SmartPA Criteria Proposal

Drug/Drug Class:	Anticoagulant Agents, Oral and Subcutaneous PDL Edit
First Implementation Date:	July 5, 2012
Proposed Date:	September 16, 2021
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.

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Program-Specific Information:	Preferred Agents	Non-Preferred Agents
	• Eliquis® • Enoxaparin • Fragmin® • Pradaxa® • Warfarin • Xarelto® 10, 15, 20 mg • Xarelto® Starter Pack	• Arixtra® • Bevyxxa® • Coumadin® • Fondaparinux • Jantoven® • Lovenox® • Savaysa® • Xarelto® 2.5 mg

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: Anticoagulant Agents, Oral and Subcutaneous
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Failure to achieve desired therapeutic outcomes with trial on 3 or more preferred agents
  - Documented trial period for preferred agents **OR**
  - Documented ADE/ADR to preferred agents **OR**
- Documented compliance on current therapy regimen
- ~~Appropriate diagnosis: Factor Xa Inhibitors, Direct Thrombin Inhibitors, Warfarin~~

~~Generic~~	~~Brand~~	~~Indication~~
~~Apixaban[3]~~	~~Eliquis®~~	~~• Prevention of stroke and systemic embolism with nonvalvular atrial fibrillation[3] • DVT prophylaxis after hip replacement[3] • DVT Prophylaxis after knee replacement[3] • Treatment of DVT and PE[3] • Prevention of recurrent DVT and/or PE[3]~~
~~Dabigatran~~	~~Pradaxa®~~	~~• Prevention of stroke and systemic embolism with nonvalvular atrial fibrillation • DVT prophylaxis after hip replacement • Treatment of DVT and PE[1] • Prevention of recurrent DVT and/or PE~~
~~Edoxaban[4]~~	~~Savaysa®~~	~~• Prevention of stroke and systemic embolism with nonvalvular atrial fibrillation[4] • Treatment of DVT and PE[1,4]~~
~~Fondaparinux~~	~~Arixtra®~~	~~• DVT prophylaxis after hip replacement • DVT Prophylaxis after knee replacement • Treatment of DVT and PE • Prevention of recurrent DVT and/or PE~~
~~Rivaroxaban[3]~~	~~Xarelto®~~	~~• Prevention of stroke and systemic embolism with nonvalvular atrial fibrillation[3] • DVT prophylaxis after hip replacement[3] • DVT Prophylaxis after knee replacement[3] • Treatment of DVT and PE[3]~~

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Generic	Brand	Indication
		• Prevention of recurrent DVT and/or PE[3]
Warfarin	Coumadin®	• Prevention of stroke and systemic embolism with nonvalvular atrial fibrillation • DVT prophylaxis after hip replacement • DVT Prophylaxis after knee replacement • Treatment of DVT and PE[1] • Prevention of recurrent DVT and/or PE • Prophylaxis and treatment of thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement[2] • Reduction in the risk of death, recurrent myocardial infarction (MI), and thromboembolic events after MI
Betrixaban[5]	Bevyxxa®	• VTE prophylaxis in adult patients hospitalized for acute medical illness who are at risk due to restricted mobility or other risk factors for VTE[5]

1 Requires initial 5-10 day therapy with a parenteral anticoagulant
2 Atrial fibrillation due to any etiology
3 Tablets may be crushed and taken by mouth or via nasogastric tube or gastric feeding tube
4 Edoxaban should not be used in patients with creatinine clearance >95 mL/min because of increased risk of ischemic stroke compared to warfarin at the highest dose studied. Creatinine clearance should be assessed before starting edoxaban for the treatment of non-valvular atrial fibrillation.
5 Safety and efficacy not established in patients with prosthetic heart valves

- Appropriate diagnosis: Low Molecular Weight Heparins (LMWH's)

