milk. It is not known if lamivudine or zidovudine are excreted in human milk. Since these drugs may pass into breast milk, it is recommended that mothers taking **LODIZ** do not breastfeed their infants.

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **LODIZ**.

Taking other medicines with LODIZ:

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines).

LODIZ interacts with trimethoprim.

Prophylactic use of co-trimoxazole may increase the concentration of the Lamivudine in the blood. The dose may need to be adjusted if the doctor confirms that you may have renal impairment.
The doctor will monitor the blood levels of Phenytoin, if you are taking this drug.

Aspirin, codeine, morphine, indomethacin, ketoprofen, naproxen, oxazepam, lorazepam, cimetidine, clofibrate, dapsone and Isoprinosine may interfere with the metabolism of Zidovudine. The doctor will monitor any significant effect, if you are currently taking any of these drugs with **LODIZ.** If you are currently on systemic pentamidine, dapsone, pyrimethamine, co-trimoxazole, amphotericin, flucytosine, ganciclovir, interferon, vincristine or vinblastine, the risk of increasing the adverse effects of Zidovudine may be potentially serious. The doctor will monitor your renal and haematological parameters and consider if any dosage adjustments may be necessary.

4. HOW TO TAKE LODIZ

Do not share medicines prescribed for you with any other person.
Always take **LODIZ** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. If you have the impression that the effect of **LODIZ** is too strong or too weak, talk to your doctor or pharmacist.

Adults and children over the age of 12 years:

- The recommended dose: one tablet orally twice daily.
- The therapy should be initiated by a doctor experienced in the management of HIV infection.

  LODIZ tablets can be taken with or without food.

- Dosage adjustments may be deemed necessary if your doctor confirms that you have renal and hepatic impairment or any increase risk of haematological adverse reactions.

If you take more LODIZ than you should:

If overdosage occurs the patient should be monitored and standard supportive treatment supplied as required.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take LODIZ:

Do not take a double dose to make up for forgotten individual doses.

5. POSSIBLE SIDE EFFECTS

LODIZ can have side effects.

LODIZ is a combination of both Lamivudine and Zidovudine and hence each of these drugs can cause side effects.

Lamivudine: The adverse events, which have been reported, are:

Nervous system disorders:

Frequent: Headache, insomnia.

Less frequent: Although no relationship to the dose of lamivudine has been reported, cases of peripheral neuropathy (or paraesthesia) have been recorded.

Musculoskeletal, connective tissue and bone disorders:

The following side effects have been reported but the frequencies are unknown: Malaise, fatigue, musculoskeletal pain.

Gastrointestinal disorders:

Frequent: Nausea, diarrhoea, vomiting, abdominal pain or cramps.

Respiratory, thoracic and mediastinal disorders :

The following side effects have been reported but the frequencies are unknown: Cough, nasal symptoms

Endocrine disorders:

The following side effects have been reported but the frequencies are unknown: Although no relationship to the dose of lamivudine has been reported, cases of pancreatitis have been recorded.

Blood and the lymphatic system disorders:

Frequent: Anaemia and neutropenia (both occasionally acute) have occurred in combination with zidovudine. Thrombocytopenia has been reported.

Investigations:

The following side effects *have been reported but the frequencies are unknown:* Transient rises in liver enzymes (AST, ALT) and rises in serum amylase have been reported.

Zidovudine: The adverse events, which have been reported, are:

Blood and the lymphatic system disorders:

Anaemia (which may require transfusions), neutropenia and leucopenia, have been reported as the most serious adverse reactions. These adverse reactions occur more often 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 patient with CD4 cell counts < 100 mm^3 reduction in the dosage or cessation of therapy may become essential.

Adverse events have been reported, in patients whose neutrophil counts haemoglobin levels and serum, vitamin B12 levels were low at the start of zidovudine therapy, and in those patients who are concurrently, taking paracetamol.

Gastrointestinal disorders:

Frequent: Nausea, vomiting, anorexia, abdominal pain, dyspepsia.

