

**Prior Authorization DRUG Guidelines**

**VIRAMUNE/XR (Nevirapine)**

Effective Date: 1/28/14

Date Developed: 1/28/14 by Catherine Sanders, MD

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Viramune is an Antiretroviral Agent, Reverse Transcriptase Inhibitor (Non-nucleoside) used in the treatment of HIV-1 infections. As a non-nucleoside reverse transcriptase inhibitor, nevirapine has activity against HIV-1 by binding to reverse transcriptase. It consequently blocks the RNA-dependent and DNA-dependent DNA polymerase activities including HIV-1 replication. It does not require intracellular phosphorylation for antiviral activity.

**Pre-Authorization Criteria:**

Viramune and Viramune XR are used in combination therapy with other antiretroviral agents for the treatment of HIV-1 infection. Therapy in antiretroviral naive patients should not be initiated in patients with elevated CD4<sup>+</sup>-cell counts unless the benefit of therapy outweighs the risk of serious hepatotoxicity (adult/postpubertal females: CD4<sup>+</sup>-cell counts >250 cells/mm<sup>3</sup>; adult males: CD4<sup>+</sup>-cell counts >400 cells/mm<sup>3</sup>).

VCHCP requires that Viramune be prescribed by an Immunology Clinic physician with current American Academy of HIV Medicine (AAHIVM) certification or a physician boarded in Infectious Disease.

**Medication Guide:**

An FDA-approved patient medication guide, which is available with the product information and at <http://www.fda.gov/downloads/Drugs/DrugSafety/ucm089818.pdf>, must be dispensed with this medication.

**Dosing: Adult:**

HIV infection: Oral:

Initial: *Immediate release*: 200 mg once daily for 14 days

Maintenance:

*Immediate release*: 200 mg twice daily (in combination with additional antiretroviral agents) if there is no rash or untoward effects during initial dosing period

*Extended release*: 400 mg once daily; maintenance therapy using the extended release must follow a 14-day initial dosing period (lead-in) using the immediate release formulation unless patient is already maintained on a nevirapine immediate release regimen

Note: If patient experiences a rash during the 14-day lead-in period, dose should not be increased until the rash has resolved. A lead-in period must always be done with immediate release formulation and regimen should not exceed 28 days; alternative treatment should be considered at that point. If a rash

occurs within the first 18 weeks of therapy, immediately check serum transaminases. Discontinue if severe rash, rash with constitutional symptoms, or rash with elevated hepatic transaminases is noted. Coadministration of prednisone during the first 6 weeks of therapy increases incidence and severity of rash; concomitant prednisone is not recommended to prevent rash. Permanently discontinue if symptomatic hepatic events occur. If therapy with any formulation is interrupted for >7 days, restart with initial dose of immediate release formulation for 14 days.

**Dosing: Pediatric:**

HIV infection: Oral:

Note: If patient experiences a rash during the 14-day lead-in period, dose should not be increased until the rash has resolved. A lead-in period must always be done with immediate release formulation and regimen should not exceed 28 days; alternative treatment should be considered at that point. If a rash occurs within the first 18 weeks of therapy, immediately check serum transaminases. Discontinue if severe rash, rash with constitutional symptoms, or rash with elevated hepatic transaminases is noted. Coadministration of prednisone during the first 6 weeks of therapy increases incidence and severity of rash; concomitant prednisone is not recommended to prevent rash. Permanently discontinue if symptomatic hepatic events occur. If therapy with any formulation is interrupted for >7 days, restart with initial dose of immediate release formulation for 14 days. (Use of nevirapine in children <15 years of age is not approved in the Canadian labeling.)

Infants and Children: *Immediate release*: 150 mg/m<sup>2</sup>/dose once daily for first 14 days (maximum: 200 mg daily); increase dose to 150 mg/m<sup>2</sup>/dose twice daily if no rash or untoward effects (maximum: 400 mg daily).

Children 6 to <18 years: *Extended release*: Dose based on body surface area (Mosteller formula); maintenance therapy using the extended release must follow a 14-day initial dosing period (lead-in) using the immediate release formulation unless patient is already maintained on a nevirapine immediate release regimen.

0.58 m<sup>2</sup> to 0.83 m<sup>2</sup>: 200 mg once daily

0.84 m<sup>2</sup> to 1.16 m<sup>2</sup>: 300 mg once daily

≥1.17 m<sup>2</sup>: 400 mg once daily (do not exceed 400 mg daily)

DHHS pediatric guidelines:

Note: Children <3 years of age: Nevirapine-based initial regimens should not be used in children previously exposed to nevirapine during prevention of maternal-to-child transmission of HIV

Children <8 years: *Immediate release*: 200 mg/m<sup>2</sup>/dose once daily for first 14 days (maximum dose: 200 mg); increase dose to 200 mg/m<sup>2</sup>/dose twice daily if no rash or untoward effects (maximum: 400 mg daily)

Children ≥8 years: *Immediate release*: 120-150 mg/m<sup>2</sup>/dose once daily for 14 days (maximum dose: 200 mg); increase dose to 120-150 mg/m<sup>2</sup>/dose twice daily if no rash or untoward effects (maximum: 400 mg daily)

Adolescents: *Immediate release*: Refer to adult dosing.

