Non-Opioid Treatment Options in Workers’ Compensation

January 21, 2016
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Presenters

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Corporate Medical Director

Matthew Foster, PharmD
Clinical Pharmacy Manager
Learning Objectives

After the completion of this activity, participants should be better able to:

• Understand the role of non-opioid analgesics in pain management
• Explain the different types of non-opioid analgesic agents
• Identify specific concerns surrounding individual non-opioid analgesic medications and understand when it is appropriate to use each agent
• Understand the role of dermatological medications in pain management
• Explain the different types of dermatological agents available for the treatment of pain
• Identify specific concerns surrounding individual dermatological medications and understand when it is appropriate to use each agent
THE USE OF NON-OPIOIDS IN CHRONIC PAIN
Pharmacologic Management of Chronic Pain

- Choice of initial agent dependent upon type of pain present
- World Health Organization (WHO) pain ladder commonly used in group health settings

1. Non-Opioid +/- Adjuvant
2. Opioid for mild to moderate pain +/- Non-Opioid +/- Adjuvant
3. Opioid for severe pain +/- Non-Opioid +/- Adjuvant

Increased or Persisting Pain
Non-Opioid Analgesics Overview

• Used to treat acute, as well as chronic pain

• Some agents have anti-inflammatory and pain relieving properties (Non-steroidal Anti-inflammatory Drugs [NSAIDs], COX-2 Inhibitors)

• Other agents provide pain relief when applied topically (topical anesthetics and analgesics)

• Considerations when using non-opioid analgesics
  - Dosing limitations
  - Duration of therapy
  - Specific side effects/precautions
  - Hypersensitivity reactions
Examples of Non-Opioid Analgesics

- Acetaminophen (Tylenol®, APAP)
- Acetylated Salicylate:
  - Aspirin (Bayer®, Ecotrin®)
- Non-Acetylated Salicylates:
  - Salsalate (Disalcid®)
  - Choline Magnesium Trisalicylate (Trilisate®)
- Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
  - Ibuprofen (Motrin®, Advil®, etc.)
  - Naproxen (Aleve®, Naprosyn®, etc.)
  - Diclofenac (Voltaren®, Flector®, etc.)
  - Meloxicam (Mobic®)
- COX-2 Selective Inhibitor, NSAID:
  - Celecoxib (Celebrex®)
Examples of Non-Opioid Analgesics (continued)

- Combination Products:
  - Butalbital-Acetaminophen-Caffeine (Fioricet®)
  - Butalbital-Aspirin-Caffeine (Fiorinal®)
- Dermatologicals: Available from various medication classes
  - Topical NSAIDs (Flector®, Voltaren®)
  - Topical anesthetics (Lidoderm®)
  - Topical analgesics (Zostrix®, Salonpas®)
  - Compounded topical formulations
Acetaminophen

Examples
Tylenol®, APAP

General Characteristics
Analgesic (pain relieving) and antipyretic (fever-reducing) actions

Dosage
- Currently 4,000 mg/day maximum (In 2011, an FDA advisory committee recommended lowering this limit to 3,000 mg/day)
- Overdose could result in acute liver toxicity (often fatal)
- Over-the-counter and combination products increase risk

Common Adverse Effects
- Liver and kidney damage (chronic use of high doses)
- Allergic reactions (rare)

Precautions
Use with caution in liver disease or chronic alcohol use
Aspirin (Acetylsalicylic Acid) - ASA

General Characteristics
- Analgesic, fever reducing, and anti-inflammatory actions
- Less commonly used due to adverse effects and availability of NSAIDs
- Frequently used for heart attack and stroke prevention more often than pain management (81 mg dose)

Common Adverse Effects
- GI disturbances – stomach ulcers (bleeding due to platelet inhibition)
- Hypersensitivity reactions – patients suffering from asthma, nasal polyps or severe allergies
- Ringing of the ears (tinnitus), increased risk of hemorrhagic stroke

Precautions
Avoid in patients with pre-existing ulcers, decreased kidney function, bleeding or clotting disorders, and in pregnancy.
Non-Acetylated Salicylates

Examples

Salsalate (Disalcid®), Choline Magnesium Trisalicylate (Trilisate®)

General Characteristics

• Lower incidence of gastric irritation, platelet inhibition, and bronchospasm
• Reduced anti-inflammatory activity

Common Adverse Effects

• Similar gastrointestinal effects, but overall incidence is lower than with non-selective NSAIDs or acetylated salicylates, such as Aspirin
• Electrolyte disturbances (hypermagnesemia, hypokalemia)

Precautions

• Avoid if allergic to aspirin or other NSAIDs, and in pregnancy
• Use with caution in patients with decreased kidney or liver function, vitamin K deficiency, hypovolemic states (dehydration, recent blood loss) and sodium-restricted diets
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Examples: Non-selective Agents
- Ibuprofen (Motrin®, Advil®)
- Naproxen (Naprosyn®, Aleve®)
- Diclofenac (Voltaren®, Flector®)
- Meloxicam (Mobic®)

General Characteristics
- Analgesic, fever reducing, and anti-inflammatory actions
- Great variability between agents

Dosage
- Adequate trial consists of an appropriate dose for 2-3 weeks
- Guidelines recommend that the lowest dose be used for the shortest duration possible
Non-Selective NSAIDs (continued)

Common Adverse Effects

- Bleeding disorders (upper GI bleed, gastric ulcers, perforation)
- Increased risk of cardiovascular events (MI, stroke, heart failure)
- Decreased kidney function (fluid retention, elevated blood pressure)
- GI effects (stomach pain, nausea, indigestion, acid reflux, diarrhea)
- Hypersensitivity reactions (bronchospasm, rash, itching)
- Miscellaneous effects (dizziness, depression, erectile dysfunction)
- Dose and duration of therapy believed to influence incidence

Precautions

- For patients at high risk for GI effects (older age, prior history of GI bleed, high dose or multiple NSAIDs) may require acid-suppressing therapy with a proton-pump inhibitor (i.e., Prilosec, Prevacid, Protonix, Nexium)
- Avoid use in patients with hypersensitivity to ASA, and in pregnancy
COX-2 Selective Inhibitors

Examples
Celecoxib (Celebrex®) is the only agent available

General Characteristics
• Selectively targets COX-2 enzyme to decrease risk of adverse GI effects
• Equally effective as non-selective NSAIDs

Common Adverse Effects
• Similar GI effects, but lower incidence
• Increased risk of cardiovascular events
• Decreased kidney function

Precautions
• Avoid if allergic to sulfonamides, aspirin, other NSAIDs, and in pregnancy
• Use with caution in patients with decreased kidney or liver function
Adverse Effects of NSAIDs
Cardiovascular Risks with Long-term Use

According to Time Passed After First-Time Myocardial Infarction (MI): A Nationwide Cohort Study (Olsen, et al., 2012)

• There is a persistent increased risk of death associated with the use of NSAIDS in general when compared to non-current use of NSAIDS

• Cox Hazard Model showed persistent, increased risk of death among patients receiving any NSAID during the five years after initial MI when compared to non-current use of NSAIDS; Diclofenac was associated with the highest risk of death

• Further investigation is warranted to clarify whether long-term caution in using these agents after MI should be recommended

• Clinical Implications: physicians should consider alternatives to NSAID therapy based on individual patient characteristics
Adverse Effects of NSAIDs

Cardiovascular Risks with Long-term Use

Systemic Review of Population-Based Controlled Observational Studies (McGettigan P., 2011)

- Compared risks with individual NSAIDS at typical doses in community settings (compared the extracted adjusted relative risk (RR) estimates)
  - NSAIDS with the highest risks (40% higher risk than non-users)
    - Rofecoxib (off-market) – RR 1.45
    - Diclofenac – RR 1.40
    - Higher doses of these agents further increased risk
  - NSAIDS with the lowest risks
    - Ibuprofen (low dose) – RR 1.18 (Risk seen only with higher doses)
    - Naproxen – RR 1.09
      - Cardiovascular risk-neutral at all doses
      - Higher risk of GI bleeding than rofecoxib
- Clinical Implications: physicians should consider alternatives to NSAID therapy based on individual patient characteristics
Adverse Effects of NSAIDs

Summary Analysis for Individual Medications 2000-2010

Note: Vertical axis indicates pooled RR.
Combination Analgesic Products

Examples
- Fioricet (acetaminophen, butalbital, caffeine)
- Fiorinal (acetylsalicylic acid, butalbital, caffeine)

General Characteristics
- Typically used for the treatment of migraine headaches
- Intended for “occasional” use only

Adverse Effects
- Rebound headaches
- GI effects (nausea, vomiting, anorexia, abdominal pain)
Non-Opioid (Non-Narcotic) Analgesics

Non-opioid analgesics are useful in the management of pain due to trauma, surgery, or arthritis. They are considered some of the first medications to try in the treatment of mild to moderate pain either alone or in the combination of opioid analgesics. Many of these agents are available without a prescription depending upon the medication and strength prescribed.

<table>
<thead>
<tr>
<th>Medications in this Class (Brand name in parenthesis)</th>
<th>Indications for Use (<strong>approval varies within class</strong>)</th>
<th>Side Effects</th>
<th>Monitoring Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen (Tylenol®)</td>
<td>Arthralgia, headache, mild pain, myalgia, osteoarthritis, and migraine</td>
<td>Liver damage, kidney damage (chronic use of high doses) and allergic reactions (rare)</td>
<td>Monitor total daily dose. Maximum recommended daily dose is 4,000 mg.</td>
</tr>
<tr>
<td>Aspirin (Bayer®, Ecotrin®, etc.)</td>
<td>Arthralgia, headache, migraine, mild pain, myalgia, osteoarthritis, and bone pain</td>
<td>Gastrointestinal ulcers, bleeding, allergic reactions (rare), abdominal pain, and nausea/vomiting</td>
<td>Monitor for gastrointestinal disturbances and bleeding.</td>
</tr>
<tr>
<td>Non-Acetylated Salicylates</td>
<td>Osteoarthritis and rheumatoid arthritis</td>
<td>Nausea, heartburn, stomach pain, dyspepsia, rash, gastrointestinal ulcers and allergic reactions</td>
<td>Monitor for gastrointestinal disturbances and bleeding.</td>
</tr>
<tr>
<td>- Salsalate (Argesic SA®)</td>
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</tr>
<tr>
<td>Butalbital-Acetaminophen - Caffeine</td>
<td>Headache and migraine</td>
<td>Liver damage, kidney damage (chronic use of high doses), abdominal pain, anxiety, diarrhea, nausea/vomiting and drowsiness</td>
<td>Monitor total daily dose of Acetaminophen. Maximum recommended daily dose is 4,000 mg.</td>
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<td>- Esgic</td>
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<td>- Fioricet</td>
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<tr>
<td>Butalbital-Aspirin-Caffeine</td>
<td>Headache, migraine, and mild to moderate pain</td>
<td>Abdominal pain, bleeding, ulcers, drowsiness, nausea/vomiting and anxiety</td>
<td>Monitor for gastrointestinal disturbances and bleeding.</td>
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<td>- Fiorinal</td>
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</tbody>
</table>
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are useful in the management of pain due to trauma, surgery, or arthritis. They are considered some of the first medications to try in the treatment of mild to moderate pain either alone or in the combination of opioid analgesics. Some of these agents are available without a prescription depending upon the medication and strength prescribed.

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<th>Side Effects</th>
<th>Monitoring Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)</td>
<td>Ankylosing spondylitis**, arthralgia**, bone pain**, migraine**, mild to moderate pain, myalgia**, and osteoarthritis</td>
<td>Bleeding, increased risk of cardiovascular events, new or worsening high blood pressure, gastrointestinal ulcers, upset stomach, decreased kidney function, and severe allergic reactions (rare)</td>
<td>Monitor mental status (for depression, suicidal ideation, anxiety, and social functioning), weight, cardiovascular health (especially in elderly and patients with pre-existing heart disease), complete blood count (CBC), liver function, kidney function, bleeding, bruising, gastrointestinal events (abdominal pain, bleeding, blood in stool, heartburn), and eye exams with prolonged use</td>
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<tr>
<td>Ibuprofen (Motrin®, Advil®)</td>
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<td>Naproxen (Naprosyn®, Anaprox®, Aleve®)</td>
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<td>Fenoprofen (Nalfon®)</td>
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<td>Ketoprofen (Orudis®)</td>
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<td>Oxaprozin (Daypro®)</td>
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<td>Indomethacin (Indocin®)</td>
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<td>Sulindac (Clinoril®)</td>
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<td>Ketorolac (Toradol®)</td>
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<td>Tolmetin (Tolectin®)</td>
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<td>Piroxicam (Feldene®)</td>
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<td>Meloxicam (Mobic®)</td>
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<td>Diclofenac (Cataflam®, Voltaren®)</td>
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<td>Nabumetone (Relafin®)</td>
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<tr>
<td>Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors)</td>
<td>Ankylosing spondylitis, bone pain, headache, moderate pain, osteoarthritis, rheumatoid arthritis, and severe pain</td>
<td>Headache, gastrointestinal ulcers, upset stomach, increased risk of cardiovascular events, decreased kidney function, and allergic reactions (rare)</td>
<td>Monitor mental status (for depression, suicidal ideation, anxiety, and social functioning), CBC, liver function, kidney function, bleeding, bruising, gastrointestinal events (abdominal pain, bleeding, blood in stool, heartburn), and weight</td>
</tr>
<tr>
<td>Celecoxib (Celebrex®)</td>
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</tbody>
</table>
DERMATOLOGICAL MEDICATIONS
Dermatologicals Overview

• Includes medications applied externally to the skin for treatment of infection, inflammation, and/or pain relief
• Typically provide pain relief directly to the area where applied
• Minimal systemic absorption – improved safety profile?
• Topical agents are available from various therapeutic classes
  – NSAIDs (i.e., Flector patches, Voltaren Gel)
  – Topical anesthetics (i.e., Lidoderm patches)
  – Topical analgesics (i.e., Zostrix, Salonpas)
• May also involve the use of compounded topical formulations
Dermatologicals Overview

2014 Top Therapeutic Classes in Workers Compensation as a Percentage of Total Spend

The top 10 classes represent 85% of the overall spend: Driven by widespread prescribing of Lidoderm, Flector, Voltaren gel, etc.

Source: 2015 Workers’ Compensation Drug Trend Report, Helios
Topical NSAIDs

Diclofenac Products

- **Flector** – FDA indicated for minor sprains, strains, and contusions
  - Usual dose is one patch applied twice daily
  - Minimal systemic absorption; however, should not be combined with oral NSAIDs due to increased cardiovascular risks

- **Voltaren Gel** – Only indicated for OA of knees and hands
  - Not evaluated for joints of the spine, hip, or shoulder
  - Should not be combined with oral NSAIDs

- **Pennsaid** – OA of knee only, not evaluated for use on other joints
  - Available in 1.5% strength (4x daily application)
  - 2% strength released 1st quarter of 2014 (2x daily application)
  - Should not be combined with oral NSAIDs
Topical NSAIDs

Diclofenac Warnings/Precautions (Oral, Topical)

Diclofenac not recommended as a first-line agent due to increased risk for cardiovascular events

Black Box Warnings:
- Coronary artery bypass graft surgery (CABG)*
- Myocardial Infarction (MI)
- Stroke
- Gastrointestinal bleeding
- Gastrointestinal perforation

*Absolute contraindication
Topical NSAIDs

Diclofenac Warnings/Precautions (Oral, Topical)

- Medication-induced hepatotoxicity: Elevation of liver function enzymes possible during treatment with all products containing diclofenac sodium (oral and topical)
- Postmarketing reports, some resulting in fatalities or transplantation
  - Liver necrosis
  - Jaundice
  - Fulminant hepatitis with and without jaundice
  - Liver failure
- Resulted in label changes to Voltaren Gel prescribing information
General Adverse Effects of Topical NSAIDs

- Rash/pruritus at application site
- Headaches
- Anemia
- Liver function test abnormalities
- Renal abnormalities
- Gastrointestinal complaints/worsening of pre-existing conditions
- Cardiovascular events/worsening of pre-existing conditions
Topical Anesthetics

- Lidoderm – Generic formulation released Sept. 16, 2013
- FDA indicated for treatment of post-herpetic neuropathy (shingles)
- Used off-label for diabetic neuropathy, other chronic pain conditions
- Commonly prescribed medication in workers’ compensation claimants – not a recommended first-line therapy for chronic neuropathic pain
- Usually one patch is applied to intact skin (covering the most painful areas) for up to 12 hours (max. three patches daily)
- Patch may be cut into smaller sizes prior to removal of the release liner
## Top 25 Medications Ranked as a % of Total Spend

Including AWP Changes

<table>
<thead>
<tr>
<th>2014 Rank</th>
<th>2013 Rank</th>
<th>Total Spend</th>
<th>Common Brand Name</th>
<th>Generic Name</th>
<th>Therapeutic Class</th>
<th>Brand and Generic AWP</th>
<th>Brand Only AWP</th>
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<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>6.8%</td>
<td>OXYCONTIN® Tablet</td>
<td>oxycodone ER</td>
<td>Opioid Analgesics</td>
<td>3.7%</td>
<td>3.7%</td>
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<td>2</td>
<td>4</td>
<td>5.7%</td>
<td>LYRICA® Capsule</td>
<td>pregabalin</td>
<td>Anticonvulsants</td>
<td>20.5%</td>
<td>20.5%</td>
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<tr>
<td>3</td>
<td>7</td>
<td>5%</td>
<td>PERCOCET® Tablet</td>
<td>oxycodone-acetaminophen</td>
<td>Opioid Analgesics</td>
<td>74.2%</td>
<td>26.6%</td>
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<td>4</td>
<td>5</td>
<td>4.4%</td>
<td>CELEBREX® Capsule</td>
<td>celecoxib</td>
<td>Anti-inflammatories</td>
<td>20.7%</td>
<td>20.7%</td>
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<tr>
<td>5</td>
<td>3</td>
<td>4.4%</td>
<td>Cymbalta® Capsule</td>
<td>duloxetine</td>
<td>Antidepressants</td>
<td>0.9%</td>
<td>3.6%</td>
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<tr>
<td>6</td>
<td>2</td>
<td>4%</td>
<td>LIDOCLERM® Patch</td>
<td>lidocaine</td>
<td>Dermatologicals</td>
<td>2.7%</td>
<td>1.6%</td>
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<tr>
<td>7</td>
<td>6</td>
<td>3.7%</td>
<td>VICODIN®, NORCO® Tablet</td>
<td>hydrocodone-acetaminophen</td>
<td>Opioid Analgesics</td>
<td>14.2%</td>
<td>45%</td>
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<td>8</td>
<td>2.4%</td>
<td>DURAGESIC® Patch</td>
<td>fentanyl</td>
<td>Opioid Analgesics</td>
<td>2.8%</td>
<td>2.3%</td>
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<td>9</td>
<td>16</td>
<td>2%</td>
<td>ROXICODONE® Tablet</td>
<td>oxycodone</td>
<td>Opioid Analgesics</td>
<td>73.6%</td>
<td>133.2%</td>
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<td>NEURONTIN® Tablet</td>
<td>gabapentin</td>
<td>Anticonvulsants</td>
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<td>13.1%</td>
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<td>10</td>
<td>1.7%</td>
<td>NEURONTIN® Capsule</td>
<td>gabapentin</td>
<td>Anticonvulsants</td>
<td>3.8%</td>
<td>28%</td>
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<td>12</td>
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<td>MOBIC® Tablet</td>
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<td>Anti-inflammatories</td>
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<td>10.1%</td>
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<td>1.4%</td>
<td>KETAMINE Powder*</td>
<td>ketamine</td>
<td>Anesthetics</td>
<td>5.9%</td>
<td>5.8%</td>
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<td>Opana® ER Tablet</td>
<td>oxymorphone ER</td>
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<td>1.3%</td>
<td>ULTRAM® Tablet</td>
<td>tramadol</td>
<td>Opioid Analgesics</td>
<td>0.3%</td>
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<td>16</td>
<td>13</td>
<td>1.2%</td>
<td>SKELEAXIN® Tablet</td>
<td>metaxalone</td>
<td>Muscle Relaxants</td>
<td>4.2%</td>
<td>3.6%</td>
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<td>17</td>
<td>24</td>
<td>1.2%</td>
<td>MS CONTIN® Tablet</td>
<td>morphine sulfate ER</td>
<td>Opioid Analgesics</td>
<td>50.5%</td>
<td>13%</td>
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<td>18</td>
<td>15</td>
<td>1.2%</td>
<td>FLECTOR® Patch</td>
<td>diclofenac</td>
<td>Dermatologicals</td>
<td>6.9%</td>
<td>6.9%</td>
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<tr>
<td>19</td>
<td>18</td>
<td>1.2%</td>
<td>ABILIFY® Tablet</td>
<td>aripiprazole</td>
<td>Antipsychotics</td>
<td>18.3%</td>
<td>18.3%</td>
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<tr>
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<td>1.1%</td>
<td>GABAPENTIN Powder*</td>
<td>gabapentin</td>
<td>Anticonvulsants</td>
<td>14.4%</td>
<td>14.1%</td>
</tr>
<tr>
<td>21</td>
<td>17</td>
<td>1%</td>
<td>FLEXERIL® Tablet</td>
<td>cyclobenzaprine</td>
<td>Muscle Relaxants</td>
<td>3.4%</td>
<td>1.8%</td>
</tr>
<tr>
<td>22</td>
<td>21</td>
<td>1%</td>
<td>NEXIUM® Capsule</td>
<td>esomeprazole</td>
<td>Ulcer Medications</td>
<td>15.4%</td>
<td>15.4%</td>
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<tr>
<td>23</td>
<td>25</td>
<td>0.9%</td>
<td>LUNESTA® Tablet</td>
<td>eszopiclone</td>
<td>Sedative-hypnotics</td>
<td>34.4%</td>
<td>36.2%</td>
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<tr>
<td>24</td>
<td>23</td>
<td>0.9%</td>
<td>TOPAMAX® Tablet</td>
<td>topiramate</td>
<td>Anticonvulsants</td>
<td>1.7%</td>
<td>9.1%</td>
</tr>
<tr>
<td>25</td>
<td>20</td>
<td>0.9%</td>
<td>AMBIEN® Tablet</td>
<td>zolpidem</td>
<td>Sedative-hypnotics</td>
<td>2.7%</td>
<td>31.5%</td>
</tr>
</tbody>
</table>

Source: 2015 Workers’ Compensation Drug Trend Report, Helios
Topical Anesthetics

Official Disability Guidelines (ODG) Criteria for use of Lidoderm patches

• Recommended for trial with evidence of localized pain of neuropathic etiology
• Evidence of a trial and failed therapy with first-line neuropathy medications
  – Tricyclic antidepressants (i.e., amitriptyline)
  – SNRI antidepressants (i.e., duloxetine)
  – Anti-epileptic medications (i.e., gabapentin, pregabalin)
• Treatment area(s), number of patches, duration of use (hrs per day) should be designated
• Short-term trial period recommended (no more than four weeks)
• No other medication changes should be made during trial period
• If improvements cannot be determined at end of trial period, Lidoderm should be discontinued
• Continued outcomes should be intermittently measured, if improvement does not continue, Lidoderm should be discontinued
Topical Anesthetics

Pliaglis (lidocaine/tetracaine) cream, Synera topical patch, and EMLA (lidocaine/prilocaine)

- Used for local anesthesia
- Not used in workers’ compensation population
- FDA indicated only for superficial aesthetic or dermal procedures
  - Dermal filler injections
  - Pulsed dye laser therapy
  - Facial laser resurfacing
  - Laser-assisted tattoo removal
  - Dermal procedures (e.g., circumcision) (EMLA)
- The dose of creams/patches that provides effective local dermal analgesia depends on the surface area & duration of the application
- Usually one Synera patch is applied for 30 minutes, Pliaglis cream is applied to area not to exceed 400 cm² for 30 minutes not to exceed 60 minutes
Topical Anesthetics

Safety Precautions for Lidocaine Use

• Avoid application to severely traumatized skin (abrasions, eczema, burns)

• Avoid application to large surface areas

• Avoid application to warm skin: Exercise, or use of thermal heat wraps/pad immediately before or during lidocaine use

• Avoid using large amounts of lidocaine

• Avoid use of occlusive dressings (skin wraps) around lidocaine site of application
Counterirritants and Miscellaneous Topical Analgesics

- **Counterirritants** – stimulate nerves that respond to coolness while depressing nerves that respond to pain
  - Methyl salicylate – similar to aspirin, also has antiinflammatory properties
  - Menthol

- **Topical analgesic**
  - Qutenza (capsaicin) – ODG recommends use only in patients who have not responded or are tolerant to other treatments

- **Common Formulations**:
  - Zostrix (capsaicin cream); Qutenza (capsaicin patch)
  - Salonpas (menthol, methyl salicylate)
  - Myoflex (trolamine salicylate)
  - New Terocin, Dendracin, Medrox (menthol, methyl salicylate, capsaicin)
Counterirritants and Miscellaneous
Topical Analgesics

• Indicated for treatment of:
  – Minor sprains and strains
  – Muscle spasms
  – Minor back pain
  – Soreness
  – Some types of arthritis

• Contain active ingredients available over-the-counter (OTC) – menthol, methyl salicylate, capsaicin

• Major cost drivers for workers’ compensation claims

• Generally not available at the pharmacy, hard to find

• Dispensed to patients directly from physicians (in-office)
Miscellaneous Topical Analgesics

Some medications responsible for the escalation in cost of claims

- **New Terocin®** (menthol, methyl salicylate, capsaicin)
- **Terocin®** (menthol, methyl salicylate, capsaicin, lidocaine)
- **Dendracin®** (menthol, methyl salicylate, capsaicin)
- **Terocin Patch®** (menthol, lidocaine), **Dendracin®** (menthol, methyl salicylate, capsaicin)
- **Medrox Ointment®** (menthol, methyl salicylate, capsaicin)
- **Medrox Patch®** (menthol, methyl salicylate, capsaicin)
# High-cost Topical Analgesics and Possible Alternatives

<table>
<thead>
<tr>
<th>Brand Names</th>
<th>Menthol</th>
<th>Methyl Salicylate</th>
<th>Capsaicin</th>
<th>Camphor</th>
<th>Lidocaine</th>
<th>AWP per 4oz or 5-10 patches</th>
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</thead>
<tbody>
<tr>
<td>Terocin®</td>
<td>10%</td>
<td>25%</td>
<td>0.025%</td>
<td>-</td>
<td>2.50%</td>
<td>$398.50</td>
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<td>New Terocin®</td>
<td>10%</td>
<td>25%</td>
<td>0.025%</td>
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<td>-</td>
<td>$426.00</td>
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<tr>
<td>Dendracin®</td>
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<td>-</td>
<td>$387.00</td>
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<tr>
<td>Dendracin®</td>
<td>10%</td>
<td>30%</td>
<td>0.0375%</td>
<td>-</td>
<td>-</td>
<td>$387.00</td>
</tr>
<tr>
<td>Medrox Ointment®</td>
<td>5%</td>
<td>20%</td>
<td>0.0375%</td>
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<td>-</td>
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<tr>
<td>Medrox Patch®</td>
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<td>20%</td>
<td>0.0375%</td>
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<td>-</td>
<td>$195.00</td>
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<tr>
<td>Terocin Patch®</td>
<td>4%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4%</td>
<td>$325.00</td>
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<table>
<thead>
<tr>
<th>Possible Alternatives</th>
<th>Menthol</th>
<th>Methyl Salicylate</th>
<th>Capsaicin</th>
<th>Camphor</th>
<th>AWP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greaseless BENGAY®</td>
<td>10%</td>
<td>15%</td>
<td>-</td>
<td>-</td>
<td>$7.93 (6 oz)</td>
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<tr>
<td>Icy Hot®</td>
<td>10%</td>
<td>30%</td>
<td>-</td>
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<tr>
<td>Ultra Strength BENGAY®</td>
<td>10%</td>
<td>30%</td>
<td>-</td>
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<tr>
<td>Arthritis Formula BENGAY®</td>
<td>8%</td>
<td>30%</td>
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<tr>
<td>Muscle Rub Cream Ultra</td>
<td>4%</td>
<td>30%</td>
<td>-</td>
<td>4%</td>
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<tr>
<td>Capsaicin Cream 0.025%</td>
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<tr>
<td>Capsaicin Cream 0.075%</td>
<td>-</td>
<td>-</td>
<td>0.075%</td>
<td>-</td>
<td>$11.90 (2 oz.)</td>
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</table>
Miscellaneous Topical Analgesics

Safety Alerts and Adverse Reactions

• **FDA Drug Safety Alert** – Regarding rare cases of serious skin injuries with use of OTC topical muscle /joint pain relievers containing menthol, methyl salicylate, capsaicin in the form of creams, lotions, ointments, patches; 1st to 3rd degree chemical burns at site of application

• **Adverse Reactions:**
  – Unpleasant burning sensation
  – Rash, itching
  – Redness, warmth, stinging
  – Swelling
  – Blisters, pain
  – Dizziness

• **Do not use:** On open wounds, cuts, damaged, or infected skin
TOPICAL COMPOUNDED MEDICATIONS
Topical Compounded Medications Overview

• Typically utilized when a commercially marketed version of a particular agent or combination of agents is not available

• Official Disability Guidelines (ODG) Stance: Not recommended as there is very limited clinical data on the efficacy or safety of these products

• Compounded as monotherapy or in combination for pain control:
  - NSAIDs – naproxen, ketoprofen, meloxicam
  - Opioids – morphine
  - Local anesthetics – lidocaine, tetracaine, prilocaine
  - Antidepressants – amitriptyline, doxepin, imipramine
  - Anticonvulsants – topiramate, gabapentin
  - Skeletal muscle relaxants – cyclobenzaprine, baclofen
  - Topical analgesics – capsaicin, menthol, methyl salicylate
Top 10 Ingredients Used in Compounded Medications
On average, topical compounded medications include 4-5 ingredients

Ranked by Spend

<table>
<thead>
<tr>
<th>2014 Rank</th>
<th>2013 Rank</th>
<th>Ingredient</th>
<th>Change in Average Daily Spend</th>
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<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>FLUTICASONE Powder</td>
<td>18.8%</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>MELOXICAM Powder</td>
<td>141.6%</td>
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<tr>
<td>3</td>
<td>2</td>
<td>FLURBIPROFEN Powder</td>
<td>21.2%</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>GABAPENTIN Powder</td>
<td>22.5%</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>KETAMINE Powder</td>
<td>3.6%</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>BACLOFEN Powder</td>
<td>27.6%</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>CYCLOBENZAPRINE Powder</td>
<td>0.1%</td>
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<tr>
<td>8</td>
<td>7</td>
<td>KETOPROFEN Powder</td>
<td>-13.9%</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>PCCA LIPODERM Cream</td>
<td>20.0%</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
<td>DICLOFENAC Powder</td>
<td>-12.7%</td>
</tr>
</tbody>
</table>

Source: 2015 Workers’ Compensation Drug Trend Report, Helios
Topical Compounded Medications

When to Use

• Compounded medications are not recommended as first-line therapy.

• Commercially available, FDA-approved medications should be adequately trialed first.

• Only if FDA-approved medications are ineffective or contraindicated in patients, compounded medications that contain FDA-approved ingredients may be considered:
  – Undertaken on a patient-by-patient basis.
  – Allergy to inactive ingredient(s) in FDA-approved medications.
  – Require different dosage strength.
  – Require different route of administration.
Topical Compounded Medications

Official Disability Guidelines (ODG) Criteria

- Include at least one medication substance/active ingredient that is the sole active ingredient in an FDA-approved prescription medication, not including OTC medications.
- Include only bulk ingredients that are components of FDA-approved medications that have been made in an FDA-registered facility & have an NDC code.
- Is not a medication that was withdrawn or removed from the market for safety reasons.
- Is not a copy of a commercially available FDA-approved medication product.
- Include only medication substances that have been supported as safe and effective for the prescribed indication by the FDA-approval process and/or by adequate medical and scientific evidence in the medical literature. This would allow off-label usage when supported by medical evidence.
- Any compounded product that contains at least one medication (or medication class) that is not recommended is not recommended. The use of compounded agents requires knowledge of the specific analgesic effect of each agent and how it will be useful for the specific therapeutic goal required.
Compounded Products

Topical Ketamine

• Currently under study for treatment of neuropathic pain in refractory cases in which all primary and secondary treatment has been exhausted.

• ODG: Only recommended for neuropathic pain in this instance

• Has shown encouraging results in non-controlled studies for Complex Regional Pain Syndrome (CRPS) type I and post-herpetic neuralgia; however, the exact mechanism of action remains undetermined.
Compounded Products

ODG list of agents not recommended for use in compounded medications

- Baclofen – No peer-reviewed literature to support topical use
- Gabapentin – No peer-reviewed literature to support topical use
- Other muscle relaxants – No evidence for use as a topical product
- Other anti-epilepsy medications – No evidence for use as a topical product
Non-Opioid Analgesics and Dermatologicals

• Non-opioids analgesics are an important component in the treatment of both acute and chronic pain.

• Dose limitations, including the ceiling effect potential, concerns for adverse effects, and patient specific risk factors are all important criteria to consider when selecting individual products.

• In older patients acetaminophen should be considered as initial and ongoing pharmacotherapy in the treatment of persistent pain, particularly musculoskeletal pain, because of its demonstrated effectiveness and good safety profile.

• Nonselective NSAIDS and COX-2 inhibitors may be considered rarely, and with extreme caution, in highly selected individuals.
Non-Opioid Analgesics and Dermatologicals

- Taking salicylates and non-steroidal anti-inflammatory medications together (including COX-2 inhibitors) should be done with caution as salicylates may increase the risk of gastrointestinal complications.

- Based on the Official Disability Guidelines (ODG), diclofenac is not recommended as a first line agent due to an increased risk of cardiovascular events.

- Research has revealed that treatment with all oral and topical diclofenac products may increase liver dysfunction as use has resulted in liver failure and death. Consideration should be given to converting this agent to a recommended first-line alternative, such as ibuprofen or naproxen.

- There are multiple therapeutic classes available as topical preparations for the treatment of pain including NSAIDs, anesthetics, and analgesics.
Non-Opioid Analgesics and Dermatologicals

• The use of Lidoderm in the treatment of neuropathic pain is not considered a first-line therapy option.

• The Official Disability Guidelines recommend that tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors (i.e., duloxetine, venlafaxine), and anticonvulsant medications (i.e. gabapentin, pregabalin) are first-line agents which should be tried before considering the use of Lidoderm.

• A short-term trial of Lidoderm is strongly recommended before chronic Lidoderm therapy is deemed necessary.

• OTC topical analgesics that are meant for local pain relief may be beneficial in certain patients.

• Some topical analgesics formulated with menthol, methyl salicylate, and capsaicin are quite costly due to their method of dispensal; however, similar more cost-effective alternatives are readily available over-the-counter nationwide.
Non-Opioid Analgesics and Dermatologicals

- Topical preparations containing menthol, methyl salicylate, and/or capsaicin in the form of creams, lotions, ointments, or patches may cause serious skin injuries.

- The use of compounded topical medications are on the rise.

- Compounded topical medications have limited clinical data for efficacy or long-term safety and are therefore not recommended as first-line therapies.

- Compounded medications should only be considered after there has been failed therapy or intolerances to traditional or first-line therapies.
References

References

Thank you!

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