

SmartPA Criteria Proposal

Drug/Drug Class:	Antiplatelet Agents PDL Edit
First Implementation Date:	December 31, 2008
Proposed Date:	September 16, 2021
Prepared For:	MO HealthNet
Prepared By:	MO HealthNet/Conduent
Criteria Status:	<input type="checkbox"/> Existing Criteria <input checked="" type="checkbox"/> Revision of Existing Criteria <input type="checkbox"/> New Criteria

Executive Summary

Purpose: The MO HealthNet Pharmacy Program will implement a state-specific preferred drug list.

Why Issue Selected: Cardiovascular disease is the cause of 36.6 percent of all deaths in the United States. Thrombotic events include acute myocardial infarction (MI) and stroke. Stroke is the third leading cause of death behind heart disease and cancer and causes significant morbidity and mortality in the U.S. Inhibitory effects on the aggregation of platelets have led to a significant decrease in the rate of vascular events for both primary and secondary cardiovascular prevention trials. Aspirin has been shown to reduce cardiovascular morbidity and mortality in both the primary and secondary setting. Other anti-thrombin drugs have been developed to improve the platelet aggregation inhibition and to improve the safety profile of this class of medications. Platelet aggregation inhibitors are useful in the treatment and prevention of cardiovascular and cerebrovascular thrombotic events.

Venous thromboembolism (VTE) is a significant public health problem in the US. The disease manifests as deep vein thrombosis (DVT) and pulmonary embolism (PE) and is a major consequence of various surgical procedures and medical conditions. DVT occurs when a thrombus, made of cellular material bound together with fibrin strands, forms in the deep venous portion of the extremities, most commonly the legs. Embolization of a thrombus results in a PE if it lodges in the pulmonary artery or one of its branches and blocks pulmonary blood flow. Clinical risk factors for VTE include immobility or paralysis, trauma or surgery involving the lower extremities, pelvis, hips or abdomen; malignancy; obesity; increased estrogen levels – including pregnancy; indwelling central venous catheters; cardiac dysfunction; or inherited hypercoagulability disorders. Treatment options include 5 days of either IV or subcutaneous (SC) unfractionated heparin, or SC low molecular weight heparin (LMWH), or selective factor Xa inhibitor or thrombin inhibitors. LMWH primarily inhibits clotting factor Xa rather than thrombin, having less of an effect on the partial thromboplastin time - eliminating the need for laboratory monitoring. In addition, because of more consistent bioavailability, there is less interpatient dose-response variation allowing for standardized dosing.

Total program savings for the PDL classes will be regularly reviewed.

Program-Specific Information:	Preferred Agents	Non-Preferred Agents
	<ul style="list-style-type: none"> Aspirin/Dipyridamole Brilinta® Clopidogrel Dipyridamole Prasugrel 	<ul style="list-style-type: none"> Aggrenox® Cilostazol Effient® Plavix® Zontivity®

- Type of Criteria: Increased risk of ADE Preferred Drug List
 Appropriate Indications Clinical Edit
- Data Sources: Only Administrative Databases Databases + Prescriber-Supplied

Setting & Population

- Drug class for review: Antiplatelet Agents
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Failure to achieve desired therapeutic outcomes with trial on 2 or more preferred agents
 - Documented trial period for preferred agents **OR**
 - Documented ADE/ADR to preferred agents **OR**
- Documented compliance on current therapy regimen **OR**
- ~~For a platelet inhibitor:~~
 - ~~Documented trial period of aspirin (trial defined as one aspirin claim in the last year) **OR**~~
 - ~~Documented ADE/ADR to aspirin~~
 - ~~May be started at the same time but the aspirin claim must be processed prior to antiplatelet claim~~
- For cilostazol:
 - Participants aged 18 years or older **AND**
 - Available first line for intermittent claudication
- For prasugrel:
 - Participants aged 75 years or younger **AND**
 - ~~Available first line for MI with stent~~
- ~~For clopidogrel, Aspirin/extended-release dipyridamole: Participants aged 18 years or older~~
- For Zontivity: Concurrent use of aspirin or clopidogrel
- ~~For aspirin/omeprazole: Documented therapeutic compliance on aspirin and omeprazole single agents (defined as 150/180 days)~~
- ~~Appropriate diagnosis or procedure allows access to preferred drugs without aspirin trial:~~

Generic	Brand	Indication
Aspirin/dipyridamole, extended release	Aggrenox®	Stroke Prevention after Recent Myocardial Infarction (MI), Recent Stroke¹
Cilostazol	Pletal®	Intermittent Claudication²
Clopidogrel	Plavix®	Stroke Prevention after Recent Myocardial Infarction (MI), Recent Stroke ACS, UA/NSTEMI, STEMI^{3*} Established Peripheral Artery Disease (PAD) Reduce rate of combined endpoint thrombotic cardiovascular (CV) events
Dipyridamole	Persantine®	Adjunctive Use in Thromboembolism Prophylaxis after Cardiac Valve Replacement⁴

Generic	Brand	Indication
Prasugrel	Effient®	<ul style="list-style-type: none"> • ACS, UA/NSTE, STEMI⁵ • Reduce rate of combined endpoint thrombotic cardiovascular (CV) events⁵ • Reduce incidence of subacute stent thrombosis
Ticagrelor	Brilinta®	<ul style="list-style-type: none"> • ACS, UA/NSTE, STEMI • Reduce rate of combined endpoint thrombotic cardiovascular (CV) events⁵ • Reduce incidence of subacute stent thrombosis • Reduce risk of first MI or stroke in patients with CAD at high risk for such events • Prevention of stroke in patients with stroke and transient ischemic attack
Vorapaxar	Zontivity®	<ul style="list-style-type: none"> • Reduce rate of combined endpoint thrombotic cardiovascular (CV) events⁷

1. In patients who have had transient ischemia or completed thrombotic stroke
2. In patients with PAD; Intermittent claudication symptom reduction as indicated by an increased walking distance
3. The benefit for patients who undergo primary percutaneous coronary intervention (PCI) is unknown
4. Adjunct to warfarin

5. Being managed with PCI
 6. Avoid maintenance doses of aspirin above 100 mg daily
 7. In patients with history of MI or with PA
- *UA/NSTE: unstable angina/non-ST elevation
*ACS: Acute Coronary Syndrome
*STEMI: ST-elevation myocardial infarction

Denial Criteria

- Lack of adequate trial on required preferred agents
- Therapy will be denied if all approval criteria are not met
- **Lack of evidence of aspirin therapy in participant's prescription claims history in the last year for Clopidogrel, Aggrenox, Dipyridamole, Brilinta, Effient or Cilostazol**
- **Absence of any of the approval diagnoses or procedures**
- For prasugrel:
 - **Patients less than 132 lbs OR**
 - Documented history of stroke/TIA
- **For Brilinta: Concurrent aspirin therapy of > 100mg/day**
- For Zontivity: Documented history of cerebral hemorrhage or stroke/TIA
- Claim exceeds maximum dosing limitation for the following:

Drug Description	Generic Equivalent	Max Dosing Limitation
BRILINTA 90 MG TABLET	TICAGRELOR	2 tablets per day
BRILINTA 60 MG TABLET	TICAGRELOR	2 tablets per day
PLAVIX 75 MG TABLET	CLOPIDOGREL	1 tablet per day
EFFIENT 5 MG TABLET	PRASUGREL	1 tablet per day
EFFIENT 10 MG TABLET	PRASUGREL	1 tablet per day
AGGRENOX 25 MG/200 MG CAPSULE	ASPIRIN/DIPYRIDAMOLE	2 capsules per day
PLETAL 100 MG TABLET	CILOSTAZOL	2 tablets per day
PLETAL 50 MG TABLET	CILOSTAZOL	2 tablets per day

Required Documentation

Laboratory Results:
MedWatch Form:

Progress Notes:
Other:

SmartPA PDL Proposal Form

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Disposition of Edit

Denial: Exception Code "0160" (Preferred Drug List)
Rule Type: PDL

Default Approval Period

1 year

References

1. Drug Effectiveness Review Project – Drug Class Review on Newer Oral Anticoagulant Agents. Center for Evidence-Based Policy, Oregon Health & Science University; January 2013/Updated March 2015.
2. Drug Effectiveness Review Project – Drug Class Review on Newer Antiplatelets Drugs. Center for Evidence-Based Policy, Oregon Health & Science University; November 2005/Updated August 2017.
3. Evidence-Based Medicine and Fiscal Analysis: "Platelet Aggregation Inhibitors Therapeutic Class Review", Provider Synergies, L.L.C., Mason, OH; November 2016.
4. Evidence-Based Medicine Analysis: "Antiplatelet Agents", UMKC-DIC; June 2021.
5. Evidence-Based Medicine and Fiscal Analysis: "Antiplatelet Agents– Therapeutic Class Review", Conduent Business Services, L.L.C., Richmond, VA; July 2021.
6. USPDI, Micromedex; 2021.
7. Facts and Comparisons eAnswers (online); 2021 Clinical Drug Information, LLC.
8. Brilinta [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; August 2021.
9. Zontivity [package insert]. Parsippany, NJ: Aralez Pharmaceuticals US Inc.; November 2019.
10. Effient [package insert]. Basking Ridge, NJ: Daiichi Sankyo, Inc.; December 2020.