

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY:	Fibromyalgia	P&T DATE:	5/9/2017
CLASS:	Pain Management	REVIEW HISTORY	9/15, 5/14, 11/12, 9/12,
LOB:	Medi-Cal	(MONTH/YEAR)	11/09, 11/06, 9/06

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

Fibromyalgia is a chronic pain disorder that leads to inflammation, widespread pain, fatigue, and sleep disruption. The symptoms are vague, making fibromyalgia challenging to diagnose. It wasn't until the last 30 years that fibromyalgia was recognized by the American Medical Association as a medical condition. Certain antidepressants, anticonvulsants, muscle relaxants, and analgesic agents are used to manage fibromyalgia. This review will examine the treatment guidelines of fibromyalgia and the currently available pharmacologic agents and their coverage criteria.

Table 1: Available Fibromyalgia Agents (Current as of 4/2017)

Formulary Agents					
Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Fml Limits	Avg. Cost per Rx	Notes
Antidepressants	Amitriptyline (Elavil)	10 mg tablet	--	\$4.98	Avoid use in members over 65 years old
		25 mg tablet	--	\$8.79	
		50 mg tablet	--	\$16.52	
		75 mg tablet	--	\$27.42	
		100 mg tablet	--	\$34.44	
	Clomipramine (Anafranil)	25 mg capsule	NF	\$440.86	Avoid use in members over 65 years old
		50 mg capsule	NF	\$477.78	
		75 mg capsule	NF	\$245.27	
	Desipramine (Norpramin)	10 mg tablet	--	\$52.49	Avoid use in members over 65 years old
		25 mg tablet	--	\$4.53	
		50 mg tablet	--	\$72.41	
		75 mg tablet	--	\$30.91	
		100 mg tablet	--	\$45.70	
	Doxepin (Sinqvan)	Silenor 3 mg tablet	NF	--	Avoid use in members over 65 years old
		Silenor 6 mg tablet	NF	--	
		10 mg/5 ml solution	--	\$6.48	Avoid use in members over 65 years old
		10 mg capsule	--	\$18.85	
		25 mg capsule	--	\$22.30	
		50 mg capsule	--	\$34.25	
		75 mg capsule	--	\$35.78	
	100 mg capsule	--	\$56.34		
	150 mg capsule	--	\$22.16		
	Imipramine (Tofranil)	10 mg tablet	--	\$6.34	Avoid use in members over 65 years old
		25 mg tablet	--	\$10.01	
		50 mg tablet	--	\$10.31	
	Nortriptyline (Pamelor)	10 mg/5 ml oral concentrate	--	\$188.77	
		10 mg capsule	--	\$7.06	
25 mg capsule		--	\$7.96		
50 mg capsule		--	\$7.06		
Citalopram (Celexa)	75 mg capsule	--	\$9.55		
	10 mg/5 ml solution	--	\$6.78		
	10 mg tablet	--	\$1.42		
	20 mg tablet	--	\$1.45		
		40 mg tablet	--	\$1.46	

