

MEDICATION COVERAGE POLICY



PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

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|--------------------------|-------------|-----------------------|------------|
| POLICY | Non-Opioids | LAST REVIEW | 5/9/2017 |
| THERAPEUTIC CLASS | Pain | REVIEW HISTORY | 2/16, 5/15 |
| LOB AFFECTED | Medi-Cal | (MONTH/YEAR) | |

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. The below criteria, limits, and requirements for certain agents are in place to ensure appropriate use of those agents.

Table 1: Available Systemic and Topical Non-Opioid Analgesics (Current as of 4/2017)

| Oral Agents | | | | | |
|---------------------------|---------------------------|----------------------------|------------------|-------------|---|
| Therapeutic Class | Generic Name (Brand Name) | Available Strengths | Formulary Limits | Cost per Rx | Notes |
| Non-Salicylate Analgesics | Acetaminophen (Tylenol) | 325 mg tablet | - | \$0.39 | Max daily limit = 4,000mg. For patients with liver disease max daily limit = 2,000mg. |
| | | 500 mg tablet | - | \$0.47 | |
| | | 650 mg ER tablet | - | \$3.64 | |
| | | 500 mg capsule | - | \$4.15 | |
| | | 80 mg chewable tablet | - | \$1.49 | |
| | | 160 mg chewable tablet | - | \$6.90 | |
| | | 80 mg dissolvable tablet | - | \$1.08 | |
| | | 160 mg dissolvable tablet | - | \$2.21 | |
| | | 160 mg/5 ml elixir | - | \$1.34 | |
| | | 160 mg/5 ml liquid | - | \$1.30 | |
| | | 160 mg/5 ml solution | - | \$30.15 | |
| | | 160 mg/5 ml suspension | - | \$1.72 | |
| | | 500 mg/15 ml liquid | - | \$6.20 | |
| | | 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 | - | \$13.04 | |
| | | 120 mg suppository | - | \$5.67 | |
| 325 mg suppository | - | \$17.05 | | | |
| 650 mg suppository | - | \$10.96 | | | |

| Therapeutic Class | Generic Name (Brand Name) | Available Strengths | Formulary Limits | Cost per Rx | Notes |
|----------------------------------|---|---------------------------------|------------------|---------------------|--|
| Salicylate Analgesics | Salsalate (Disalcid) | 500 mg tablet | - | \$82.50 | |
| | | 750 mg tablet | - | \$105.12 | |
| 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 | |
| | Diclofenac (Zorvolex) | 400 mg capsule | NF | -- | |
| | | 18 mg capsule | NF | \$289.37 | |
| | Diclofenac Potassium (Zipsor, Cataflam) | 35 mg capsule | NF | -- | |
| | | Zipsor 25 mg capsule | NF | -- | |
| | Diclofenac Sodium DR, XR | 50 mg tablet | - | \$27.60 | |
| | | 25 mg DR tablet | NF | \$44.62 | |
| | | 50 mg DR tablet | - | \$10.48 | |
| | | 75 mg DR tablet | - | \$6.01 | |
| | Etodolac (Lodine) | 100 mg DR tablet | - | \$26.56 | Diclofenac XR 100mg (Voltaren XR) is dosed once daily |
| | | 200 mg capsule | - | \$50.36 | |
| | | 300 mg capsule | - | \$65.11 | |
| | | 400 mg tablet | - | \$39.48 | |
| | Ibuprofen (Motrin) | 400 mg tablet | - | \$43.36 | |
| | | 500 mg tablet | - | \$43.36 | |
| | | 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 | |
| | Indomethacin (Indocin) | 100 mg/5 ml suspension | - | \$5.66 | |
| | | 50 mg/1.25 ml suspension drops | - | \$6.05 | |
| | | 25 mg capsule | - | \$9.08 | |
| | | 50 mg capsule | - | \$12.63 | |
| | | 75 mg ER capsule | - | \$93.28 | |
| | Ketoprofen | 50 mg rectal suppository | - | -- | |
| | | 25 mg/5 ml oral suspension | - | \$411.82 | |
| | Ketorolac | 200 mg ER capsule | NF | \$98.75 | |
| | Meloxicam (Mobic) | 10 mg tablet | NF | \$14.69 | |
| 7.5 mg tablet | | QL | \$1.57 | Limit 2 tablets/day | |
| Nabumetone | 15 mg tablet | QL | \$3.01 | Limit 1 tablet/day | |
| | 500 mg tablet | - | \$25.37 | | |
| Naproxen (Naprosyn, EC-Naproxen) | 750 mg tablet | - | \$23.09 | | |
| | 250 mg tablet | - | \$2.14 | | |
| | 375 mg tablet | - | \$3.27 | | |
| | 500 mg tablet | - | \$4.15 | | |
| | 500 mg DR tablet | - | \$26.02 | | |
| Piroxicam (Feldene) | 125 mg/5 ml suspension | - | \$59.65 | | |
| | 10 mg capsule | NF | -- | | |
| Sulindac (Clinoril) | 20 mg capsule | NF | \$29.89 | | |
| | 150 mg tablet | - | \$8.31 | | |
| | | 200 mg tablet | - | \$11.11 | |

| 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 | | |
| 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; PA | \$64.56 | Reserved as step therapy to treatment failure of 3 formulary NSAIDs, including meloxicam or etodolac |
| | | 1.5% solution | NF | \$187.70 | |
| | | 3% gel | NF | -- | |
| | Diclofenac epolamine (Flector) | 1.3% patch | NF | \$317.75 | |
| | Indomethacin (Indocin) | 50 mg suppository | - | -- | |
| Other | Benzocaine | 10% mucosal gel | - | \$2.81 | |
| | | 20% oral gel | - | \$3.37 | |
| | | 20% spray | NF | \$32.50 | |
| | Capsaicin (Muscle Relief, Arthritis Pain Relief) | 0.025% cream | - | \$2.87 | |
| | | 0.075% cream | - | \$17.65 | |
| | | 0.1% cream | - | \$7.79 | |
| | Lidocaine (Lidoderm) | 5% patch | PA | \$234.45 | Reserved for treatment failure to two forms of conventional neuropathic agents in patients with neuropathy |
| | Other Lidocaine (2% Jelly, Viscous Solution) | 3% cream | NF | \$35.44* | *Est. cost for 28.35-g tube |
| | | 4% cream | NF | \$3.72* | *\$22.35 = Est. cost for 30-g tube |
| | | 5% anorectal cream | NF | \$18.00* | *Est. cost for 30-g tube |
| | | 3% lotion | NF | \$365.8* | *Est. cost for 118 ml |
| 4% lotion | | NF | \$82.72* | *Est. cost for 88-g tube | |
| 5% ointment | | NF | \$116.33* | *\$286.50 = Est cost for 30-day supply | |
| 2% jelly | | - | \$16.70 | | |

| | | | | | |
|--|---------------------------------|-------------------------|----|-----------|--|
| | | 2% viscous solution | - | \$5.02 | |
| | | 4% mucosal solution | - | \$5.05 | |
| | Lidocaine-Prilocaine | 2.5-2.5% cream | QL | \$57.59 | 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

⊞ 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).

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

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)

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:** None
- 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

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-Gjevre, 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.

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 |

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| Update to Policy | HPSJ Coverage Policy – Pain – Non-Opioid 2017-05.docx | 5/2017 | Johnathan Yeh, PharmD |
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Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy