VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

NORVIR (Ritonavir)

Effective Date: 1/28/14

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

Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20

Norvir is an Antiretroviral Agent, Protease Inhibitor used in the treatment of HIV-1 infections. Norvir binds to the site of HIV-1 protease activity and inhibits cleavage of viral Gag-Pol polyprotein precursors into individual functional proteins required for infectious HIV. This results in the formation of immature, noninfectious viral particles.

Pre-Authorization Criteria:
Norvir is used for the treatment of HIV-1 infection as part of a multidrug regimen.
Note: Use as a pharmacokinetic "booster" for other protease inhibitors is an unlabeled use and not covered.

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

Dosing: Adult:
Note: Must be given in combination with other antiretroviral agents. Norvir® tablets are not bioequivalent to Norvir® capsules. Gastrointestinal side effects or paresthesias may be more common initially when patients are switching from the capsule to the tablet formulation.
Treatment of HIV infection: Manufacturer's labeling: Oral (Note: Not recommended as the primary protease inhibitor in any regimen [DHHS, 2013]): Initiate dose at 300 mg twice daily, then increase by 100 mg twice daily every 2-3 days to recommended dosage of 600 mg twice daily (maximum: 600 mg twice daily)

Pharmacokinetic "booster" in combination with other protease inhibitors (unlabeled use): Oral:100-400 mg daily in 1-2 divided doses (DHHS, 2013)
Note: Recommended as the "booster" component in the following preferred regimens in treatment-naive patients: Atazanavir and tenofovir/emtricitabine, or darunavir and tenofovir/emtricitabine (DHHS, 2013). In patients without evidence of PI resistance, once-daily booster-dosing of 100 mg ritonavir may be preferred to 200 mg daily due to less gastrointestinal and metabolic adverse events. Refer to individual protease inhibitor monographs; specific dosage recommendations often require adjustment of both agents.

Dosing: Pediatric:

Note: Must be given in combination with other antiretroviral agents. Norvir® tablets are not bioequivalent to Norvir® capsules. Gastrointestinal side effects or paresthesias may be more common initially when patients are switching from the capsule to the tablet formulation.
Treatment of HIV infection: Manufacturer's labeling:
Infants >1 month and Children: Oral: Initiate dose at 250 mg/m^2/dose twice daily; titrate dose upward every 2-3 days by 50 mg/m^2 twice daily to recommended dosage of 350-400 mg/m^2/dose twice daily (maximum dose: 600 mg twice daily). If 400 mg/m^2/dose twice daily is not tolerated, the highest tolerated dose may be used for maintenance therapy. Note: Oral solution should not be administered to neonates before a postmenstrual age (first day of mother's last period to birth plus the time elapsed after birth) <44 weeks.

Adolescents: Refer to adult dosing.

Administration:
Administer all formulations with food, per the manufacturer. DHHS guidelines recommend administering the tablets with food and administering capsules or oral solution with food, if possible, to improve tolerability (DHHS, 2013). Liquid formulations usually have an unpleasant taste. Consider mixing it with chocolate milk or a liquid nutritional supplement and taking within 60 minutes. Whenever possible, administer oral solution with calibrated dosing syringe. Shake solution well before use. Tablets should be swallowed whole; do not chew, break, or crush.

Dosing: Geriatric :
Refer to adult dosing.

Dosing: Renal Impairment:
No dosage adjustment necessary.

Dosing: Hepatic Impairment:
Mild-to-moderate impairment (Child-Pugh class A or B): No dosage adjustment necessary; however, ritonavir levels may be decreased in moderate impairment and patient response should be monitored. Severe impairment (Child-Pugh class C): Not recommended (has not been studied).

Dosage Forms: U.S.:
Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Capsule, Oral:
Norvir: 100 mg [contains alcohol, usp]
Solution, Oral:
Norvir: 80 mg/mL (240 mL) [contains alcohol, usp, fd&c yellow #6 (sunset yellow), propylene glycol, saccharin sodium; peppermint-caramel flavor]
Tablet, Oral:
Norvir: 100 mg

Generic Equivalent Available: U.S.-No

Exceptions:
Norvir is not to be used as monotherapy and is not recommended as the primary protease inhibitor in any regimen.
Etravirine plus tipranavir or atazanavir or fosamprenavir with "boosted" ritonavir are not recommended regimens and are not to be used. "Boosted" ritonavir is an unlabeled use and therefore not covered.

Contraindications:
Hypersensitivity to ritonavir or any component of the formulation; concurrent alfuzosin, amiodarone, cisapride, dihydroergotamine, ergonovine, ergotamine, flecainide, lovastatin, methylergonovine, midazolam (oral), pimozide, propafenone, quinidine, sildenafil (when used for the treatment of pulmonary arterial hypertension [eg, Revatio®]), simvastatin, St John's wort, triazolam, and voriconazole (when ritonavir ≥800 mg/day)

Adverse Reactions:
>10%: hypercholesterolemia, hypertriglyceridemia, nausea, diarrhea, vomiting, dysgeusia, increased GGT, weakness, increased CPK.
Other Severe Less Common Reactions: hypersensitivity reactions, fat redistribution, immune reconstitution syndrome, PR interval prolongation, AV block, diabetes mellitus, pancreatitis, hepatotoxicity, toxic epidermal necrolysis, exfoliative dermatitis, erythema multiforme, thrombocytopenia, neutropenia, autoimmune disorders.

U.S. BOXED WARNING:
Ritonavir may intereact with many medications, including antiarrhythmics, ergot alkaloids, and sedatives/hypnotics, resulting in potentially serious and/or life-threatening adverse events due to inhibited drug metabolism.

References:

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4. 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 Diseases Society of America (IDSA)," May 7, 2013. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf
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14. Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children, “Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection,” August 16, 2010. Available at http://www.aidsinfo.nih.gov
15. www.uptodate.com: Ritonavir: Drug Information
16. www.epocrates.com: Norvir Drug Information

Revision History:

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