



Introduction to Pharmaceutical Compounds

January 1, 2014

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About Central

Introduction

- **Central Rexall Drugs Inc. (“Central”)** is a fully licensed compounding pharmacy that has been in existence for **over 115 years**. It is a member of the PCCA, IACP and Good Neighbor network of pharmacies.
- **As of May 2014**, it is licensed in approximately **40 U.S. states** with licenses pending or in process in the remaining states. For an up-to-date list of licenses, please contact the Sabrina Aguilar at sabrina@centraldrugs.net.
- Central specializes in compounding topical medications for pain, neuropathy, scar and wound.
- Overseeing Central’s day-to-day operations is Trent Brockmeier, a seasoned operations executive from the West Coast with experience scaling a variety of distribution businesses.

The Central Advantage

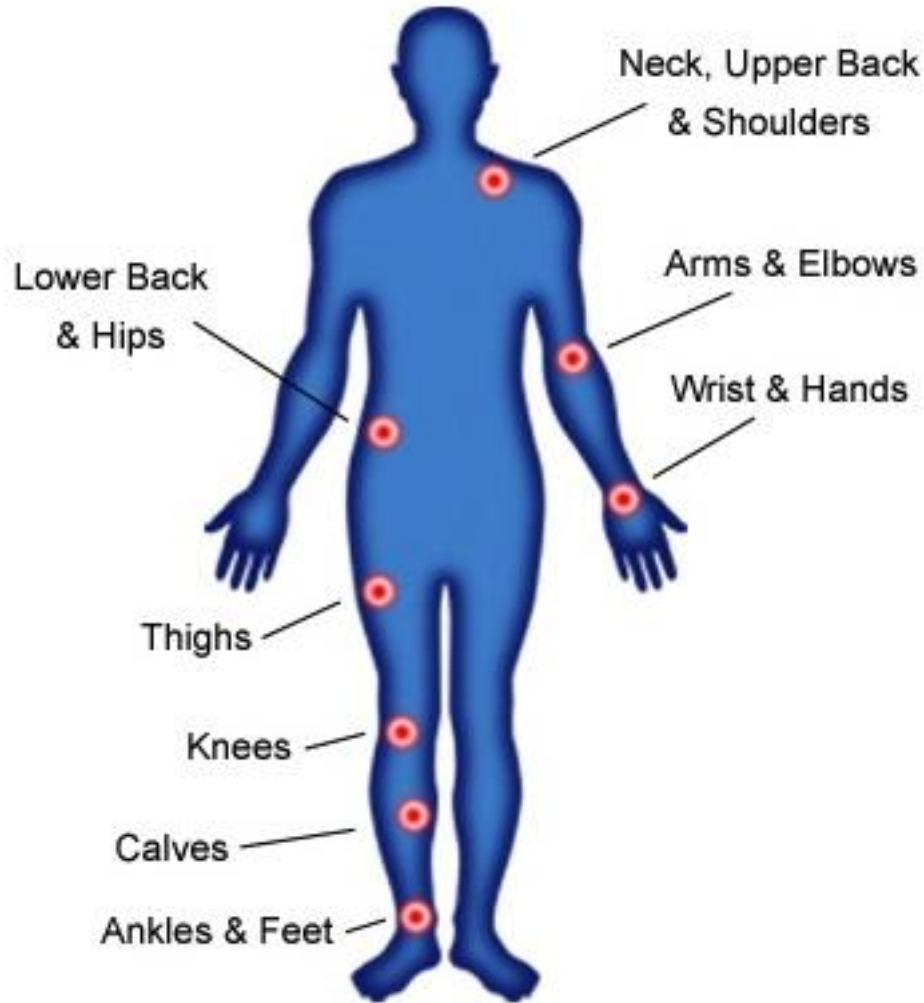
- **Customer Service**. Central's customer service representatives contact every patient the say day the script is received, usually within 30 minutes. These representatives also maintain close relationships with the prescriber's staff.
- **State Licenses**. Central is expecting to be licensed in all 50 states in 2014.
- **Co-Pay Reduction & Low Cash Pay**. Central offers a program through a third-party that reduces co-pays to \$15 (on average) and allows a cash-pay option for most topical creams at \$0.25/gram.
- **Technology**. Central has partnered with a technology company to offer prescribers a unique e-prescribing alternative. Central also has a web-portal for sales reps to track their sales.

