

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY	Non-Opioids	LAST REVIEW	12/11/2018
THERAPEUTIC CLASS	Pain Management	REVIEW HISTORY (MONTH/YEAR)	5/17, 2/16, 9/15, 5/15, 5/14, 11/12, 9/12, 11/09, 11/06, 9/06
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

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are frequently used to manage mild to moderate nociceptive pain. NSAIDs may be used in acute or chronic pain, but patients older than 65 years or who have a history of gastrointestinal bleeds may want to consider topical NSAID therapy over oral formulations in chronic pain management. Musculoskeletal relaxants have also demonstrated some efficacy for management of chronic back pain. For neuropathic pain, the mainstay of treatment are tricyclic antidepressants, gabapentin, and SNRIs. Patients with neuropathic pain respond poorly to opioids and NSAIDs. Topical therapies for neuropathic pain include capsaicin cream and various topical lidocaine formulations. Fibromyalgia is a type of neuropathic pain that is 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.

The below criteria, limits, and requirements are in place to ensure appropriate use of non-opioid agents for use in managing pain.

Table 1: Available Systemic Non-Opioid Agents (Current as of 12/2018)

Oral Agents					
Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Formulary Limits	Cost per Rx	Notes
Non-Salicylate Analgesics	Acetaminophen (Tylenol)	325 mg tablet	-	\$0.29	Max daily limit = 4,000mg. For patients with liver disease max daily limit = 2,000mg.
		500 mg tablet	-	\$0.34	
		650 mg ER tablet	-	\$3.20	
		500 mg capsule	-	\$2.29	
		80 mg chewable tablet	-	\$1.59	
		160 mg chewable tablet	-	\$3.84	
		80 mg dissolvable tablet	-	\$0.76	
		160 mg dissolvable tablet	-	\$0.93	
		160 mg/5 ml elixir	-	\$0.90	
		160 mg/5 ml liquid	-	\$0.95	
		160 mg/5 ml solution	-	\$29.69	
		160 mg/5 ml suspension	-	\$2.15	
		500 mg/15 ml liquid	-	\$2.89	
		80 mg/ml suspension drops	-	--	
		100 mg/ml suspension drops	-	--	
		80 mg/0.8 ml drops	-	\$4.87	
100 mg/ml drops	-	--			
80 mg suppository	-	\$9.62			
120 mg suppository	-	\$4.82			
325 mg suppository	-	\$6.79			
650 mg suppository	-	\$8.18			

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Formulary Limits	Cost per Rx	Notes
Salicylate Analgesics	Salsalate (Disalcid)	500 mg tablet	-	\$54.93	
		750 mg tablet	-	\$88.06	
NSAIDs	Aspirin	325 mg tablet	-	\$0.13	
		325 mg DR tablet	-	\$0.23	
	Celecoxib (Celebrex)	50 mg capsule	PA	--	Reserved as step therapy to treatment failure of 3 formulary NSAIDs, including meloxicam or etodolac
		100 mg capsule		\$26.83	
		200 mg capsule		\$75.92	
		400 mg capsule	NF	\$79.87	
	Diclofenac (Zorvolex)	18 mg capsule	NF	--	
		35 mg capsule	NF	--	
	Diclofenac Potassium (Zipsor, Cataflam)	Zipsor 25 mg capsule	NF	--	
		50 mg tablet	-	\$23.25	
	Diclofenac Sodium DR, XR	25 mg DR tablet	NF	\$44.62	
		50 mg DR tablet	-	\$9.38	
		75 mg DR tablet	-	\$6.01	
		100 mg DR tablet	-	\$33.74	Diclofenac XR 100mg (Voltaren XR) is dosed once daily
	Etodolac (Lodine)	200 mg capsule	-	\$37.95	
		300 mg capsule	-	\$52.55	
		400 mg tablet	-	\$38.07	
		500 mg tablet	-	\$43.34	
	Ibuprofen (Motrin)	100 mg tablets/chewable tablets	-	\$9.53	Ibuprofen 100mg is available as tablets and chewable tablets
		200 mg tablet	-	\$0.38	
		400 mg tablet	-	\$1.36	
		600 mg tablet	-	\$1.82	
		800 mg tablet	-	\$3.12	
		100 mg/5 ml suspension	-	\$4.96	
	Indomethacin (Indocin)	50 mg/1.25 ml suspension drops	-	\$6.18	
		25 mg capsule	-	\$9.39	
		50 mg capsule	-	\$10.75	
		75 mg ER capsule	-	\$58.64	
	Ketoprofen	50 mg rectal suppository	-	--	
		25 mg/5 ml oral suspension	NF	--	
	Ketorolac	200 mg ER capsule	NF	--	
	Meloxicam (Mobic)	10 mg tablet	NF	\$19.91	
7.5 mg tablet		QL	\$1.52	Limit 2 tablets/day	
Nabumetone	15 mg tablet	QL	\$1.33	Limit 1 tablet/day	
	500 mg tablet	-	\$11.26		
Naproxen (Naprosyn, EC-Naproxen)	750 mg tablet	-	\$11.50		
	250 mg tablet	-	\$1.95		
	375 mg tablet	-	\$3.10		
	500 mg tablet	-	\$13.91		
	500 mg DR tablet	-	\$30.09		
	550 mg tablet	-	\$10.31		
Piroxicam (Feldene)	125 mg/5 ml suspension	NF	\$231.40		
	10 mg capsule	NF	--		
Sulindac (Clinoril)	20 mg capsule	NF	--		
	150 mg tablet	-	\$6.97		
		200 mg tablet	-	\$8.70	

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Formulary Limits	Cost per Rx	Notes
Skeletal Muscle Relaxants	Baclofen (Lioresal)	10 mg tablet	-	\$8.00	
		20 mg tablet	-	\$14.33	
	Carisoprodol (Soma)	250 mg tablet	NF	\$63.00	
		350 mg tablet	NF	\$6.66	
	Chlorzoxazone (Parafon Forte, Lorzone)	Lorzone 375 mg tablet	NF	--	
		500 mg tablet	NF	--	
		Lorzone 750 mg tablet	NF	--	
	Cyclobenzaprine (Flexeril)	5 mg tablet	-	\$5.00	
		10 mg tablet	-	\$2.59	
	Dantrolene Sodium (Dantrium)	25 mg capsule	NF	\$153.40	
		50 mg capsule	NF	\$144.97	
		100 mg capsule	NF	--	
	Metaxalone (Skelaxin)	800 mg tablet	NF	\$313.49	
	Methocarbamol (Robaxin)	500 mg tablet	-	\$8.17	
750 mg tablet		-	\$3.44		
Orphenadrine (Norflex)	100 mg XR tablet	NF	--		
Tizanidine (Zanaflex)	2 mg tablet	-	\$16.54	Only tablets are formulary. Capsules are non-formulary.	
	4 mg tablet	-	\$22.44		
Antidepressants	Amitriptyline (Elavil)	10 mg tablet	--	\$4.64	Avoid use in members over 65 years old
		25 mg tablet	--	\$7.14	
		50 mg tablet	--	\$10.25	
		75 mg tablet	--	\$25.78	
		100 mg tablet	--	\$25.34	
		150 mg tablet	--	\$48.83	
	Clomipramine (Anafranil)	25 mg capsule	NF	\$193.51	Avoid use in members over 65 years old
		50 mg capsule	NF	\$163.35	
		75 mg capsule	NF	\$561.62	
	Desipramine (Norpramin)	10 mg tablet	--	\$39.93	Avoid use in members over 65 years old
		25 mg tablet	--	\$44.18	
		50 mg tablet	--	\$59.26	
		75 mg tablet	--	--	
		100 mg tablet	--	\$68.73	
		150 mg tablet	--	--	
	Doxepin (Siquan)	Silenor 3 mg tablet	NF	--	Avoid use in members over 65 years old
		Silenor 6 mg tablet	NF	--	
		10 mg/5 ml solution	--	\$2.12	Avoid use in members over 65 years old
		10 mg capsule	--	\$15.10	
		25 mg capsule	--	\$21.31	
		50 mg capsule	--	\$31.14	
		75 mg capsule	--	\$44.68	
		100 mg capsule	--	\$59.68	
150 mg capsule	--	\$19.46			
Imipramine (Tofranil)	10 mg tablet	--	\$5.98	Avoid use in members over 65 years old	
	25 mg tablet	--	\$8.37		
	50 mg tablet	--	\$9.97		
Nortriptyline (Pamelor)	10 mg/5 ml oral concentrate	PA; QL	\$55.90	Reserved for inability to consume capsules or tablets my mouth.	
	10 mg capsule	--	\$6.58		
	25 mg capsule	--	\$8.48		
	50 mg capsule	--	\$7.00		
	75 mg capsule	--	\$9.76		
Citalopram (Celexa)	10 mg/5 ml solution	PA; QL	\$12.87	Reserved for inability to consume capsules or tablets my mouth.	
	10 mg tablet	--	\$1.06		
	20 mg tablet	--	\$1.39		
	40 mg tablet	--	\$1.43		

