

LIDOTHOL- lidocaine and menthol patch
Advanced Rx Pharmacy of Tennessee, LLC

Disclaimer: This drug has not been found by FDA to be safe and effective, and this labeling has not been approved by FDA. For further information about unapproved drugs, click here.

Lidothol - Lidocaine 4.5%, Menthol 5% Patch

SPL Medguide

Lidothol (Lidocaine 4.5% / Menthol 5% Patch)

For Topical Use Only

Do not use:

- On the face or rashes
- On wounds, damaged, or infected skin
- In the eyes, mouth or other mucous membranes
- On genitals
- With a heating pad

Ask a doctor before use if:

- You are allergic to topical products or any ingredients in this product
- You are pregnant or breast feeding
- You are under age 18

When using this product:

- Wash hands after applying or removing patch
- Avoid contact with eyes
- If eye contact occurs, rinse thoroughly with water

Stop use and consult your physician if:

- Rash, irritation, or itching develops
- Condition worsens Keep out of reach of children

Lidothol Patient Information.

Before you begin using this medication: read this entire patient information sheet. If you have any questions, please consult your physician or pharmacist. Inform your physician if your condition does not improve or if it worsens.

This information may not include all of the details needed to use Lidothol safely and effectively. Discuss use with your doctor or pharmacist.

What is Lidothol?

A topical pain relief patch consisting of the local anesthetic Lidocaine (4.5%) and the topical analgesic Menthol (5%).

What is Lidothol used for?

The patch assists patients in the management of mild to moderate acute pain or mild to moderate aches. Lidothol is applied to the skin at the specific region experiencing these pain symptoms. The synthesis of Lidocaine and Menthol is a highly effective combination of pain relievers working to alleviate discomfort while the root cause is being managed and treated by your healthcare providers.

DO NOT USE:

- If you are allergic to any of the ingredients in this product
- On wounds or damaged skin
- With a heating pad
- If you are pregnant, planning to become pregnant, or breastfeeding

What are the possible side effects with Lidothol?

- Common: itching or redness of the skin following application
- NOTE: The majority of patients experience no significant adverse events following patch application. Serious side effects, are, in general, related to accidental toxicity of medication by applying considerably more than directed by your doctor or pharmacist or by ingesting the contents of the patch.
- Tell your healthcare provider about all the medicines you take. This includes prescription and nonprescription medicines, vitamins, and herbal supplements.
- Avoid excessive alcohol usage, since it may increase the potential for Central Nervous System (CNS) effects such as dizziness, confusion, lightheadedness and orthostatic hypotension.

This is not a complete list of the possible side effects. For more information, talk with your doctor or pharmacist. You may report side effects to FDA at 1--800--FDA--1088 or www.fda.gov/medwatch

KEEP OUT OF REACH OF CHILDREN Rx ONLY

DIRECTIONS FOR USE

Adults and children 12 years and over:

Apply 1 to 2 patches to the affected area of intact skin. Lidothol should be removed after 12 hours of continuous use and remain off for at least 12 hours.

1. Determine area of patch application. If the pain area is smaller than the patch, patches may be cut into smaller sizes with scissors. Safely discard the remaining unused pieces of cut patches where children and pets cannot reach.
2. Remove the transparent protective film (clear plastic barrier) before application of patches to the skin. Apply immediately after removing the protective film.
3. Apply 1 patch to the affected area so that the patch covers all or most of the painful area.
4. Remove patch if irritation occurs.

Children under 12 years of age: Consult a doctor

WARNINGS

1. Do not use:
2. On wounds, cuts, damaged or infected skin
3. On eyes, mouth, genitals, or other mucous membranes

2. Consult physician for children under 12 years of age

3. Stop and consult your prescriber if pain worsens

Call your healthcare provider right away if you experience any of the following warning signs or any other unusual symptoms of concern:

- Shortness of breath
- Swelling or numbness of the tongue or throat
- Severe headache or vomiting
- Dizziness or faintness
- Changes in vision or speech

General information for safe and effective use of Lidothol

Do not use this product for another indication. Do not give this drug to anyone else, even if they have the same condition. This product is intended for use as prescribed by a physician.

How should I store Lidothol?

Store product at room temperature at 65°F to 75°F (18°C to 24°C). Keep away from heat or sunlight. Protect from excessive moisture. Safely discard product after expiration date posted on the product label. Discard patches away from small children or animals.

DO NOT use the product after the expiration date printed on the box.

This insert provides the most important information about Lidothol. If you would like more information, talk with your healthcare provider or pharmacist. There is additional information in the following sections intended for healthcare professionals.

What are the active ingredients in Lidothol?

The patch consists of 4.5% Lidocaine and 5% Menthol.

What are the inactive Ingredients in Lidothol?

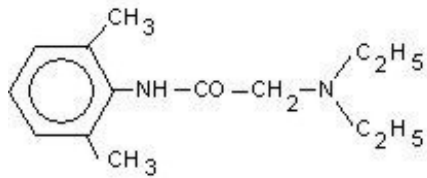
Alcohol, Carboxymethylcellulose Sodium, Dihydroxyaluminum Aminoacetate, Glycerine, Kaolin, Partially Neutralized Polyacrylate, Phenoxyethanol, Polysorbate 80, Polyvinyl Pyrrolidone, Tartaric Acid, Tetrasodium EDTA, Water

Description

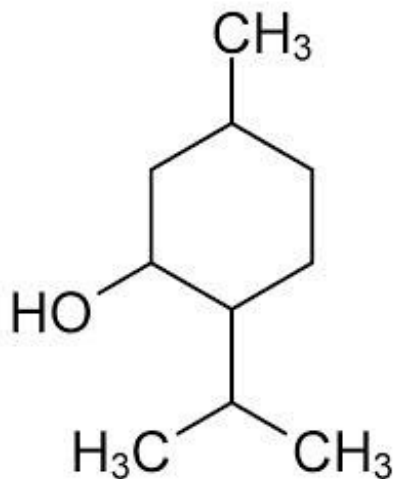
Lidothol is a prescription topical patch, packaged with 15 medicated patches: 5 re-sealable pouches containing 3 patches each. Lidocaine is present in a 4.5% concentration (w/w). It is chemically designated as 2--(diethylamino)--N--(2,6--dimethylphenyl) acetamide and has an empirical formula of C₁₄H₂₂N₂O. The molecular weight of Lidocaine is 234.34 g/mol. Menthol is present in a 5% concentration (w/w). The chemical name is (1R,2S,5R)--2--isopropyl--5--methylcyclohexanol. The empirical formula for Menthol is C₁₀H₂₀O with a molecular weight of 156.27 g/mol.

Lidothol (Lidocaine 4.5% / Menthol 5% Patch) consists of an adhesive hydrogel containing Lidocaine 4.5% and Menthol 5%, applied to flexible woven polyester backing and protected by a plastic film. The protective film is removed prior to application to the skin. The size of the patch is 12cm x 8cm.

Lidocaine is chemically designated as 2--(diethylamino)--N--(2,6--dimethylphenyl), has an octanol: water partition ration of 43 at pH 7.4, and has the following structure:



Menthol is chemically designated as 2--Isopropyl--5--methylcyclohexanol. It contains colorless, hexagonal crystals, usually needle--like; fused masses or crystalline powder with a pleasant, peppermint--like odor. It has a melting point between 31°C to 36° C. Menthol has the following structure:



Each adhesive patch contains 76.5mg of Lidocaine and 85mg of Menthol. It also contains the following inactive ingredients: Alcohol, Carboxymethylcellulose Sodium, Dihydroxyaluminum Aminoacetate, Glycerine, Kaolin, Partially Neutralized Polyacrylate, Phenoxyethanol, Polysorbate 80, Polyvinyl Pyrrolidone, Tartaric Acid, Tetrasodium EDTA, Water

Clinical Pharmacology

Lidocaine is a topical anesthetic and stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anesthetic action.

Menthol has local anesthetic and counterirritant qualities. It also acts as a weak kappa (κ) opioid receptor agonist. Menthol chemically triggers the cold--sensitive TRPM--8 receptors in the skin, which are responsible for the well--documented cooling sensation that occurs when applied to the skin. Menthol's analgesic properties are not fully understood; however, they are mediated through a selective activation of κ --opioid receptors. Menthol also blocks voltage--sensitive sodium channels, reducing neural activity that may stimulate muscle tissue.

Pharmacodynamics

Menthol works by targeting the κ --opioid receptor on the TRPM8 neuron. The TRPM8 neuron is normally activated at temperatures between (8° -- 28° C). Menthol causes the

neuron to fire at temperatures above normal activation, which triggers the characteristic cooling sensation. Also because of Menthol's specific targeting of the κ -opioid receptor, it is endowed with analgesic properties.

