SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Lysodol Gel

2. Qualitative and quantitative composition

Composition:

- Aceclofenac BP 1.5% w/w
- Oleum Lini (containing predominantly Alpha Linolenic Acid) 3% w/w
- Methyl salicylate BP 10 % w/w
- Capsaicin USP 0.01% w/w
- Menthol USP 5 % w/w
- Benzyl alcohol BP 1% w/w (as preservative)
- Gel base q.s

Excipients with known effects: Propylene Glycol and Isopropyl Alcohol.

For full list of excipients, see section 6.1

3. Pharmaceutical form

Topical gel

Lysodol Gel (Aceclofenac, Oleum Lini, Methyl salicylate, Capsaicin, Menthol, Benzyl alcohol gel)
Description: Creamish coloured semi solid capsicum odour gel

4. Clinical particulars

4.1 Therapeutic indications

It is indicated for the treatment of rheumatic pain, muscle pain, arthralgia and Musculo-skeletal pain.

4.2 Posology and method of administration

Route of administration: Topical
Posology
This medicine is for external use only. Use it in the dose and duration as advised by your doctor.

Check the label for directions before use. Clean and dry the affected area and apply the gel. Wash your hands after applying, unless hands are the affected area.

4.3 Contraindications

Known hypersensitivity (e.g., anaphylactic reactions and serious skin reactions) to aceclofenac or any components of the drug product.
History of asthma, urticaria, or other allergic-type reactions after taking aspirin or

other NSAIDs. Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients.

4.4 Special warnings and precautions for use

The use of Aceclofenac with concomitant NSAIDs including cyclooxygenase- 2 selective inhibitors should be avoided.

Respiratory disorders:

Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients.

Cardiovascular, Renal and Hepatic Impairment:

The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. Renal function should be monitored in these patients.

Renal:

The importance of prostaglandins in maintaining renal blood flow should be taken into account in patients with impaired cardiac or renal function, those being treated with diuretics or recovering from major surgery.

Hepatic:

If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), It should be discontinued.

Cardiovascular and cerebrovascular effects:

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy. Patients with congestive heart failure (NYHA-I) and patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with aceclofenac after careful consideration. As the cardiovascular risks of aceclofenac may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be re- evaluated periodically.

Gastrointestinal bleeding, ulceration and perforation:

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events. **SLE and mixed connective tissue disease:** In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis.

Hypersensitivity reactions:

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug.

4.5 Interaction with other medicinal products and other forms of interaction Other analgesics including cyclooxygenase-2 selective inhibitors:
Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects.
Anti-hypertensives:

NSAIDs, may reduce the effect of activity antihypertensives. The risk of acute renal insufficiency, which is usually reversible, may be increased in some patients with compromised renal function (e.g. dehydrated patients or elderly patients) when ACE- inhibitors or angiotensin II receptor antagonists are combined with NSAIDs.
Diuretics:

Aceclofenac, like other NSAIDs, may inhibit the activity of diuretics. Diuretics can increase the risk of nephrotoxicity of NSAIDs. Although it was not shown to affect blood pressure control when co-administered with bendrofluazide, interactions with other diuretics cannot be ruled out.
Cardiac glycosides like digoxin:

NSAIDs may exacerbate cardiac failure, reduce GFR (glomerular filtration rate) and inhibit the renal clearance of glycosides, resulting in increased plasma glycoside levels. The combination should be avoided unless frequent monitoring of glycoside levels can be performed.
Lithium:

Several NSAID drugs inhibit the renal clearance of lithium, resulting in increased serum concentrations of lithium. The combination should be avoided unless frequent monitoring of lithium can be performed.
Methotrexate: The possible interaction between NSAIDs and methotrexate should be born in mind also when low doses of methotrexate are used, especially in patients with decreased renal function. When combination therapy has to be used, the renal function should be monitored. Caution should be exercised if both an NSAID and methotrexate are administered within 24 hours of each other, since NSAIDs may increase plasma levels, resulting in increased toxicity.
Mifepristone:

NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding.

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin.

Quinolone antibiotics:

Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):

Increased risk of gastrointestinal bleeding.

