SmartPA Criteria Proposal

Drug/Drug Class:	Antiplatelet Agents PDL Edit
First Implementation Date:	December 31, 2008
Proposed Date:	September 17, 2020
Prepared For:	MO HealthNet
Prepared By:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☒Revision of Existing Criteria ☐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
	• **Aspirin/Dipyridamole** • Brilinta® • Clopidogrel • Dipyridamole • Prasugrel	• **Aggrenox®** • Aspirin/Omeprazole • Cilostazol • Effient® • Plavix® • Yosprala™ • 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 ~~**or ticlopidine**~~: 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 Stroke[1]
Cilostazol	Pletal®	• Intermittent Claudication[2]
Clopidogrel	Plavix®	• Stroke Prevention after Recent Myocardial Infarction (MI), Recent Stroke • ACS, UA/NSTEMI, STEMI[3*] • Established Peripheral Artery Disease (PAD)

Generic	Brand	Indication
		• Reduce rate of combined endpoint thrombotic cardiovascular (CV) events
Dipyridamole	Persantine®	• Adjunctive Use in Thromboembolism Prophylaxis after Cardiac Valve Replacement[4]
Prasugrel	Effient®	• ACS, UA/NSTE, STEMI[5] • Reduce rate of combined endpoint thrombotic cardiovascular (CV) events[5] • Reduce incidence of subacute stent thrombosis
Ticagrelor	Brilinta®	• ACS, UA/NSTE, STEMI • Reduce rate of combined endpoint thrombotic cardiovascular (CV) events[5] • Reduce incidence of subacute stent thrombosis
Vorapaxar	Zontivity®	• Reduce rate of combined endpoint thrombotic cardiovascular (CV) events[7]

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
- Claim exceeds maximum dosing limitation for the following:

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

Required Documentation

Laboratory Results:	☐	Progress Notes:	☐
MedWatch Form:	☐	Other:	☐

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 2020.
5. Evidence-Based Medicine and Fiscal Analysis: "Antiplatelet Agents– Therapeutic Class Review", Conduent Business Services, L.L.C., Richmond, VA; July 2020.
6. Lippincott, Williams, Wilkins. PDR Electronic Library, Montvale NJ; 2020.
7. USPDI, Micromedex; 2020.
8. Facts and Comparisons eAnswers (online); 2020 Clinical Drug Information, LLC.