

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY	Parkinson's Disease	P&T DATE	5/8/2018
THERAPEUTIC CLASS	Neurological Disorders	REVIEW HISTORY	2/17, 2/16, 9/12, 5/11,
LOB AFFECTED	Medi-Cal	(MONTH/YEAR)	9/07

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

Anti-parkinson's medications are used to relieve symptoms of Parkinson's Disease. The purpose of this coverage policy is to review the coverage criteria of HPSJ's formulary antiparkinsonian agents (Table 1).

Table 1: Available Antiparkinsonian Agents (Current as of 4/2018)

Generic (Brand)	Strength & Dosage form	Formulary Limit	Cost per Rx	Notes
Dopamine precursor/dopamine decarboxylase inhibitor				
Levodopa/carbidopa (Sinemet, Sinemet CR, Parcopa, Rytary, Duopa)	Carbidopa 10 mg-levodopa 100 mg oral disintegrating tablet (ODT)	F	--	
	Carbidopa 10 mg-levodopa 100 mg tablet	F	\$18.24	
	Carbidopa 25 mg-levodopa 100 mg ODT	F	--	
	Carbidopa 25 mg-levodopa 100 mg tablet	F	\$29.78	
	Carbidopa 25 mg-levodopa 250 mg ODT	F	--	
	Carbidopa 25 mg-levodopa 250 mg tablet	F	\$26.06	
	Carbidopa extended-release (ER) 25 mg-levodopa 100 mg tablet	F	--	
	Carbidopa ER 50 mg-levodopa 200 mg tablet	F	--	
	Rytary ER 23.75 mg-95 mg capsule	NF	\$730.94	
	Rytary ER 36.25 mg-145 mg capsule	NF	\$650.16	
	Rytary ER 48.75 mg-195 mg capsule	NF	--	
	Rytary ER 61.25 mg-245 mg capsule	NF	--	
Duopa (4.63 mg Carbidopa- 20 mg Levodopa per 1 ml) suspension	NF	--		
Anticholinergic Agents				
Biperiden (Akinetone)	Akinetone 2 mg tablet	NF	--	Carved out to fee for service
Benztropine (Cogentine)	Benzotropine 0.5 mg tablet	NF	--	
	Benzotropine 1 mg tablet	NF	--	
	Benzotropine 2 mg tablet	NF	--	
	Benzotropine 1 mg/ml solution	NF	--	
Trihexyphenidyl (Artane)	Trihexyphenidyl 2 mg tablet	NF	--	
	Trihexyphenidyl 5 mg tablet	NF	--	
	Trihexyphenidyl 0.4 mg/ml elixir	NF	--	
MAO-B inhibitors				
Rasagiline mesylate (Azilect)	Rasagiline mesylate 0.5 mg tablet	PL	--	Must be prescribed by Neurologist
	Rasagiline mesylate 1 mg tablet	PL	\$379.36	
Selegiline HCL (Zelapar, Eldepryl)	Selegiline 5 mg capsule	F	\$66.37	
	Selegiline 5 mg tablet	F	\$75.84	
	Emsam 24 hr transdermal patches:			
	6 mg/24 h	NF	--	
	9 mg/24 h	NF	--	
	12 mg/24 h	NF	--	
	Zelapar 1.25 mg ODT	NF	--	
Safinamide (Xadago)	Xadago 50 mg tablet	NF	--	
	Xadago 100 mg mg tablet	NF	--	
Dopamine agonists				
Apomorphine (Apokyn)	Apokyn 30 mg/3 ml cartridge	NF	--	
Bromocriptine mesylate (Parlodel, Cycloset)	Bromocriptine 2.5 mg tablet	F	\$145.11	
	Bromocriptine 5 mg capsule	F	\$191.79	
	Cycloset 0.8 mg tablets	NF	--	
Pramipexole Di-HCL (Mirapex, Mirapex ER)	Pramipexole 0.125 mg tablet	QL	\$6.06	Restricted to 90 tablets per month.
	Pramipexole 0.25 mg tablet	QL	\$4.70	

