VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

INVIRASE (Saquinavir)

Effective Date: 1/28/14

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

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Invirase is an Antiretroviral Agent, Protease Inhibitor used in the treatment of HIV-1 infections. Invirase 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:
Invirase is used for treatment of HIV-1 infections and must be used in combination with ritonavir. Invirase may also be used with other antiretroviral agents.
Pretreatment EKG should be done and therapy is not to be initiated if pretreatment QT interval is >450 msec.

VCHCP requires that Invirase 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/UCM229206.pdf, must be dispensed with this medication.

Dosing: Adult:
Saquinavir should always be used with concomitant ritonavir.
HIV infection: Oral: 1000 mg twice daily given in combination with ritonavir 100 mg twice daily. This combination should be given together and within 2 hours after a full meal in combination with a nucleoside analog.
Dosage adjustments when administered in combination therapy: Saquinavir: 1000 mg twice daily administered with lopinavir 400 mg/ritonavir 100 mg (Kaletra™) twice daily; no additional ritonavir is necessary

Dosing: Pediatric:
HIV infection: Oral: Children >16 years: Refer to adult dosing.

Administration:
Administer saquinavir and ritonavir at the same time and within 2 hours after a full meal. Patients unable to swallow capsules may open capsules and mix contents with 15 mL of syrup (or sorbitol if diabetic or glucose intolerant) or with 3 teaspoons of jam. Mixture should be stirred for 30-60 seconds and then administered entirely. Suspension should be at room temperature prior to administration.

Dosing: Geriatric:
Clinical studies did not include sufficient numbers of patients ≥65 years of age. Use caution due to increased frequency of organ dysfunction.

Dosing: Renal Impairment:
No dosage adjustment necessary. However, has not been studied in severe renal impairment or ESRD.

Dosing: Hepatic Impairment:
Mild to moderate impairment (Child-Pugh classes A and B): No dosage adjustment necessary.
Severe impairment (Child-Pugh class C): Use is contraindicated when coadministered with ritonavir.

Dosage Forms: U.S.:
Excipient information presented when available (limited, particularly for generics); consult specific product labeling.
Capsule, Oral:
Invirase: 200 mg
Tablet, Oral:
Invirase: 500 mg

Generic Equivalent Available: U.S.-No

Exclusions:
Invirase is not to be used if not concomitantly used with ritonavir.
Do not use if pretreatment EKG reveals QT interval >450 msec.
Therapy is to be discontinued promptly if viral suppression response is lost, as continuation may increase the likelihood of cross-resistance to other protease inhibitors.

Contraindications:
Hypersensitivity to saquinavir or any component of the formulation; congenital or acquired QT prolongation, refractory hypokalemia or hypomagnesemia, concomitant use of other medications that both increase saquinavir plasma concentrations and prolong the QT interval; complete AV block (without implanted ventricular pacemaker) or patients at high risk of complete AV block; severe hepatic impairment; coadministration of saquinavir/ritonavir with alfuzosin, amiodarone, bepridil, cisapride, dofetilide, ergot derivatives, flecainide, lidocaine (systemic), lovastatin, midazolam (oral), pimozide, propafenone, quinidine, rifampin, sildenafil (when used for pulmonary artery hypertension [eg, Revatio®]),simvastatin, trazodone, or triazolam

Adverse Reactions:
>10%: nausea
Other severe less common adverse reactions: altered cardiac conduction including prolongation of QT interval, potentially leading to torsade de pointes and prolongation of PR interval, potentially leading to heart block, fat redistribution, immune reconstitution syndrome, increased cholesterol, hyperglycemia, diabetes mellitus, hypertriglyceridemia, pancreatitis, hepatotoxicity, hypersensitivity reactions, Stevens-Johnson syndrome, hemolytic anemia, thrombocytopenia, pancytopenia, autoimmune disorders.

References:

1. Collier AC, Coombs RW, DA, et al, "Treatment of Human Immunodeficiency Virus Infection With Saquinavir, Zidovudine, and Zalcitabine," *N Engl J Med*, 1996, 334(16):1011-7. [PubMed 8598838]
2. Deeks SG, Smith M, Holodniy M, et al, "HIV-1 Protease Inhibitors. A Review for Clinicians," *JAMA*, 1997, 277(2):145-53. [PubMed 8990341]
3. 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
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
5. Hilts AE and Fish DN, "Dosage Adjustment of Antiretroviral Agents in Patients With Organ Dysfunction," *Am J Health Syst Pharm*, 1998, 55:2528-33. [PubMed 9853641]
6. Hsu A, Granneman GR, Cao G, et al, "Pharmacokinetic Interactions Between Two Human Immunodeficiency Virus Protease Inhibitors, Ritonavir and Saquinavir," *Clin Pharmacol Ther*, 1998, 63(4):453-64. [PubMed 9585800]
7. Kakuda TN, Struble KA, and Piscitelli SC, "Protease Inhibitors for the Treatment of Human Immunodeficiency Virus Infection," *Am J Health Syst Pharm*, 1998, 55(3):233-54. [PubMed 9492254]
8. Kaul DR, Cinti SK, Carver PL, et al, "HIV Protease Inhibitors: Advances in Therapy and Adverse Reactions, Including Metabolic Complications," *Pharmacotherapy*, 1999, 19(3):281-98. [PubMed 10221367]
9. McDonald CK and Kuritzkes DR, "Human Immunodeficiency Virus Type 1 Protease Inhibitors," *Arch Intern Med*, 1997, 157(9):951-9. [PubMed 9140265]
10. Mueller BU, "Antiviral Chemotherapy," *Curr Opin Pediatr*, 1997, 9(2):178-83. [PubMed 9204247]
11. Noble S and Faulds D, "Saquinavir: A Review of Its Pharmacology and Clinical Potential in the Management of HIV Infection," *Drugs*, 1996, 52(1):93-112. [PubMed 8799687]
12. Rana KZ and Dudley MN, "Human Immunodeficiency Virus Protease Inhibitors," *Pharmacotherapy*, 1999, 19(1):35-59. [PubMed 9917077]
13. Rhone SA, Hogg RS, Yip B, et al, "The Antiviral Effect of Ritonavir and Saquinavir in Combination Amongst HIV-Infected Adults: Results From a Community-Based Study," *AIDS*, 1998, 12(6):619-24. [PubMed 9583602]
14. Singh M, Arora R, and Jawad E, "HIV Protease Inhibitors Induced Prolongation of the QT Interval: Electrophysiology and Clinical Implications," *Am J Ther*, 2010, 17(6):e193-201. [PubMed 19636247]
15. Vella S and Floridia M, "Saquinavir. Clinical Pharmacology and Efficacy," *Clin Pharmacokinet*, 1998, 34(3):189-201. [PubMed 9533981]
16. 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

17. www.uptodate.com: Saquinavir: Drug Information
18. www.epocrates.com: Invirase Drug Information

REVISION HISTORY:

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