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Fml Limits	Avg. Cost per Rx	Notes
Antidepressants	Escitalopram (Lexapro)	5 mg/5 ml solution	--	\$122.03	
		5 mg tablet	--	\$4.86	
		10 mg tablet	--	\$4.68	
		20 mg tablet	--	\$5.24	
	Fluoxetine (Prozac)	20 mg/5 ml solution	--	\$26.57	Long half-life: consider in patients who have partial non-compliance issues.
		10 mg capsule	--	\$1.92	
		20 mg capsule	--	\$1.10	
		40 mg capsule	--	\$9.78	
		90 mg DR capsule	NF	--	
		10 mg tablet	NF	\$9.46	Formulary alternative = 10 mg capsule
		20 mg tablet	NF	--	Formulary alternative = 20 mg capsule
	Fluvoxamine (Luvox)	25 mg tablet	--	\$16.94	
		50 mg tablet	--	\$26.60	
		100 mg tablet	--	\$20.25	
		100 mg ER capsule	NF	--	Formulary alternative = fluvoxamine tablets
		150 mg ER capsule	NF	\$218.59	
	Paroxetine hydrochloride (Paxil/Paxil CR)	Paxil 10 mg/5 ml suspension	--	\$198.75	
		10 mg tablet	QL	\$3.44	Limit 30 per 30 days
		20 mg tablet	QL	\$3.57	
		30 mg tablet	QL	\$7.87	
		40 mg tablet	QL	\$4.97	
		12.5 mg ER tablet	PA; QL	\$102.76	Reserved for failure of 2 months of dose-optimized paroxetine. Limit 30 per 30 days.
		25 mg ER tablet	PA; QL	\$118.81	
		37.5 mg ER tablet	PA; QL	\$106.88	
	Paroxetine mesylate (Brisdelle, Pexeva)	7.5 mg capsule	NF	--	Formulary alternative = Paroxetine HCl
		30 mg tablet	NF	--	
		40 mg tablet	NF	--	
	Sertraline (Zoloft)	20 mg/ml oral concentrate	QL	\$67.05	Limit 300 ml per 30 days
		25 mg tablet	QL	\$1.32	Limit 60 per 30 days
		50 mg tablet	QL	\$2.58	
		100 mg tablet	QL	\$3.09	
	Venlafaxine (Effexor/Effexor XR)	25 mg tablet	QL	\$19.86	Limit 90 per 30 days
		37.5 mg tablet	QL	\$20.12	Limit 90 per 30 days
		50 mg tablet	QL	\$19.83	Limit 90 per 30 days
		75 mg tablet	QL	\$18.84	Limit 90 per 30 days
		100 mg tablet	QL	\$10.84	Limit 90 per 30 days
		37.5 mg XR capsule	QL	\$6.31	Limit 60 per 30 days
		75 mg XR capsule	QL	\$8.08	Limit 60 per 30 days
		150 mg XR capsule	QL	\$7.93	Limit 60 per 30 days
		37.5 mg XR tablet	NF	--	Formulary alternative = 37.5 mg XR capsule
		75 mg XR tablet	NF	--	Formulary alternative = 75 mg XR capsule
		150 mg XR tablet	NF	--	Formulary alternative = 150 mg XR capsule
	Duloxetine (Cymbalta)	20 mg DR capsule	PA; QL	\$39.75	Limit 60 capsules per 30 days
		30 mg DR capsule	PA; QL	\$46.47	
		40 mg DR capsule	NF	--	Formulary alternative = Two 20 mg XR capsules
		60 mg DR capsule	PA; QL	\$14.59	Limit 30 capsules per 30 days

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Fml Limits	Avg. Cost per Rx	Notes
Antidepressants	Desvenlafaxine (Khedezla)	50 mg ER tablet	NF	--	Formulary alternative = Desvenlafaxine succinate
		100 mg ER tablet	NF	--	
	Desvenlafaxine fumarate	50 mg ER tablet	NF	--	
		100 mg ER tablet	NF	--	
	Desvenlafaxine succinate (Pristiq)	25 mg ER tablet	NF	\$29.84	
		50 mg ER tablet	PA	\$45.44	Reserved for patients diagnosed with MDD who have failed dose optimized venlafaxine and duloxetine
	100 mg ER tablet	PA	\$60.05		
	Milnacipran (Savella)	12.5 mg tablet	PA	--	Reserved for treatment failure of dose-optimized Venlafaxine for at least 2 months
		25 mg tablet	PA	\$45.08	
		50 mg tablet	PA	\$278.83	
		100 mg tablet	PA	\$233.09	
		12.5 mg-25 mg-50 mg titration pack	NF	\$253.92	
	Levomilnacipran (Fetzima)	20 mg ER capsule	PA	\$318.65	Reserved for treatment failure of dose optimized venlafaxine and duloxetine for 2 months each
		40 mg ER capsule	PA	\$316.90	
80 mg ER capsule		PA	\$304.83		
120 mg ER capsule		PA	\$319.62		
20 mg-40 mg titration pack		NF	\$294.87		
Anticonvulsants	Gabapentin (Neurontin)	100 mg capsule	-	\$3.44	Reserved for treatment failure to 2 months each of a tricyclic antidepressant AND Gabapentin
		300 mg capsule	-	\$5.50	
		400 mg capsule	-	\$4.68	
		600 mg capsule	-	\$15.06	
		800 mg capsule	-	\$50.72	
		250 mg/5 ml solution	-	\$34.00	
	Pregabalin (Lyrica)	25 mg capsule	PA	\$415.42	
		50 mg capsule	PA	\$429.50	
		75 mg capsule	PA	\$369.33	
		100 mg capsule	PA	\$427.75	
		150 mg capsule	PA	\$429.17	
		200 mg capsule	PA	\$409.95	
		225 mg capsule	PA	\$371.16	
300mg capsule	PA	\$362.13			
Muscle Relaxants	Cyclobenzaprine (Flexiril)	5 mg tablet	-	\$5.00	
		10 mg tablet	-	\$2.59	
NSAIDs	Aspirin	325mg tablet	-	\$0.12	
		325 mg DR tablet	-	\$0.20	
	Celecoxib (Celebrex)	50mg capsule	ST; PA	\$44.13	Reserved as step therapy to treatment failure of 3 formulary NSAIDs, including meloxicam or etodolac
		100 mg capsule		\$82.02	
		200 mg capsule		\$96.00	
		400 mg capsule	NF	--	
	Diclofenac (Zorvolex)	18 mg capsule	NF	\$289.37	
		35 mg capsule	NF	--	
	Diclofenac Potassium (Zipsor, Cataflam)	Zipsor 25 mg capsule	NF	--	
		50 mg tablet	-	\$27.60	
	Diclofenac Sodium DR, XR	25 mg DR tablet	NF	\$44.62	
		50 mg DR tablet	-	\$10.48	
75 mg DR tablet		-	\$6.01		
100 mg DR tablet		-	\$26.56	Diclofenac XR 100mg (Voltaren XR) is dosed once daily	