Lidocaine is an amide--type local anesthetic agent and is suggested to stabilize neuronal membranes by inhibiting the ionic fluxes required for the initiation and conduction of impulses.

The penetration of Lidocaine into intact skin after application of patch is sufficient to produce an analgesic effect, but less than the amount necessary to produce a complete sensory block.

Pharmacokinetics

Absorption:

The amount of Lidocaine and Menthol systemically absorbed is directly related to both the duration of application and the surface area over which it is applied.

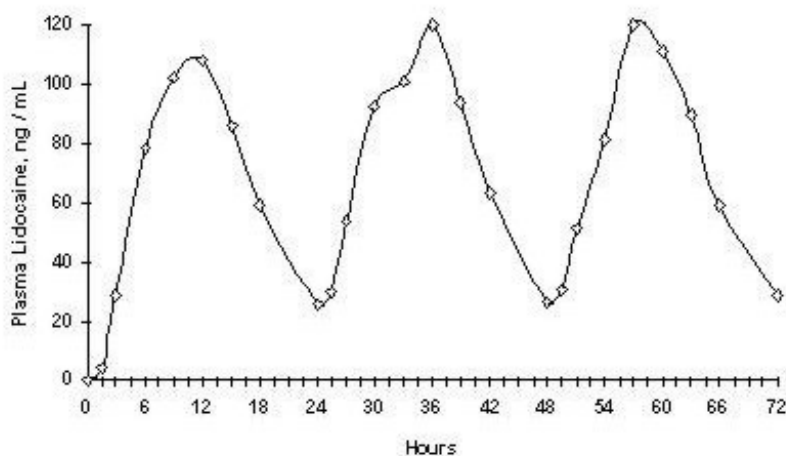
In a pharmacokinetic study, three Lidocaine 5% patches were applied over an area of 420 cm² of intact skin on the back of

normal volunteers for 12 hours. Blood samples were withdrawn for a determination of Lidocaine concentration during the application and for 12 hours after removal of patches. The results are summarized in table 1.

Repeated application of three days indicated that the Lidocaine concentration does not increase with daily use. The mean plasma pharmacokinetic profile for the 15 healthy volunteers is shown in Figure 1. When Lidocaine 5% patch is used according to the recommended dosing instructions, only $3 \pm 2\%$ of the dose applied is expected to be absorbed. At least 95% (665 mg) of Lidocaine will remain in a used patch. Mean peak blood concentration of Lidocaine is about 0.13 $\mu\text{g}/\text{mL}$ (about 1/10 of the therapeutic concentration required to treat cardiac arrhythmias).

Figure 1

Mean Lidocaine blood concentrations after three consecutive daily applications of three Lidocaine 5% patches simultaneously for 12 hours per day in healthy volunteers (n = 15).



Distribution:

When Lidocaine is administered intravenously to healthy volunteers, the volume of distribution is 0.7 to 2.7 L/kg (mean 1.5

± 0.6 SD, n = 15). At concentrations produced by application of Lidocaine Patch 5%, Lidocaine is approximately 70% bound to plasma proteins, primarily alpha-1-acid glycoprotein. At much higher plasma concentrations (1 to 4 µg/mL of free base), the plasma protein binding of Lidocaine is concentration dependent. Lidocaine crosses the placental and blood brain barriers, presumably by passive diffusion.

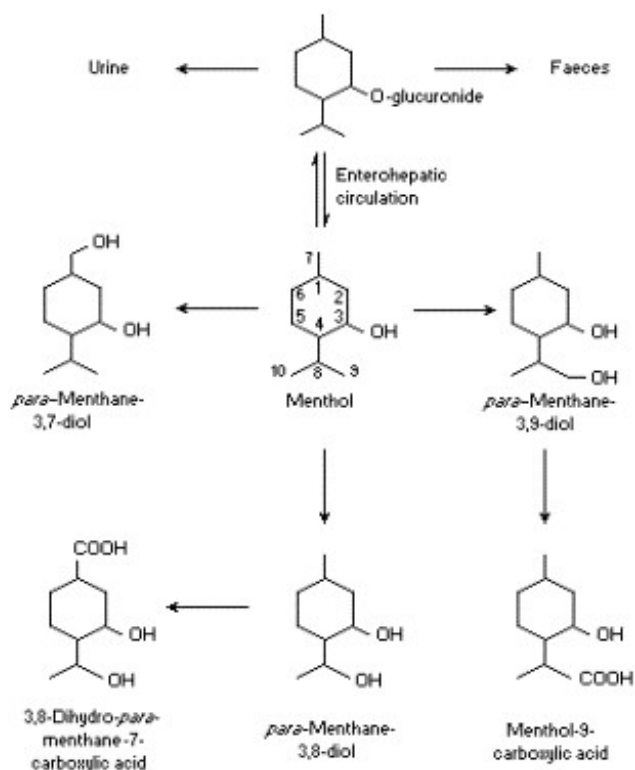
Metabolism:

It is not known if Lidocaine is metabolized in the skin. Lidocaine is metabolized rapidly by the liver to a number of metabolites, including monoethylglycinexylidie (MEGX) and glycinexylidide (GX), both of which have pharmacologic activity similar to, but less potent than that of Lidocaine. A minor metabolite, 2,6-xylidine, has unknown pharmacologic activity but is carcinogenic in rats. The blood concentration of this metabolite is negligible following application of Lidocaine Patch 5%.

Following intravenous administration, MEGX and GX concentrations in serum range from 11% to 36% and from 5% to 11% of Lidocaine concentrations, respectively.

Humans rapidly metabolize Menthols primarily in the liver by the microsomes, using the enzyme CYP2A6. Cytochrome P450-mediated oxidation occurs in humans, yielding various alcohol and hydroxy acid derivatives. These are eliminated in the urine unchanged or conjugated with glucuronic acid.

Figure 1. Proposed metabolic pathway of menthol



Excretion:

Lidocaine and its metabolites are excreted by the kidneys. Less than 10% of Lidocaine is excreted unchanged. The half-life of Lidocaine elimination from plasma following IV administration is 81 to 149 minutes (mean 107 ± 22 SD, n=15). The systemic clearance

is 0.33 to 0.90 L/min (mean 0.64 ± 0.18 SD, n=15).

Menthols are largely eliminated as glucuronides. In an experiment, 79% of a 1g (Quick, 1928) and 78% of a 10--20mg (Atzl et al., 1972) oral dose of Menthol was eliminated as the glucuronic acid conjugate within 6 h after administration to volunteers. Of a dose of 47 mg/kg bw [^3H]-Menthol, 82% was eliminated in the urine 17 hours after administration.

Smaller amounts were distributed in the feces and ileum; only 1% of the activity remained in the liver (Clegg et al., 1982).

Indications and Usage

Lidothol is a formulation used to assist patients in the treatment of mild to moderate acute or chronic aches or pain. Muscle or joint pain can be due to muscle or ligament strains, simple backache, tendonitis, osteoarthritis, rheumatoid arthritis, peripheral neuropathies such as diabetic neuropathy or post herpetic neuralgia, and other complex regional pains. It can also be used to help with certain types of headaches, but use with caution when applying in order to avoid eye contact.

Other uses may be considered if deemed clinically relevant.

Contraindications

Lidothol is contraindicated in patients with a known history of sensitivity to local anesthetics of the amide type, or to any other component of the product.

Warnings and Precautions

Methemoglobinemia

Cases of methemoglobinemia have been reported in association with local anesthetic use. Although all patients are at risk for methemoglobinemia, patients with glucose-6-phosphate dehydrogenase deficiency, congenital or idiopathic methemoglobinemia, cardiac or pulmonary compromise, infants under 6 months of age, and concurrent exposure to oxidizing agents or their metabolites are more susceptible to developing clinical manifestations of the condition. If local anesthetics must be used in these patients, close monitoring for symptoms and signs of methemoglobinemia is recommended.

Signs and symptoms of methemoglobinemia may occur immediately or may be delayed some hours after exposure and are characterized by a cyanotic skin discoloration and abnormal coloration of the blood. Methemoglobin levels may continue to rise; therefore, immediate treatment is required to avert more serious central nervous system and cardiovascular adverse effects, including seizures, coma, arrhythmias, and death. Discontinue Lidothol and any other oxidizing agents. Depending on the severity of the symptoms, patients may respond to supportive care, i.e., oxygen therapy, hydration. More severe symptoms may require treatment with methylene blue, exchange transfusion, or hyperbaric oxygen.

Excessive dosage or short interval between doses can result in high plasma levels and serious adverse effects. Patients should be instructed to strictly adhere to the

recommended dosage and administration guidelines set forth in this literature and on your prescription label. The management of serious adverse reactions may require the use of resuscitative equipment, oxygen or other resuscitative drugs.

