Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

NEORELAX A 8mg Tablet

2. Qualitative and quantitative composition

Each film coated tablet contains:
Aceclofenac BP 100mg
Thiocolchicoside 8mg
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film coated tablet

Brown coloured, round shaped, biconvex, film coated tablets, plain on both sides..

4. Clinical particulars

4.1 Therapeutic indications

Aceclofenac with Thiocolchicoside 8mg Tablets is indicated for the relief of painful spasm associated with degenerative vertebral disorders & vertebral static problem, torticollis, dorsal pain, low back pain, traumalogical and neurological disorders, inflammation & other painful conditions associated with skeletal muscles.

4.2 Posology and method of administration

Tablet should be taken on a full stomach. Unless prescribed otherwise by the Physician, it should be given one tablet twice for severe muscle cramps. Use in children under the age of 15 years is not recommended

4.3 Contraindications

Neorelax should not be used in individuals who exhibit hypersensitivity to thiocolchicoside, aceclofenac, or any of the substances used in its formulation. It is also contraindicated for patients with a history of allergic or anaphylactic reactions to aspirin or NSAIDs, those with a history of peptic ulcers or gastrointestinal bleeding, individuals with moderate to severe renal impairment, those prone to asthma attacks, bronchospasms, acute rhinitis, urticaria, or those who are hypersensitive to these types of drugs. Additionally, Neorelax is not recommended for use during pregnancy and lactation, as well as in cases of severe heart failure or severely impaired hepatic or renal function, especially during the last three months of pregnancy.

4.4 Special warnings and precautions for use

Thiocolchicoside is not recommended for use in children. In cases of diarrhea, it is advisable to adjust the dosage as needed. Elderly individuals are at a higher risk of experiencing more severe consequences such as gastrointestinal bleeding, ulcerative perforation,

haematemesis, and melena. These adverse events can occur at any point during treatment, even without prior warning symptoms or a history of such issues. If gastrointestinal bleeding or ulceration occurs in patients taking aceclofenac, it is recommended to discontinue the drug. Close medical monitoring is crucial for patients with severe hepatic impairment.

When prescribing aceclofenac, caution should be exercised in elderly patients with renal, hepatic, or cardiovascular impairments, as well as in those concurrently taking other medications. It is advisable to use the lowest effective dose and regularly monitor renal function. Allergic reactions, including anaphylactic or anaphylactoid reactions, can occur even in individuals with no previous exposure to the drug.

It is important to consider the role of prostaglandins in maintaining renal blood flow in patients with impaired cardiac or renal function, those on diuretics, or those recovering from major surgery. The effects on renal function due to aceclofenac are typically reversible upon discontinuation of the medication. Caution is also warranted in patients with a history of coagulation disorders and liver dysfunction.

Long-term treatment with aceclofenac requires monitoring of renal and hepatic function, as well as regular blood counts. Persistent elevation of hepatic enzyme levels necessitates discontinuation of aceclofenac. Close medical supervision is essential for patients exhibiting symptoms indicative of gastrointestinal disorders, those with a history suggestive of gastrointestinal ulceration, ulcerative colitis, Crohn's disease, bleeding tendencies, or haematological abnormalities.

4.5 Interaction with other medicinal products and other forms of interaction

Aceclofenac

Lithium: Aceclofenac, like many NSAIDs, may increase plasma concentration of lithium and thus, increases their risk of its toxicity.

Cardiac Glycosides (Digoxin): Through their renal effects, NSAIDs may increase plasma glycoside levels, exacerbate cardiac failure and reduce the glomerular filtration rate (GFR) in patients receiving glycosides.

Diuretics: Aceclofenac, like other NSAIDs, may inhibit the activity of diuretics. Although it was not shown to affect blood pressure control when co-administered with bendrofluazide, interactions with other diuretics cannot be ruled out. When concomitant administration with potassium-sparing diuretics is employed, serum potassium should be monitored. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Anticoagulants: Like other NSAIDs, aceclofenac may enhance the activity of anticoagulants such as warfarin. Close monitoring of patients on combined anticoagulant and aceclofenac therapy should be undertaken.

Antihypertensive Drugs: NSAIDs may reduce the effect of 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 angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists are combined with NSAIDs. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

Antidiabetic Agents: Clinical studies have shown that diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However, there have been isolated reports of hypoglycemic and hyperglycemic effects. Thus, with aceclofenac, consideration should be given to adjustment of the dosage of hypoglycemic agents.

Methotrexate: Caution should be exercised if NSAIDs 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 to 12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Corticosteroids: Concomitant administration of aceclofenac with corticosteroids may increase the risk of GI ulceration or bleeding.

Anti-Platelet Agents and Selective Serotonin Reuptake Inhibitors (SSRIs): Concomitant administration of aceclofenac with these drugs may increase the risk of GI bleeding.

Ciclosporin: Ciclosporin nephrotoxicity may be increased by the effect of NSAIDs on renal prostaglandins.