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Fml Limits	Avg. Cost per Rx	Notes
NSAIDs	Etodolac (Lodine)	200 mg capsule	-	\$50.36	
		300 mg capsule	-	\$65.11	
		400 mg tablet	-	\$39.48	
		500 mg tablet	-	\$43.36	
	Ibuprofen (Motrin)	100 mg tablets/ chewable tablets	-	\$5.72	Ibuprofen 100mg is available as tablets and chewable tablets
		200 mg tablet	-	\$0.35	
		400 mg tablet	-	\$1.66	
		600 mg tablet	-	\$2.28	
		800 mg tablet	-	\$3.44	
		100 mg/5 ml suspension	-	\$5.66	
		50 mg/1.25 ml suspension drops	-	\$6.05	
	Indomethacin (Indocin)	25 mg capsule	-	\$9.08	
		50 mg capsule	-	\$12.63	
		75 mg ER capsule	-	\$93.28	
		50 mg rectal suppository	-	--	
		25 mg/5 ml oral suspension	-	\$411.82	
	Ketoprofen	200 mg ER capsule	NF	\$98.75	
	Ketorolac	10 mg tablet	NF	\$14.69	
	Meloxicam (Mobic)	7.5 mg tablet	QL	\$1.57	Limit 2 tablets/day
		15 mg tablet	QL	\$3.01	Limit 1 tablet/day
	Nabumetone (Relafen)	500 mg tablet	-	\$25.37	
		750 mg tablet	-	\$23.09	
	Naproxen (Naprosyn, EC-Naproxen)	250 mg tablet	-	\$2.14	
		375 mg tablet	-	\$3.27	
		500 mg tablet	-	\$4.15	
		500 mg DR tablet	-	\$26.02	
		125 mg/5 ml suspension	-	\$59.65	
Piroxicam (Feldene)	10 mg capsule	NF	--		
	20 mg capsule	NF	\$29.89		
Sulindac (Clinoril)	150 mg tablet	-	\$8.31		
	200 mg tablet	-	\$11.11		

PA = Prior Authorization Required; QL = Quantity Limit; NF = Non-Formulary

⊕ 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 HSPJ Medical Review Guidelines (UM06).

