

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	Clotting Disorders, Arrhythmias, Stroke	P&T DATE:	9/11/2018
THERAPEUTIC CLASS:	Cardiovascular	REVIEW HISTORY: (MONTH/YEAR)	5/17, 2/16, 5/15, 2/15, 11/14, 7/14, 2/13, 11/12, 9/12, 4/12, 5/11, 2/10, 1/10
LOB AFFECTED:	Medi-Cal		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

The below criteria, limits, and requirements for certain agents are in place to ensure appropriate use of those agents using standards of care as set by clinical practice guidelines, including but not limited to the Chest Guidelines. Areas include VTE/DVT, and other coagulopathies as well as anti-arrhythmic agents.

Anticoagulant/Antiplatelet agents (Current as of 4/2018)

Therapeutic Class	Generic (Brand)	Strength	Form Limits	Avg Cost per month	Indication			Notes
					Afi b	VT E	PP X	
Oral Anticoagulants								
Target Specific Oral Anti-coagulants (TSOACs)	Rivaroxaban (Xarelto)	Tablets:						
		10 mg	QL, PA*	\$167.84	x	x	x	Max 35 tablets per 365 days
		15 mg	QL, PA*	\$435.61	x	x	x	Max 42 tablets per 3 months
		20 mg	QL, PA*	\$392.79	x	x	x	Max 30 tablets per 30 days
		Starter Pack:						
		15/20 mg	NF	\$854.90	x	x	x	
	Apixaban (Eliquis)	Tablets:						
		2.5 mg	QL; PA*	\$354.67	x	x	x	Max 70 tablets per 365 days
		5mg	QL; PA*	\$373.90	x	x	x	Max 74 tablets per 30 days
		Starter Pack:						
			5 mg	NF	\$620.17	x	x	x
	Dabigatran (Pradaxa)	Capsules:						
		75 mg	NF	\$324.62	x			
		110 mg	NF	\$380.84			x	
		150 mg	QL	\$352.67	x	x	x	Max 60 capsules per 30 days
	Edoxaban (Savaysa)	Tablets:						
		15 mg	NF	\$403.92	x	x		
		30 mg	NF	\$403.92		x		
	Betrixaban (Bevyxxa)	Capsules:						
		40 mg	NF	\$540.00		x		
80 mg		NF	\$540.00		x			
Vitamin K Antagonists (VKA)	Warfarin	Tablets:						
		1 mg	--	\$6.94	x	x	x	--
		2 mg	--	\$6.11	x	x	x	--
		2.5 mg	--	\$7.92	x	x	x	--
		3 mg	--	\$5.14	x	x	x	--
		4 mg	--	\$5.56	x	x	x	--
		5 mg	--	\$5.47	x	x	x	--
		6 mg	--	\$5.66	x	x	x	--
		7.5 mg	--	\$5.57	x	x	x	--
	10 mg	--	\$6.10	x	x	x	--	
	JANTOVEN	1 mg	NF	--	x	x	x	
		2 mg	NF	\$9.13	x	x	x	
		2.5 mg	NF	\$6.62	x	x	x	
	3 mg	NF	\$5.07	x	x	x		
	4 mg	NF	\$3.88	x	x	x		

	5 mg	NF	\$4.19	x	x	x	
	6 mg	NF	\$6.36	x	x	x	
	7.5 mg	NF	\$13.84	x	x	x	
	10 mg	NF	\$0.24	x	x	x	

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Form Limits	Avg Cost per month	Notes/Restriction Language
Injectable Agents					
Unfractionated Heparin	Heparin Flush/ Heparin Vials	10 Unit/ml	--	--	--
		100 Unit/mL	--	--	--
		1,000 Unit/mL	--	--	--
		5,000 Unit/mL	--	\$26.45	--
		10,000 Unit/mL	--	\$2.90	--
		20,000 Unit/mL	--	--	--
Fractionated Heparin	Enoxaparin (Lovenox)	Prefilled Syringes:			No prior authorization is required if less than 10 days' supply as bridge therapy. Maximum of 2 syringes per day and 3 courses per 180 days. Submit PA for larger quantities.
		30 mg/0.3 mL	QL	\$64.69	
		40 mg/0.4 mL	QL	\$111.84	
		60 mg/0.6mL	QL	\$168.42	
		80 mg/0.8 mL	QL	\$239.15	
		100 mg/mL	QL	\$332.09	
		120 mg/0.8 mL	QL	\$380.74	
150 mg/mL	QL	\$453.56			