Prevention of maternal-fetal HIV transmission (DHHS [perinatal], 2012): Note: Nevirapine is used in combination with zidovudine in select situations (eg, infants born to mothers with only intrapartum therapy or no therapy). Use is not recommended in women receiving standard recommended antenatal antiretroviral prophylaxis.

**Dosing: Geriatric:**

Refer to adult dosing.

**Dosing: Renal Impairment:**

*Immediate release:*

$Cl_{cr} \geq 20$  mL/minute: No dosage adjustment necessary.

$Cl_{cr} < 20$  mL/minute: No dosage adjustment provided in manufacturer's labeling (has not been studied).

*Extended release:* No dosage adjustment provided in manufacturer's labeling (has not been studied).

Hemodialysis: An additional 200 mg *immediate release* dose is recommended following dialysis.

**Dosing: Hepatic Impairment:**

Permanently discontinue if symptomatic hepatic events occur.

*U.S. labeling:*

Mild impairment (Child-Pugh class A):

*Immediate release:* No dosage adjustment provided in manufacturer's labeling; use with caution.

*Extended release:* Not studied.

Moderate-to-severe impairment (Child-Pugh class B or C): Use is contraindicated.

**Dosage Forms: U.S.:**

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Suspension, Oral:

Viramune: 50 mg/5 mL (240 mL) [contains methylparaben, propylparaben]

Generic: 50 mg/5 mL (240 mL)

Tablet, Oral:

Viramune: 200 mg [scored]

Generic: 200 mg

Tablet Extended Release 24 Hour, Oral:

Viramune XR: 100 mg, 400 mg

Generic Equivalent Available: U.S.-May be product dependent

**Administration:**

Oral: May be administered with or without food; may be administered with an antacid or didanosine.

Shake suspension gently prior to administration; the use of an oral dosing syringe is recommended, especially if the dose is  $\leq 5$  mL; if using a dosing cup, after administration, rinse cup with water and also administer rinse. Extended release tablets must be swallowed whole and not crushed, chewed, or divided.

**Exclusions:**

Viramune is not to be used as monotherapy.

Viramune is not to be used in patients with moderate-to-severe hepatic impairment (Child-Pugh class B or C)

Viramune is not to be used in occupational or nonoccupational postexposure prophylaxis (PEP) regimens.

Viramune-based initial regimens should not be used in children previously exposed to nevirapine during prevention of maternal-to-child transmission of HIV due to increased risk of resistance and treatment failure. (Protease inhibitor-based initial regimens preferred in this population.)

**Adverse Reactions:**

>10%: rash, cholesterol increased, LDL increased, neutropenia, ALT increased, symptomatic hepatic events (including hepatitis and hepatic failure-risk higher in ARV-naïve women with CD4 counts >250 cells/mm<sup>3</sup> and ARV-naïve men with CD4 counts >400 cells/mm<sup>3</sup>.)

Other Serious Less Common Reactions: immune reconstitution syndrome, rhabdomyolysis, fat redistribution, skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, stomatitis, severe, autoimmune disorders.

**U.S. BOXED WARNING:**

Severe, life-threatening, and sometimes fatal skin reactions; reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, hypersensitivity reactions with rash, constitutional findings, and organ dysfunction; 14-day start with 200 mg qday decreases frequency of rash; monitor closely during 1st 18wk of treatment with greatest risk in 1st 6weeks; check transaminase levels immediately for patients who develop rash within 1st 18weeks of treatment; discontinue treatment and seek medical care if signs and symptoms of severe skin

Severe, life-threatening, and sometimes fatal hepatotoxicity; may present with non-specific prodromal hepatitis signs and symptoms, often associated with rash, and progress to hepatic failure; increased risk if female or high CD4 count at treatment start; greatest risk if female with CD4 count >250, including pregnant women on antiretroviral combination treatment; hepatic failure reported in non-HIV patients on nevirapine for post-exposure prophylaxis; contraindicated for occupational and non-occupational post-exposure prophylaxis; monitor closely during 1st 18weeks of treatment with greatest risk in 1st 6weeks; can occur in both genders, all CD4 counts, and at any time during treatment; discontinue treatment and seek medical care if hepatitis signs or symptoms or increased transaminases combined with rash or other systemic symptoms; do not restart treatment after hepatic injury or hypersensitivity reaction; do not restart treatment after severe skin or hypersensitivity reaction.

**References:**

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2. DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents, "Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, Department of Health and Human Services," February 12, 2013;1-267. Available at <http://www.aidsinfo.nih.gov>
3. DHHS Panel on Opportunistic Infections (OI) in HIV-Infected Adults and Adolescents, "Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents: Recommendations from the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the HIV Medicine Association (HIVMA) of the Infectious

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  13. [www.epocrates.com](http://www.epocrates.com): Nevirapine Drug Information

## Revision History:

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