Generic	Brand	Indication
Dalteparin	Fragmin®	• Prophylaxis of DVT which may lead to PE in abdominal surgery and at risk for thromboembolic complications • Prophylaxis of DVT which may lead to PE in hip replacement surgery • Prophylaxis of DVT which may lead to PE in severely restricted mobility during acute illness • Prophylaxis of ischemic complications in unstable angina and non-Q wave MI[8] • Extended treatment of symptomatic VTE (proximal DVT and/or PE) in cancer patients to reduce recurrence of VTE
Enoxaparin	Lovenox®	• Prophylaxis of DVT which may lead to PE in abdominal surgery and at risk for thromboembolic complications • Prophylaxis of DVT which may lead to PE in hip replacement surgery[6] • Prophylaxis of DVT which may lead to PE in knee replacement surgery • Prophylaxis of DVT which may lead to PE in severely restricted mobility during acute illness • Treatment of acute DVT with or without PE[7] • Prophylaxis of ischemic complications in unstable angina and non-Q wave MI[8] • Treatment of acute ST-segment elevation MI [STEMI] managed medically or with subsequent percutaneous coronary intervention[8]

6 During and following hospitalization
7 Approved for *inpatient* treatment of acute DVT *with or without PE* when administered in conjunction with warfarin; approved for *outpatient* treatment of DVT *without PE* when administered in conjunction with warfarin
8 In conjunction with ASPIRIN

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Denial Criteria

- Lack of adequate trial on required preferred agents
- Therapy will be denied if all approval criteria are not met
- Claim exceeds maximum dosing limitation for the following:

Drug Description	Generic Equivalent	Max Dosing Limitation
PRADAXA 150 MG	DABIGATRAN	2 tablets per day
PRADAXA 75 MG	DABIGATRAN	2 tablets per day
PRADAXA 110 MG	DABIGATRAN	2 tablets per day
LOVENOX 30 MG/0.3 ML	ENOXAPARIN	0.6 mL per day
LOVENOX 150 MG/1 ML	ENOXAPARIN	2 mL per day
LOVENOX 120 MG/0.8 ML	ENOXAPARIN	1.6 mL per day
LOVENOX 60 MG/0.6 ML	ENOXAPARIN	1.2 mL per day
LOVENOX 80 MG/0.8 ML	ENOXAPARIN	1.6 mL per day
LOVENOX 100 MG/1 ML	ENOXAPARIN	2 mL per day
LOVENOX 40 MG/0.4 ML	ENOXAPARIN	0.8 mL per day
LOVENOX 300 MG/3 ML	ENOXAPARIN	3 mL per day
ARIXTRA 10 MG/0.8 ML	FONDAPARINUX	0.8 mL per day
ARIXTRA 2.5 MG/0.5 ML	FONDAPARINUX	0.5 mL per day
ARIXTRA 5 MG/0.4 ML	FONDAPARINUX	0.4 mL per day
ARIXTRA 7.5 MG/0.6 ML	FONDAPARINUX	0.6 mL per day
XARELTO 10 MG	RIVAROXABAN	1 tablet per day
XARELTO 15 MG	RIVAROXABAN	1 tablet per day
XARELTO 20 MG	RIVAROXABAN	1 tablet per day
XARELTO 2.5 MG	RIVAROXABAN	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. Evidence-Based Medicine Analysis: “Direct Factor Xa Inhibitor Agents and Miscellaneous Anticoagulants”, UMKC-DIC; June 2021.
2. Evidence-Based Medicine Analysis: “Low Molecular Weight Heparins (LMWH)”, UMKC-DIC; Updated June 2021.
3. Evidence-Based Medicine and Fiscal Analysis: “Anticoagulants Agents: Oral and Subcutaneous – Therapeutic Class Review”, Conduent Business Services, L.L.C., Richmond, VA; July 2021.
4. USPDI, Micromedex; 2021.
5. Facts and Comparisons eAnswers (online); 2021 Clinical Drug Information, LLC.

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