1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

TRANGEL ULTRA

(Diclofenac Diethylamine, Methyl Salicylate, Menthol, Capsicum Oleoresin Gel)

Gel for topical administration

2. QUALITATIVE AND QUANTITATIVE COPOSITION

Label claim

Each gm contains

Diclofenac Diethylamine B.P.

eq. to Diclofenac Sodium B.P. ...10 mg

Methyl Salicylate B.P. …80 mg

Menthol B.P. …60 mg

Capsicum Oleoresin USP …0.15 mg

Gel Base … Q.S.

List of Excipients:

Carbopol 934 B.P

Polyethylene Glycol B.P.

Sodium Methyl Paraben B.P.

Sodium Propyl Paraben B.P.

Triethanolamine B.P.

Isopropyl Alcohol B.P.

Tween -80 B.P

Freshly boiled purified water BP

3. PHARMACEUTICAL FORM

Gel for topical administration

TRANGEL ULTRA is available as Off white, smooth homogeneous, semisolid preparation filled in 20 gm lami tubes.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

It is used to provide pain relief in following conditions:

Low Back Pain, Sprains, Strains, Tendonitis, Muscle Stiffness (Wry neck), Hand/Neck/Shoulder Pain.

4.2 Posology and method of administration

a) A sufficient quantity of gel should be applied and rub gently over the affected part 2-3 times daily or as prescribed by the physician.

b) Wash hands thoroughly after each application.

External application.

4.3 Method of administration

Adults:

Trangel Ultra is applied to the skin 3 or 4 times daily and rubbed in gently. The amount needed depends on the size of the painful site.

Do not massage vigorously. The duration of treatment depends on the indication and the response obtained. Treatment beyond two weeks is not recommended with Trangel Ultra.

Children:

Dosage recommendations and indications have not been established for the use of Trangel Ultra in children.

4.4 Contraindications

Trangel Ultra is contra-indicated in those patients who are hypersensitive to NSAIDs and other ingredients in the formulation.

4.4 Special warnings and precautions for use

Warning

For external use only.

Wash your hands thoroughly after application of the gel.

Avoid contact with the eyes.

Limit use to intact skin. Do not apply to open wounds

If irritation persists discontinue use and contact your Doctor

Precautions

Avoid local application of any other drug in the form of gel/cream/ointment/lotion when using Trangel Ultra.

Keep out of reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

The concurrent use of NSAIDs and warfarin has been associated with severe, sometimes fatal, haemorrhage. The exact mechanism of the interaction between NSAIDs and warfarin is unknown,

but may involve enhanced bleeding from NSAIDs induced gastrointestinal ulceration or an additive effect of anticoagulation by warfarin and inhibition of platelet function by NSAIDs.
Systemic reactions are unlikely to occur when Trangel Ultra is used as recommended. Nevertheless, the possibility of such an interaction should be borne in mind.

4.6 Fertility, pregnancy and lactation

Fertility

Advise females of reproductive potential who desire pregnancy that NSAIDs, including Trangel Ultra, may be associated with a reversible delay in ovulation.

Pregnancy

Risk Summary Use of NSAIDs, including Trangel Ultra, during the third trimester of pregnancy increases the risk of premature closure of the fetal ductus arteriosus. Avoid use of NSAIDs, including Trangel Ultra, in pregnant women starting at 30 weeks of gestation (third trimester).

Lactation

Patients with any pre-existing illness or any allergy especially to aspirin or aspirin-like products. This should be used only if clearly needed during pregnancy or lactation.

4.7 Effects on ability to drive and use machines

One should not drive a vehicle if the medicine makes you drowsy, dizzy or lowers your blood-pressure extensively. Pharmacists also advise patients not to drink alcohol with medicines as alcohol intensifies drowsiness side-effects.

4.8 Undesirable effects

Trangel Ultra is generally very well tolerated; however, transient skin irritation or redness may be seen. Consult your doctor if such irritation or redness develops.
Methyl salicylate one of the continent of Trangel Ultra can be absorbed into the bloodstream after topical application. However, overdoses of oil of wintergreen are highly toxic.
Most instances of human toxicity due to methyl salicylate are a result of over-application of topical analgesics, especially involving children, some people have intentionally ingested large amounts of oil of wintergreen. Salicylate, the major metabolite of methyl salicylate, may be quantities in blood, plasma or serum to confirm a diagnosis of poisoning in hospitalized patients or to assist in an autopsy.

-While the risk of absorbing Diclofenac from Trangel Ultra into your bloodstream is low, an NSAID can cause life-threatening heart or circulation problems such as heart attack or stroke, especially if you use it long term.

4.9 Overdose

-Low systemic absorption of topically applied Diclofenac makes overdosage highly unlikely.