Medical Overview

Art of Compounding Medications

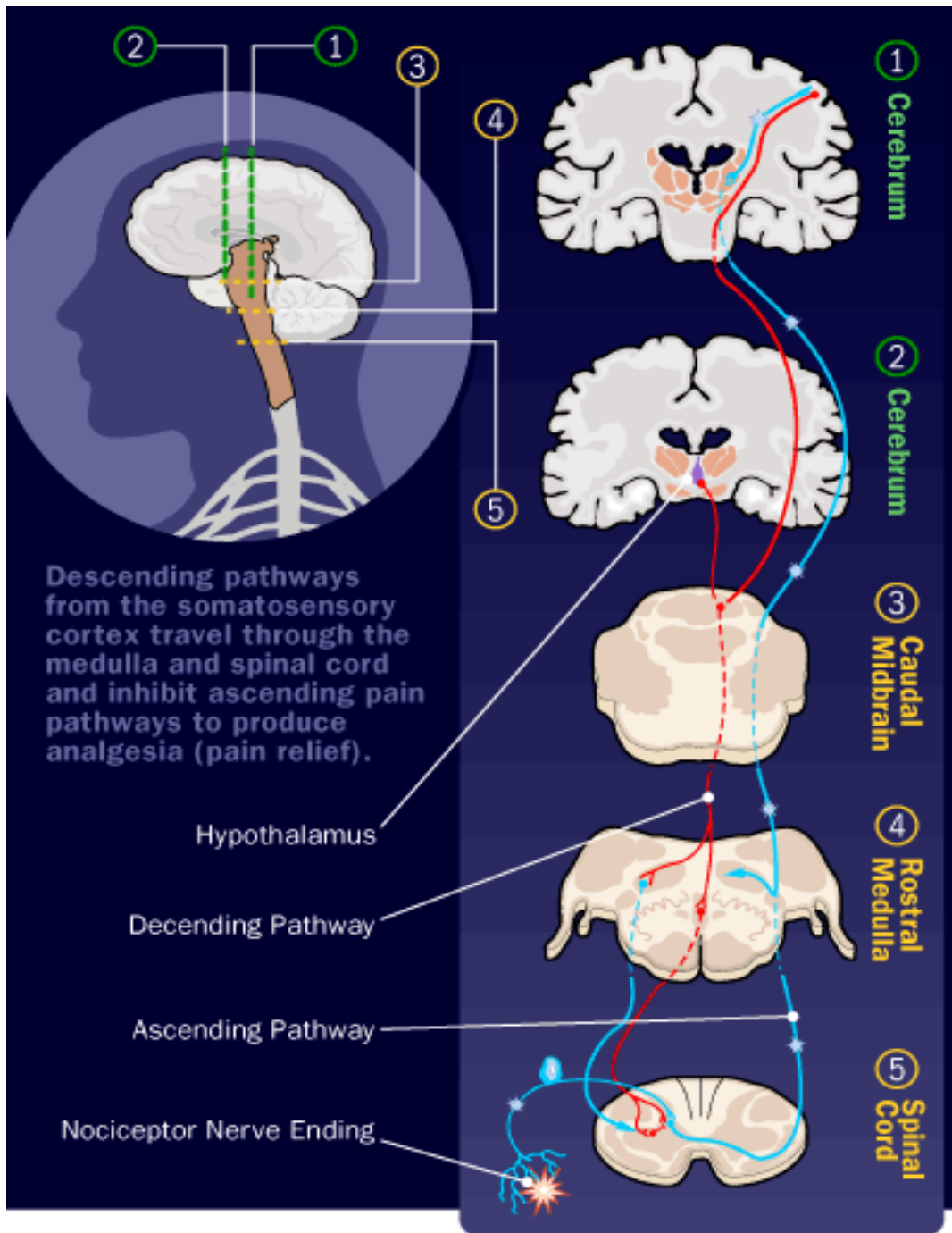
- **Not a manufactured drug. Individual medications “compounded” (mixed) after receiving a prescription.**
- **Custom-designed with the patient in mind.**
- **Physician and compounding pharmacist work together to ensure patient is prescribed an appropriate strength and dosage.**
- **Each of the individual medications have been FDA approved for the purposes of compounding.**

