Medication Policy Manual

**Policy No:** dru357

**Topic:** Zontivity™, vorapaxar

**Date of Origin:** July 11, 2014

**Committee Approval Date:** July 10, 2015

**Next Review Date:** July 2016

**Effective Date:** August 1, 2015

**IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

Vorapaxar (Zontivity) is an oral antiplatelet medication used to reduce the risk of a stroke or heart attack in patients who have had a previous heart attack or who have peripheral artery disease (PAD).
Policy/Criteria

I. Most contracts require prior authorization approval of vorapaxar (Zontivity) prior to coverage. Vorapaxar (Zontivity) may be considered medically necessary in patients requiring antiplatelet therapy when all of criteria A through C below are met.
   A. Patient has one of the following:
      1. History of myocardial infarction (MI; heart attack)
      OR
      2. Diagnosis of peripheral artery disease (PAD)
   AND
   B. There is clinical documentation that treatment with clopidogrel (with or without concomitant aspirin) has not been tolerated or is contraindicated.
   AND
   C. Vorapaxar (Zontivity) will be given in combination with clopidogrel or aspirin unless both have not been tolerated or are contraindicated.

II. Administration, Quantity Limitations, and Authorization Period
   A. OmedaRx considers vorapaxar (Zontivity) to be a self-administered medication.
   B. When prior authorization is approved, vorapaxar (Zontivity) may be authorized in quantities of 30 tablets every 30 days.
   C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Vorapaxar (Zontivity) is considered not medically necessary in patients with active bleeding or in patients with a history of stroke, transient ischemic attack, or intracranial hemorrhage.

IV. Vorapaxar (Zontivity) is considered investigational when used for all other conditions.
Position Statement

- Significant safety concerns exist with the use of vorapaxar (Zontivity) in some patient populations; therefore, its use should be reserved for those patients in whom it has been shown to be safe and effective.

- The safety and efficacy of vorapaxar (Zontivity) have only been demonstrated when added to standard antiplatelet therapy such as clopidogrel with or without concomitant aspirin. There is limited clinical experience with the use of vorapaxar (Zontivity) in conjunction with other antiplatelet drugs.

Clinical Efficacy

- Vorapaxar (Zontivity) was approved based on one randomized, placebo-controlled trial in 26,449 patients with a history of myocardial infarction (MI), ischemic stroke, or peripheral artery disease (PAD). The primary efficacy endpoint evaluated was the composite of cardiovascular (CV) death, MI, stroke, or urgent coronary revascularization; however, this was later changed to a composite of CV death, MI, or stroke (originally the major secondary endpoint). [1,2]

- Patients received concomitant antiplatelet therapy according to the local standard of care for their study site (e.g. aspirin, generic clopidogrel). [1,2]

* At two years, treatment was discontinued in patients with a history of stroke due to an increased risk of intracranial hemorrhage.

* At three years, the original endpoint had occurred in significantly more patients in the placebo group than the vorapaxar (Zontivity) group [12.4% vs 11.2%, respectively; hazard ratio for vorapaxar (Zontivity) 0.88; 95% confidence interval: 0.82, 0.95; p = 0.001].

* The rate of moderate to severe bleeding events was significantly greater in patients receiving vorapaxar (Zontivity) versus placebo. This included intracranial hemorrhage [1.0% and 0.5% for the vorapaxar (Zontivity) and placebo groups, respectively; p < 0.001].

* A significant proportion of subjects (>20%) dropped out of the study prematurely, potentially leading to a loss of randomization and under-reporting of safety events.

- Vorapaxar (Zontivity) has been evaluated in two additional randomized controlled trials, one each in only patients following MI and only patients following ischemic stroke. In both trials, the addition of vorapaxar (Zontivity) to standard therapy did not significantly decrease the rate of CV events, but did significantly increase rates of bleeding events. [3,4]

Safety [1]

- As with most other antiplatelets, the most common adverse events associated with vorapaxar (Zontivity) are related to bleeding. Vorapaxar (Zontivity) carries a boxed warning for increased risk of bleeding events, and should not be initiated in patients...
with active pathological bleeding, or who have a history of stroke, transient ischemic attack or intracranial hemorrhage.

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### Codes

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### References