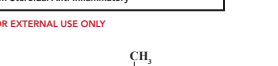
LOXOPROFEN

LOXOTOP™ PAP 100mg Patch

Non-Steroidal Anti-Inflammatory

Rx

FOR EXTERNAL USE ONLY



Product Description
Patch preparation comprising ointment, uniformly spread over a support with the surface of the ointment covered by a liner. The ointment surface is white to light yellow in color. The ointment has a fragrance of mentha oil.

Formulation
Each 100 mg patch comprises 10g of ointment which contains the following:
Loxoprofen sodium hydrate, JP..... 113.4 mg (100 mg as anhydride).

CLINICAL PARTICULARS

1. Indications
Loxoprofen (LOXOTOP™ PAP) is indicated for anti-inflammation and analgesia in the following diseases and symptoms: Osteoarthritis, myalgia, posttraumatic swelling and pain.

2. Dosage and Route of Administration
Apply to the affected area once daily.

3.Contraindications
Loxoprofen (LOXOTOP™ PAP) is contraindicated in the following patients.

- Patients with a history of hypersensitivity to any ingredients of this product.
- Patients with or with a history of aspirin-induced asthma (induction of asthmatic attack with nonsteroidal anti-inflammatory-analgesics, etc.) [May induce an aspirin-induced asthmatic attack.]

4. Special warnings and precautions for use

4.1. Careful Administration
This product should be administered with caution in the following patients: Patients with bronchial asthma (as the disease state may be exacerbated.)

4.2 Clinically Significant Adverse Reactions
Shock, Anaphylaxis: Shock or anaphylaxis (decreased blood pressure, urticaria, laryngeal oedema, dyspnoea, etc.) may occur. Patients should be carefully monitored. If any abnormalities are observed, use of this drug should be discontinued immediately and appropriate measures should be taken.

4.3. Important Precautions

- It is important to note that treatment with anti-inflammatory-analgesic agents is a symptomatic treatment, not a causal treatment.
- For treatment of skin inflammation caused by infectious disease, this product may cause a risk of masking the signs and symptoms of the infectious disease, therefore,the appropriate antibacterial and/or antifungal drugs must be administered in combination with this product to the affected part of the skin, under careful observation and caution.
- Therapies other than drug treatment must also be considered in using this product in the management of chronic diseases (osteoarthritis and others). The patient's clinical condition should be closely monitored with caution against the development of adverse reactions.

4.4. Use in the Elderly
This product should be used with careful monitoring of dermal condition of application area, in the elderly patients.

4.5. Pediatric Use
The safety of this product in low birth weight infants, newborn infants, infants and toddlers, children and adolescents has not been established (because there has been little experience of its use in pediatric patients).

4.6. Precautions Concerning Use
Site of Application:

- Do not apply this product onto area of damaged or non-intact skin or mucosal membrane.
- Do not apply this product onto area of eczema and rash.

5. Interactions with other Medicinal Products and other Forms of Interactions
Not applicable to both contraindications and precautions for coadministration.

6. Pregnancy and Lactation

- This product should be administered to women who are or are possibly pregnant only when the anticipated therapeutic benefits are considered to outweigh any potential risk. [The safety of this product in these populations has not been established.]
- It has been reported that constriction of the fetal ductus arteriosus is observed when woman in the late stage of pregnancy received other nonsteroidal anti-inflammatoryanalgesic drugs for external use.
- Renal impairment and decreased urine output in foetuses as well as accompanying oligohydramnios have been reported following use of cyclooxygenase inhibitors (oral dosage form or suppository) in pregnant women.

7. Effects on Ability to Drive and Use Machines
There is no data available on effects on ability to drive and use machines.

8. Adverse Drug Reaction(s)

8.1. Shock, Anaphylaxis (The Incidence Unknown)

8.2. Other Adverse Drug Reactions

	0.5% to <3%	<0.5%	Incidence Unknown
Hypersensitivity	Pruritus, erythema, contact dermatitis, rash	Haemorrhage subcutaneous, skin irritation, pigment precipitation	Blister, swelling
Gastrointestinal		Stomach discomfort, upper abdominal pain, diarrhoea, loose stools	
Hepatic		Increased AST(GOT), increased ALT(GPT), increased γ-GTP	
Other		Edema	

9. Overdose and Treatment
There is no data available on overdose.

PHARMACOLOGICAL PROPERTIES

1. Pharmacodynamic properties

1.1. Mechanism of Action
After being absorbed transdermally, loxoprofen sodium hydrate is biotransformed into an active metabolite trans-OH form (SRS coordination) to exert its excellent anti-inflammatory and analgesic effects in acute inflammations, chronic inflammations and pain.

1.1.1. Anti-inflammatory effects
Loxoprofen (LOXOTOP™ PAP) has been demonstrated significant anti-inflammatory effects on both acute inflammations such as carrageenin-induced edema (rat) and chronic inflammations such as adjuvant arthritis (rat).

1.1.2. Analgesic effects
Loxoprofen (LOXOTOP™ PAP) has been demonstrated to show the analgesic effect in the Randall-Selitto test (inflamed paw pressuring method: rat), and in the chronic adjuvant arthritis pain test (rat).

1.2 Pharmacokinetic properties

1.2.1. Plasma Concentration
Each of 14 Japanese healthy male adult volunteers was subjected to repeated administration of two Loxoprofen (LOXOTOP™ PAP) on the back once a day for five days, showing detection of loxoprofen and its trans-OH form (active metabolite) in the plasma immediately after the start of the administration with their plasma concentrations gradually increasing over the period of the administration before reaching steady state in four or five days after the administration at low levels compared to those achieved by the equivalent oral dose of the same drug until, upon the discontinuation of the administration, they rapidly disappeared from the plasma to concentrations below the limit of quantitative determination (LQD).

1.2.2. Tissue Penetration
Administration of 3.5cm2 of the Loxoprofen (LOXOTOP™ PAP) (containing 14C-loxoprofen) to the rat dorsal skin for a time period of 24 hours showed that the concentration of radioactivity in the skeletal muscle immediately under the patch administered area of the skin was 3.6- to 24-fold higher than that in the skeletal muscle under the patch non-administered area of the skin, confirming the formation of the trans-OH form of 14C-loxoprofen as its active metabolite.

1.2.3. Metabolism
An in vitro test of loxoprofen sodium hydrate for metabolism inhibition using human hepatic microsome showed that the drug did not inhibit the metabolism of substrates for cytochrome P450 enzymes (CYP1A1/2, 2A6, 2B6, 2C8/9, 2C19, 2D6, 2E1 and 3A4) even at a concentration of 200μM equivalent to 1,000 times or more than the maximum plasma concentration observed by administration of Loxoprofen (LOXOTOP™ PAP) in a dose of one patch a day.

1.2.4. Urinary Excretion
Each of 14 Japanese healthy male adult volunteers was subjected to repeated administration of two Loxoprofen (LOXOTOP™ PAP) on the back once a day for five days, showing that the daily urinary excretion of loxoprofen, its trans-OH form (active metabolite) and cis-OH form remained almost constant after the elapse of 24 hours following the administration with the total cumulative excretion rate of 2.67% from the start of the administration until 48 hours after the discontinuation of the administration.

PHARMACEUTICAL PARTICULARS

1.1 Shelf life
24 months

1.2 Storage conditions
This product must be stored in light-proof tightly-sealed container.
Do not store above 30°C.

1.3 Instructions for use/handling

1.3.1. Expiration date for use
This product must be used before the expiration date indicated on the package or label.

1.3.2. Instructions for use/handling
After removing the patch from the pouch for use, be sure to close it securely by gently pressing both sides of its zip-lock portion against each other.

Dosage Forms and Packaging Available (pack size):
5 patches per pouch x 10's (Box of 50 pouches).

Caution: Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

Keep out of reach of children.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph. Seek medical attention immediately at the first sign of any adverse drug reaction.

MANUFACTURED BY

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Nakaniikawa-gun, Toyama, Japan.

REGISTRATION NUMBER

DR-XY#####

DATE OF FIRST AUTHORIZATION

DD-MMM-YYYY

IMPORTER AND MARKETING AUTHORIZATION HOLDER

Km. 14 West Service Rd. South Superhighway, cor. Edison Ave., Sun Valley, Parañaque, Metro Manila

DATE OF REVISION OF THE TEXT

May 30, 2022