Common Pain Points

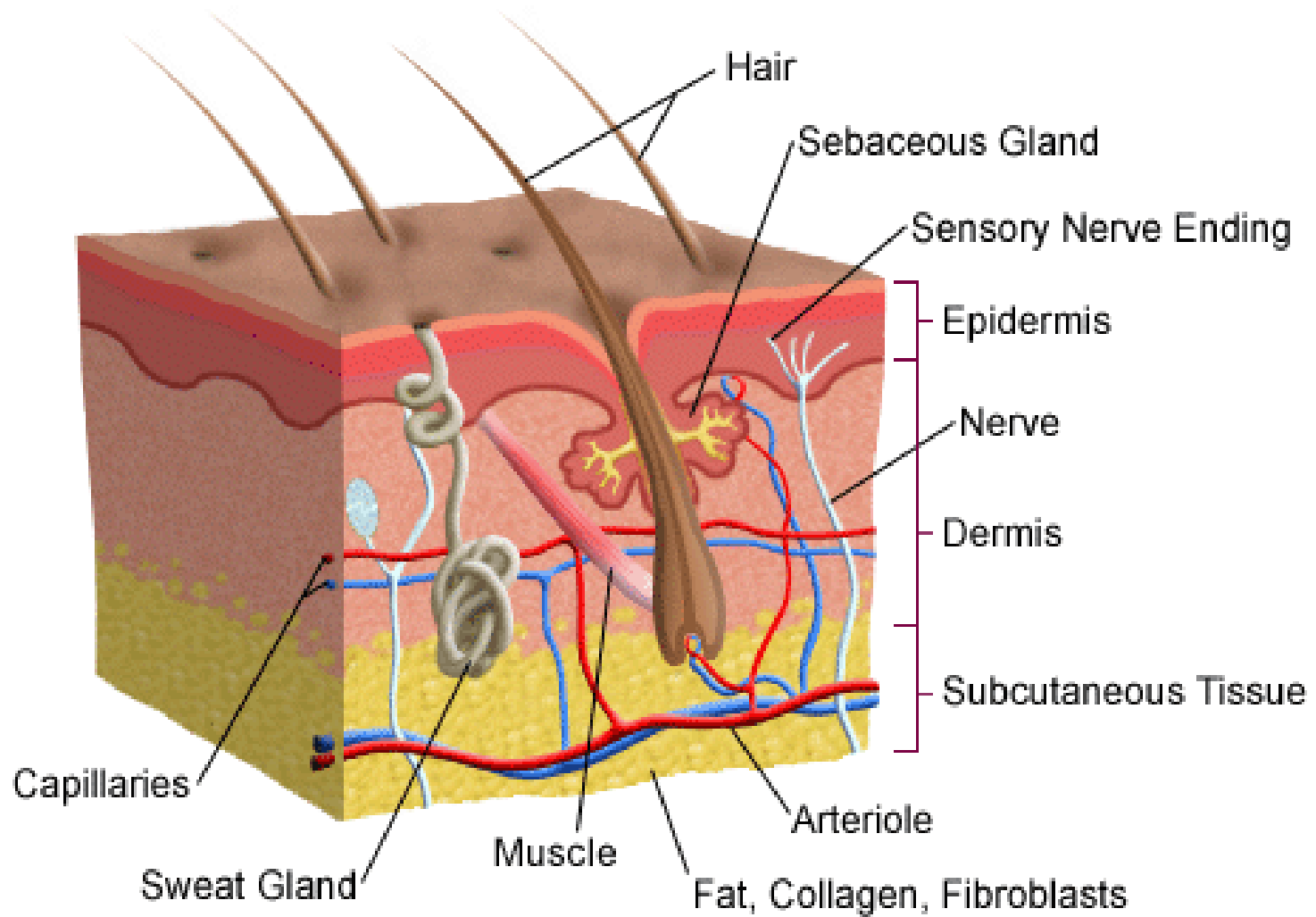


Confidential Information

How Pain Works



The Skin



Skin Layers

- **Types of skin layer properties:**
 - **Lipophilic (Greek, “fat loving”)**
 - **Lipophobic (Greek, “fat hating”)**
- **In the past, these different types of skin layers and properties limited the effectiveness of topical medications.**
- **Medications need both Lipid (lipophilic) and Aqueous (lipophobic) properties to penetrate the skin to therapeutic depths.**