Quinolone Antimicrobials: Convulsions may occur due to an interaction between quinolones and NSAIDs. This may occur in patients with or without a previous history of epilepsy or convulsions. Therefore, caution should be exercised when considering the use of a quinolone in patients who are already receiving a NSAID

Thiocolchicoside

There is no data on drug interactions of thiocolchicoside. However, when administered concomitantly with similar drugs, the patient should be closely monitored. Drug interactions associated with aceclofenac are similar to those observed with other NSAIDs.

4.6 Fertility, pregnancy, and lactation

The drug in not recommended in pregnant & breast feeding women.

4.7 Effects on ability to drive and use machines.

There are no data available of the effect on driving vehicles and using machines. Although only
rare cases of drowsiness have been reported, this has to be taken into account when driving vehicles
and operating machines.

4.8 Undesirable effects

Aceclofenac

The majority of adverse reactions reported have been reversible and of a minor nature. The most frequent are GI disorders, in particular dyspepsia, abdominal pain, nausea and diarrhoea, and occasional dizziness. If serious adverse reactions occur, aceclofenac should be withdrawn. Gastrointestinal: The most commonly observed adverse events are GI in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melena, hematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease have been reported following administration. Less frequently, gastritis has been observed. Pancreatitis has been reported very rarely. Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consist of a non-specific allergic reaction and/or anaphylaxis or respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnea. Cardiovascular and Cerebrovascular: Edema, hypertension, palpitation, flushing, hot flushes, vasculitis and cardiac failure have been reported in association with NSAID treatment. Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with an increased risk of arterial thrombotic events (e.g., myocardial infarction or stroke). Neurological and Special Senses: Optic neuritis, somnolence, reports of aseptic meningitis (especially in patients with existing auto immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease) with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation, malaise, confusion, and drowsiness. Renal: Interstitial nephritis. Hematological: Agranulocytosis, aplastic anaemia. Miscellaneous: In patients with varicella, serious cutaneous and soft tissue infections have been reported in association with NSAID treatment. Other rarely reported adverse reactions of aceclofenac include the following: Renal and Urinary: Renal insufficiency, abnormal serum creatinine levels, increased blood urea, renal failure, nephrotic syndrome. Respiratory: Dyspnea, bronchospasm, stridor. Hepatic: Abnormal hepatic enzyme levels, hepatitis, jaundice, increased blood alkaline phosphatase. Blood and Lymphatic System: Anemia, bone marrow depression, granulocytopenia, thrombocytopenia, neutropenia, hemolytic anemia. Skin and Subcutaneous Tissue Disorders: Pruritus, rash, photosensitivity reactions, dermatitis urticaria, angioedema, purpura, erythema multiforme, exfoliative dermatitis, bullous dermatoses, severe mucocutaneous skin reactions (including Stevens-Johnson Syndrome

and Toxic Epidermal Necrolysis) Ear and Labyrinth Disorders: Tinnitus, vertigo. Eye Disorders: Visual disturbance. Nervous System: Paraesthesia, tremor, somnolence, headache, dysgeusia. Psychiatric Disorders: Depression, abnormal dreams, confusion, hallucinations, insomnia. Metabolism: Hyperkalemia. General Disorders: Edema, fatigue, leg cramps.

Thiocolchicoside

Gastrointestinal Disturbances: These can manifest as nausea, vomiting, diarrhoea, and abdominal discomfort. In some cases, more severe gastrointestinal issues such as gastritis, gastrointestinal bleeding, or ulcerative perforation may occur.

Allergic Reactions: Allergic reactions to thiocolchicoside can range from mild skin rashes and itching to more severe allergic responses like anaphylactic reactions.

*Central Nervous System Effects***:** Some individuals may experience dizziness, headache, or sleepiness when using thiocolchicoside.

Muscle Weakness: Thiocolchicoside is a muscle relaxant, and while it is intended to reduce muscle stiffness, excessive use or sensitivity to the drug may lead to muscle weakness.

Hypersensitivity Reactions: In rare instances, individuals may exhibit hypersensitivity to thiocolchicoside, leading to symptoms such as skin rash, itching, or swelling.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

There have been no reports on overdose until now. Management of acute poisoning with NSAIDs essentially consists of supportive and symptomatic measures. Standard supportive measures should be adopted as required.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Aceclofenac ATC code: M01A B16

Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) with marked analgesic and antiinflammatory properties

The mode of action of aceclofenac is largely based on the inhibition to prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclooxygenase (COX). COX enzymes are involved in conversion of arachidonic acid into prostaglandin (PGs). Prostaglandins are usually

responsible for causing pain, inflammation, and fever. Aceclofenac blocks the enzyme COX and thereby inhibit PGs synthesis, thus, produces analgesic and anti-inflammatory effects.

Thiocolchicoside ATC Code: M03BX05

Potent competitive antagonist of GABA AR functions; In vitro – Thiocolchicoside only binds to GABA – A and strychnine sensitive glycine receptors. Thiocolchicoside acting as a GABA – A receptor antagonist, its myorelaxant effects could be exerted at a glycinergic mechanism of action cannot be excluded. The characteristics of the interaction of Thiocolchicoside with GABA – A circulating metabolite, the glucuronidated derivative. In vivo, the muscle relaxant properties of thiocolchicoside and its main metabolite have been demonstrated in various predictive models of rats and rabbits. The lack of myorelaxants effect of Thiocolchicoside in spinalized rats suggests a predominant supraspinal action for this compound. Thiocolchicoside was also found to possess models after oral, subcutaneous, intraperitoneal and intramuscular administration. Moreover, in pharmaco-EEG studies, the thiocolchicoside and its main metabolite were shown to be devoid of any sedative effect. Thiocolchicoside (TCC) is used clinically for its muscle relaxant, antiinflammatory, and analgesic properties. Neorelax A 8 mg works by acting on the central nervous system but it does not heal a muscle, because muscles are self-healing, but mask the pain to allow the body time to heal itself. Thiocolchicoside also works on the brain. This medication works to reduce your brain's ability to sense pain, allowing you to relax. It also blocks the pain sensations that your body's nerves send to your brain. In most cases, thiocolchicoside is used in addition to therapy or exercise, or both. It is important to bear in mind that muscles will take a while to come back to their relaxed position, so just because a drug helps stop the pain, do not get back into normal activity levels.

5.2 Pharmacokinetic properties

Aceclofenac

After oral administration, aceclofenac is rapidly and completely absorbed as unchanged drug. Peak plasma concentrations are reached approximately 1.25 to 3.00 hours following ingestion. Aceclofenac penetrates into the synovial fluid, where the concentrations reach approximately 57% of those in plasma. The volume of distribution is approximately 25 liters. The mean plasma elimination half-life is around 4 hours. Aceclofenac is highly protein-bound (>99%). Aceclofenac circulates mainly as unchanged drug. The main metabolite detected in plasma is 4'- hydroxyaceclofenac. Approximately two- thirds of the administered dose is excreted via the urine, mainly as hydroxymetabolites. No changes in the pharmacokinetics of aceclofenac have been detected in the elderly.

Thiocolchicoside:

Absorption: By oral administration, thiocolchicoside is well absorbed from the gastrointestinal tract.

Metabolism: It metabolized into 3 main metabolites. The two main circulating forms were the thiocolchicoside aglycon and the glucuronidated derivative of thiocolchicoside, which is active.
Distribution: In humans the binding of thiocolchicoside to human serum proteins is low (13%) and not dependent on the therapeutic concentration of thiocolchicoside and serum albumin is mainly involved in serum protein binding. It shows its effect in 1-2 hours after oral administration and peak plasma level is achieved in about 0.7 hours.
Elimination: Elimination half-life is about 2.5-5 hours. It's effect is continued for 24 hours. For Healthy Volunteers: After oral administration to these healthy volunteers no traces of thiocolchicoside are detected. The active glucoronidated metabolite appears rapidly in plasma with a median T max (Time to reach maximum plasma concentration of a drug) at 1 hour, and is eliminated with a mean apparent terminal half – life of about 7 hours. After a single 8 mg oral administration of thiocolchicoside, the mean cumulative area under curve (AUC) of thiocolchicoside and its glucuronidated metabolite, which reflects exposure to the active entities, is about 500ng.h/ml. After oral administration of (14C) – radio labelled thiocolchicoside, 79% of the dose is recovered in faeces and 20% in urine.

5.3 Preclinical safety data
No data available.

6. Pharmaceutical particulars

6.1 List of excipients
Maize Starch BP
Lactose Monohydrate BP
Microcrystalline Cellulose BP (Ph 101)
Maize Starch BP (For Paste)
Polyvinylpyrrolidone BP (Pvp K-30)
Purified Water BP
Sodium Starch Glycollate BP
Colloidal Anhydrous Silica BP
Purified Talc BP
Magnesium Stearate BP
Insta Moistshield (Ic-Ms-5950-R)
Isopropyl Alcohol BP
Methylene Chloride
Wincoat Wt-01943 Brown

6.2 Incompatibilities
None known

6.3 Shelf life
36 months

6.4 Special precautions for storage:
Store in a dry place below 30˚C. Protect from light.

6.5 Nature and contents of container

Printed heat seal lacquer coated Aluminium foil for blisterpacking. Clear transparent PVC film PVdC coating

Pack size 3 x 10'S Blister pack

6.6 Special precautions for disposal and other handling:

No special requirements

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:

Meyer Organics Pvt.Ltd

Manufacturing site address:

Meyer Organics Pvt Ltd

10-D, 2nd Phase, Peenya Industrial Area, Bangalore - 560058, India

8. Marketing authorization number

CTD9891

9. Date of first registration

07/12/2022

10. Date of revision of the text:

17/09/2023

11. Dosimetry:

Not Applicable

12. Instructions for Preparation of Radiopharmaceuticals:

Not Applicable