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Formulary Limits	Avg. Cost per Rx	Notes
Antidepressants (cont.)	Escitalopram (Lexapro)	5 mg/5 ml solution	PA; QL	\$106.67	Reserved for inability to consume capsules or tablets my mouth.
		5 mg tablet	--	\$4.56	
		10 mg tablet	--	\$4.11	
		20 mg tablet	--	\$5.02	
	Fluoxetine (Prozac)	20 mg/5 ml solution	PA; QL	\$23.88	Reserved for inability to consume capsules or tablets my mouth. Long half-life: consider in patients who have partial non-compliance issues.
		10 mg capsule	--	\$1.19	
		20 mg capsule	--	\$1.05	
		40 mg capsule	--	\$5.85	
		90 mg DR capsule	NF	--	Formulary alternative = 10mg, 20mg, 40mg capsules
		10 mg tablet	NF	\$19.31	
		20 mg tablet	NF	--	
	Fluvoxamine (Luvox)	60 mg tablet	NF	--	
		25 mg tablet	--	\$20.39	
		50 mg tablet	--	\$25.48	
		100 mg tablet	--	\$21.59	
		100 mg ER capsule	NF	--	Formulary alternative = fluvoxamine tablets
	Paroxetine hydrochloride (Paxil/Paxil CR)	150 mg ER capsule	NF	\$218.59	
		Paxil 10 mg/5 ml suspension	PA; QL	\$214.74	Reserved for inability to consume capsules or tablets my mouth.
		10 mg tablet	QL	\$3.43	Limit 30 per 30 days
		20 mg tablet	QL	\$2.82	
		30 mg tablet	QL	\$6.59	
		40 mg tablet	QL	\$4.83	
		12.5 mg ER tablet	PA; QL	\$101.14	Reserved for failure of 2 months of dose-optimized paroxetine. Limit 30 per 30 days.
		25 mg ER tablet	PA; QL	\$139.78	
	37.5 mg ER tablet	PA; QL	\$58.09		
	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	PA; QL	\$54.84	Reserved for inability to consume capsules or tablets my mouth. Limit 300 ml per 30 days.
		25 mg tablet	QL	\$1.34	Limit 60 per 30 days
		50 mg tablet	QL	\$2.44	
		100 mg tablet	QL	\$3.04	
	Venlafaxine (Effexor/Effexor XR)	25 mg tablet	QL	\$14.56	Limit 90 per 30 days
		37.5 mg tablet	QL	\$12.17	Limit 90 per 30 days
		50 mg tablet	QL	\$17.42	Limit 90 per 30 days
		75 mg tablet	QL	\$13.12	Limit 90 per 30 days
		100 mg tablet	QL	\$4.40	Limit 90 per 30 days
		37.5 mg XR capsule	QL	\$6.26	Limit 60 per 30 days
		75 mg XR capsule	QL	\$7.37	Limit 60 per 30 days
		150 mg XR capsule	QL	\$7.64	Limit 60 per 30 days
		37.5 mg XR tablet	NF	\$15.76	Formulary alternative = 37.5 mg XR capsule
		75 mg XR tablet	NF	--	Formulary alternative = 75 mg XR capsule
		150 mg XR tablet	NF	\$15.83	Formulary alternative = 150 mg XR capsule
	Duloxetine (Cymbalta)	225 mg XR tablet	NF	\$197.36	Formulary alternative = 150 mg + 75 mg XR capsule
20 mg DR capsule		QL	\$52.98	Limit 60 capsules per 30 days	
30 mg DR capsule		QL	\$37.93		
40 mg DR capsule		NF	--	Formulary alternative = Two 20 mg XR capsules	
	60 mg DR capsule	QL	\$23.98	Limit 30 capsules per 30 days	

Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Fml Limits	Avg. Cost per Rx	Notes
Antidepressants (cont.)	Desvenlafaxine (Khedezla)	50 mg ER tablet	NF	--	Formulary alternative = Desvenlafaxine succinate 50mg, 100mg ER tablets
		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	\$42.80	Reserved for patients diagnosed with MDD who have failed dose optimized venlafaxine and duloxetine.
		50 mg ER tablet	PA	\$33.34	
		100 mg ER tablet	PA	\$31.49	
	Milnacipran (Savella)	12.5 mg tablet	PA	--	Reserved for treatment failure of dose optimized venlafaxine and duloxetine for 2 months each. Starter pack is limited to 1 fill per 180 days.
		25 mg tablet	PA	\$355.77	
		50 mg tablet	PA	\$341.12	
		100 mg tablet	PA	\$241.06	
		12.5 mg-25 mg-50 mg titration pack	PA	\$311.98	
	Levomilnacipran (Fetzima)	20 mg ER capsule	PA	\$344.73	Reserved for treatment failure of dose optimized venlafaxine and duloxetine for 2 months each. Starter pack is limited to 1 fill per 180 days.
		40 mg ER capsule	PA	\$353.99	
		80 mg ER capsule	PA	\$354.55	
120 mg ER capsule		PA	\$358.57		
20 mg-40 mg titration pack		PA	\$341.50		
Anticonvulsants	Gabapentin (Neurontin)	100 mg capsule	-	\$3.46	Reserved for treatment failure to 2 months each of a tricyclic antidepressant AND Gabapentin.
		300 mg capsule	-	\$5.36	
		400 mg capsule	-	\$4.69	
		600 mg tablet	-	\$12.13	
		800 mg tablet	-	\$20.14	
		250 mg/5 ml solution	-	\$49.61	
	Pregabalin (Lyrica)	25 mg capsule	PA	\$485.20	
		50 mg capsule	PA	\$528.13	
		75 mg capsule	PA	\$466.11	
		100 mg capsule	PA	\$545.49	
		150 mg capsule	PA	\$538.88	
		200 mg capsule	PA	\$549.14	
		225 mg capsule	PA	\$441.49	
300mg capsule	PA	\$448.35			
ST = Step therapy; QL = Quantity Limit; PA = Prior Authorization Required; NF = Non-Formulary					

Table 2: Available Topical Non-Opioid Agents (Current as of 12/2018)

Topical Agents					
Therapeutic Class	Generic Name (Brand Name)	Available Strengths	Formulary Limits	Est. Cost per 30 days	Notes
NSAID	Diclofenac Sodium (Voltaren, Solaraze, Pennsaid)	1% gel	ST; AL	\$47.51	Reserved as step therapy to treatment failure of 3 formulary NSAIDs, including meloxicam or etodolac
		1.5% solution	NF	\$56.10	
		3% gel	NF	--	
	Diclofenac epolamine (Flector)	1.3% patch	NF	\$376.52	
	Indomethacin (Indocin)	50 mg suppository	-	--	
Other	Benzocaine	10% mucosal gel	-	\$2.81	
		20% oral gel	-	\$3.31	
		20% spray	NF	--	
	Capsaicin (Muscle Relief, Arthritis Pain Relief)	0.025% cream	-	\$2.08	
		0.075% cream	-	\$7.31	
		0.1% cream	-	\$4.53	
	Lidocaine (Lidoderm)	5% patch	PA	\$212.68	Reserved for treatment failure to two forms of conventional neuropathic agents in patients with neuropathy
	Other Lidocaine (2% Jelly, Viscous Solution)	3% cream	-	\$44.52	
		4% cream	-	\$29.27	
		5% anorectal cream	-	--	
		3% lotion	NF	--	
		4% lotion	NF	--	
		5% ointment	NF	\$196.40	
		2% jelly	-	\$12.74	
		2% viscous solution	-	\$5.83	
4% mucosal solution	-	\$9.27			
Lidocaine-Prilocaine	2.5-2.5% cream	QL	\$36.12	Limit 30gm/month	
Lidocaine-Hydrocortisone	3-0.5% cream applicator	NF	\$38.04*	*Est. cost for 30-day supply (applicators)	
Lidocaine-Hydrocortisone	3-0.5% cream tube	NF	\$33.45*	*Est. cost for 28.35-g tube	
Lidocaine-Tetracaine	7-7% cream	NF	\$220.05*	*Est. cost for 30-g tube	

ST = Step therapy; QL = Quantity Limit; PA = Prior Authorization Required; NF = Non-Formulary; AG = Age Limit

⊕ 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).

Non-Salicylate Analgesics

Acetaminophen capsules, tablets, drops, elixir, suspension

Acetaminophen Formulations

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** FDA recommends limiting to 4G/day for patients due to risk of liver damage and drug overdose. In patients with liver impairment or liver disease, the FDA recommends avoiding Acetaminophen intake or restricting Acetaminophen to 2G/day.

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 (except for Meloxicam 7.5mg—Limit 2 tablets per day; Meloxicam 15mg—Limit 1 tablet per day)
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Indomethacin 25mg/5mL suspension, Naproxen 125mg/5mL suspension

Skeletal Muscle Relaxants

Baclofen (Lioresal), Cyclobenzaprine (Flexeril), Methocarbamol (Robaxin), Tizanidine (Zanaflex tablets)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Carisoprodol (Soma), Chlorzoxazone (Parafon Forte), Dantrolene, Metaxalone (Skelaxin), and Orphenadrine (Norflex)

Antidepressants

Amitriptyline (Elavil), Imipramine (Tofranil), Doxepin (Sinequan)

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

Citalopram (Celexa), Escitalopram (Lexapro), Fluoxetine (Prozac), Nortriptyline (Pamelor), Fluvoxamine

- Coverage Criteria:**
 - Solutions: Reserved for documented inability to consume capsules or tablets by mouth.
- Limits:** None
- Required Information for Approval:** Solutions: Documented inability to consume capsules or tablets by mouth.
- Other Notes:** None
- Non-Formulary:**
 - Fluoxetine tablets
 - Fluoxetine DR 90mg capsules
 - Fluvoxamine capsules

Duloxetine (Cymbalta)

- Coverage Criteria:** None
- Limits:**
 - 20mg, 30mg capsules: Limited to 60 capsules per 30 days.
 - 60mg capsules: Limited to 30 capsules per 30 days.
- Required Information for Approval:** N/A
- 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.
- Non-formulary:** Duloxetine 40mg capsules

Sertraline (Zoloft)

- Coverage Criteria:**
 - Tablets: None
 - Solutions: Reserved for documented inability to consume capsules or tablets by mouth.
- Limits:**
 - Tablets: Limited to 60 tablets per month.
 - Solutions: Limited to 300mL per 30 days.
- Required Information for Approval:** Solutions: Documented inability to consume capsules or tablets by mouth.
- Other Notes:** None

Venlafaxine (Effexor IR/XR)

- Coverage Criteria:** None
- Limits:**
 - Immediate Release: Limited to 90 tablets per 30 days.
 - Extended Release: Limited to 60 capsules per 30 days.
- 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 dose-optimized Paroxetine IR for at least 2 months.
 - Solutions: Reserved for documented inability to consume capsules or tablets by mouth.
- Limits:**
 - Tablets: Limited to 30 tablets per 30 days.
 - Solutions: None
- Required Information for Approval:**
 - Paroxetine CR: prescription history showing at least 2 consecutive months of dose-optimized Paroxetine IR
 - Solutions: Documented inability to consume capsules or tablets by mouth.

- Other Notes:** None
- Non-Formulary:** Paroxetine mesylate

Desvenlafaxine (Pristiq), Levomilnacipran (Fetzima), Milnacipran (Savella)

- 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 succinate 25 mg ER 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

Topical NSAID Formulations

Diclofenac Sodium (Voltaren Gel), Indomethacin (Indocin Suppositories)

Diclofenac Sodium (Voltaren Gel)

- Coverage Criteria:** Voltaren Gel 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

Indomethacin (Indocin Suppositories)

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

Other Topical Formulations

Capsaicin Cream, Lidocaine 2% Viscous Solution, Lidocaine 2% Jelly, Lidocaine 3% Cream, Lidocaine 4% Cream, Lidocaine 3% Lotion, Lidocaine 4% Lotion, Lidocaine 5% Anorectal Cream, Lidocaine 5% Ointment, Lidocaine (Lidoderm Patch), Lidocaine-Prilocaine Cream, Lidocaine-Hydrocortisone, Lidocaine-Tetracaine

Capsaicin Cream, Lidocaine 2% Viscous Solution, Lidocaine 3% Cream, Lidocaine 4% Cream, Lidocaine 5% Anorectal Cream

- Coverage Criteria:** Lidocaine 5% anorectal cream is reserved for relief of pain or itching due to anorectal disorder.
- Limits:** None

- Required Information for Approval:** N/A
- Other notes:** None
- Non-Formulary:** Lidocaine 3% Lotion, Lidocaine 4% Lotion, Lidocaine 5% Ointment

Lidocaine-Prilocaine Cream

- Coverage Criteria:** None
- Limits:** Limit 30gm per day
- Required Information for Approval:** N/A
- Other notes:** None
- Non-Formulary:** Lidocaine-Hydrocortisone, Lidocaine-Tetracaine

Lidocaine 5% (Lidoderm Patch)

- Coverage Criteria:** Lidoderm patches are reserved for patients with peripheral neuropathy AND treatment failure of two (2) dose optimized conventional treatments (e.g. TCA, SNRI, gabapentin).
- Limits:** None
- Required Information for Approval:** Diagnosis of neuropathic pain AND drug refill history showing at least two dose-optimized conventional forms (e.g. Gabapentin 1,600mg/day, Venlafaxine IR/XR 150-225mg/day, Amitriptyline 25-75mg/day), 8 weeks each
- Other notes:** None

CLINICAL JUSTIFICATION:

NSAIDs are an effective choice of therapy for acute and chronic nociceptive pain, but they are often under-utilized due to concerns of gastrointestinal side effects. While oral NSAIDs should be avoided in high risk patients, they should not be ruled out from all patients. High risk factors include age (>65 years old), patients with a history of GI bleed/peptic ulcer, moderate-severe renal insufficiency, congestive heart failure, patients on chronic anticoagulant/antiplatelet therapy; patients with high risk factors may want to consider topical NSAID therapy or non-NSAID therapy. Furthermore, not all NSAIDs are created equal. NSAIDs that are more COX-2 selective (Celecoxib, Etodolac, and Meloxicam) tend to have a lower risk of gastrointestinal effects compared to non-selective NSAIDs (ibuprofen, naproxen, diclofenac, indomethacin, etc). In clinical trials, Etodolac and Celecoxib were equally efficacious and demonstrated improved GI tolerability compared to non-selective NSAIDs. Meloxicam's efficacy varied between slightly inferior and equally efficacious but showed improved GI tolerability compared to non-selective NSAIDs. Celecoxib was associated with a significantly higher risk of myocardial infarction. Both Etodolac and Meloxicam had no reports of MI events. Patients currently on an effective pain management therapy with an NSAID may want to consider prophylaxis with proton-pump inhibitors (PPIs). One trial compared Celecoxib to Diclofenac + Omeprazole in arthritis patients who recently suffered GI hemorrhages. The results showed combination therapy of a non-selective NSAID and PPI were equal GI tolerability to that of Celecoxib.

Diclofenac gel is commonly prescribed in elderly patients with osteoarthritis. Diclofenac gel was compared to oral Diclofenac and the results were no difference in efficacy between the two treatment groups. Diclofenac gel was also more tolerable compared to oral Diclofenac. Topical Diclofenac may be useful for patients with a very specific, localized pain site since it only works on the applied area. The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) guidelines both agree that topical NSAID formulations are second line to oral NSAID therapy.

Whether or not topical Lidocaine is effective for chronic back pain has been highly debated topic. Recent evidence suggests Lidocaine patch is not superior to placebo for treatment of chronic back pain. However, Lidocaine is approved for post-herpetic neuralgia and neuropathic pain. Therefore, patients with chronic back pain derived from neuropathic origin may benefit from topical Lidocaine. Like Diclofenac gel, topical Lidocaine relieves only localized pain. Since tricyclic antidepressants (TCAs), gabapentin are the mainstay therapies of neuropathic pain, lidocaine patch is reserved for treatment failure to conventional neuropathic treatment agents. While lidocaine 5% patch is the only formulation approved for neuropathic pain, topical lidocaine 2% jelly, 2% mucosal solution, 4% mucosal solution, 3% cream, 4% cream, and 5% anorectal cream may serve as additional non-opioid alternatives in some localized, painful conditions. In particular, lidocaine 4% cream and 5% anorectal cream are often used in vulvodynia.⁵ Most topical lidocaine formulations are on formulary without restrictions. However, lidocaine 5% anorectal cream requires PA to ensure appropriate use, given its limited indications for anorectal disorders.

There is no established evidence supporting increased effectiveness of one skeletal muscle relaxant over another. The agents have been observed to either be comparable or have slightly higher effectiveness compared to placebo. Although there is insufficient evidence of the comparative risk of abuse among all skeletal muscle relaxants, Carisoprodol is classified as a controlled substance and therefore has an increased risk of abuse. This agent will maintain its status as being a non-formulary agent. Dantrolene is an agent that can also be used as a skeletal muscle relaxant but it has a black box warning for its potential hepatotoxicity risk that is increased in females, persons over 35 years of age, and persons taking other medications. The increased incidence has been noted more so in persons taking >800 mg/day versus 400mg/day.⁴

Exercise is recommended as the first step to managing fibromyalgia and should be continued even in patients on pharmacologic therapies.⁶ 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.⁷ 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.⁸ NSAIDs may be used to supplement antidepressants, and GABA analogs for pain relief.⁹

REFERENCES

1. Chen YF, Jobanputra P, Barton P, et al. Cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs (etodolac, meloxicam, celecoxib, rofecoxib, etoricoxib, valdecoxib and lumiracoxib) for osteoarthritis and rheumatoid arthritis: a systematic review and economic evaluation. *PubMed Health*. 2008. Available from: <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0015006>. (Accessed April 27, 2015).
2. Nair B and Taylor-Gjevve, R. A review of topical diclofenac use in musculoskeletal disease. *Pharmaceuticals*. 2010. 3: 1892-1909.
3. Hashmi JA, Baliki MN, Huang L, et al. Lidocaine patch (5%) is no more potent than placebo in treating chronic back pain when tested in a randomized double-blind, placebo-controlled brain imaging study. *Molecular Pain*. 2012. 8:29. doi:10.1186/1744-8069-8-29.
4. Dantrium® [prescribing information]. Rochester, MI: JHP Pharmaceuticals, LLC: 2011.
5. Haefner HK, et al. The Vulvodynia Guideline. *Journal of Lower Genital Tract Disease*. 2005;9(1)40–51.
6. Busch AJ, Schachter CL, Overend TJ, Peloso PM, Barber KA. Exercise for fibromyalgia: a systematic review. *J Rheumatol*. 2008; 35(6): 1130.
7. 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.
8. 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.
9. Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. *JAMA*. 2004; 292(19):2388.
10. Macfarlane GJ, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis*. 2017;76:318–328.
11. Fitzcharles MA, et al. Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome. *Canadian Rheumatology Association Societe Canadienne de Rheumatologie*. 2012;1-45.
12. 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.
13. 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.
14. 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	Non-Opioid Pain Management Coverage Policy.docx	4/2015	Jonathan Szkotak, PharmD, BCACP
Update to Policy	HPSJ Coverage Policy – Pain – Non-Opioid 2015-05.docx	5/2015	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Pain – Non-Opioid 2016-02.docx	2/2016	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Pain – Non-Opioid 2017-05.docx	5/2017	Johnathan Yeh, PharmD
Update to and Merge of Non-Opioid and Fibromyalgia Policies	HPSJ Coverage Policy – Pain – Non-Opioid 2018-12.docx	12/2018	Matthew Garrett, PharmD

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