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Form Limits	Avg Cost per month	Notes/Restriction Language
Antiplatelet Agents	Aspirin	Tablets:			--
		81 mg	--		
		325 mg	--	\$	
	Clopidogrel (Plavix)	75 mg	--	\$3.49	--
		300mg	NF	--	
	Dipyridamole (Persantine)	Tablets:			--
		25 mg	--	\$4.90	
		50 mg	--	\$23.86	
		75 mg	--	\$21.50	
		Solution:			
	5 mg/ml (10 ml)	NF	--		
	Prasugrel (Effient)	5 mg	PA	\$389.33	Reserved for patients status post stent placement or medical management of acute coronary syndrome for patients intolerant to Clopidogrel or Ticagrelor
		10 mg	PA	\$384.59	
	Ticagrelor (Brilinta)	90 mg	QL	\$330.41	60 tablets per 30 days
		60mg	ST	\$345.88	Step therapy to 12 months of Dual Oral Antiplatelet Therapy (DAPT) with Clopidogrel, Ticagrelor, or Prasugrel.
	Dipyridamole/Aspirin (Aggrenox)	Tablets:			Restricted to secondary CVA prevention.
		25mg-200 mg	PA	\$261.17	
	Cilostazol (Pletal)	Tablets:			--
		50 mg	--	\$16.70	
		100 mg	--	\$8.44	
Vorapaxar (Zontivity)	Tablets:				
	2.08 mg	NF			

Drug Class	Generic Name (Brand Name)	Available Strengths	Form Limits	Avg Cost per month	Notes/Restriction Language
Anti-arrhythmic Agents	CLASS I				
	Quinidine Sulfate	Tablets:			
		200 mg IR	--	--	--
		300 mg IR	--	--	--
	Quinidine Sulfate	300 mg ER	--	--	--
		ER tablet			
		324mg	--	\$77.20	--
	Quinidine Gluconate	Injection:			
		80 mg/mL	--	--	--
		ER Capsule:			
	Disopyramide Phosphate (Norpace, Norpace CR)	100 mg	--	--	--
		150 mg	--	--	--
		IR Capsule:			
		100 mg	--	\$21.60	--
		150 mg	--	\$22.34	--
		Capsule:			
	Mexiletine	150 mg	--	\$72.00	--
		200 mg	--	\$101.92	--
		250 mg	--	\$149.21	--
	Flecainide	Tablet:			
		50 mg	--	\$31.22	--
100 mg		--	\$51.11	--	
150 mg		--	\$157.62	--	
Propafenone (Rythmol, Rythmol SR)	IR Tablet:				
	150 mg	--	\$19.82	--	
	225 mg	--	\$34.43	--	
	300 mg	--	\$95.69	--	
	ER Capsules:				
	225 mg	--	\$247.03	--	
	325 mg	--	\$373.37	--	
425 mg	--	\$352.03	--		
Beta Blockers	CLASS II				
	See hypertension coverage policy				
	CLASS III				
	Amiodarone (Cordarone, Pacerone)	Tablet:			
		100 mg	NF	--	--
		200 mg	--	\$7.71	--
		400 mg	NF	--	--
	Dofetilide (Tikosyn)	Capsules:			
		125 mcg		\$297.26	
		250 mcg		\$293.88	
		500 mcg		--	
	Dronedarone (Multaq)	Tablet:			
		400 mg	PA	\$504.23	Reserved for patients 55 and younger or with treatment failure of Amiodarone and high risk of pulmonary fibrosis or optic neuropathy without NYHA class II-III heart failure with recent exacerbation, NYHA Class IV heart failure, or LVEF ≤ 35%
	Sotalol (Betapace, Betapace AF, Sotylize)	Tablet:			
		80 mg	--	\$11.38	--
120 mg		--	\$19.45	--	
160 mg		-	\$22.05	--	
240 mg		--	--	--	
Oral Solution:					
5 mg/ ml	NF	--	--		

CLASS IV				
Calcium Channel Blockers	See hypertension coverage			
CARDIAC GLYCOSIDES				
Digoxin (Digitek, Digox, Lanoxin)	Oral Solution (60 ml):			
	50 mcg/ ml	--	\$124.02	--
	Tablet:			
	125 mcg	--	\$69.18	--
	250 mcg	--	\$54.83	--
	Lanoxin Tablets:			
	62.5 mcg	NF	--	
	125 mcg	NF	--	
	187.5 mcg	NF	--	
250 mcg	NF	--		

NF = Non-formulary

⊕ CLINICAL JUSTIFICATION:

Overall, Target Specific Oral Anti-coagulants (TSOACs) have similar treatment efficacy to Vitamin K Antagonists (VKAs), but have lower risk of major bleeding. All studies were designed to test non-inferiority to Warfarin. Though this is the case, there is limited evidence regarding post-marketing surveillance safety. Extension Studies only followed patients at most 12-18 months. Warfarin has been on the market for decades, while the oldest TSOAC has been on the market less than 10 years. Given the gravity of ensuring therapeutic coverage with an anticoagulant, patients who are high risk for stroke in Afib (CHADS2 \geq 2) qualify for TSOAC treatment. TSOACs did not demonstrate superiority to warfarin in treating VTE, therefore, patients must fail to achieve therapeutic INRs while on warfarin therapy, or have a recurrent thrombotic event, before TSOACs will be approved for DVT/PE.

For Acute Coronary Syndrome (ACS), Clopidogrel and Prasugrel showed equal efficacy with the exception of the diabetic subgroup. These patients fared better on Prasugrel than Clopidogrel. Prasugrel is a more potent anti-platelet drug, and as a result, had more bleeding risk in studies, so much so, that it carries a black box warning for increased risk of intracranial bleed in patients with previous history of stroke or TIA. Therefore, Clopidogrel is the preferred agent.

HPSJ formulary is open and includes all classes of antiarrhythmic agents. One exception exists with respect to dronedarone. HPSJ restricts this to members with a trial history of amiodarone due to the heart failure risks that dronedarone might pose.

⊕ EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Vitamin K Antagonists ***Warfarin (Coumadin, Jantoven)***

Warfarin (Coumadin)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** Warfarin is the gold standard for anticoagulation management. It is the preferred agent for DVT treatment

Target Specific Oral Anticoagulants ***Rivaroxaban (Xarelto), Apixaban (Eliquis), Dabigatran (Pradaxa), Edoxaban (Savaysa)***

Rivaroxaban (Xarelto)

- Coverage Criteria:**

- 20mg or 15mg: None (Quantity limits apply).
- 10mg: Reserved for post-TKA/THA DVT Prophylaxis
- Limits:**
 - 20mg: 30 tablets/month,
 - 15mg: 42 tablets per 90 days
 - 10mg: PA required
- Required Information for Approval:** For 10mg strength, submit documentation of eminent THA/TKA procedure.
- Other Notes:** none
- Non-Formulary: Xarelto Starter Pack**

Apixaban (Eliquis)

- Coverage Criteria:**
 - 5mg: None,
 - 2.5mg: Reserved for secondary prevention of DVT/PE post treatment, or as renally adjusted Atrial Fibrillation Treatment.
- Limits:**
 - 5mg: 74 per 30 days,
 - 2.5mg: PA required
- Required Information for Approval:** For renally adjusted Eliquis, Age, body weight, and Serum Creatinine are required for review.
- Other Notes:** Renally dose-adjusted Apixaban appropriate for members having any two of the following: Age ≥80 years, body weight ≤60 kg, or serum creatinine ≥1.5 mg/dL.
- Non-Formulary: Eliquis Starter Pack**

Dabigatran (Pradaxa)

- Coverage Criteria:** None
- Limits:** 150mg: 60 capsules/month
- Required Information for Approval:** N/A
- Other Notes:** Patients with poor renal function, use warfarin instead.
- Non-Formulary:** Pradaxa 75 mg and 110 mg, Savaysa

Injectable Agents

Unfractionated Heparin, Enoxaparin (Lovenox)

Unfractionated Heparin

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None

Enoxaparin (Lovenox)

- Coverage Criteria:** No prior authorization is required if < 10 days supply as bridge therapy. Maximum of 2 syringes per day and 3 courses per 180 days.
- Limits:** 2 syringes per day for 10 day supply, 3 courses per 180 days.
- Required Information for Approval:** N/A
- Other Notes:** Please submit PA if used for any other indication than bridge to warfarin, if total days' supply exceeds 10. Include chart notes with diagnosis and treatment course.

Antiplatelet Agents

Aspirin, Clopidogrel (Plavix), Cilostazol (Pletal), Ticagrelor (Brilinta), Prasugrel (Effient), Dipyridamole (Persantine), Dipyridamole/Aspirin (Aggrenox), Vorapaxar (Zontivity)
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Aspirin, Clopidogrel (Plavix), Cilostazol (Pletal), Dipyridamole (Persantine)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Dipyridamole 5 mg/ ml solution, Vorapaxar (Zontivity)

Ticagrelor (Brilinta)

- Coverage Criteria:** None (Quantity limits apply)
- Limits:**
 - 90mg: 60 tablets/month,
 - 60mg: Step therapy to 12 months of DAPT Therapy.
- Required Information for Approval:** N/A
- Other Notes:** none

Prasugrel (Effient)

- Coverage Criteria:** Reserved for patients status post stent placement or medical management of acute coronary syndrome for patients intolerant to Clopidogrel (Plavix)
- Limits:** None
- Required Information for Approval:** Prior Authorization form with chart notes documenting treatment failure or intolerance to Clopidogrel (Plavix)
- Other Notes:** Prasugrel should not be used in patients with a previous history of CVA, due to increased risk of bleed. Patients on Ticagrelor should not use more than 100mg aspirin daily.

