

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY	Parkinson's Disease	P&T DATE	5/11/2021
THERAPEUTIC CLASS	Neurological Disorders	REVIEW HISTORY	5/20, 5/19, 5/18, 2/17,
LOB AFFECTED	Medi-Cal	(MONTH/YEAR)	2/16, 9/12, 5/11, 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 2/2021)

Generic (Brand)	Strength & Dosage form	Formulary Limit	Cost per Rx	Notes	
Dopamine precursor/dopamine decarboxylase inhibitor					
Carbidopa (Lodosyn)	Carbidopa 25 mg tablets	NF			
Levodopa (Inbrija)	Levodopa (Inbrija) 42 mg capsules for inhalation	NF			
Levodopa/carbidopa (Sinemet, Sinemet CR, Parcopa, Rytary, Duopa)	Carbidopa 10 mg-levodopa 100 mg ODT	F	\$80.09		
	Carbidopa 10 mg-levodopa 100 mg tablet	F	\$12.04		
	Carbidopa 25 mg-levodopa 100 mg ODT	F	--		
	Carbidopa 25 mg-levodopa 100 mg tablet	F	\$13.38		
	Carbidopa 25 mg-levodopa 250 mg ODT	F	--		
	Carbidopa 25 mg-levodopa 250 mg tablet	F	\$19.89		
	Carbidopa extended-release (ER) 25 mg-levodopa 100 mg tablet	F	\$29.22		
	Carbidopa ER 50 mg-levodopa 200 mg tablet	F	\$23.34		
	Rytary ER 23.75 mg-95 mg capsule	NF	\$514.83		
	Rytary ER 36.25 mg-145 mg capsule	NF	\$922.54		
	Rytary ER 48.75 mg-195 mg capsule	NF	\$922.54		
	Rytary ER 61.25 mg-245 mg capsule	NF	--		
	Duopa suspension (4.63 mg Carbidopa- 20 mg Levodopa per 1 ml)	NF	--		
Anticholinergic Agents					
Biperiden (Akinetone)	Akinetone 2 mg tablet	NF	--		
Benztropine (Cogentine)	Benzotropine 0.5 mg tablet	NF	--	Carved out to fee for service	
	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	\$125.99		
Selegiline HCL (Zelapar, Eldepryl)	Selegiline 5 mg capsule	F	\$64.60		
	Selegiline 5 mg tablet	F	--		
	Zelapar 1.25 mg ODT	NF	--		
	Emsam 24 hr transdermal patches:				
	6 mg/24 h	NF	--		
	9 mg/24 h	NF	--		
12 mg/24 h	NF	--			
Safinamide (Xadago)	Xadago 50 mg tablet	NF	--		
	Xadago 100 mg tablet	NF	--		
Dopamine agonists					
Apomorphine (Apokyn)	Apokyn 30 mg/3 ml cartridge	NF	--		
	Kynmobi 10 mg sublingual tablets	NF	--		

