monitored for evidence of withdrawal and methadone dose should be adjusted accordingly.

Pregnancy: Category C. There are no adequate and well-controlled studies in pregnant women. Nevirapine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Lactation: Data indicate that nevirapine readily crosses the placenta and is found in breast milk. It is recommended that HIV-infected mothers not breast-feed their infants to avoid risking postnatal transmission of HIV. Mothers should discontinue nursing if they are receiving nevirapine.

SIDE EFFECTS

The most clinically important adverse events associated with nevirapine therapy are rash and increases in liver function tests. Cases of hypersensitivity reactions have been observed.

The major clinical toxicity of nevirapine is rash, with nevirapine-attributable rash occurring in 16% of patients in combination regimens in Phase II/III controlled studies. Thirty-five percent of patients treated with nevirapine experienced rash compared with 19% of patients treated in control groups of either zidovudine + didanosine or zidovudine alone. Severe or life-threatening rash occurred in 6.6% of nevirapine-treated patients compared with 1.3% of patients treated in the control groups.

Rashes are usually mild to moderate, maculopapular erythematous cutaneous eruptions; with or without pruritus, located on the trunk, face and extremities. The majority of severe rashes occurred within the first 28 days of treatment. 25% of the patients with severe rashes required hospitalization, and one patient required surgical intervention. Overall, 7% of patients discontinued nevirapine due to rash.

With respect to laboratory abnormalities, asymptomatic elevations in GGT levels are more frequent in nevirapine recipients than in controls. Because clinical hepatitis has been reported in nevirapine-treated patients, monitoring of ALT (SGPT) and AST (SGOT) is strongly recommended, especially during the first six months of nevirapine treatment (See Warnings and Precautions). Decreased neutrophils (< 750/mm³), platelets (< 50,000/mm³) and Hb (< 8.0 g/dL), and increased total bilirubin (> 2.5 mg/dL) have also been reported.

OVERDOSAGE

There is no known antidote for nevirapine overdosage.

STORAGE

Store below 30°C

PRESENTATION

Nevimune Tablets : Blister pack of 10 tablets
Container pack of 60 tablets

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Cipla

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

Nevirapine Tablets 200 mg

Nevimune

WARNING

SEVERE, LIFE-THREATENING SKIN REACTIONS, INCLUDING FATAL CASES, HAVE OCCURRED IN PATIENTS TREATED WITH NEVIRAPINE. THESE HAVE INCLUDED CASES OF STEVENS-JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS, AND HYPERSENSITIVITY REACTIONS CHARACTERIZED BY RASH, CONSTITUTIONAL FINDINGS AND ORGAN DYSFUNCTION. PATIENTS DEVELOPING SIGNS OR SYMPTOMS OF SEVERE SKIN REACTIONS OR HYPERSENSITIVITY REACTIONS MUST DISCONTINUE NEVIRAPINE AS SOON AS POSSIBLE (SEE WARNINGS).

SEVERE AND LIFE-THREATENING HEPATOTOXICITY, INCLUDING FATAL HEPATIC NECROSIS, HAS OCCURRED IN PATIENTS TREATED WITH NEVIRAPINE (SEE WARNINGS). RESISTANT VIRUS EMERGES RAPIDLY AND UNIFORMLY WHEN NEVIRAPINE IS ADMINISTERED AS MONOTHERAPY. THEREFORE, NEVIRAPINE SHOULD ALWAYS BE ADMINISTERED IN COMBINATION WITH ANTIRETROVIRAL AGENTS.

COMPOSITION

Nevimune Tablets
Each uncoated tablet contains
Nevirapine ..... 200 mg

DESCRIPTION

Nevimune is a non-nucleoside reverse transcriptase inhibitor with activity against **HIV-1**. Nevirapine binds directly to reverse transcriptase and blocks the RNA-dependent and DNA-dependent DNA polymerase activities by causing a disruption of the enzyme's catalytic site. The HIV-2 reverse transcriptase and human DNA polymerases (such as DNA polymerases α,β,γ or δ) are not inhibited by nevirapine.

In cell culture, nevirapine demonstrated additive to synergistic activity against HIV in drug combination regimens with zidovudine, didanosine, stavudine, lamivudine, saquinavir and indinavir.

INDICATIONS

Nevimune is indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 infection. Resistant virus emerges rapidly and uniformly when nevirapine is administered as monotherapy. Therefore, nevirapine should always be administered in combination with at least one additional antiretroviral agent.

DOSAGE AND ADMINISTRATION

The recommended dose for nevirapine is one 200 mg tablet daily for the first 14 days (this lead-in period should be used because it has been found to lessen the frequency of rash), followed by one 200 mg tablet twice daily, in combination with antiretroviral agents. For concomitantly administered antiretroviral therapy, the full prescribing information for those drugs should be consulted.

Monitoring of patients

Clinical chemistry tests, which include liver function tests, should be performed prior to initiating nevirapine therapy and at appropriate intervals during therapy (See Warnings and Precautions).

Dosage Adjustment

Nevirapine should be discontinued if patients experience severe rash or a rash accompanied by constitutional findings (See Warnings and Precautions). Patients experiencing rash during the 14-day lead-in period of 200 mg/day should not have their nevirapine dose increased until the rash has resolved (See Warnings and Precautions).

Nevirapine administration should be interrupted in patients experiencing moderate or severe liver function test abnormalities (excluding GGT), until the liver function test elevations have returned to baseline. Nevirapine may then be restarted at 200 mg per day. Increasing the daily dose to 200 mg twice daily should be done with caution, after extended observation. Nevirapine should be permanently discontinued if moderate or severe liver function test abnormalities recur (See Warnings and Precautions).

Patients who interrupt nevirapine dosing for more than 7 days should restart the recommended dosing, using one 200 mg tablet daily for the first 14 days (lead-in) followed by one 200 mg tablet twice daily. No data are available to recommend a dosage of nevirapine in patients with hepatic dysfunction, renal insufficiency, or undergoing dialysis.

CONTRAINDICATIONS

Nevirapine is contraindicated in patients with clinically significant hypersensitivity to any of the components contained in the tablet or the oral suspension.

WARNINGS AND PRECAUTIONS

Severe, life-threatening skin reactions, including fatal cases, have occurred in patients treated with nevirapine. These have included cases of Stevens-Johnson syndrome, toxic epidermal necrolysis, and hypersensitivity reactions characterized by rash, constitutional findings, and organ dysfunction. Patients developing signs or symptoms of severe skin reactions or hypersensitivity reactions (including, but not limited to, severe rash or rash accompanied by fever, blisters, oral lesions, conjunctivitis, facial edema, muscle or joint aches, general malaise and/or significant hepatic abnormalities) must discontinue nevirapine as soon as possible.

Nevirapine therapy must be initiated with a 14-day lead-in period of 200 mg/day which has been shown to reduce the frequency of rash. If rash is observed during this lead-in period, dose escalation should not occur until the rash has resolved (See Dosage and Administration).

Severe or life-threatening hepatotoxicity, including fatal fulminant hepatitis (transaminase elevations, with or without hyperbilirubinemia, prolonged partial thromboplastin time, or eosinophilia), has occurred in patients treated with nevirapine. Some of these cases began in the first few weeks of therapy, and some were accompanied by rash. Nevirapine administration should be interrupted in patients experiencing moderate or severe ALT or AST abnormalities until these return to baseline values. Nevirapine should be permanently discontinued if liver function abnormalities recur upon readministration. Monitoring of ALT and AST is strongly recommended, especially during the first six months of nevirapine treatment (See Side Effects, Dosage and Administration).

The duration of clinical benefit from antiretroviral therapy may be limited. Patients receiving nevirapine or any other antiretroviral therapy may continue to develop opportunistic infections and other complications of HIV infection, and therefore should remain under close clinical observation by physicians experienced in the treatment of patients with associated HIV diseases.

When administering nevirapine as part of an antiretroviral regimen, the complete product information for each therapeutic component should be consulted before initiation of treatment.

IMPAIRED RENAL AND HEPATIC FUNCTION

Nevirapine is extensively metabolized by the liver and nevirapine metabolites are extensively eliminated by the kidney. However, the pharmacokinetics of nevirapine have not been evaluated in patients with either hepatic or renal dysfunction. Therefore, nevirapine should be used with caution in these patient populations.

DRUG INTERACTIONS

The induction of CYP3A by nevirapine may result in lower plasma concentrations of other concomitantly administered drugs that are extensively metabolized by CYP3A. Thus, if a patient has been stabilized on a dosage regimen for a drug metabolized by CYP3A, and begins treatment with nevirapine, dose adjustments may be necessary.

Rifampin/Rifabutin: There are insufficient data to assess whether dose adjustments are necessary when nevirapine and rifampin or rifabutin are coadministered. Therefore, these drugs should only be used in combination if clearly indicated and with careful monitoring.

Ketoconazole: Nevirapine and ketoconazole should not be administered concomitantly. Coadministration of nevirapine and ketoconazole results in a significant reduction in ketoconazole plasma concentrations.

Oral Contraceptives: There are no clinical data on the effects of nevirapine on the pharmacokinetics of oral contraceptives. Nevirapine may decrease plasma concentrations of oral contraceptives (also other hormonal contraceptives); therefore, these drugs should not be administered concomitantly with nevirapine.

Methadone: Based on the known metabolism of methadone, nevirapine may decrease plasma concentrations of methadone by increasing its hepatic metabolism. Narcotic withdrawal syndrome has been reported in patients treated with nevirapine and methadone concomitantly. Methadone-maintained patients beginning nevirapine therapy should be