Dipyridamole/Aspirin (Aggrenox)

- Coverage Criteria:** Restricted to secondary CVA prevention.
- Limits:** None
- Required Information for Approval:** Prior Authorization form and chart notes documenting a history of previous CVA.
- Other Notes:** None

Antiarrhythmic Agents
<i>Quinidine Sulfate/Gluconate, Disopyramide Phosphate, Mexiletine, Flecainide, Propafenone (Rythmol), Amiodarone (Cordarone, Pacerone), Sotalol, Dofetilide (Tikosyn), Dronedarone (Multaq), Digoxin</i>

Quinidine Sulfate/Gluconate, Disopyramide Phosphate, Mexiletine, Flecainide, Propafenone, Sotalol

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None

Amiodarone

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Amiodarone 100 mg and 400 mg, Tikosyn

Dronedarone

- Coverage Criteria:** It is reserved for patients older than 55 OR with treatment failure of or are intolerant to amiodarone or other antiarrhythmics AND without NYHA Class II or III HF with exacerbation/hospitalization within the previous 4 weeks, NYHA Class IV HF, or LVEF \leq 35%.
- Limits:** None
- Required Information for Approval:** Documented treatment failure of amiodarone, chart notes documenting current ejection fraction (if applicable), and no recent hospitalization within the past 4 weeks as evidenced by HPSJ records.
- Other Notes:** Claims for members older than 55 will pass through; no prior authorization is required.

Digoxin

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None

REFERENCES

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2. Kearon C, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest. 2016; 149(2):315-352.
3. Adam S, et al. Comparative Effectiveness of Warfarin and New Oral Anticoagulants for the Management of Atrial Fibrillation and Venous Thromboembolism: A Systematic Review. Ann Int Med. 2012; 157(11): 796-807
4. Slot, B., Berge E. Factor Xa inhibitors versus vitamin K antagonists for preventing cerebral or systemic embolism in patients with atrial fibrillation (Review). Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No.: CD008980.
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7. Nishiura RA, Otto CM, Bonow RO, et. al., 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017.
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9. Bonaca MP, Scirica BM, Creager MA, et al., Circulation. 2013 Apr 9;127(14):1522-9, 1529e1-6. doi: 10.1161/CIRCULATIONAHA.112.000679. Epub 2013 Mar 15.
10. Bohula EA, Aylward PE, Bonaca MP, et al., Efficacy and Safety of Vorapaxar With and Without a Thienopyridine for Secondary Prevention in Patients With Previous Myocardial Infarction and No History of Stroke or Transient Ischemic Attack: Results from TRA 2°P-TIMI 50. Circulation. 2015 Nov 17;132(20):1871-9. doi: 10.1161/CIRCULATIONAHA.114.015042. Epub 2015 Sep 3.

✚ REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Plavix_PVD and Stent Rvw w TC 1-15-08_2.doc	1/2010	Allen Shek PharmD BCPS
Update to Policy	Plavix study 2-8-10.docx	2/2010	Allen Shek PharmD BCPS
Update to Policy	Multaq 5-4-11.doc	5/2011	Allen Shek PharmD BCPS
Update to Policy	Antiplatelet Class Review 2-12-10.docx	4/2012	Allen Shek PharmD BCPS
Update to Policy	Rivaroxaban Monograph V6.doc	9/2012	Allen Shek PharmD BCPS
Update to Policy	Formulary Realignment 9-18-12.xlsx	9/2012	Allen Shek PharmD BCPS
Update to Policy	Formulary Realignment PT 11-20-12.xlsx	11/2012	Allen Shek PharmD BCPS
Update to Policy	Xarelto revisit 2013-2-19.docx	2/2013	Allen Shek PharmD BCPS
Update to Policy	Ticagrelor Drug Monograph 204-05-29.docx	7/2014	Jonathan Szkotak, PharmD BCACP
Update to Policy	Apixaban Monograph 11-2014.docx	11/2014	Jonathan Szkotak, PharmD BCACP
Update to Policy	Anti-coagulants 2-17-2015.docx	2/2015	Jonathan Szkotak, PharmD BCACP
Update to Policy	HPSJ Coverage Policy – Cardiovascular – Clotting Disorders 2015-05.docx	5/2015	Jonathan Szkotak, PharmD BCACP
Update to Policy	HPSJ Coverage Policy – Cardiovascular – Clotting Disorders, Arrhythmias, Stroke 2016-05.docx	2/2016	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Cardiovascular – Clotting Disorders, Arrhythmias, Stroke 2017-05.docx	5/2017	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Cardiovascular – Clotting Disorders, Arrhythmias, Stroke 2018-09.docx	9/2018	Johnathan Yeh, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy