What You Need to Know About Compounded Prescription Drugs

Mark Pew, Senior Vice President, PRIUM
- 35+ years in P&C, 20+ years in Work Comp
- Created PRIUM’s award-winning Chronic Pain Intervention Program in 2003, Intervention Triage in 2010, Texas Closed Formulary turnkey in 2011, Centers with Standards in 2012, TaperRx in 2014
- From March 2012 thru September 2017 …
  - 453 presentations, 33,563 people, 41 states + DC
  - 20 national webinars
- Published and quoted in CLM Magazine, Risk & Insurance, Business Insurance, WorkCompCentral, WorkCompWire, Insurance Thought Leadership, etc
- IAIABC Medical Issues Committee, SIIA Work Comp Committee, CompSense Pharmacy group in CA (chairman) & NY
- 2016 & 2017 Best Blog recipient
- 2018 Magna Comp Laude recipient
- 2017 IAIABC Samuel Gompers award

Blog: LinkedIn.com/in/markpew
Twitter: @RxProfessor
What is a compound?

Highly recommended reading …

*Compounding is Confounding Workers’ Compensation, CompPharma 2014*

**Compounds Definition**

- Pharmacy compounding = Art & Science of preparing personalized medications for patients
- Compounding pharmacies in the USA dates to early 1800’s
- By the 1990’s, compounding occurred in hospitals, home healthcare pharmacies and retail drugstores
- Professional Compounding Centers of America
  www.pccarx.com
Compounds

Definition

- Not proven to be more effective than commercially available, manufactured drugs
  - Anecdotal stories but no suitable references ("evidence")
- Using compounds pose potential risks to patients
  - Lack of dosage control / education for patient
- Could create drug interactions
  - Within the compound
  - The compound interacting with other oral drugs or supplements
- Most are not FDA approved
  - In other words ... Off-label (and "experimental")

Compounds

Definition

- Regulation of compounds varies from state to state
- National standards have been created by Pharmacy Compounding Accreditation Board (PCAB) - www.pcab.org/consumers
  - Verification the pharmacy is not on probation for issues related to compounding quality, public safety or controlled substances
  - Verification that the pharmacy is properly licensed in each state it does business in
  - An extensive on-site evaluation by a PCAB surveyor, all of whom are compounding pharmacists trained in evaluating compliance with PCAB’s quality standards, which includes:
    - An assessment of the pharmacy’s system for assuring and maintaining staff competency
    - A review of facilities and equipment
    - Review of records and procedures required to prepare quality compounded medications
    - Verification that the pharmacy uses ingredients from FDA registered and or licensed sources
    - Review of the pharmacy’s program for testing compounded preparations

Compounds

Dangerous

- Remember New England Compounding in 2012 that caused meningitis outbreak?
  - A Federal inspection found:
    - Greenish-yellow residue on sterilization equipment
    - Surfaces coated with levels of mold and bacteria that exceeded the company’s own environmental limits
    - An air-conditioner that was shut off nightly despite the importance of controlling temperature and humidity
    - Supplied drugs to hospitals around the USA including those affiliated with Harvard, Yale and Mayo Clinic
  - 64 people died, 14,000 people exposed, 313 became ill, 700 others have recurring fungal infections
  - 14 people arrested (former owners and employees)

www.nytimes.com/2012/10/27/health/fda-finds-unsanitary-conditions-at-new-england-compounding-center.html?_r=0
What are the clinical applications?
Compounds
Clinical applications

- Reasons why they may be medically appropriate:
  - Used for an FDA-approved indication
  - The requested formulation is FDA-approved
  - The strength requested is not commercially available and does not exceed the FDA-approved strength of the product
  - Not being used for cosmetic or erectile dysfunction purposes

- EXAMPLES:
  - Dosage formulation must be changed to allow a person with dysphagia (trouble swallowing) to have a liquid formulation of a commercially available tablet-only product
  - Obtain the exact strength needed of the active ingredient
  - Avoid ingredients that a particular patient has an allergy to
  - Add flavoring to medication to make it more palatable.

www.caremark.com/portal/asset/FEP_Rationale_CompoundHighDollarLimit.pdf
Revised 6/13/14

Compounds
Clinical applications

- If there is an FDA-approved drug that is medically appropriate for a patient, the FDA-approved product should be prescribed and used

- Compounded drugs do not undergo the same premarket review and thus lack an FDA finding of safety and efficacy and lack an FDA finding of manufacturing quality

- The FDA does not consider compounding large volumes of copies, or what are essentially copies, of any approved commercially-available drug to fall within the scope of traditional pharmacy practice

www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm310215.htm

Compounds
Clinical applications

- In Work Comp, most compounded medications are pain management as topical creams
- Topical compounds are considered 2nd or 3rd line therapy, primarily recommended for neuropathic pain when antidepressants and anticonvulsants have failed
- Outside of Work Comp, compounds mostly used for:
  - Hormone replacement
  - Dermatology
  - Children’s formulations
  - Anti-cancer treatment
- Why not pain management? Why is Work Comp different?

Physician Dispensing and Compounded Medications – a Legislative and Regulatory Update, HELIOS webinar on 10/22/14
What are the trends?

Compounds Trends – Express Scripts

- From 2013 to 2014:
  - Use increased 45%
    - Use increased 71.9% from 2012 to 2013
  - Among injured workers, 2.2% used a compound
  - High-compounding pharmacies (compounds are more than 67% of their total prescriptions) increased prices by 51.5%
    - Low-compounding pharmacies increased by 8.7%
    - Price increased by 41% from 2012 to 2013
  - 20 states have adopted rules to-date
    - Tactics include fee schedule reimbursement, maximum limits/caps, ingredient-level billing and reporting requirements

The 2014 Drug Trend Report - Workers' Compensation, The Express Scripts Lab, April 2015
### Compounds Trends – Express Scripts

- **Top 5 compounded ingredients:**
  - Gabapentin (anti-epileptic)
  - Ketamine (anesthetic)
  - Fluticasone Propionate (steroid)
  - Tramadol (narcotic-like pain reliever)
  - Meloxicam (NSAID)

- These accounted for **86.1%** of all prescription compounds.

### Compounds Top 20 Ingredients

<table>
<thead>
<tr>
<th>Rank</th>
<th>Drug Name</th>
<th># of Rx</th>
<th># of Claims</th>
<th>Total Pay</th>
<th>Avg Cost per Rx</th>
<th>Avg Cost per Claim</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gabapentin</td>
<td>4,581</td>
<td>2,230</td>
<td>$2,161,633</td>
<td>$472</td>
<td>$1,773</td>
</tr>
<tr>
<td>2</td>
<td>Gabapentin</td>
<td>3,300</td>
<td>1,480</td>
<td>$1,192,235</td>
<td>$317</td>
<td>$2,752</td>
</tr>
<tr>
<td>3</td>
<td>Bactrim</td>
<td>5,081</td>
<td>1,000</td>
<td>$1,583,319</td>
<td>$227</td>
<td>$887</td>
</tr>
<tr>
<td>4</td>
<td>Fluticasone Propionate</td>
<td>1,882</td>
<td>345</td>
<td>$516,189</td>
<td>$2,758</td>
<td>$6,036</td>
</tr>
<tr>
<td>5</td>
<td>Fluoxetine</td>
<td>967</td>
<td>967</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>6</td>
<td>Tramadol</td>
<td>1,967</td>
<td>1,000</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>7</td>
<td>Fluticasone Propionate</td>
<td>1,007</td>
<td>967</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>8</td>
<td>Salbutamol</td>
<td>3,388</td>
<td>345</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>9</td>
<td>Ketamine HCL</td>
<td>2,637</td>
<td>1,000</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>10</td>
<td>Fluticasone Propionate</td>
<td>1,241</td>
<td>427</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>11</td>
<td>Amantadine HCL</td>
<td>457</td>
<td>181</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>12</td>
<td>Ketamine HCL</td>
<td>457</td>
<td>181</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>13</td>
<td>Amifamidine</td>
<td>1,192</td>
<td>716</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>14</td>
<td>Fluticasone Propionate</td>
<td>1,241</td>
<td>427</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>15</td>
<td>Fluticasone Propionate</td>
<td>1,241</td>
<td>427</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>16</td>
<td>Fluticasone Propionate</td>
<td>1,241</td>
<td>427</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>17</td>
<td>Fluticasone Propionate</td>
<td>1,241</td>
<td>427</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>18</td>
<td>Fluticasone Propionate</td>
<td>1,241</td>
<td>427</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>19</td>
<td>Fluticasone Propionate</td>
<td>1,241</td>
<td>427</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
<tr>
<td>20</td>
<td>Fluticasone Propionate</td>
<td>1,241</td>
<td>427</td>
<td>$506,322</td>
<td>$536</td>
<td>$5,574</td>
</tr>
</tbody>
</table>

Source: Texas Department of Insurance, Workers’ Compensation Research and Evaluation Group, 2016.

### Compounds Trends – Texas

#### Number and Cost of Ingredients (Lines) by N-drug Status

<table>
<thead>
<tr>
<th>Year</th>
<th>Compounded drug: Number of Ingredients (Lines)</th>
<th>Share in Billing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N-drug</td>
<td>Y-drug</td>
</tr>
<tr>
<td>2010</td>
<td>468</td>
<td>897</td>
</tr>
<tr>
<td>2011</td>
<td>310</td>
<td>492</td>
</tr>
<tr>
<td>2012</td>
<td>156</td>
<td>595</td>
</tr>
<tr>
<td>2013</td>
<td>81</td>
<td>411</td>
</tr>
<tr>
<td>2014</td>
<td>51</td>
<td>843</td>
</tr>
<tr>
<td>2015</td>
<td>17</td>
<td>791</td>
</tr>
</tbody>
</table>

Source: Texas Department of Insurance, Workers’ Compensation Research and Evaluation Group, 2016.
Compounds Trends – Texas

Cost of Compounded Drugs by Bill Lines, by N-drug Status
Source: Texas Department of Insurance, Workers’ Compensation Research and Evaluation Group, 2016

<table>
<thead>
<tr>
<th>Year</th>
<th>N-drug</th>
<th>Y-drug</th>
<th>Other</th>
<th>Total Pharmacy</th>
<th>Total Cost Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>$97,867</td>
<td>$122,639</td>
<td>$5,669,421</td>
<td>$5,889,927</td>
<td>$159,756,432</td>
</tr>
<tr>
<td>2011</td>
<td>$57,053</td>
<td>$70,060</td>
<td>$5,977,639</td>
<td>$6,104,752</td>
<td>$153,104,682</td>
</tr>
<tr>
<td>2012</td>
<td>$37,277</td>
<td>$77,449</td>
<td>$9,147,604</td>
<td>$9,262,331</td>
<td>$139,845,705</td>
</tr>
<tr>
<td>2013</td>
<td>$42,827</td>
<td>$89,485</td>
<td>$12,870,432</td>
<td>$13,002,743</td>
<td>$126,258,717</td>
</tr>
<tr>
<td>2014</td>
<td>$25,731</td>
<td>$99,098</td>
<td>$13,801,131</td>
<td>$13,925,959</td>
<td>$111,392,973</td>
</tr>
<tr>
<td>2015</td>
<td>$9,373</td>
<td>$109,847</td>
<td>$11,784,603</td>
<td>$11,903,824</td>
<td>$103,710,192</td>
</tr>
</tbody>
</table>

Compounds Trends – Texas

Number and Cost by Compounded Drug
Source: Texas Department of Insurance, Workers’ Compensation Research and Evaluation Group, 2016

<table>
<thead>
<tr>
<th>Year</th>
<th># of Compounded Drugs</th>
<th># of Ingredients (Lines)</th>
<th>Total Cost</th>
<th>Avg Cost per Compounded Drug</th>
<th>Avg # of Ingredients (Lines) per Compounded Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>18,502</td>
<td>50,747</td>
<td>$5,889,927</td>
<td>$318</td>
<td>2.7</td>
</tr>
<tr>
<td>2011</td>
<td>18,344</td>
<td>55,605</td>
<td>$6,104,752</td>
<td>$333</td>
<td>3.0</td>
</tr>
<tr>
<td>2012</td>
<td>20,554</td>
<td>68,928</td>
<td>$9,262,331</td>
<td>$451</td>
<td>3.4</td>
</tr>
<tr>
<td>2013</td>
<td>19,662</td>
<td>60,167</td>
<td>$13,002,743</td>
<td>$661</td>
<td>3.1</td>
</tr>
<tr>
<td>2014</td>
<td>21,370</td>
<td>67,865</td>
<td>$13,925,959</td>
<td>$652</td>
<td>3.2</td>
</tr>
<tr>
<td>2015</td>
<td>16,180</td>
<td>56,158</td>
<td>$11,903,824</td>
<td>$736</td>
<td>3.5</td>
</tr>
</tbody>
</table>

• Two observations from their research …
  • The top 10 individual prescribing doctors (or pain management clinics) accounted for 50 percent of all bills
  • The majority of the bills have a NDC that is not identified in the pharmacy closed formulary
What do guidelines say about them?

Compounds
Official Disability Guidelines

- Not first-line therapy
  1. In general, commercially available, FDA-approved drugs should be given an adequate trial
  2. If these are found to be ineffective or are contraindicated in individual patients, compound drugs that use FDA-approved ingredients may be considered

  • NOTE: There is fairly good evidence that the use of gabapentin and gabapentin-like compounds results in decreased opioid consumption

Compounds
Official Disability Guidelines

- Criteria for Compound drugs:
  1. Include at least one drug substance (or active ingredient) that is the sole active ingredient in an FDA-approved prescription drug, not including OTC drugs.
  2. Include only bulk ingredients that are components of FDA-approved drugs that have been made in an FDA-registered facility and have an NDC code.
  3. Is not a drug that was withdrawn or removed from the market for safety reasons.
  4. Is not a copy of a commercially available FDA-approved drug product.
5. Include only drug 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.

6. Any compounded product that contains at least one drug (or drug 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.

Are all compounds appropriate?
Are all compounds inappropriate?
Is just say “no” a viable option?
Or should they be reviewed on a case-by-case basis?

Can they be considered as alternative treatment?

Compounds
"Anecdotal" story

Dear Customer

Subject: Dermatome Health Solutions Inquiry From Website

I’ve been using Compounds Cream since Dec. 14, 2013. Having extreme neuropathy in left foot area started after 10 day flexor tendon surgery. At which time I had no neuropathy. At that time I had Type 2 Diabetes, high blood pressure, high lipids, sleep apnea, high cholesterol, hypothyroidism, I was once a smoker, I suffer from Lupus, chronic fatigue syndrome. I started using Compounds Cream daily in the morning and nightly. The neuropathy in my feet is undeletable. I now feel better, less tired, less falling. The product is the answer to neuropathy. The benefit is in my feet and in my body. 50 percent. I have experienced some decrease in neuropathy as well.

Thank you for your product. This product has improved my condition. I cut a section of my toe off and didn’t even know. Tell everyone and tell them it works. This would be Madame Munters. Thank you so much for COMPATABLE. Island

Dermatome Health Solutions
Compounds
Optum’s 17 Questions

1. Has an adequate trial of first-line, oral medications been completed?
   • If you’re seeing a compounded medication without first-line, oral medications, investigate why.

2. Are first-line oral agents available?
   • There could be a shortage of commercially available first-line oral agents, or perhaps none exist.

3. Why is the patient unable to use oral medicines?
   • It’s helpful to know why the patient cannot tolerate oral medicines, such as trouble swallowing.

4. Are there any comorbidity conditions that might prevent the use of oral formulations?
   • Underlying conditions may necessitate the use of a topical approach to pain management rather than using oral nonsteroidal anti-inflammatory drugs (NSAIDs).

5. Does the patient have any allergies that might prevent the use of oral formulations?
   • An oral medication that does not contain the allergens may perform as well, if not better.

6. Have other non-compounded, topical medications been tried?
   • Many commercially available and over-the-counter topical medications may provide the same relief.

7. Is the condition being treated compensable?
   • Ensure the purpose of the compounded medication is related to the injury.

8. Are all the ingredients appropriate for the condition being treated?
   • For example, a prescription for anticonvulsants wouldn’t make sense for an injury that doesn’t involve neuropathic pain.

9. Are the ingredients effective according to evidence-based guidelines?
   • What do the Official Disability Guidelines (ODG) and American College of Occupational and Environmental Medicine (ACOEM) say about the ingredients of the compounded medication in relation to the injury?

10. Does the prescriber have any literature to support the use of the compound?
    • Compounded medications are not subject to clinical trials; however, studies may exist on the efficacy of the individual ingredients and/or the compound itself.

11. Is there therapy class duplication with current oral medications?
    • Therapeutic duplication increases the risk of drug-drug interactions, over-medicating, and other complications.

12. Is there ingredient duplication within the compounded medication itself?
    • Lidocaine and Benzocaine, for example, are both local anesthetics, and not necessary in one compound.
Compounds
Optum’s 17 Questions

13. Has there been an associated decrease in opioid utilization?
   • If the opioid level has remained the same—or increased—because of the ingredients in the compounded medication, it may not be the right course of therapy.

14. Has the patient demonstrated improvement in function and/or quality of life?
   • No reported improvement is a red flag that the medication therapy is in need of review.

15. How long does the prescriber plan on prescribing the compound medication?
   • The patient, payer, and physician should be aligned in their understanding of the treatment plan, its intended duration, and objectives.

16. Will a compounded medication cost less long-term than multiple oral medications?
   • All things being equal, look at the overall costs and determine what is the safest, most cost-effective approach.

17. How does the pricing of the compounded medication compare with the cost to create it?
   • Identify the price at the ingredient level and compare it to the price paid for the compounded formulation.

www.optum.com/articles/evaluating-compounded-medications

So what is Texas doing?
Compounds
The Adjustment

• Amending §§ 134.500, 134.530, and 134.540
• Amendments change the definition of closed formulary to exclude any prescription drug created through compounding, and require preauthorization for all prescription drugs created through compounding for claims subject to and not subject to certified networks.
• The proposed rule changes are not intended to prohibit the use of medically necessary compound medications in the workers’ compensation system. Rather, they are intended to ensure that injured employees have access to all health care reasonably required by the nature of the injury as and when needed.


Compounds
The Adjustment

• Timeline:
• Informal draft published: 06/16/17
• Informal Comment deadline: 07/07/17
• Anticipated formal proposal: December 2017

Compounds
The Adjustment

• Changes (definitions):
• §134.500.(a)(3)(B) any prescription drug created through compounding (any compound that contains a drug identified with a status of “N” in the current edition of the ODG Treatment in Workers’ Comp (ODG) / Appendix A. ODG Workers’ Compensation Drug Formulary, and any updates)
• §134.500.(b) This section will become effective for all drugs that are prescribed and dispensed for outpatient use on or after MM/DD/YY (intended to be a date certain approximately sixty days after the rule amendment is finally adopted)

Compounds
The Adjustment

• Changes (preauthorization, not subject to certified networks):
  • §134.530(h)(1)(B) any prescription drug created through compounding [any compound that contains a drug identified with a status of “N” in the current edition of the ODG Treatment in Workers’ Comp (ODG) / Appendix A, ODG Workers’ Compensation Drug Formulary, and any updates];
  • §134.530(h) This section will become effective for all drugs that are prescribed and dispensed for outpatient use on or after MM/DD/YY (intended to be a date certain approximately sixty days after the rule amendment is finally adopted).

In other words …

Compounds can be used
But their medical necessity needs to be validated

✓
Mark RxProfessor Pew
Senior Vice President
(678) 735-7309 Office
mpew@prium.net

Blog: LinkedIn.com/in/markpew
Twitter: @RxProfessor