Apomorphine (Kynmobi)	Kynmobi 15 mg sublingual tablets	NF	--	
	Kynmobi 20 mg sublingual tablets	NF	--	
	Kynmobi 25 mg sublingual tablets	NF	--	
	Kynmobi 30 mg sublingual tablets	NF	--	
	Kynmobi 10/15/20/25/30 mg sublingual titration kit	NF	--	
Amantadine (Gocovri; Osmolex ER)	Amantadine 100 mg capsule	NF	--	Carved out to fee for service
	Amantadine 100 mg tablet		--	
	Amantadine 50 mg/5 ml Syrup		--	
	Gocovri ER Capsules 68.5 mg		--	
	Gocovri ER Capsules 137 mg		--	
	Osmolex ER: 129 mg tablets		--	
	Osmolex ER: 193 mg tablets		--	
	Osmolex ER: 258 mg tablets		--	
Bromocriptine mesylate (Parlodel, Cycloset)	Bromocriptine 2.5 mg tablet	F	\$82.87	
	Bromocriptine 5 mg capsule	F	\$250.35	
	Cycloset 0.8 mg tablets	NF	--	
Pramipexole Di-HCL (Mirapex, Mirapex ER)	Pramipexole 0.125 mg tablet	QL	\$1.93	Restricted to 90 tablets per month.
	Pramipexole 0.25 mg tablet	QL	\$1.96	
	Pramipexole 0.5 mg tablet	QL	\$2.57	
	Pramipexole 0.75 mg tablet	QL	\$2.84	
	Pramipexole 1 mg tablet	QL	\$2.51	
	Pramipexole 1.5 mg tablet	QL	\$4.28	
	Pramipexole ER 0.375 mg tablet	NF	--	
	Pramipexole ER 0.75 mg tablet	NF	--	
	Pramipexole ER 1.5 mg tablet	NF	\$813.34	
	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	\$3.00	Restricted to 90 tablets per month.
	Ropinirole 0.5 mg tablet	QL	\$2.27	
	Ropinirole 1 mg tablet	QL	\$2.95	
	Ropinirole 2 mg tablet	QL	\$2.74	
	Ropinirole 3 mg tablet	QL	\$3.22	
	Ropinirole 4 mg tablet	QL	\$4.19	
	Ropinirole 5 mg tablet	QL	\$4.07	
	Ropinirole HCL ER 2 mg tablet	NF	--	
	Ropinirole HCL ER 4 mg tablet	NF	--	
	Ropinirole HCL ER 6 mg tablet	NF	--	
	Ropinirole HCL ER 8 mg tablet	NF	--	
Ropinirole HCL ER 12 mg tablet	NF	--		
Rotigotine (Neupro)	Neupro 1 mg/24 hr patch	NF	--	
	Neupro 2 mg/24 hr patch	NF	--	
	Neupro 3 mg/24 hr patch	NF	--	
	Neupro 4 mg/24 hr patch	NF	\$4.19--	
	Neupro 6 mg/24 hr patch	NF	--	
	Neupro 8 mg/24 hr patch	NF	--	
COMT inhibitors				
Entacapone (Comtan)	Entacapone 200 mg tablet	NF	\$58.76	Maximum of 8 tablets per day
Tolcapone (Tasmar)	Tolcapone 100 mg tablet	NF	--	
Opicapone (Ongentys)	Ongentys 25 mg tablets	NF	--	
	Ongentys 50 mg tablets	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	--	
Adenosine A2A receptor antagonist				
Istradefylline (Nourianz)	Nourianz 20 mg tablets		--	PA required. Reserved for patients experiencing at least 2 hours of "off" time per day despite treatment. Patients must have tried and failed treatment with dopamine agonists and COMPT inhibitors for "off" symptoms for at least four weeks.
	Nourianz 40 mg tablets	F	--	

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

Levodopa/carbidopa (Sinemet, Sinemet CR, Parcopa, Rytary, Duopa), Carbidopa (Lodosyn)

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, Carbidopa (Lodosyn), Inbrija (Levodopa)

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), Safinamide (Xadago)

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, Kynmobi), 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, Kynmobi), 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)

COMPT inhibitors

Entacapone (Comtan), Tolcapone (Tasmar), Opicapone (Ongentys)

Entacapone (Comtan)

- Coverage Criteria:** None
- Limits:** Maximum of 8 tablets per day
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Tolcapone (Tasmar), Opicapone (Ongentys)

Adenosine A2A receptor antagonist

Nourianz (istradefylline)

Nourianz (istradefylline)

- Coverage Criteria:** Reserved for patients experiencing at least 2 hours of “off” time per day despite treatment. Patients must have tried and failed treatment with dopamine agonists and COMT inhibitors for “off” symptoms for at least four weeks.
- Limits:** Maximum of 1 tablet per day.
- Required Information for Approval:** Chart note documentation of treatment failure with Dopamine agonist and COMT inhibitors
- Other Notes:** None

● **CLINICAL JUSTIFICATION**

HPSJ’s Parkinson’s management policy is based on recommendations by the *American Academy of Neurology*. Either Levodopa or non-ergot dopamine agonists (DA) can be used to initiate symptomatic therapy.¹⁴ selegiline are less effective.^{1,14} 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**

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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.
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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.
13. Inbrija Package insert.
14. J. M. Miyasaki, W. Martin, O. Suchowersky, W. J. Weiner, A. E. Lang. Practice parameter: Initiation of treatment for Parkinson's disease: An evidence-based review Report of the Quality Standards Subcommittee of the American Academy of Neurology. January 08, 2002; 58 (1).
15. NOURIANZ™ (istradefylline) package insert.
16. KYNMOBI™ (apomorphine HCl) package insert.
17. ONGENTYS™ (opicapone) package insert.

● **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
Update to Policy	HPSJ Coverage Policy – Neurological Disorders – Parkinson's Disease 2019-05.docx	5/2019	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy – Neurological Disorders – Parkinson's Disease 2019-05.docx	5/2019	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy – Neurological Disorders – Parkinson's Disease.docx	5/2020	Matthew Garrett, PharmD
Update to Policy	Parkinson's Disease	5/2021	Matthew Garrett, 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.