	Pramipexole 0.5 mg tablet	QL	\$6.40	
	Pramipexole 0.75 mg tablet	QL	\$5.28	
	Pramipexole 1 mg tablet	QL	\$5.40	
	Pramipexole 1.5 mg tablet	QL	\$9.88	
	Pramipexole ER 0.375 mg tablet	NF	--	
	Pramipexole ER 0.75 mg tablet	NF	--	
	Pramipexole ER 1.5 mg tablet	NF	--	
	Pramipexole ER 2.25 mg tablet	NF	--	
	Pramipexole ER 3 mg tablet	NF	--	
	Pramipexole ER 3.75 mg tablet	NF	--	
	Pramipexole ER 4.5 mg tablets	NF	--	
Ropinirole HCL (Requip, Requip XL)	Ropinirole 0.25 mg tablet	QL	\$15.93	Restricted to 90 tablets per month.
	Ropinirole 0.5 mg tablet	QL	\$5.30	
	Ropinirole 1 mg tablet	QL	\$14.70	
	Ropinirole 2 mg tablet	QL	\$5.28	
	Ropinirole 3 mg tablet	QL	\$15.82	
	Ropinirole 4 mg tablet	QL	\$15.85	
	Ropinirole 5 mg tablet	QL	\$17.26	
	Ropinirole HCL ER 2 mg tablet	NF	--	
	Ropinirole HCL ER 4 mg tablet	NF	\$109.31	
	Ropinirole HCL ER 6 mg tablet	NF	--	
	Ropinirole HCL ER 8 mg tablet	NF	--	
Rotigotine (Neupro)	Neupro 1 mg/24 hr patch	NF	--	
	Neupro 2 mg/24 hr patch	NF	\$639.26	
	Neupro 3 mg/24 hr patch	NF	--	
	Neupro 4 mg/24 hr patch	NF	--	
	Neupro 6 mg/24 hr patch	NF	--	
	Neupro 8 mg/24 hr patch	NF	--	
COMT inhibitors				
Entacapone (Comtan)	Entacapone 200 mg tablet	NF	\$268.20	
Tolcapone (Tasmar)	Tolcapone 100 mg tablet	NF	--	
Dopamine precursor/dopamine decarboxylase inhibitor/COMT inhibitor				
Levodopa/carbidopa/entacapone (Stalevo)	Levodopa/carbidopa/entacapone 50 mg/12.5 mg/200 mg tablets	NF	--	
	Levodopa/carbidopa/entacapone 75 mg/18.75 mg/200 mg tablets	NF	--	
	Levodopa/carbidopa/entacapone 100 mg/25 mg/200 mg tablets	NF	--	
	Levodopa/carbidopa/entacapone 125 mg/31.25 mg/200 mg tablets	NF	--	
	Levodopa/carbidopa/entacapone 150 mg/37.5 mg/200 mg tablets	NF	--	
	Levodopa/carbidopa/entacapone 200 mg/50 mg/200 mg tablets	NF	--	

QL = Quantity Limit; NF = Non-formulary; PL = Must be prescribed by Neurologist

● **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).

Dopamine precursor/dopamine decarboxylase inhibitor
<i>Levodopa/carbidopa (Sinemet, Sinemet CR, Parcopa, Rytary, Duopa)</i>

Carbidopa-levodopa disintegrating tablet (Parcopa), Carbidopa-levodopa tablet (Sinemet), Carbidopa ER-levodopa tablet (Sinemet CR)

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

- Non-Formulary:** Carbidopa ER-levodopa capsule (Rytary), Duopa (4.63 mg Carbidopa- 20 mg Levodopa per 1 ml) suspension

Anticholinergic Agents

Biperiden (Akinetone), Benztropine (Cogentine), Trihexyphenidyl (Artane)

- Non-Formulary:** Biperiden (Akinetone), Benztropine (Cogentine), Trihexyphenidyl (Artane)
- Other Notes:** Benztropine (Cogentine), Trihexyphenidyl (Artane) carved out to Fee for service

MAO-B inhibitors

Rasagiline mesylate (Azilect), Selegiline HCL (Zelapar, Eldepryl, Emsam)

Rasagiline mesylate (Azilect)

- Coverage Criteria:** Must be initiated by a neurologist.
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None

Selegiline HCL (Zelapar, Eldepryl)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Emsam 24 hr transdermal patches, Safinamide (Xadago)

Dopamine agonists

Apomorphine (Apokyn), Bromocriptine mesylate (Parlodel, Cycloset), Pramipexole Di-HCL (Mirapex, Mirapex ER), Ropinirole HCL (Requip, Requip XL), Rotigotine (Neupro)

Bromocriptine mesylate (Parlodel)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Cycloset, Apomorphine (Apokyn), Rotigotine (Neupro)

Pramipexole Di-HCL (Mirapex), Ropinirole HCL (Requip)

- Coverage Criteria:** None
- Limits:** 90 tablets per 30 days
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Pramipexole Di-HCL ER (Mirapex ER), Ropinirole HCL ER (Requip XL)

● CLINICAL JUSTIFICATION

HPSJ's Parkinson's management policy is based on recommendations by the *American Academy of Neurology*. In general, Parkinson's Disease can be effectively managed with carbidopa/levodopa (Sinemet), while dopamine agonists (bromocriptine, pramipexole, and ropinirole) and selegiline are less effective.¹ Additionally, there is insufficient evidence that sustained-release Sinemet offers a clinical advantage over immediate-release Sinemet in treatment of motor complications.¹⁻³ While first-line therapy with Sinemet is effective, progression of Parkinson's Disease leads to motor fluctuations (e.g., off time and dyskinesia). These can be effectively managed with entacapone and rasagiline.⁴ Alteration in dosing frequencies of Dopamine agonist or Levodopa is also used to manage motor fluctuations. According to a double-blind, randomized study investigating rotigotine vs. ropinirole vs. placebo in advanced PD patients, rotigotine showed similar efficacy to ropinirole, but rotigotine was associated with application site reactions.⁵ There is insufficient evidence that extended-release pramipexole and ropinirole provide a clinical advantage over their immediate-release counterparts.^{6,7} Therefore, HPSJ limits the use of rasagiline, extended-release pramipexole and ropinirole, rotigotine, and tolcapone. Although anticholinergic agents are used as initial therapy associated with Parkinson's disease, only few are FDA approved for Parkinson's disease.

☒ REFERENCES

1. American Academy of Neurology. Practice Parameter: Initiation of Treatment for Parkinson's Disease: An Evidence-Based Review. *Neurology*. 2002;58(1):11-17.
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4. American Academy of Neurology. Practice Parameter: Treatment of Parkinson Disease with Motor Fluctuations and Dyskinesia (An Evidence-Based Review). *Neurology*. 2006;66(7):983-995.
5. Mizuno Y, Nomoto M, Hasegawa K et al. Rotigotine vs. ropinirole in advanced stage Parkinson's disease: A double-blind study. *Parkinsonism & Related Disorders*. 2014;20(12):1388-1393.
6. Hametner EM, Seppi K, Poewe W. Role and clinical utility of pramipexole extended release in the treatment of early Parkinson's disease. *Clinical Interventions in Aging*. 2012;7:83-88.
7. Nashatizadeh MM, Lyons KE, Pahwa R. A review of ropinirole prolonged release in Parkinson's disease. *Clinical Interventions in Aging*. 2009;4:179-186.
8. Mirapex [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; Revised July 2016.
9. Requip [package insert]. Research Triangle Park, NC: GlaxoSmithKline; Revised September 2016.
10. Parkinson's disease medications for medical professionals. How is Parkinson's disease treated? Parkinson's Disease Clinic and Research Center University of California, San Francisco
11. Martin Paspe Cruz, Xadago (Safinamide) A Monoamine Oxidase B Inhibitor for the Adjunct Treatment of Motor Symptoms in Parkinson's Disease. [P.T.](#) 2017 Oct; 42(10): 622-624,637.
12. Xadago [Package insert]. Zambon SpA. 2017

● REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Dopamine Agonists in RLS 9-11-07.docx	9/2007	Allen Shek, PharmD
Update to Policy	Formulary Realignment 5-11.xlsx	5/2011	Allen Shek, PharmD
Update to Policy	Formulary Realignment PT 9-18-12.xlsx	9/2012	Allen Shek, PharmD
Update to Policy	HPSJ Coverage Policy – Neurological Disorders – Parkinson's Disease 2016-02.docx	02/2016	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Neurological Disorders – Parkinson's Disease 2017-02.docx	02/2017	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Neurological Disorders – Parkinson's Disease 2018-05.docx	5/2018	Johnathan Yeh, PharmD

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

☒ All antiparkinsonism medications not mentioned in this coverage policy are specifically carved out from Medi-Cal Managed Care Plans, and should be billed directly to Medi-Cal Fee-For-Service. The **Managed Medi-Cal Prescription Drug Carve-Out** list can be found at www.hpsj.com/medication-coverage-policies/ or www.hpsj.com/pharmacy. Please note that Medi-Cal FFS may require submission of a Treatment Authorization Request (TAR) to determine appropriateness of the treatment prior to coverage.