# Uses, Common Types, and Costs of Compounded Topical Pain Creams

# and

# Patient Preferences Regarding Compounded Topical Pain Creams

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# Our Research

1. Timothy B. McPherson, Patrick E. Fontane, Kelsey D. Jackson, Kathleen S. Martin, Tricia Berry, Rasma Chereson, and Rhonda Bilger. Prevalence of Compounding in Independent Community Pharmacy Practice. Journal of the American Pharmacists Assoc. 2006;46:568.
2. Valerie Yancey, Richard Yakimo, Anne Perry, and Timothy McPherson. Perceptions of pharmaceutical care among pharmacists offering compounding services. Journal of the American Pharmacists Assoc. 2008;48:508.
3. Timothy McPherson and Patrick Fontane. Patient-centered care in the community-based compounding practice setting. Journal of the American Pharmacists Assoc. 2010;50:37.
4. Timothy McPherson, Patrick Fontane, Reethi Iyengar, Rochelle Henderson. Utilization and Costs of Compounded Medications for Commercially Insured Patients, 2012-2013. Journal of Managed Care and Specialty Pharmacy 2016;22:172-81
5. Timothy McPherson, Patrick Fontane, Rhonda Bilger. Patient Experiences with Compounded Medications. Journal of the American Pharmacists Assoc., submitted. Supported by Focus Script LLC.

# Compounded Products Are Used to Treat a Variety of Medical Conditions

1. Bioidentical hormone replacement therapy (50%)
2. Topical pain creams (23%)
3. Thyroid disorders (6%)
4. Sinus/nasal conditions
5. Infections
6. Other
    - Dermatologic conditions
    - Migraine
    - Erectile dysfunction
    - Lupus
    - Gastrointestinal conditions

McPherson, Fontane, Bilger – JAPhA submitted; McPherson et al JMCP 2016

# Compounded Topical Pain (CTP) Cream Users

- N=107
- Respondents represented 17 states
- 77% female
- Age 35 – 96, average 67 years
  - Approximately 80% of users between 48 – 83 years
- 79% considered themselves to be in fair or good health
- 86% of CTP users indicated that the prescribing physician was the first person to suggest using a compounded medication

McPherson, Fontane, Bilger – JAPhA submitted

# Duration of CTP Use

| Statistic | Months |
|---|---|
| Range | 0 - 48 |
| 25th %ile | 1 |
| Mean | 8 |
| 75th %ile | 12 |

McPherson, Fontane, Bilger –unpublished data

# Uses for CTP

- Arthritis pain – 29%
  - Foot, knee, hip
- Non-specified pain – 26%
  - Foot, knee, hip, shoulder, back, neck
- Neuropathic pain or neuralgia – 12%
  - Post-herpetic, post-surgical, or diabetic
- 56% of respondents used CTP in addition to other medications
- CTP has been widely used in workers compensation patients

# Some Drugs Commonly Used in CTP

- Gabapentin
- Baclofen
- Cyclobenzaprine HCl
- Ketamine
- Diclofenac Na
- Flurbiprofen
- Lidocaine
- Bupivacaine HCl
- Amitriptyline
- Combinations of up to 6 drugs within the same product
  - 3, 4, and 5 drug combinations were the most common

McPherson et al JMCP 2016; McPherson, Fontane, Bilger – unpublished data

# Cream Bases for CTP

- Proprietary formulas for transdermal delivery
  - Versabase® (PCCA)
  - Pracasil-Plus® (PCCA)
  - Lipoderm® (PCCA)
  - Pentravan® (Fagron)
  - Transdermal Pain Base ® (Medisca)

## Commonly Requested Compounds

[redacted]

### Pain

- ★ **For All Pain Formulas**
  - Dispense: 60 grams (may increase quantity once patient established)
  - SIG: apply 1-2 grams to affected area (rub in well for 1 minute) 3-4 times per day PRN
  - Ketamine is a controlled substance (schedule III) → max of 5 refills
- ★ **Inflammatory Pain**
  - Ketoprofen 10% in Lipoderm
    - 60 grams = $55
  - Piroxicam 5% in Lipoderm
    - 60 grams = $65
- ★ **Musculoskeletal Pain**
  - Pain MSK #1
    - Cyclobenzaprine HCl 2% / Ketoprofen 10% in Lipoderm
    - 60 grams = $65
  - Pain MSK #2
    - Guaifenesin 10% / Magnesium Sulfate Heptahydrate 10% in Lipoderm
    - 60 grams = $55
- ★ **Neuropathic Pain (General)**
  - Pain Neuro #1
    - Baclofen 10% / Ketoprofen 10% / Lidocaine 10% in Lipoderm
    - 60 grams = $80
  - Pain Neuro #2
    - Baclofen 2% / Clonidine HCl 0.2% / Gabapentin 10% / Ketamine 5% in Lipoderm
    - 60 grams = $100
  - Pain Neuro #3
    - Amitriptyline HCl 2% / Clonidine HCl 0.01% in Lipoderm
    - 60 grams = $55
  - Pain Neuro #4
    - Amitriptyline HCl 2% / Clonidine HCl 0.2% / Gabapentin 5% / Ketamine 5% / Ketoprofen 5% in Lipoderm
    - 60 grams = $85
  - Pain Neuro #5
    - Amitriptyline HCl 2% / Diclofenac Na 5% / Gabapentin 5% in Lipoderm
    - 60 grams = $75
  - Pain Neuro #6
    - Amitriptyline HCl 2% / Baclofen 3% / Ibuprofen 10% / Lidocaine 5% in Lipoderm
    - 60 grams = $60
- ★ **Neuropathic Pain (Diabetic)**
  - Pain Neuro DM #1
    - Nifedipine 2% / Pentoxifylline 5% in Lipoderm
    - 60 grams = $65
  - Pain Neuro DM #2
    - Clonidine HCl 0.2% / Gabapentin 6% / Ketamine 10% / Nifedipine 2% in Lipoderm
    - 60 grams = $95

Form distributed by a local pharmacy physician offices in February 2019

# Costs of CTP

- Two types of cost data
  - Patient-reported out of pocket cost, irrespective of insurance coverage
    - Our 2017 patient survey data
  - Ranking of aggregate annual costs to insurers
    - Express Scripts database - JMCP 2016 paper
      - Large pharmacy benefit manager and mail order pharmacy
    - Data reflect patients with commercial insurance coverage (no worker's compensation, Medicare/Medicaid, or TriCare claims)

# Out of Pocket Cost Reported by CTP Users

- Costs are not normalized to days supply

| Statistic | All Responses | Insured | No Insurance |
|---|---|---|---|
| Mean | $24 | $16 | $48 |
| Median | $10 | $7 | $50 |
| 25th %ile | $1 | $1 | $19 |
| 75th %ile | $40 | $17 | $70 |
| Number of responses | 103 | 76 | 25 |

McPherson, Fontane, Bilger –unpublished data

# Average Out of Pocket Cost for CTP was Similar to Non-Compounded Prescriptions

| Statistic | All CTP Users | Insured | No insurance |
|---|---|---|---|
| Mean | $24 | $16 | $48 |
| Median | $10 | $7 | $50 |

- Average out of pocket cost for all prescriptions for insured patients in 2017: $28
  M Aitken. Medicine Use and Spending in the U.S. A Review of 2017 and outlook to 2022. https://www.iqvia.com
- Average cash price for a non-insured prescription in the US in 2017: $68
  Kaiser Family Foundation. Health costs and budgets - prescription drugs. https://www.kff.org/
- Prices listed on local pharmacy CTP form ranged $55 - $100

McPherson, Fontane, Bilger –unpublished data

# Costs of CTP from Insurance Claims Data Demographics for 2013

**TABLE 1** Demographic Data

| | 2012 | 2013 | Change |
|---|---|---|---|
| **Eligible members** | 22,314,101 | 22,745,508 | 431,407 (1.9%) |
| **Prescription medication users** | 14,960,649 | 15,110,518 | 149,869 (1.0%) |
| Prevalence of prescription medication users (%) | 67.0 | 66.4 | -0.9 |
| Average age, years (SD) | 36.9 (20.7) | 36.8 (20.6) | -0.1 yr |
| Female | 11,508,347 | 11,713,474 | 1.8% |
| Percent female | 51.6 | 51.5 | -0.2 |
| Compound users | 245,285 | 323,501 | 78,216 (31.9%) |
| Prevalence of compound users (%) | 1.1 | 1.4 | 27.3 |
| Average age, years (SD) | 41.8 (21.3) | 42.3 (21.1) | 0.5 yr |
| Female | 162,471 | 212,590 | 30.8% |
| Percent female | 66.2 | 65.7 | -0.8 |

*SD = standard deviation.*

McPherson et al, *J Manag Care Spec Pharm.* 2016;22(2):172-81

# CTP Drugs Led the Most Frequently Compounded Ingredients for Adults in 2013

- Ranked by number of compounded claims the drug appeared in

**TABLE 3** Ten Most Frequently Compounded Drugs by User Age and Sex, 2013

| Rank | <10 Years | | 10-19 Years | | 20-29 Years | | 30-39 Years | |
|---|---|---|---|---|---|---|---|---|
| | F | M | F | M | F | M | F | M |
| 1 | Omeprazole | Omeprazole | Baclofen | Baclofen | Baclofen | Baclofen | Gabapentin | Gabapentin |
| 2 | Lansoprazole | Lansoprazole | Cyclobenzaprine HCl | Cyclobenzaprine HCl | Gabapentin | Cyclobenzaprine HCl | Progesterone | Baclofen |
| 3 | Enalapril maleate | Enalapril maleate | Gabapentin | Lidocaine HCl viscous | Cyclobenzaprine HCl | Gabapentin | Baclofen | Cyclobenzaprine HCl |
| 4 | Nystatin | Oseltamivir | Lidocaine HCl viscous | Methylcobalamin | Ketamine HCl | Ketamine HCl | Cyclobenzaprine HCl | Ketamine HCl |
| 5 | Oseltamivir | Hydrocortisone | Diclofenac sodium | Salicylic acid | Diclofenac sodium | Diclofenac sodium | Ketamine HCl | Diclofenac sodium |
| 6 | Hydrocortisone | Nystatin | Salicylic acid | Gabapentin | Progesterone | Lidocaine | Diclofenac sodium | Lidocaine |
| 7 | Zinc oxide | Zinc oxide | Lidocaine | Diclofenac sodium | Lidocaine | Lidocaine HCl viscous | Lidocaine | Bupivacaine HCl |
| 8 | Ursodiol | Baclofen | Hydrocortisone | Omeprazole | Bupivacaine HCl | Flurbiprofen | Bupivacaine HCl | Flurbiprofen |
| 9 | Atenolol | Spironolactone | Ketamine HCl | Lidocaine | Flurbiprofen | Bupivacaine HCl | Flurbiprofen | Lidocaine HCl |
| 10 | Baclofen | Triamcinolone acetonide | Bupivacaine HCl | Ketamine HCl | Lidocaine HCl | Lidocaine HCl | Testosterone | Testosterone |

| Rank | 40-49 Years | | 50-59 Years | | 60-69 Years | | ≥70 Years | |
|---|---|---|---|---|---|---|---|---|
| | F | M | F | M | F | M | F | M |
| 1 | Progesterone | Baclofen | Progesterone | Gabapentin | Progesterone | Gabapentin | Gabapentin | Gabapentin |
| 2 | Gabapentin | Gabapentin | Estradiol | Baclofen | Estradiol | Baclofen | Baclofen | Baclofen |
| 3 | Baclofen | Cyclobenzaprine HCl | Testosterone | Cyclobenzaprine HCl | Gabapentin | Cyclobenzaprine HCl | Cyclobenzaprine HCl | Cyclobenzaprine HCl |
| 4 | Cyclobenzaprine HCl | Ketamine HCl | Gabapentin | Testosterone | Baclofen | Testosterone | Diclofenac sodium | Diclofenac sodium |
| 5 | Testosterone | Diclofenac sodium | Baclofen | Ketamine HCl | Testosterone | Ketamine HCl | Ketamine HCl | Ketamine HCl |
| 6 | Estradiol | Testosterone | Cyclobenzaprine HCl | Diclofenac sodium | Cyclobenzaprine HCl | Diclofenac sodium | Lidocaine | Testosterone |
| 7 | Ketamine HCl | Lidocaine | Estriol | Lidocaine | Diclofenac sodium | Lidocaine | Bupivacaine HCl | Lidocaine |
| 8 | Diclofenac sodium | Bupivacaine HCl | Diclofenac sodium | Bupivacaine HCl | Ketamine HCl | Bupivacaine HCl | Progesterone | Bupivacaine HCl |
| 9 | Lidocaine | Flurbiprofen | Ketamine HCl | Flurbiprofen | Estriol | Flurbiprofen | Lidocaine HCl | Lidocaine HCl |
| 10 | Bupivacaine HCl | Lidocaine HCl | Lidocaine | Lidocaine HCl | Lidocaine | Lidocaine HCl | Estradiol | Triamcinolone acetonide |

*F = female; HCl = hydrochloride; M = male.*

McPherson et al, *J Manag Care Spec Pharm.* 2016;22(2):172-81

# CTP Drugs Led the Most Expensive Compounded Ingredients for Adults in 2013

- Rank by total cost billed, i.e. Number of claims x ingredient cost

**TABLE 4** Ten Most Expensive Ingredients in Compounded Medications by User Age and Sex, 2013

| Rank | <10 Years | | 10-19 Years | | 20-29 Years | | 30-39 Years | |
|---|---|---|---|---|---|---|---|---|
| | F | M | F | M | F | M | F | M |
| 1 | Oseltamivir | Oseltamivir | Gabapentin | Gabapentin | Gabapentin | Gabapentin | Gabapentin | Gabapentin |
| 2 | Lansoprazole | Omeprazole | Fluticasone proprionate | Fluticasone proprionate | Fluticasone proprionate | Ketamine HCl | Ketamine HCl | Ketamine HCl |
| 3 | Fluticasone proprionate | Lansoprazole | Flurbiprofen | Flurbiprofen | Ketamine HCl | Flurbiprofen | Fluticasone proprionate | Flurbiprofen |
| 4 | Omeprazole | Methylcobalamin | Ketamine HCl | Ubiquinol | Flurbiprofen | Fluticasone proprionate | Flurbiprofen | Fluticasone proprionate |
| 5 | Sildenafil | Leucovorin calcium | Custom Lipo-Max | Ketamine HCl | Custom Lipo-Max | Custom Lipo-Max | Custom Lipo-Max | Testosterone |
| 6 | Tacrolimus | Sildenafil | Cyclobenzaprine HCl | Custom Lipo-Max | Pracasil Plus | Cyclobenzaprine HCl | Cyclobenzaprine HCl | Cyclobenzaprine HCl |
| 7 | Nystatin | Ubiquinol | Pracasil Plus | Cyclobenzaprine HCl | Cyclobenzaprine HCl | Baclofen | Pracasil Plus | Custom Lipo-Max |
| 8 | Pracasil Plus | Sodium bicarbonate | Baclofen | Oseltamivir | Baclofen | Lipoderm base | Baclofen | Baclofen |
| 9 | Baclofen | Tacrolimus | Lipoderm base | Pracasil Plus | Mometasone furoate | Pracasil Plus | Lipoderm base | Lipoderm base |
| 10 | Sodium bicarbonate | PCCA-Plus | Oseltamivir | Baclofen | Lipoderm base | Mometasone furoate | Bupivacaine HCl | Ethoxy diglycol |

| Rank | 40-49 Years | | 50-59 Years | | 60-69 Years | | ≥70 Years | |
|---|---|---|---|---|---|---|---|---|
| | F | M | F | M | F | M | F | M |
| 1 | Gabapentin | Gabapentin | Gabapentin | Gabapentin | Gabapentin | Gabapentin | Gabapentin | Gabapentin |
| 2 | Ketamine HCl | Ketamine HCl | Ketamine HCl | Ketamine HCl | Ketamine HCl | Ketamine HCl | Ketamine HCl | Ketamine HCl |
| 3 | Flurbiprofen | Flurbiprofen | Flurbiprofen | Flurbiprofen | Flurbiprofen | Flurbiprofen | Flurbiprofen | Flurbiprofen |
| 4 | Fluticasone proprionate | Custom Lipo-Max | Custom Lipo-Max | Custom Lipo-Max | Custom Lipo-Max | Custom Lipo-Max | Custom Lipo-Max | Custom Lipo-Max |
| 5 | Custom Lipo-Max | Cyclobenzaprine HCl | Cyclobenzaprine HCl | Cyclobenzaprine HCl | Cyclobenzaprine HCl | Cyclobenzaprine HCl | Cyclobenzaprine HCl | Cyclobenzaprine HCl |
| 6 | Cyclobenzaprine HCl | Fluticasone proprionate | Fluticasone proprionate | Baclofen | Baclofen | Baclofen | Baclofen | Baclofen |
| 7 | Baclofen | Baclofen | Baclofen | Testosterone | Fluticasone proprionate | Alprostadil | Lipoderm base | Lipoderm base |
| 8 | Lipoderm base | Testosterone | Lipoderm base | Lipoderm base | Lipoderm base | Lipoderm base | Ketoprofen | Ketoprofen |
| 9 | Pracasil Plus | Lipoderm base | Progesterone | Fluticasone proprionate | Progesterone | Testosterone | Diclofenac sodium | Testosterone |
| 10 | Progesterone | Ethoxy diglycol | Diclofenac sodium | Bupivacaine HCl | Mometasone furoate | Fluticasone proprionate | Bupivacaine HCl | Diclofenac sodium |

*F = female; HCl = hydrochloride; M = male.*

McPherson et al, *J Manag Care Spec Pharm.* 2016;22(2):172-81

# Compounded Claim Costs Spiked in 2014 but Have Decreased Since 2015

- Data refer to all compounded claims, not only CTP
- 2013 – Compounded claims cost approx. $20* per member.
  Average ingredient cost was $308 per compounded claim.
  *Estimated from data in Drug Trend Report and JMCP 2016
- 2014: Compounded claims cost $46.04 per member.
  Average ingredient cost was $701 per claim.
  Compounded Rx were the drug class with 3rd highest cost.
- 2015: Compounded Rx cost $20.62 per member.
  Cannot estimate ingredient cost per claim.
  Compounded Rx were the drug class with 9th highest cost.
- 2016, 2017: Compounded Rx not in top 15 most expensive drug classes

Express Scripts Drug Trend Reports, 2010 – 2017, available at http://lab.express-scripts.com/lab/drug-trend-report/

# Patient Preferences for Manufactured versus Compounded Prescriptions

- Three indicators of patient perceptions of CTP
  - Reasons for using a compounded product
  - Satisfaction with CTP
  - Satisfaction with CTP as compared to previous products used for the same condition

# Why did you and your physician decide to use this compounded medication? Please mark all that apply.

| Reason | % of CTP Users |
|---|---|
| I don't know - my physician made the decision for me | 48 |
| Previous medications failed to provide relief from my medical condition | 40 |
| Previous medications caused significant side effects | 20 |

McPherson, Fontane, Bilger –unpublished data

# CTP User Satisfaction with the Compounded Product

| Indicate your level of satisfaction with: | Very Dissatisfied (%) | Somewhat Dissatisfied (%) | Somewhat Satisfied (%) | Very Satisfied (%) |
|---|---|---|---|---|
| Relief from the medical condition | 3 | 5 | 39 | 53 |
| Overall satisfaction | 7 | 10 | 23 | 60 |
| Out of pocket cost | 2 | 3 | 29 | 66 |

n = 99-101 per item

McPherson, Fontane, Bilger –unpublished data

# CTP User Satisfaction with the Compounded Product as Compared to Previous Medications

CRx = compounded product

| How does the CRx compare to previous medications in terms of: | CRx Much Worse (%) | CRx Somewhat Worse (%) | CRx About the Same (%) | CRx Somewhat Better (%) | CRx Much Better (%) |
|---|---|---|---|---|---|
| Relief from the medical condition | 0 | 2 | 11 | 40 | 47 |
| Side effects | 0 | 3 | 16 | 7 | 74 |
| Out of pocket cost | 11 | 6 | 22 | 20 | 41 |

n = 68-83 per item

McPherson, Fontane, Bilger –unpublished data

# Demand for CTP is Projected to Increase Through 2025

- Global Market Insights projects an increasing market for compounded medications in general through 2025.
- Steady growth in pain management market is also predicted
  https://www.gminsights.com/industry-analysis/us-compounding-pharmacies-market

# Thoughts on Safety and Efficacy of CTP

- We are not qualified to comment on safety or efficacy of CTP
- Most CTP users were somewhat or very satisfied with relief from their medical condition
- Cline and Turrentine review found mixed results for single agent and combination pain products
  Dermatitis 2016;27;263-271.
- Brutcher et al RCT found no benefit of CTP over 3 months in patients with neuropathic, nociceptive, or mixed pain.
  Ann Intern Med doi:10.7326/M18-2736
  Author-stated limitations:
  - Single CTP formulation per group
  - Diversity of pain conditions

# What specific recommendations (if any) would you like to see come from the committee's report?

- Consider recommending a prioritized research agenda to address questions that are not answered with available data
  - Why do prescribers choose CTP?
  - Can an in vitro assay predict efficacy of CTP?
    - Drug transport through porcine skin in a Franz cell is the traditional model
    - A model for assessing drug combinations would be useful

Thank You