PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 10/02/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

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

Various guidelines mention Zontivity:

- **Chronic Coronary Disease:** The guidelines for the management of patients with chronic coronary disease (2023) from the American Heart Association (AHA) and the American College of Cardiology (ACC) address Zontivity.[3] It is

noted that in the TRAP 2P TIMI 50 trial, at a mean follow-up of 3 years, patients with a history of MI, ischemic stroke, or PAD randomized to either Zontivity, on a background of aspirin therapy, had a reduced number of ischemic events or died from common from CV causes after 3 years compared with placebo. However, patients experienced more major and intracranial bleeding.

- **Peripheral Arterial Disease:** Guidelines for the management of lower extremity peripheral arterial disease from the AHA, ACC, and other organizations state that in patients with symptomatic peripheral arterial disease, the benefit of adding Zontivity to existing antiplatelet therapy is uncertain.[4]

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.

- **Zontivity® (vorapaxar tablets (Wraser)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Patient with a Previous Myocardial Infarction (MI) or Peripheral Arterial Disease (PAD).** Approve for 1 year if the patient meets ALL of the following (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 COVERED

- **Zontivity® (vorapaxar tablets (Wraser)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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 history 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.

REFERENCES

1. Zontivity® tablets [prescribing information]. Ridgeland, MS: Wraser; October 2022.
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. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2023;82(9):833-955.
4. Gornik HL, Aronow HE, Goodney PP, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SIR/VESS guideline for the management of lower extremity peripheral artery disease. *J Am Coll Cardiol*. 2024;83(24):2497-2604.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	10/02/2024