Antidepressants

Amitriptyline (Elavil), Nortriptyline (Pamelor), Imipramine (Tofranil), Doxepin (Sinequan), Fluoxetine capsules (Prozac), Fluvoxamine tablets, Citalopram (Celexa), Escitalopram (Lexapro)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Clomipramine (Anafranil), Doxepin (Silenor), Fluoxetine tablets, Fluoxetine DR capsules, Fluvoxamine capsules,

Sertraline (Zoloft)

- Coverage Criteria:** None
- Limits:** 60 tablets per month
- Required Information for Approval:** N/A
- Other Notes:** None

Venlafaxine (Effexor IR/XR)

- Coverage Criteria:** None
- Limits:** 3 tablets/XR capsules per day
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Venlafaxine XR tablets

Paroxetine HCl IR/CR (Paxil)

- Coverage Criteria:**
 - Paroxetine IR—None
 - Paroxetine CR—Reserved for treatment failure/intolerance to Paroxetine IR for at least 2 months
- Limits:** 1 tablet per day
- Required Information for Approval:** Paroxetine CR—prescription history showing at least 2 consecutive months of dose-optimized Paroxetine IR
- Other Notes:** None
- Non-Formulary:** Paroxetine mesylate

Duloxetine (Cymbalta), Milnacipran (Savella)

- Coverage Criteria:** Reserved for treatment failure of dose-optimized Venlafaxine IR/XR for 2 months.
- Limits:**
 - Duloxetine 20mg & 30mg capsules: Limit 2 capsules per day
 - Duloxetine 60mg capsule: Limit 1 capsule per day
- Required Information for Approval:** Prescription history showing 2 consecutive fills of Venlafaxine (doses >150mg/day).
- Other Notes:** There is no evidence that Duloxetine dosages of more than 60 mg/day confer additional benefit, even in patients who do not respond to a 60 mg dose, and higher doses are associated with a higher rate of adverse reactions..

Desvenlafaxine (Pristiq), Levomilnacipran (Fetzima)

- Coverage Criteria:** Reserved for patients with treatment failure of dose-optimized Venlafaxine IR/XR and Duloxetine for 2 months each.
- Limits:** None
- Required Information for Approval:** Prescription history showing 2 consecutive fills of Venlafaxine (doses >150mg/day) and 2 consecutive fills of Duloxetine (60mg/day).
- Other Notes:** None
- Non-Formulary:** Desvenlafaxine (Khedezla), Desvenlafaxine fumarate, Desvenlafaxine 25 mg tablets

Anticonvulsants

Gabapentin (Neurontin)

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

Pregabalin (Lyrica)

- Coverage Criteria:** Lyrica is step therapy to treatment failure of a tricyclic antidepressant (eg Amitriptyline, Nortriptyline, etc) AND Gabapentin at doses greater than or equal to 1800mg/day for at least 8 weeks.
- Limits:** None
- Required Information for Approval:** Prescription history showing at least 2 consecutive fills of gabapentin (≥ 1800 mg/day) AND 2 consecutive fills of dose-optimized tricyclic antidepressants.
- Other Notes:** None

Muscle Relaxant

Cyclobenzaprine (Flexeril)

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

Oral Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Celecoxib (Celebrex), Diclofenac Sodium, Diclofenac Potassium (Cataflam), Etodolac (Lodine), Ibuprofen (Motrin), Indomethacin (Indocin), Meloxicam (Mobic), Nabumetone, Naproxen (Naprosyn), Sulindac (Clinoril)

Celecoxib (Celebrex)

- Coverage Criteria:** Celebrex is step therapy to 3 formulary NSAIDs, including Meloxicam or Etodolac, unless patient is at high risk of gastrointestinal events. High risk factors include age >65 , previous history of gastroduodenal ulcer, gastrointestinal bleed/perforation; concomitant use of anticoagulants or long term corticosteroids.
- Limits:** None
- Required Information for Approval:** Drug refill history showing fills of two 3 formulary NSAIDs, one of them being Meloxicam or Etodolac or documentation that member has a history of GI bleeds/ulcers or that member is chronically using anticoagulants/corticosteroids.
- Other Notes:** None

Diclofenac Sodium, Diclofenac Potassium (Cataflam), Etodolac (Lodine), Ibuprofen (Motrin), Indomethacin (Indocin), Meloxicam (Mobic), Nabumetone, Naproxen (Naprosyn), Sulindac (Clinoril)