Ciclosporin, Tacrolimus:

Administration of NSAID drugs together with ciclosporin or tacrolimus is thought to increase the risk of nephrotoxicity due to decreased synthesis of prostacyclin in the kidney. During combination therapy it is therefore important to carefully monitor renal function.

Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There are indications of an increased risk of haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

Antidiabetic agents: Clinical studies have shown that diclofenac can be given together with oral antidiabetic agents with influencing their clinical effect. However, there have been isolated reports of hypoglycaemic and hyperglycaemic effects. Thus, with Aceclofenac Tablets, consideration should be given to adjustment of the dosage of hypoglycaemic agents.

4.6 Pregnancy and lactation Pregnancy:

Unknown. Human and animal studies are not available. Please consult your doctor.

Lactation:

LYSODOL Gel is probably safe to use during lactation. Limited human data suggests that the drug does not represent a significant risk to the baby. The baby's skin should not come into direct contact with the treated area of skin. Water-miscible cream/gel is preferred as ointments may expose the baby to harmful effects of LYSODOL Gel via licking.

Safety for use of Capsaicin, menthol and methyl salicylate in lactation has not been established; therefore, the potential benefit of the product should be weighed against the possible risks to the mother and child.

4.7 Effects on ability to drive and use machines

Not available

4.8 Undesirable effects

GI disorders (e.g. dyspepsia, abdominal pain, nausea, vomiting, diarrhoea, flatulence, constipation, malaena, haematemesis, ulcerative stomatitis, gastritis), rash, ruber, urticaria, enuresis, headache, dizziness, paraesthaesia, drowsiness; asthma, bronchospasm, dyspnoea, pruritus, purpura, angioedema. Ml, stroke, acute coronary syndrome, oedema, HTN, cardiac failure; nephritis, nephritic syndrome, renal failure; abnormal liver function, hepatitis, jaundice; visual disturbance, optic neuritis; thrombocytopenia, neutropenia, agranulocytosis, aplastic and haemolytic anaemias. Rarely, pancreatitis, exfoliative and bullous demnatoses (e.g. epidemnal necrolysis, erythema multiforme, Steven Johnson syndrome, toxic epidermal necrolysis). Potentially Fatal: GI bleeding, ulceration or perforation.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after Authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Pharmacovigilance Electronic Reporting System (PvERS)
https://pv.pharmacyboardkenya.org/

4.9 Overdose

Do not use more than prescribed dose. Taking more medication will not improve your symptoms; rather they may cause poisoning or serious side-effects. If you suspect that you or anyone else who may have overdosed of LYSODOL Gel, please go to the emergency department of the closest hospital or nursing home. Bring a medicine box, container, or label with you to help doctors with necessary information.
Do not give your medicines to other people even if you know that they have the same condition, or it seems that they may have similar conditions. This may lead to overdosage. Please consult your physician or pharmacist or product package for more information.
Symptoms of Aceclofenac overdose

Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal irritation, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, hypotension, respiratory depression, fainting, occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.
Symptoms of methyl salicylate overdose

Salicylate intoxication can occur after ingestion or topical application of methyl salicylate. Mild chronic salicylate intoxication, or salicylism, usually occurs only after repeated use of large doses. Salicylism can also occur following excessive topical application of salicylates. Symptoms include dizziness, tinnitus, deafness, sweating, nausea and vomiting, headache, and confusion, and may be controlled by reducing the dosage. Symptoms of more severe intoxication or of acute poisoning following overdose include hyperventilation, fever, restlessness, ketosis, and respiratory alkalosis and metabolic acidosis. Depression of the CNS may lead to coma; cardiovascular collapse and respiratory failure may also occur.
Symptoms of menthol overdose

Ingestion of significant quantities is reported to cause symptom: severe abdominal pain, nausea, vomiting, vertigo, ataxia, drowsiness, and coma; instant collapse in infants after the local application of menthol to their nostrils. Seizures may be the first clinical sign of severe toxicity of camphor; however, seizures are usually selflimited. Severe toxicity of camphor can result in delirium, visual hallucinations, cerebral edema, and status epilepticus. Systemic toxicity may include hypotension, tachycardia, respiratory failure, and death. Treatment The stomach should be emptied by gastric lavage or administration of oral activated charcoal Fluid and electrolyte management is the mainstay of treatment with the immediate aim of correction of acidosis, hyperpyrexia, hypokalaemia and dehydration if present. Any convulsions must be controlled first through supportive care including anticonvulsant therapy.

