VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

EDURANT (Rilpivirine)

Effective Date: 1/28/14
Date Developed: 1/28/14 by Catherine Sanders, MD
Date Approved by P&T Committee: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20, 2/2/21, 5/4/21
(ARCHIVED 8/3/21)

Edurant is an Antiretroviral Agent, Reverse Transcriptase Inhibitor (Non-nucleoside) used in the treatment of HIV-1 infections. Rilpivirine 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:

For use in combination with Vocabria® (cabotegravir tablets), for short-term treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine,

Or

For use as an oral lead-in to assess the tolerability of rilpivirine prior to administration of Cabenuva® (cabotegravir, rilpivirine extended-release injectable suspensions)

Or

As oral therapy for patients who will miss planned injection dosing with Cabenuva.

Additionally, Edurant remains indicated for use in combination with other antiretroviral agents, for the treatment of HIV-1 infection in antiretroviral treatment-naïve patients ≥ 12 years of age and weighing ≥ 35 kg with plasma HIV-1 RNA ≤ 100,000 copies/mL at the start of therapy.

Oral lead-in therapy should be used for approximately 1 month (at least 28 days) to assess the tolerability of rilpivirine prior to the initiation of Cabenuva.

VENTURA COUNTY
HEALTH CARE PLAN

~~T~~treatment of HIV-1 infections in antiretroviral treatment-naïve patients with HIV-1 RNA less than or equal to 100,000 copies/mL at the start of therapy

Note: to be used in combination with at least 2 other antiretroviral agents.
Note: VCHCP requires that Edurant be prescribed by an Immunology Clinic physician with current American Academy of HIV Medicine (AAHIVM) certification or a physician boarded in Infectious Disease.

Note: not recommended for patients less than 18 years of age

Dosing: Adult:
Treatment of HIV-1 infection (treatment-naïve): Oral: 25 mg once daily.
NOTE: Do not use rilpivirine-based regimens in patients with preantiretroviral therapy CD4 count <200 cells/mm^3 and/or HIV RNA >100,000 copies/mL

Oral lead-in*:* 25 mg once daily, in combination with oral cabotegravir, for ~1 month (≥28 days) prior to initiation of cabotegravir and rilpivirine injections, to assess tolerability to rilpivirine. **Note:** Final oral dose should be taken on the same day as initiation of injections.

Dosing: Pediatric:
Children and Adolescents ≥12 years and ≥35 kg: Oral: 25 mg once daily.

Dosing: Renal Impairment:
Mild-to-moderate renal impairment: No dosage adjustment necessary.
Severe or end-stage renal impairment: Use with caution; no dosage adjustment necessary (DHHS, 2012)
Hemodialysis/peritoneal dialysis: Due to extensive protein binding, significant removal by hemodialysis or peritoneal dialysis is unlikely.

Dosing: Hepatic Impairment:
Mild-to-moderate impairment (Child-Pugh class A or B): No dosage adjustment necessary.
Severe impairment (Child-Pugh class C): No dosage adjustment provided in the manufacturer's labeling

Dosage Forms: U.S.:
Tablet, Oral: 25 mg

The recommended daily dose of Edurant is one 25 mg tablet in combination with one 30 mg tablet of Vocabria. Edurant should be taken with Vocabria once daily at approximately the

same time each day with a meal. The last oral dose should be taken on the same day that injections with Cabenuva are started.

If a patient plans to miss a scheduled Cabenuva injection visit by more than 7 days, take daily therapy to replace up to two consecutive monthly injection visits. The recommended daily dose of Edurant is one 25 mg tablet and one 30 mg tablet of Vocabria, taken once daily at approximately the same time each day with a meal. The first dose of oral therapy should be taken approximately 1 month after the last injection dose of Cabenuva and continued until the day injection dosing is restarted.

Administration:
Administer with a normal- to high-calorie meal. Taking with a protein supplement drink alone does not increase absorption.

Contraindications:
Current use of carbamazepine, dexamethasone (>1 dose), oxcarbazepine, phenobarbital, phenytoin, proton pump inhibitors (PPIs), rifabutin, rifampin, rifapentine, or St. John's wort.

Adverse Reactions:
>10%-cholesterol increased, LDL increased, ALT increased, AST increased
Other Serious Less Common Reactions: Depression, suicidality, fat redistribution, hepatotoxicity, imjune reconstitution syndrome, autoimmune disorders.

Exclusions:
Edurant is not for use in treatment-experienced patients.

References:
1. Azijn H, Tirry I, Vingerhoets J, et al, "TMC278, a Next-Generation Nonnucleoside Reverse Transcriptase Inhibitor (NNRTI), Active Against Wild-Type and NNRTI-Resistant HIV-1," *Antimicrob Agents Chemother*, 2010, 54(2):718-27. [PubMed 19933797]
2. Cohen CJ, Molina JM, Cahn P, et al, "Efficacy and Safety of Rilpivirine (TMC278) Versus Efavirenz at 48 Weeks in Treatment-Naive HIV-1-Infected Patients: Pooled Results from the Phase 3 Double-Blind Randomized ECHO and THRIVE Trials," *J Acquir Immune Defic Syndr*, 2012, 60(1):33-42. [PubMed 22343174]
3. Cohen CJ, Molina JM, Cassetti I, et al, "Week 96 Efficacy and Safety of Rilpivirine in Treatment-Naive HIV-1 Infected Patients in Two Phase II Randomized Trials," *AIDS*, 2013, 7(6):939-50. [PubMed 23211772]
4. 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
5. Fulco PP and McNicholl IR, "Etravirine and Rilpivirine: Nonnucleoside Reverse Transcriptase Inhibitors With Activity Against Human Immunodeficiency Virus Type 1

Strains Resistant to Previous Nonnucleoside Agents," *Pharmacotherapy*, 2009, 29(3):281-94. [PubMed 19249947]
6. MacArthur RD, "Clinical Trial Report: TMC278 (Rilpivirine) Versus Efavirenz as Initial Therapy in Treatment-Naïve, HIV-1-Infected Patients," *Curr Infect Dis Rep*, 2011, 13(1):1-3. [PubMed 21308448]
7. Molina JM, Clumeck N, Orkin C, et al, "Rilpivirine Efficacy, Virology and Safety in ARV Treatment-Naïve Patients With Viral Load ≤100,000 HIV-1 RNA c/mL: ECHO and THRIVE 96 Week Results," *J Int AIDS Soc*, 2012, 15(6):18250. [PubMed 23234922]
8. Nelson M, Amaya G, Clumeck N, et al, "Efficacy and Safety of Rilpivirine in Treatment-Naive HIV-1-Infected Patients With Hepatitis B Virus/Hepatitis C Virus Coinfection Enrolled in the Phase III Randomized, Double-Blind ECHO and THRIVE Trials," *J Antimicrob Chemother*, 2012, 67(8):2020-8. [PubMed 22532465]
9. Pozniak AL, Morales-Ramirez J, Katabira E, et al, "Efficacy and Safety of TMC278 in Antiretroviral-Naïve HIV-1 Patients: Week 96 Results of a Phase IIb Randomized Trial," *AIDS*, 2010, 24(1):55-65. [PubMed 19926964]
10. www.uptodate.com: Rilpivirine: Drug Information
11. www.epocrates.com: Edurant Drug Information

REVISION HISTORY:

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Revision	Content	Contributors	Review/Revision

VENTURA COUNTY
HEALTH CARE PLAN

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1/24/17	No	Catherine Sanders, MD; Robert Sterling, MD	Annual review
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