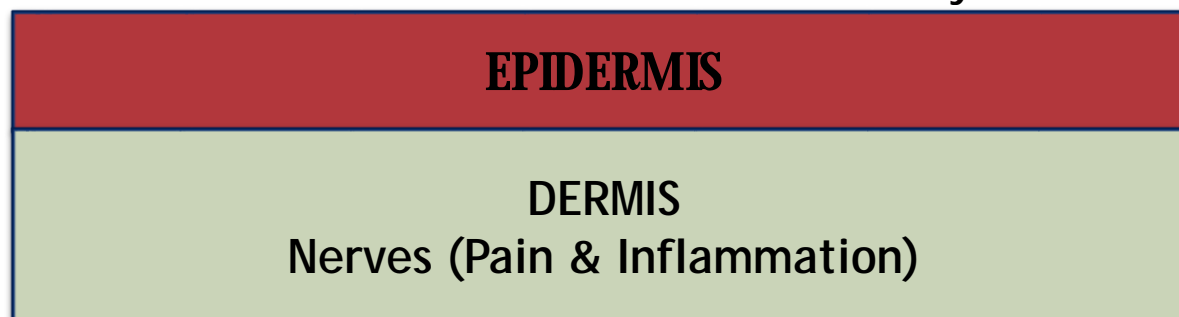
Skin Layers (cont.)

Property Required
to Penetrate:

LIPID

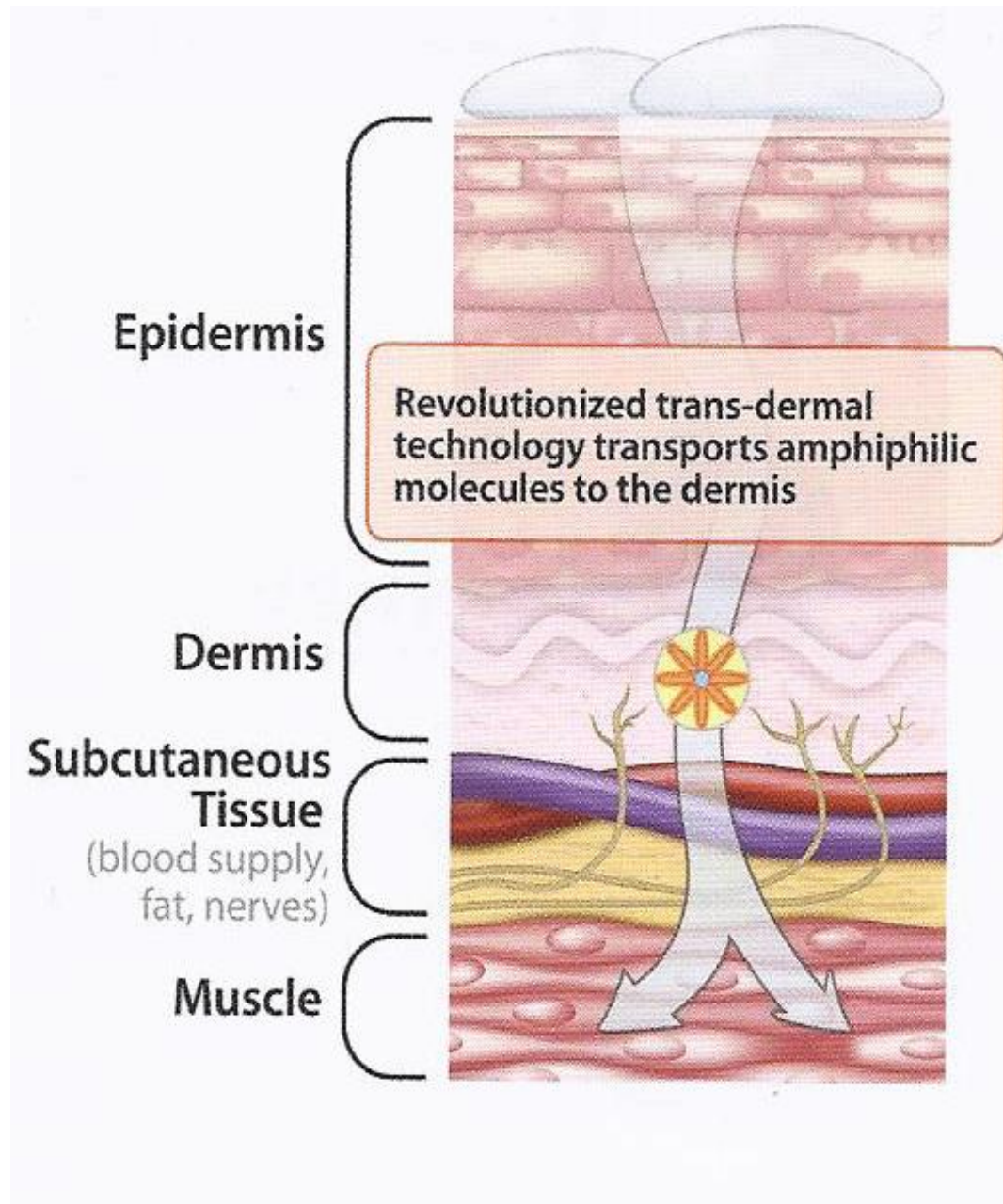
AQUEOUS

Layers of Skin



- The general rule is “like dissolves like.”
- A Lipid substance will pass through the Epidermis because both substances are alike. However, a Lipid is not able to penetrate the Dermis because they are opposite in chemistry (e.g. oil & water). Instead, an Aqueous substance is required to do so.

Transdermal Delivery



Medication Classes

Medication Classes

- **It is common practice in medicine to designate classes of medication according to their most common or familiar use.**
- **Prescription topical pain creams commonly include five classes of medications.**
 - **NMDA Receptor Antagonist**
 - **NSAID's**
 - **Muscle Relaxants**
 - **Anti-Spasmodics**
 - **Local Anesthetics**

NMDA Receptor Antagonist

- **N-Methyl-D-aspartate (NMDA)**
- **NMDA receptor antagonists are a class of anesthetics that work to antagonize, or inhibit the action of the N-methyl d-aspartate receptor (NMDAR).**
- **Ketamine (a Schedule III Controlled Substance) is a NMDA Receptor Antagonist that is commonly found in prescription topical pain creams.**

NMDA Receptor Antagonist - Ketamine

- **Schedule III Controlled Substance**
- **Found to be effective at reducing neuropathic pain and typically prescribed for the following indications:**
 - **Complex Regional Pain Syndrome (CRPS or RSD)**
 - **Radiculopathy**
 - **Post Herpetic Neuralgia (PHN)**
 - **Peripheral Sensitization (after a peripheral nerve lesion)**
 - **Fibromyalgia**
 - **Diabetic Neuropathy**
 - **Chemo Induced Neuropathy**
 - **Post Surgical Neuropathic Pain**
 - **Idiopathic Proctodynia**
 - **Trigeminal neuralgia**
 - **Phantom limb pain**

NSAIDs

- **Non-steroidal anti-inflammatory drugs, usually abbreviated “NSAIDs.”**
- **Classified as drugs that provide analgesic and antipyretic (fever-reducing) effects, and, in higher doses, anti-inflammatory effects.**
- **The most prominent branded members of this group of drugs are aspirin, ibuprofen, and naproxen.**

NSAIDs – Flurbiprofen, Diclofenac, etc.

- **Common NSAIDs found in prescription topical pain creams include Flurbiprofen, Diclofenac and Mefenamic Acid.**
- **These medications are typically prescribed to provide relief for the following:**
 - **OA and RA**
 - **Postoperative pain**
 - **Mild pain due to inflammation and tissue injury**
 - **Tendonitis**
 - **Sprains and Strains**
 - **Sports or overuse-type injuries**

Muscle Relaxants

- **Common Muscle Relaxants found in prescription topical pain creams include Baclofen, Cyclobenzaprine, Orphenadrine and Imipramine.**
- **These medications are typically prescribed to provide relief for the following:**
 - **Low back pain and neck pain**
 - **Skeletal muscle spasms**
 - **Fibromyalgia**
 - **Myofascial Pain Syndrome**
 - **Radiculopathy**
 - **Acute painful musculoskeletal conditions**

Anti-Spasmodics

- **Common Anti-Spasmodics found in prescription topical pain creams include Baclofen and Gabapentin.**
- **These medications are typically prescribed to provide relief for the following:**
 - **Fibromyalgia**
 - **Chronic neuropathic pain**
 - **CRPS**
 - **Post Herpetic Neuralgia**
 - **Diabetic neuropathy**
 - **Chemo induced neuropathy**

Local Anesthetics

- **Common local anesthetics found in prescription topical pain creams include Lidocaine and Tetracaine.**
- **These medications are antipruritic (anti-itch) and are typically prescribed to provide numbness at the pain site.**

Prescription Combinations

Diagnosis

Inflammatory

| |
|----------------------|
| Epicondylitis |
| Musculoskeletal Pain |
| Osteoarthritis |
| Plantar fasciitis |
| Rheumatoid arthritis |
| Tendinosis |
| Tendonitis |

Neuropathic

| |
|---|
| CIPN - Acute |
| CIPN - Chronic |
| CRPS/RSD - Phase 1 |
| CRPS/RSD - Phase 2 |
| Developing Neuropathy - Acute Phase W/ Inflammation |
| Diabetic Peripheral Neuropathy |
| General Neuropathy |
| General Neuropathy |
| Phantom Limb Pain |
| Post Herpetic Neuralgia - Acute |
| Post Herpetic Neuralgia - Chronic |
| Trigeminal neuralgia |

Combination

| |
|-------------------------------------|
| Failed back syndrome |
| Fibromyalgia |
| Myofascial Pain Syndrome |
| Radiculopathy |
| TMJ |
| Musculoskeletal Pain & Inflammation |

Prescription Form – Medication Combinations

- Musculoskeletal Pain, Inflammation**
Ketamine 10% (C-III), Baclofen 2%, Cyclobenzaprine 2%, Flurbiprofen 10%, Gabapentin 6%, Lidocaine 2%
- Musculoskeletal Pain, Inflammation**
Flurbiprofen 20%, Baclofen 2%, Cyclobenzaprine 2%, Gabapentin 6%, Lidocaine 5%
- Tendinosis, Strictures, Scarring**
Flurbiprofen 10%, Baclofen 2%, Verapamil 10%

- General Neuropathy**
Ketamine 10% (C-III), Baclofen 2%, Cyclobenzaprine 2%, Flurbiprofen 10%, Gabapentin 6%, Lidocaine 2%
- Chemotherapy Induced Peripheral Neuropathy, Diabetic Peripheral Neuropathy**
Ketamine 10% (C-III), Baclofen 2%, Gabapentin 6%, Imipramine 3%, Nifedipine 2%, Lidocaine 2%
- RSD/CRPS, Trigeminal Neuralgia, Phantom Limb Pain, Developing Neuropathy**
Ketamine 10% (C-III), Clonidine 0.2%, Gabapentin 6%, Imipramine 3%, Mefenamic Acid 3%, Lidocaine 2%

- Fibromyalgia, Radiculopathy, Failed Back Syndrome**
Ketamine 10% (C-III), Baclofen 2%, Cyclobenzaprine 2%, Diclofenac 3%, Gabapentin 6%, Lidocaine 2%
- Myofascial Pain Syndromes, TMJ**
Flurbiprofen 10%, Baclofen 2%, Cyclobenzaprine 2%, Gabapentin 6%, Orphenadrine 5%, Lidocaine 2%
- Myofascial Pain, Post Laminectomy, Greater Neuropathic Components**
Ketamine 10% (C-III), Baclofen 2%, Cyclobenzaprine 2%, Flurbiprofen 10%, Gabapentin 6%, Lidocaine 2%

A Strong Foundation – The Base

- **Lipoderm Base + DMSO Driver**
- **Lipoderm base (LIPID) is formulated to hold medications in a way that can be applied to the skin and effectively carried to the site of pain.**
- **DMSO driver (Aqueous) is added to make the skin more receptive to the uptake of the medication.**
- **Combination of the Lipoderm base and DMSO driver allows the compounded medications to pass through the skin and be delivered to the site of pain.**

Anti-Inflammatory Combinations

- Inflammation is normally accompanied by stiff and sore muscles.

- **Common Anti-Inflammatory Combinations:**

- Musculoskeletal Pain, Inflammation**

- Ketamine 10% (C-III), Baclofen 2%, Cyclobenzaprine 2%, Flurbiprofen 10%, Gabapentin 6%, Lidocaine 2%

- Musculoskeletal Pain, Inflammation**

- Flurbiprofen 20%, Baclofen 2%, Cyclobenzaprine 2%, Gabapentin 6%, Lidocaine 5%

- **How anti-inflammatory combinations work:**

- Numbs the area via a local anesthetic, Lidocaine.
- After ~15 minutes the NSAIDs penetrate transdermally and exert anti-inflammatory effects.

Neuropathic Pain Combinations

- **Common Neuropathic Pain Combinations:**

- General Neuropathy**
Ketamine 10% (C-III), Baclofen 2%, Cyclobenzaprine 2%, Flurbiprofen 10%, Gabapentin 6%, Lidocaine 2%
- Chemotherapy Induced Peripheral Neuropathy, Diabetic Peripheral Neuropathy**
Ketamine 10% (C-III), Baclofen 2%, Gabapentin 6%, Imipramine 3%, Nifedipine 2%, Lidocaine 2%
- RSD/CRPS, Trigeminal Neuralgia, Phantom Limb Pain, Developing Neuropathy**
Ketamine 10% (C-III), Clonidine 0.2%, Gabapentin 6%, Imipramine 3%, Mefenamic Acid 3%, Lidocaine 2%
- Myofascial Pain, Post Laminectomy, Greater Neuropathic Components**
Ketamine 10% (C-III), Baclofen 2%, Cyclobenzaprine 2%, Flurbiprofen 10%, Gabapentin 6%, Lidocaine 2%

- **Effective in all types of neuropathic pain, especially when nerve damage is present.**

- Ketamine (an NMDA receptor antagonist) quiets the nerve noise at the source of the pain.
- Muscle relaxants/anti-spasmodics help calm the usual muscle tremors accompanied with Post-Herpetic Neuralgia (PHN).
- Imipramine has been found effective at treating diabetic induced neuropathy. A higher concentration of Ketamine would be appropriate for more severe cases of diabetic induced neuropathy.

Topical Delivery

Adverse Effects of Oral NSAIDs

- **30 million people reported taking oral NSAIDs regularly.**
- **107,000 were hospitalized for NSAID-related complications among arthritis patients alone.**
- **Much higher in Osteoarthritis (OA) and Rheumatoid Arthritis (RA) patients.**

Topical Advantages

- **Overcome the disadvantages of oral drug administration.**
 - **First pass metabolism**
 - **Peptic ulcer**
 - **Gastrointestinal hemorrhage**
- **Local enhanced drug delivery to affected tissues with a reduced incidence of systemic adverse effects.**
- **Plasma concentrations (amount of medication in bloodstream) after topical administration are generally less than 5% of those in oral administration.**

Topical Advantages (cont.)

- **Meniscus and Cartilage concentrations are 4-7 times higher than after oral administration.**
- **Concentrations in tendon sheath are also significantly greater than plasma concentrations after topical administration.**

Topical Competition (branded)

Topical Competition

- **Branded prescription medications marketed to physicians to alleviate pain include the following:**
 - **Voltaren®**
 - **Flector Patch®**
 - **Pennsaid®**
 - **Lidoderm®**

Voltaren & Flector

- **1% Diclofenac Gel (Voltaren)**
 - #1 prescribed topical NSAID
 - Typically prescribed to relieve the pain of OA in the knees, ankles, feet, elbows, wrists and hands.
- **1.3% Diclofenac Patch (Flector)**
 - Typically prescribed to relieve pain caused by minor strains, sprains or bruises.
 - 12 hours on 12 hours off
 - 2 hour period
- **Custom compounded formulations can include 3% Diclofenac without the restrictions of a patch. Muscle relaxants and local anesthetics can also be included to help manage pain.**

Pennsaid

- **1.5% Diclofenac Gel**
- **Typically prescribed to relieve the pain of OA of the knee, off-label use on other joints is common.**
- **High concentration of DMSO (45.5%)**
- **Custom compounded formulations can include DMSO at a lower concentration to provide effective delivery without drying out the skin.**

Lidoderm

- **5% Lidocaine Patch**
- **Typically prescribed to relieve pain from Post Herpetic Neuralgia. Off label use for other indications resulting in acute pain are common.**
- **If used for PHN, Lidocaine is no longer the most effective medication. Primary research demonstrates much higher efficacy in treating PHN with topical ketamine and gabapentin, which can be included in custom compounded formulations.**

Sales Process

Main Physician Call Points

- **Orthopedic**
- **Pain Management**
- **Sports Medicine**
- **Podiatry**
- **Anesthesiologist
(pain medicine)**
- **Physiatrist**
- **Rheumatology**
- **Neurologist**
- **Oncology**
- **Family Medicine**

Cold-Call

- **Build a relationship with the gatekeeper (receptionist, nurse, Physician Assistants, etc.).**
- **Explain the offering:**
 - **“We compound custom pain/anti-inflammatory creams that are similar to Voltaren or Flector Patch but with analgesic action as well.”**
 - **“We compound topical pain and anti-inflammatory creams.”**
 - **“Topical alternative to opioids”**
- **Ask to speak with available healthcare providers.**
- **Schedule lunch to present to the physician(s).**