5. Pharmacological properties

5.1 Pharmacodynamic properties Mechanism of Action:

Aceclofenac: Through COX-2 inhibition, aceclofenac down regulates the production of various inflammatory mediators including prostaglandin E2 (PGE2), IL-111, and TNF from lhe arachidonic acid (M) pathway. Inhibition of ll-6 is thought to be mediated by diclofenac converted from aceclofenac. Suppressed action of inflammatory cytokines decreases the production of reactive oxygen species. Aceclofenac is shown to decreased production of nitrous oxide in human articular chondrocytes. In addition, aceclofenac interferes with neutrophil adhesion to endothelium by decreasing the expression of L-selectin (CD62L), which is a cell adhesion molecule expressed on lymphocytes. Aceclofenac is proposed to stimulate the synthesis of glycosaminoglycan in human osteoarthritic cartilage which may be mediated through its inhibitory action on IL-1 production and activity. The chrondroprotective effects are generated by 4'-hydroxyaceclofenac which suppresses IL-1 mediated production of promatrix metalloproteinase-1 and metalloproteinase-3 and interferes with the release of proteoglycan from chrondrocytes.

Oleum lini: Oleum Lini improves the patient's condition by performing the following functions: Increasing the blood supply at the site of application.

Capsaicin: Capsaicin has been shown to reduce the amount of substance P associated with inflammation -however this is not believed to be its main mechanism in the relief of pain Capsaicin's mechanism of action is attributed to "defunctionalization" of nociceptor fibers by inducing a topical hypersensitivity reaction on the skin. This alteration in pain mechanisms is due to many of the

following: temporary loss of membrane potential, inability to transport neurotrophic factors leading to altered phenotype, and reversible retraction of epidermal and dermal nerve fiber terminals.

Menthol: acts on cold receptors. It constricts capillaries and decreases their permeability, gives sensation of coolness. Menthol provides local revulsive and moderate analgesic actions.

Methyl salicylate: is a derivative of salicylic acid, which has local irritant action. Methyl salicylate causes formation of a great number of biologically active substances and their output into blood because of irritation of skin receptors. There is a release of P substance from neurons. Decrease of P substance in nerve endings cause decrease of pain sensation. In addition, Methyl salicylate as one of the group of nonsteroidal anti-inflammatory drugs inhibits synthesis of prostaglandins because of cyclooxygenase inhibition that decreases swelling and infiltration of inflamed tissues.

5.2 Pharmacokinetic properties

LYSODOL Gel is a non-steroidal anti-inflammatory drug (NSAID). II works by blocking the release of certain chemical messengers that cause pain and inflammation (redness and swelling).

6. Pharmaceutical particulars

6.1 List of excipients

Sr. No.	Ingredients	Specification
1.	Propylene glycol	BP
2.	Diethylamine	BP
3.	Isopropyl alcohol	BP
4.	Disodium edetate	BP
5.	Carbomer	BP
6.	Cresmer RH 40 (Hydrogenated Castor Oil)	BP
7.	Butylated hydroxy toluene	BP
8.	Macrogols cetostearyl ether	BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store protected from heat & light at a temperature not exceeding 30°C.

Do not freeze.

Keep all medicines out of reach of children.

6.5 Nature and contents of container

30 gm Lami tube

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

Galaxy Pharmaceuticals Ltd.

P.O.Box 39107-00623,

3rd Parklands 1st floor Doctors Park,

Nairobi, Kenya. Country: Kenya

8. Marketing authorisation number(s)

H2022/CTD8882/20310

9. Date of first authorisation/renewal of the authorisation

15/12/2022

10. Date of revision of the text

20/08/2026