PRIOR AUTHORIZATION POLICY

POLICY: Cardiology – Zontivity Prior Authorization Policy
- Zontivity® (vorapaxar tablets – Aralez)

REVIEW DATE: 11/09/2022

OVERVIEW

Zontivity, a protease-activated receptor-1 antagonist, is indicated for the reduction of thrombotic cardiovascular (CV) events in patients with **a history of myocardial infarction (MI) or with peripheral arterial disease (PAD)**.[1] The agent has been shown to reduce the rate of a combined endpoint of cardiovascular death, MI, stroke, and urgent coronary revascularization.

Studies involving Zontivity involved adding the agent to aspirin and/or clopidogrel. Use Zontivity with aspirin and/or clopidogrel according to indicated uses or the standard of care. The clinical use of Zontivity with other antiplatelet medications is limited, as well as data involving Zontivity as the only antiplatelet agent. In a subgroup analysis of the pivotal data, patients weighing < 60 kg who received Zontivity did not have a favorable outcome regarding the primary composite endpoint of CV death, MI, stroke, or urgent coronary revascularization.[1,2]

Guidelines

According to American Heart Association and the American College of Cardiology guidelines on the management of patients with lower extremity PAD (2016), the overall clinical benefit of Zontivity added to existing antiplatelet therapy in patients with symptomatic PAD is uncertain.[3]

Safety

Zontivity has a Boxed Warning regarding the risk of bleeding.[1] Zontivity is contraindicated in patients with a history of stroke, transient ischemic attack, or intracranial hemorrhage (ICH). Antiplatelet medications, including Zontivity, increase the risk of bleeding, including ICH and fatal bleeding.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Zontivity. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Zontivity is recommended in patients who meet the following criteria:

FDA-Approved Indication

1. **Patient with a Previous Myocardial Infarction (MI) or Peripheral Arterial Disease (PAD).** Approve for 1 year if the patient meets the following criteria (A, B, and C):
   - **A)** Patient weighs ≥ 60 kg; AND
   - **B)** Patient is receiving Zontivity in combination with aspirin and/or clopidogrel; AND
   - **C)** Patient has been determined by the prescriber to be at high risk for future thrombotic events.

Note: Examples of high risk include that the patient has experienced multiple myocardial infarctions, has undergone many urgent coronary revascularization procedures, has had placement of coronary artery stents, or the patient has other concomitant diseases that increase cardiovascular risk such as diabetes.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Zontivity is not recommended in the following situations:

1. **Acute Coronary Syndrome (ACS) that Occurred Recently (within < 14 days).** In the TRACER (Thrombin Receptor Antagonist for Clinical Event Reduction in acute coronary syndrome) study, adding Zontivity to standard therapy in those who experienced an ACS increased the risk of major bleeding and did not result in clinical benefits.

2. **Patient with a Prior History of Stroke, Transient Ischemic Attack (TIA), or Intracranial Hemorrhage (ICH).** Zontivity is contraindicated for use in patients with a of stroke, TIA, or ICH due to an increased risk of ICH in this population.

3. **Concurrent Use of Effient® (prasugrel tablets) or Brilinta® (ticagrelor tablets).** There is limited clinical experience involving use of Zontivity with antiplatelet agents (e.g., Effient, Brilinta) other than aspirin and/or clopidogrel.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Zontivity® tablets [prescribing information]. Parsippany, NJ: Aralez; November 2019.
2. Morrow DA, Braunwald E, Bonaca MP, et al, for the TRA 2P-TIMI 50 Steering Committee and Investigators. Vorapaxar in the Secondary Prevention of Atherothrombotic Events. *N Engl J Med*. 2012;366(15):1404-1413.
3. Gerhard-Herman MD, Gornik HL, Shishehbor MH, et al. 2016 AHA/ACC guideline in the management of patients with lower extremity peripheral artery disease. *J Am Coll Cardiol*. 2017;69(11):e1465-1508.
4. Tricoci P, Huang Z, Held C, et al, for the TRACER Investigators. Thrombin-receptor antagonist vorapaxar in acute coronary syndromes. *N Engl J Med*. 2012;366(1):20-33.