The Physician Interaction

- **Show physician the compound prescription form and educate him or her on the medications.**
- **Ask open-ended questions:**
 - What kind of topicals do you currently use?
 - Why haven't you used topicals in treating pain before?
 - Have you ever used compounding before?
- **Customize the sales approach.**
- **Pitch quality of compounded medications and emphasis on customer service.**

Know the Audience

- Research the clinic and the physician.
- Know the physician's background and try to make a personal connection.
- Understand the physician's needs by his or her practice area.
 - **Pain Specialist:** Prefers an alternative to opioids. Topical pain creams are not addictive, unlike oral pain meds.
 - **Orthopedics:** Similar to Voltaren/Flector Patch/Pennsiad but less expensive and at more effective concentration.
 - **Family Practice:** Strength of an opioid without the systemic effects. Patients can use it and receive pain relief throughout the work day.

Know the Current Prescribing Habits

- **To the extent possible, determine whether the physician is currently prescribing prescription topical pain creams.**
 - **If so, what pharmacy is being used? Local or national? Who is the rep currently getting his business? What is the rep's connection to the physician?**
 - **If not, what is the physician currently prescribing for pain indications? An oral medication? A prescription patch?**
 - **Has the physician prescribed topical pain medications in the past, but stopped doing so? If so, why? Did the pharmacy provide bad quality or service?**

Customize Sales Approach

- **You currently use topicals, great! What kind? Voltaren?**
 - **Our anti-inflammatory is similar to Voltaren in that it uses Diclofenac but at a higher concentration in conjunction with other anti-inflammatory medications, muscle relaxants and local anesthetics.**
- **You have yet to use topicals? What are your hesitations?**
 - **Reference other local physicians**
 - **Provide patient testimonials**
 - **Hand out primary research highlighting the safe and effective use of topical analgesics and anti-inflammatories.**

Educate the Physician

- **Explain the medications included in the formulations.**
- **Ask about patients' common indications.**
 - What diagnosis do you typically see?
 - What are you doing for patients with OA, Tendonitis, LBP?
 - Do you have patients looking for an alternative to prescription medication or that would like to take less prescription medication?
- **Provide specific indications to help drive interest:**
 - **“I imagine you treat a lot of lower back pain.”**
 - A combination pain cream has been successful in managing low back pain. In fact, it is the most common indication we see for prescription pain creams.
 - **Orthopedic specialist deal with issues relating to major joints in the body**
 - With our anti-inflammatory cream you're getting drug concentrations in the meniscus and cartilage that are 4-7 times higher than oral administration without systemic absorption

Pitch Quality & Customer Service

- **Topical compounded medications utilize a premium base and DMSO drivers.**
 - Lipoderm ActiveMax by Professional Compounding Centers of America (PCCA) is specially formulated to hold numerous medications together and effectively deliver those medications to the point of pain.
 - DMSO drivers enhance drug delivery with minimal systemic absorption.
- **High-quality plastic pumps made by TopiPump.**
- **Fast & Free Delivery.**
 - Prescriptions are shipped within 48 hours.
 - Overnight shipping at no charge to the patient.

Pitch Quality & Customer Service (cont.)

- **Availability of co-pay reduction through third-party provider reducing most patients co-pay to \$15.**
- **Compounding pharmacists and pharmacy technicians available to answer any questions from prescribing physicians or patients.**
- **Many physicians are not happy with the performance of fly-by-night compounding pharmacies and sales organizations. Central is well-staffed and ensures customer services is paramount for both the physician and the patient.**

Offer a Prescription Trial

- **A good way to wrap-up is to recommend the product to the physician, MA/PA, or associate within the clinic who may have an applicable pain indication.**
 - This will be written as an actual prescription.
 - If the physician specifies a formulation containing a controlled substance for their own personal use, then it must be signed off by another doctor.
- **Positive feedback from doctors, associates within the clinic, friends and family, builds a great relationship for future business.**

Follow Up

- **Address any hesitations**
- **Ask about a specific patient they've been treating that might benefit from the cream**
- **Ask questions regarding the research you handed out, offer highlights or testimonials**
- **Recommend application for certain diagnosis**
- **Ask physician to give Central one chance to provide an excellent compounded product and superior customer service to the patient and the physician's office.**

The End.



Central Rexall Drugs Inc.
125 East Thomas Street
Hammond, Louisiana 70401
office: 877.258.3477

Trent Brockmeier, COO
cell: 985.205.2044
trent@centraldrugs.net

www.centraldrugs.net