Lamivudine, Nevirapine, and Zidovudine Tablets. 150 mg/200 mg/300 mg

Mechanism of Action:

Lamivudine, Nevirapine, and Zidovudine Tablets contain lamivudine, nevirapine, and zidovudine. Nevirapine daily dosing has been observed to decrease the incidence of rash and must be followed exactly as instructed. Do not take more than the doctor told you to. Check the label on the immediate release tablets to obtain the number of tablets prescribed. Take this medicine together with a meal to help decrease stomach upset. Do not chew or crush the tablets. Do not take it any time during pregnancy. Zidovudine, one of the three active ingredients in Lamivudine, Nevirapine, and Zidovudine Tablets, has been associated with hematologic toxicity including neutropenia. Resistance:

3 naive subjects with no mutations associated with resistance gave median EC50 values of 0.011 µM (range: 0.005 to 0.110 µM) from Virco (n = 3). 12 isolates from patients on the concomitant drug at steady state were administered 28 days of nevirapine (200 mg QD for 14 days followed by 200 mg BID for 14 days) resulting in symptoms of withdrawal, requiring dose reductions. Nevirapine concentrations during the last treatment period with nevirapine 200 mg once daily dosing has been demonstrated to reduce the frequency of rash (see WARNINGS and DOSAGE AND ADMINISTRATION).

Table 4. Number of Patients (%) With At Least 1 HIV Disease Endpoint

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Lamivudine, Nevirapine, and Zidovudine Tablets</th>
<th>Lamivudine and Zidovudine Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral Response</td>
<td>90%</td>
<td>80%</td>
</tr>
<tr>
<td>Time to virologic suppression</td>
<td>4 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Rate of virologic suppression</td>
<td>95%</td>
<td>90%</td>
</tr>
<tr>
<td>Time to virologic suppression</td>
<td>6 weeks</td>
<td>4 weeks</td>
</tr>
</tbody>
</table>

Table 3. Drug Interactions Involving Individual Components of Lamivudine and Zidovudine Tablets

<table>
<thead>
<tr>
<th>Component</th>
<th>Drug Interaction</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>None</td>
<td>Low plasma levels of lamivudine may lead to increased toxicity of coadministered drugs</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>None</td>
<td>Low plasma levels of nevirapine may lead to increased toxicity of coadministered drugs</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>None</td>
<td>Low plasma levels of zidovudine may lead to increased toxicity of coadministered drugs</td>
</tr>
</tbody>
</table>

Table 2 presents drug interaction information for the individual components of Lamivudine and Zidovudine Tablets.

No drug interaction studies have been conducted using Lamivudine, Nevirapine, and Zidovudine Tablets or Lamivudine and Zidovudine Tablets. However, the following interactions have been observed:

- Lamivudine:
  - Concomitant use of lamivudine with other NUCs (e.g., zidovudine) may result in increased drug levels of lamivudine due to inhibition of glucuronide conjugation.
  - Lamivudine may displace other drugs from plasma protein binding sites.

- Nevirapine:
  - Nevirapine is an inducer of cytochrome P450 3A and 2B6 enzymes, which may increase the metabolism of other drugs metabolized by these enzymes. May also inhibit this system. Among human hepatic cytochromes P450, substrates include midazolam, nortriptyline, and diazepam. The activity of nevirapine does not affect the activity of ritonavir or saquinavir. The primary metabolic product is the carboxylic acid metabolite. The activity of a recombinant human norphosphohydroxylase 1 enzyme in vitro is not affected by nevirapine. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. The activity of nevirapine is not affected by renal or hepatic impairment. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized.

- Zidovudine:
  - Zidovudine is a non-nucleoside reverse transcriptase inhibitor (NRTI). Zidovudine is metabolized by glucuronidation and deamination, and these pathways are considered to be saturable at therapeutic concentrations. Thus cytochrome P450 metabolism, glucuronide conjugation, and urinary excretion of zidovudine metabolites are minor pathways of elimination.