- Coverage Criteria:** None
- Limits:** None
 - Meloxicam 7.5mg—Limit 2 tablets per day
 - Meloxicam 15mg—Limit 1 tablet per day
- Required Information for Approval:** N/A
- Other Notes:** None

CLINICAL JUSTIFICATION

Exercise is recommended as the first step to managing fibromyalgia and should be continued even in patients on pharmacologic therapies.¹ For patients requiring pharmacologic therapies, tricyclic antidepressants (e.g. Amitriptyline) are usually first-line and prescribed at low doses to prevent over-sedation. An indirect comparison of Amitriptyline to Duloxetine or Milnacipran showed Amitriptyline was superior to the latter two—improving pain relief, fatigue, and sleep disturbance.² For patients who do not respond to tricyclic antidepressants, Cyclobenzaprine may be considered as an alternative due to its structural similarities to tricyclic antidepressants. For patients suffering fatigue due to fibromyalgia, Venlafaxine, Duloxetine, Milnacipran, or Selective Serotonin Reuptake Inhibitors (SSRIs) may be preferred. Venlafaxine, while not indicated for treatment of fibromyalgia, is a Serotonin-Norepinephrine Reuptake Inhibitor (SNRI) just as Duloxetine and has evidence to support its use in fibromyalgia and pain when used at higher doses. For patients who difficulty sleeping at night, Gabapentin and Pregabalin may be helpful.³ NSAIDs may be used to supplement antidepressants, and GABA analogs for pain relief.⁴

REFERENCES

1. Busch AJ, Schachter CL, Overend TJ, Peloso PM, Barber KA. Exercise for fibromyalgia: a systemic review. *J Rheumatol*. 2008; 35(6): 1130.
2. Häuser W, Petzke F, Üçeyler N, Sommer C. Comparative efficacy and acceptability of amitriptyline, duloxetine and milnacipran in fibromyalgia syndrome: a systematic review with meta-analysis. *Rheumatology (Oxford)*. 2011; 50(3): 532.
3. Häuser W, Wolfe F, Tölle T, Üçeyler N, Sommer C. The role of antidepressants in the management of fibromyalgia syndrome: a systematic review and meta-analysis. *CNS Drugs*. 2012; 26(4): 297-307.
4. Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. *JAMA*. 2004; 292(19):2388.
5. Macfarlane GJ, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis*. 2017;76:318–328.
6. Fitzcharles MA, et al. Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome. *Canadian Rheumatology Association Societe Canadienne de Rheumatologie*. 2012;1-45.
7. Tzellos TG, et al. Gabapentin and pregabalin in the treatment of fibromyalgia: a systematic review and a meta-analysis. *J Clin Pharm Ther*. 2010;35(6):639-56.
8. Hauser W, Bernardy K, Uceyler N, Sommer C. Treatment of fibromyalgia syndrome with gabapentin and pregabalin--a meta-analysis of randomized controlled trials. *Pain*. 2009;145(1-2):69-81.
9. Moore R, Wiffen PJ, Derry S, Rice ASC. Gabapentin for chronic neuropathic pain and fibromyalgia in adults. *Cochrane Database of Systematic Reviews* 2014, Issue 4. Art. No.: CD007938. DOI: 10.1002/14651858.CD007938.pub3

REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Lyrica 9-06.doc	9/2006	Allen Shek, PharmD
Updated Policy	Antidepressants SSRI & SNRI Review 11-06.doc	11/2006	Allen Shek, PharmD
Updated Policy	Fibromyalgia review_11-17-09.doc	11/2009	Allen Shek, PharmD
Updated Policy	Savella Review 9-18-2012	9/2012	Allen Shek, PharmD
Updated Policy	Savella Review 11-20-2012	11/2012	Allen Shek, PharmD
Updated Policy	Antidepressant Class Review 2014-05-29.docx	5/2014	Jonathan Szkotak, PharmD
Updated Policy	HPSJ Coverage Policy – Pain – Fibromyalgia 2015-09.docx	9/2015	Jonathan Szkotak, PharmD
Updated Policy	HPSJ Coverage Policy – Pain – Fibromyalgia 2017-05.docx	5/2017	Johnathan Yeh, PharmD

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