Accidental Exposure in Children

Even a used Lidothol patch contains a large amount of Lidocaine. The potential exists for a small child or a pet to suffer serious adverse effects from chewing or ingesting a new or used Lidothol patch, although the risk with this formulation has not been evaluated. It is important for patients to store and dispose of Lidothol beyond the reach of children, pets and others. (See HANDLING AND DISPOSAL)

Excessive Dosing

Excessive dosing by applying Lidothol to larger areas for longer than the recommended wearing time could result in increased absorption of Lidocaine and high blood concentrations, leading to serious adverse effects. Lidocaine toxicity could be expected at Lidocaine blood concentrations above 5 µg/mL. The blood concentration of Lidocaine is determined by the rate of systemic absorption and elimination. Longer duration of application, application of more than the recommended number of patches, smaller patients, or impaired elimination may all contribute to increasing the blood concentration of Lidocaine. With recommended dosing of Lidothol, the average blood concentration is about 0.13 µg/mL, but concentration higher than 0.25 µg/mL have been observed in some patients.

Because of the possibility of sedation, patients should be cautioned regarding the use of heavy machinery or automobiles, also any activities made hazardous by decreased alertness.

Hepatic Disease

Patients with severe hepatic disease are at greater risk of developing toxic blood concentrations of Lidocaine, because of their inability to metabolize Lidocaine normally.

Allergic Reactions

Patients allergic to para--aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to Lidocaine. However, Lidothol should be used with caution in patients with a history of drug sensitivities, especially if the etiologic agent is uncertain.

Non-intact Skin

Application to broken or inflamed skin, although not tested, may result in higher blood concentrations of Lidocaine from increased absorption. Lidothol is only recommended for use on intact skin.

Eye Exposure

The contact of Lidothol with eyes, although not studied, should be avoided based on the findings of severe eye irritations with the use of similar products in animals. If eye contact occurs, immediately wash out the eye with water or saline and protect the eye until sensation returns.

External Heat Sources

Placement of external heat sources, such as heating pads or electric blankets, over

patches is not recommended as this has not been evaluated and may increase plasma Lidocaine levels.

Drug Interactions: Antiarrhythmic Drugs

Lidothol should be used with caution in patients receiving Class 1 antiarrhythmic drugs (such as tocainide and mexiletine) since the toxic effects are additive and potentially synergistic.

Local Anesthetics

When Lidothol is used concurrently with other products containing local anesthetic agents the amount absorbed from all formulations must be considered.

Carcinogenesis, Mutagenesis, Impairment of Fertility Carcinogenesis

A minor metabolite, 2,6--xylidine, has been found to be carcinogenic in rats. The blood concentration of this metabolite is negligible following application of Lidothol

Mutagenesis

Lidocaine is not mutagenic in Salmonella/mammalian microsome test nor clastogenic in chromosome aberration assay with human lymphocytes and mouse micronucleus test.

Impairment of Fertility

The effect of Lidothol on fertility has not been studied.

PREGNANCY:

The safety of Lidothol has not been established during pregnancy. There are no well-controlled studies in pregnant women. Lidothol should not be used during pregnancy unless absolutely needed. Discuss with physician prior to using Lidothol during pregnancy.

NURSING MOTHERS:

The effect of Lidothol on the nursing infant has not been evaluated. Lidothol has not been studied in nursing mothers. Caution should be exercised when Lidothol is administered to a nursing mother.

PEDIATRIC/GERIATRIC USE:

Safety and effectiveness in pediatric and geriatric patients have not been established.

Adverse Reactions

The most common adverse reactions occur at the application site, including dermatitis, itching or scaling. These tend to be dose--limiting and diminish with time.

Serious adverse experiences following the administration of Lidothol are similar in nature to those observed in other amide anesthetic--containing agents. These adverse experiences are, in general, dose--related and may result from high plasma levels caused by excessive dosage, rapid absorption, or may result from hypersensitivity, idiosyncrasy, or a diminished tolerance on the part of the patient. Serious adverse experiences are generally systemic in nature. During or immediately after treatment with Lidothol, the skin at the site of application may develop redness, blisters, bruising, burning sensation, depigmentation, dermatitis, or mild irritation.

Allergic Reactions

Allergic and anaphylactoid reactions associated with Lidocaine, although rare, can occur. They are characterized by angioedema, bronchospasm, dermatitis, dyspnea, hypersensitivity, laryngospasm, pruritus, shock, and urticaria. If they occur, consult your doctor.

Drug Interactions

Patients that are administered local anesthetics may be at increased risk of developing methemoglobinemia when concurrently exposed to the following oxidizing agents

Class

Nitrates/Nitrites

Local Anesthetics

Antineoplastic agents

Antibiotics

Antimalarials

Anticonvulsants

Other drugs

Examples

nitroglycerin, nitroprusside, nitric oxide, nitrous oxide

benzocaine, lidocaine, bupivacaine, mepivacaine, tetracaine, prilocaine, procaine, articaine, ropivacaine

cyclophosphamide, flutamide, rasburicase, ifosfamide, hydroxyurea

dapsone, sulfonamides, nitrofurantoin, para-aminosalicylic acid

chloroquine, primaquine

phenytoin, sodium valproate, phenobarbital

acetaminophen, metoclopramide, sulfa drugs (i.e., sulfasalazine), quinine

Dosage and Administration

Apply Lidothol to intact skin to cover the most painful area. Apply no more than four patches per day. Each patch should not be applied for more than 12 hours in a given 24-- hour period. Patches may be cut into smaller sizes with scissors prior to removal of the protective film. Clothing may be worn over the area of application. Smaller areas of treatment are recommended in a debilitated patient, or a patient with impaired elimination.

If irritation or a burning sensation occurs during application, remove the patch and do not reapply until the irritation subsides.

When Lidothol is used concurrently with other products containing local anesthetic

agents, the amount absorbed from all formulations must be considered.

Lidothol may not stick if it gets wet. Avoid contact with water, such as bathing, swimming or showering.

Overdosage

There have been no reports of over--dosage with Lidothol. Signs of overdosage would include vomiting, drowsiness, coma, respiratory depression, and seizures. In the case of overdosage, discontinue the product immediately, treat the patient symptomatically, and institute supportive measures.

How Supplied

Lidothol is supplied in the following dosage form:

15 Patches: 3 per re--sealable pouch, 5 pouches

NDC: 80425-0252-01

Manufactured For:

Terrain Pharmaceuticals

50 West Liberty Street, Suite 1080

Reno, NV 89501

Distributed by: Advanced Rx Pharmacy of Tennessee, LLC

877.985.4377

Storage and Handling

HANDLING AND DISPOSAL:

Wash hands immediately after applying or removing Lidothol. Eye contact with Lidothol should be avoided. Do not store patch outside the sealed envelope. Apply immediately after removal from the protective envelope. Fold used patches so the adhesive side sticks to itself, then safely discard used patches or pieces of cut patches where children and pets cannot access them. Lidothol should be kept out of reach of children.

STORAGE:

Store at room temperature of 65°F to 75°F (18°C to 24°C). Keep away from heat or sunlight. Protect from excessive moisture. The product can be considered safe and effective to use when maintained under these recommended conditions within the posted expiration date.

Principal Display Panel

Packed By:
AdvancedRx
NashvilleTN, 37217



Store at 20°-25°C (68°-77°F)

Caution: Federal law PROHIBITS Transfer of this drug to any person other than the patient for whom it was prescribed

LIDOTHOL PATCH

#15

NDC: 80425-0252-01 Source NDC: 53225-1025-01
Lot: 15LP Expires: 4/30/2025



LIDOTHOL PATCH #15
NDC: 80425-0252-01
Source NDC: 53225-1025-01
Lot: 15LP Exp:4/30/2025

TERRAIN PHARMAC
S/N: 000000122565

LIDOTHOL

lidocaine and menthol patch

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:80425-0252(NDC:53225-1025)
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
LIDOCAINE (UNII: 98PI200987) (LIDOCAINE - UNII:98PI200987)	LIDOCAINE	4.5 g
MENTHOL (UNII: L7T10EIP3A) (MENTHOL - UNII:L7T10EIP3A)	MENTHOL	5 g

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:80425-0252-1	15 in 1 BOX	01/10/2023	
1		1 in 1 PATCH; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
unapproved drug other		01/10/2023	

Labeler - Advanced Rx Pharmacy of Tennessee, LLC (117023142)

Establishment

Name	Address	ID/FEI	Business Operations
Advanced Rx Pharmacy of Tennessee, LLC		117023142	repack(80425-0252)

Revised: 1/2023

Advanced Rx Pharmacy of Tennessee, LLC