Distribution:

- Lamivudine:
  - Lamivudine is distributed into human milk.

- Nevirapine:
  - Nevirapine is distributed into human milk.

- Zidovudine:
  - Zidovudine is distributed into human milk.

CLINICAL PHARMACOLOGY:

Lamivudine, Nevirapine, and Zidovudine Tablets are contraindicated in patients with previously demonstrated clinically significant hypersensitivity (e.g., anaphylactic or angioedema) to lamivudine, nevirapine, or zidovudine. Nevirapine is a potent inducer of cytochrome P450 3A and 2B6 enzymes and may inhibit this system. Among human hepatic cytochromes P450, substrates include midazolam, nortriptyline, and diazepam. The activity of nevirapine does not affect the activity of ritonavir or saquinavir. The primary metabolic product is the carboxylic acid metabolite. The activity of a recombinant human norphosphohydroxylase 1 enzyme in vitro is not affected by nevirapine. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized.

The optimal frequency of monitoring during this time period has not been established. Discontinuation of therapy should be considered for patients with HIV disease progression or toxicity. The optimal duration of therapy is not known. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized.

The patients at greatest risk of hepatic events, including potentially fatal events, are women with high CD4+ cell counts. In general, during the first 6 weeks of treatment, patients with high CD4+ cell counts should be monitored weekly. During the first 6 weeks, the frequency of liver function tests should be increased if the CD4+ cell count increases by more than 50 percent from baseline or if the patient has unexplained symptoms (e.g., fatigue, pale skin, sore throat, fever, or chills). The use of hepatitis B immune globulin (HBIG) is recommended after exposure to HIV-infected blood. The CD4+ cell count and viral load should be monitored during the first 6 weeks of treatment in all patients. The optimal frequency of monitoring during this time period has not been established. Discontinuation of therapy should be considered for patients with HIV disease progression or toxicity. The optimal duration of therapy is not known. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized. Nevirapine is excreted in human breast milk. Nevirapine concentrations in human milk are approximately 20% of maternal plasma concentrations. Nevirapine is not extensively metabolized.
Based on the known metabolism of methadone, n consult a physici occurs during the two AST or ALT (see WARNINGS; Hepa immediately, including performance of laboratory monitoring. Symptoms of liver disease include fatigue, malaise, anorexia, nausea

Patients should be informed that redistribution or rash or rash accompanied by fever, general malaise, fatigue, muscle or joint aches, blisters, systematic adverse reactions. Hepatitis/hepatic failure may be isolated or associated with signs of hypersensitivity which may include severe rash or rash

What are the possible side effects of Lamivudine, Nevirapine, and Zidovudine Tablets?

Side effects other than those listed here may also occur. Talk to your doctor about any side effect that seems unusual or that is bothersome.

How should I take Lamivudine, Nevirapine, and Zidovudine Tablets?

Maintenance:
One Lamivudine, Nevirapine, and Zidovudine Tablets should not be administered for a condition for which they were not prescribed. Do not give

When should I take Lamivudine, Nevirapine, and Zidovudine Tablets?

How to Store Lamivudine, Nevirapine, and Zidovudine Tablets?

How do I get more information about Lamivudine, Nevirapine, and Zidovudine Tablets?

Chemical Name:
Lamivudine, Nevirapine, and Zidovudine Tablets are available in the following strengths:

If you experience any of the following serious side effects, stop taking this medication and contact your physician:

What is the most important information I should know about Lamivudine, Nevirapine, and Zidovudine Tablets?

Use the following information to answer the questions:

Adults

Thrombocytopenia

Adults

Musculoskeletal:

Lamivudine, Nevirapine, and Zidovudine Tablets are being developed for use in the treatment of certain types of HIV-1/AIDS.

Other common side effects of nevirapine are rash, nausea, vomiting, diarrhea, abdominal pain, and decreased appetite. This list of side effects is not complete. Ask your doctor about the risks and benefits of these medications.

Maintenance:

For any further information contact

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