Drug/Drug Class: Antiplatelet Agents PDL Edit  
First Implementation Date: December 31, 2008  
Revised Date: January 6, 2022  
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:

<table>
<thead>
<tr>
<th>Preferred Agents</th>
<th>Non-Preferred Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin/Dipyridamole</td>
<td>Aggrenox®</td>
</tr>
<tr>
<td>Brilinta®</td>
<td>Cilostazol</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Effient®</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>Plavix®</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>Zontivity®</td>
</tr>
</tbody>
</table>

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

- Documented compliance on current therapy regimen OR
- 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 AND

  - 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: Documented diagnosis of intermittent claudication
  - Participants aged 18 years or older
- For prasugrel: participants aged 75 years or younger
  - 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:

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin/dipyridamole, extended release</td>
<td>Aggrenox®</td>
<td>Stroke Prevention after Recent Myocardial Infarction (MI), Recent Stroke</td>
</tr>
<tr>
<td>Cilostazol</td>
<td>Pletal®</td>
<td>Intermittent Claudication</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Plavix®</td>
<td>Stroke Prevention after Recent Myocardial Infarction (MI), Recent Stroke, ACS, UA/NSTEMI, STEMI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Established Peripheral Artery Disease (PAD)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduce rate of combined endpoint thrombotic cardiovascular (CV) events</td>
</tr>
<tr>
<td>Dipyridamole</td>
<td>Persantine®</td>
<td>Adjunctive Use in Thromboembolism Prophylaxis after Cardiac Valve Replacement</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>Effient®</td>
<td>ACS, UA/NSTE, STEMI</td>
</tr>
<tr>
<td>Generic</td>
<td>Brand</td>
<td>Indication</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
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</tr>
</tbody>
</table>
| Ticagrelor | Brilinta<sup>©</sup> | • Reduce rate of combined endpoint thrombotic cardiovascular (CV) events<sup>5</sup>  
• 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<sup>©</sup> | • Reduce rate of combined endpoint thrombotic cardiovascular (CV) events<sup>2</sup> |

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 PAD  
*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:

<table>
<thead>
<tr>
<th>Drug Description</th>
<th>Generic Equivalent</th>
<th>Max Dosing Limitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRILINTA 90 MG TABLET</td>
<td>TICAGRELOR</td>
<td>2 tablets per day</td>
</tr>
<tr>
<td>BRILINTA 60 MG TABLET</td>
<td>TICAGRELOR</td>
<td>2 tablets per day</td>
</tr>
<tr>
<td>PLAVIX 75 MG TABLET</td>
<td>CLOPIDOGREL</td>
<td>1 tablet per day</td>
</tr>
<tr>
<td>EFFIENT 5 MG TABLET</td>
<td>PRASUGREL</td>
<td>1 tablet per day</td>
</tr>
<tr>
<td>EFFIENT 10 MG TABLET</td>
<td>PRASUGREL</td>
<td>1 tablet per day</td>
</tr>
<tr>
<td>AGGRENEX 25 MG/200 MG CAPSULE</td>
<td>ASPIRIN/DIPYRIDAMOLE</td>
<td>2 capsules per day</td>
</tr>
<tr>
<td>PLETAL 100 MG TABLET</td>
<td>CILOSTAZOL</td>
<td>2 tablets per day</td>
</tr>
<tr>
<td>PLETAL 50 MG TABLET</td>
<td>CILOSTAZOL</td>
<td>2 tablets per day</td>
</tr>
</tbody>
</table>

**Required Documentation**

Laboratory Results:  
Progress Notes:  
MedWatch Form:  
Other:

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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

6. USPDI, Micromedex; 2021.
7. Facts and Comparisons eAnswers (online); 2021 Clinical Drug Information, LLC.