Nervous system disorders:

Frequent: Headache, paraesthesia, asthenia, insomnia.

Skin and subcutaneous tissue disorders:

Frequent: Rash.

Musculoskeletal. connective tissue and bone disorders:

Frequent: Myalgia, malaise.

Nausea, was considerably more common in all studies in patients receiving zidovudine, the other adverse events were not consistently reported to be more frequent in occurrence than in the placebo recipients.

Vomiting, anorexia, malaise and asthenia were more common in zidovudine-treated patients with early HIV disease, whilst severe headache, myalgia and insomnia were more common in. zidovudine Treated patients with advanced HIV disease.

General disorders and administration site conditions:

Frequent: Fever.

The following side effects have *been reported but the frequencies* are *unknown:* Somnolence, diarrhoea, dizziness, sweating, dyspnoea, flatulence, taste perversion, pain in the chest, loss of mental acuity, anxiety, urinary frequency, depression, generalised pain, chills, cough, urticaria, pruritus and an influenza- like syndromes, have been recorded as other adverse events associated with the use of **LODIZ**.

The occurrence of these and other less frequent adverse events was similar in both zidovudine and placebo-treated patients. The incidence of nausea and other frequently reported clinical adverse events consistently decrease over time during the first few weeks of therapy with zidovudine, this was indicated by available data from both placebo-controlled and open-labelled studies.

The relationship between the following events, which have been reported on, and the use of zidovudine is difficult to evaluate, if the medically complicated situations, which characterise advanced HIV disease is considered.

Hepato-biliarv disorders:

The following side effects have been reported but the frequencies are unknown: Lactic acidosis in the absence of hypoxaemia, liver disorders such as severe hepatomegaly with steatosis.

Musculoskeletal, connective tissue and bone disorders:

The following side effects have been reported but the frequencies are unknown: Myopathy.

Blood and the lymphatic system disorders:

The following side effects *have been reported but the frequencies* are *unknown:* Pancytopenia with marrow hypoplasia and isolated thrombocytopenia.

Investigations:

The following side effects have been reported but the frequencies are unknown: Raised blood levels of liver enzymes and bilirubin.

Endocrine disorders:

The following side effects have been reported but the frequencies are unknown: Pancreatitis.

Musculoskeletal, connective tissue and bone disorders:

The following side effects have been reported but the frequencies are unknown: Nail, skin and oral mucosa pigmentation.

Nervous system disorders:

The following side effects have been reported but the frequencies are unknown: In patients receiving open-label therapy with zidovudine, convulsions and other cerebral events have also been recorded. The beneficial effect of zidovudine on HIV-associated neurological disorders has overall been proven by the weight of evidence.

A reduction or suspension of zidovudine therapy may assist in the assessment and management of these conditions, if the severity of the symptoms warrants it. **LODIZ** should be discontinued and separate preparations of zidovudine and lamivudine should be administered, if symptoms become intolerable.

Not all side effects reported for **LODIZ** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **LODIZ**, please consult your doctor, pharmacist or other healthcare professional for advice.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

6. STORING AND DISPOSING OF LODIZ

Store at or below 30 °C. Protect from light and moisture.

STORE ALL MEDICINES OUT OF THE REACH OF CHILDREN.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. PRESENTATION OF LODIZ

1. 60 tablets are packed in a white 110 ml HDPE container (heavy weight) closed with cap containing induction sealing wad.
2. 60 tablets are packed in white round 75 ml HDPE container (heavy weight) with stock ribbed polypropylene closure with induction sealing wad.

8. IDENTIFICATION OF LODIZ

White modified capsule shaped, biconvex, film-coated tablets, debossed with ‘C’ and ‘60’ on one side and plain on the other side.

9. REGISTRATION NUMBER / REFERENCE NUMBER

A40/20.2.8/0381

10. NAME AND ADDRESS OF REGISTRATION HOLDER

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