-In the event of accidental ingestion, resulting in significant systemic side-effects general therapeutic measures normally adopted to treat poisoning with non-steroidal anti- inflammatory drugs should be used.

-Management of overdosage with NSAIDs essentially consists of supportive and symptomatic measures. There is no typical clinical picture resulting from Diclofenac overdosage. Gastric lavage and use of activated charcoal can be examined, especially if time has passed since the ingestion.

5.0 Pharmacological properties

5.1 Pharmacodynamic properties

Mechanisms of Action/Effect

-Trangel Ultra is an analgesic, anti-inflammatory preparation for topical application.

-Trangel Ultra containing Diclofenac diethylammonium relieves pain, reduces oedema, and shorten the time to return to normal functions, in inflammation of traumatic or rheumatic origin.

Diclofenac has been shown to inhibit prostaglandin biosynthesis; and this is regarded as an important factor in its mechanism of action.

-Methyl salicylate is a salicylic acid derivative that is used topically as a counter-irritant in rubefacient preparations for the relief of pain in musculoskeletal, joint had soft tissue disorders. Like other salicylates, methyl salicylate may be absorbed through intact skin. methyl salicylate is extensively metabolized to salicylic acid in the dermal and subcutaneous tissues following topical administration.

-Menthol is a common counter-irritant in various topical analgesic preparations. When applied to the skin, menthol dilates the blood vessels, causing a sensation of coldness followed by an analgesic effect.

-Methyl Salicylate is Counter irritant which inflames the effected part, improves blood flow, makes warmth the affected part and enhances deeper penetration of the drug hence works faster. Menthol Provides a soothing, cooling and analgesic effect.

5.2 Pharmacokinetic properties

Absorption

The amount of Diclofenac absorbed through skin is proportional to the contact time and skin area covered with the Gel, and depends on the total topical dose and on skin hydration. About 6% of the

active substance is absorbed after topical application of 2.5 gm per 500 cm2. Absorption of Diclofenac increases threefold if an occlusive dressing is applied for 10 hours. Methyl salicylate is speedily absorbed when applied cutaneously. Percutaneous absorption of methyl salicylate is enhanced by exercise, heat occlusion, or disruption of integrity of the skin. Both the rate and extent of absorption increase after repeated application. Menthol is known to be well absorbed after topical application.

Distribution

Diclofenac can be detected in the plasma, synovial tissue and synovial fluid after topical application. The peak plasma concentrations of Diclofenac are about 100 times lower after topical application than after oral administration. 99.7% of Diclofenac binds to serum proteins, mainly to albumin. 50-80% of salicylic acid binds to serum proteins.

The distribution of Menthol after topical application is unknown.

Systemic exposure with recommended use of diclofenac sodium gel (4 x 4 g per day applied to 1 knee) is on average 17 times lower than with oral treatment. (Basis: treatment with diclofenac sodium gel of 1 knee, 4 times a day versus 50 mg, 3 times a day of oral diclofenac tablets). The amount of diclofenac sodium that is systemically absorbed from diclofenac sodium gel is on average 6% of the systemic exposure from an oral form of diclofenac sodium.

The average peak plasma concentration with recommended use of diclofenac sodium gel (4 x 4 g per day applied to 1 knee) is 158 times lower than with the oral treatment.

The pharmacokinetics of diclofenac sodium gel has been tested under conditions of moderate heat (application of a heat patch for 15 minutes prior to gel application) and of moderate exercise (first gel application followed by a 20-minute treadmill exercise). No clinically relevant differences of systemic absorption and of tolerability were found between applications of diclofenac sodium gel (4 x 4 g per day on 1 knee) with and under the conditions tested. However, the pharmacokinetics of diclofenac sodium gel were not tested under the condition of heat application following gel application. Therefore, concurrent use of diclofenac sodium gel and heat is not recommended.

5.3 Preclinical safety data

There are no other preclinical safety data of relevance to the prescriber apart from those already detailed in the SPC

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Carbopol 934 B.P

Propylene Glycol B.P.

Sodium Methyl Paraben B.P.

Sodium Propyl Paraben B.P.

Triethanolamine B.P.

Isopropyl Alcohol B.P.

Tween 80 B.P.

Freshly boiled purified water B.P.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store on or below 30°C. Keep medicine out of reach of children. Do not freeze

6.5 Nature and contents of container

1x20 gm tube in carton.

6.6 Instructions for use and handling and disposal

No special requirements.

7. Marketing authorization holder

Applicant's Name	:	**Rene Pharmacy (R) Ltd.**
Address	:	KN 82 street, NDAMAGE Building, Nyarugenege District, opp. T-2000 New, B.P. 6033, Kigali, Rwanda.

8. Number(s) in the national register of finished pharmaceutical products

----

9. Date of first authorization/renewal of the authorization

----

10. DATE OF REVISION OF THE TEXT

February, 2017