Summary Product Characteristics

1. Name of the medicinal product

ACLORAX T4 TABLETS (Aceclofenac 100 mg & Thiocolchicoside 4 mg Tablets)

2. Qualitative and quantitative composition

Each film coated tablet Contains :

Aceclofenac BP	100 mg.
Thiocolchicoside BP	4 mg.

For the full list of excipients, See Section 6.1

3. Pharmaceutical form

Yellow color, round, Biconvex, film coated tablet without break line.

4. Clinical Particulars

4.1 Therapeutic indications

Aceclofenac & Thiocolchicoside tablet is a medicine that is used for the treatment of muscle stiffness in spine, muscle stiffness in muscle diseases, muscle stiffness in the joint diseases, Lumbago, muscle stiffness in nerve diseases, Pain caused by nonarticular rheumatism and other diseases.

4.2 Posology and method of administration

Aceclofenac

Adults

The recommended dose is 200 mg daily, taken as two divided doses. Paediatric population

There are no clinical data on the use of Aceclofenac in children and therefore it is not recommended for use in children under 18 years of age.

Elderly

The elderly, who are more likely to be suffering from impaired renal, cardiovascular or hepatic function and receiving concomitant medication, are at increased risk of serious consequences of adverse reactions.

If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

The pharmacokinetics of Aceclofenac are not altered in elderly patients, therefore it is not considered necessary to modify the dose or dose frequency.

Renal insufficiency

There is no evidence that the dosage of Aceclofenac needs to be modified in patients

with mild renal impairment, but as with other NSAIDs caution should be exercised.

Hepatic insufficiency

There is some evidence that the dose of Aceclofenac should be reduced in patients with hepatic impairment and it is suggested that an initial daily dose of 100 mg be used.

Thiocolchicoside:

For the oral form 8 mg:

The recommended and maximal dose is 8 mg every 12 hours (i.e. 16 mg per day).

Th

e treatment duration is limited to 7 consecutive days.

Both for oral and for IM*:*

Doses exceeding recommended doses or long-term use should be avoided. Paediatric population
Aceclofenac & Thiocolchicoside tablets should not be used in children and adolescents under 16 years of age because of safety concerns

Method of administration

Swallow the tablet whole with a glass of water. Do not crush or chew the tablets. Never change the dose of your medicine without talking to your doctor first. Continue to take your tablets for as long as your doctor recommends.

4.3Contraindications
Hypersensitivity to Aceclofenac or to any of the Excipients listed in section 6.1

Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

NSAIDS are contraindicated in patients who have previously shown hypersensitivity reactions (eg. Asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin, or other non-steroidal anti-inflammatory drugs.

Hepatic failure and renal failure (see section 4.4).

Patients with established congestive heart failure (NYHA II-IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

History of gastrointestinal bleeding or perforation, related to previous NSAIDS therapy. Active bleedings or bleeding disorders.
Aceclofenac should not be prescribed during pregnancy, especially during the last trimester of pregnancy, unless there are compelling reasons for doing so. The lowest effective dosage should be used (see section 4.6).

4.4Special warnings and precautions for use

Before using Aceclofenac & Thiocolchicoside tablet inform your doctor of the current medications over the counter products (e.g. vitamins, herbal supplements, etc), allergies, pre-existing dieases and current health conditions (e.g., pregnancy, upcoming surgery etc),. Some health conditions make you more susceptible to the

side effects of the drug.

Important counselling points include:

- Avoid driving and operate dangerous machinery
- Gastro-intestinal disorders
- History of gastroulceration
- Limit alcoholic beverages
- Patients recovering after a surgery
- Severe cardiac impairment
- Severe renal impairment
- Severe hepatic impairment
- Usage of diuretics

4.5Interaction 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 including GI bleeding (see section 4.4).

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. 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.

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. When concomitant administration with potassium-sparing diuretics is employed, serum potassium should be monitored.

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 (see section 4.4).

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4). Close monitoring of patients on combined anti-coagulants and Aceclofenac Tablets therapy should be undertaken.

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 (see section 4.4).

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.

4.6Fertility,pregnancy and lactation Aceclofenac:

Pregnancy:

There is no information on the use of Aceclofenac during pregnancy. Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage, cardiac malformation or gastroschisis after use of prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality.

In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, Aceclofenac should not be given unless clearly necessary. If Aceclofenac is used by a women attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

Cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);

renal dysfunction, which may progress to renal failure with oligo-hydroamniosis; the mother and the neonate, at the end of pregnancy, to: Possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.

Inhibition of uterine contractions resulting in delayed or prolonged labour .

Consequently, aceclofenac is contraindicated during the third trimester of pregnancy (see section 4.3)

Lactation:

There is no information on the secretion of Aceclofenac to breast milk, there was however no notable transfer of radio labelled (14C) Aceclofenac to the milk of lactating rats.

The use of Aceclofenac Tablets should therefore be avoided in pregnancy and lactation unless the potential benefits to the other outweigh the possible risks to the foetus.

Fertility;

The use of Aceclofenac tablets may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility withdrawal of Aceclofenac tablets should be considered .

Thiocolchicoside:

Pregnancy:

There are limited data on the use of thiocolchicoside in pregnant women. Therefore, the potential hazards for the embryo and foetus are unknown.

Studies in animals have shown teratogenic effects.

Lactation

Since it passes into the mother's milk, the use of Thiocolchicoside is contraindicated during breastfeeding.

Fertility:

In a fertility study performed in rats, no impairment of fertility was seen at doses up

to 12 mg/kg, i.e. at dose levels inducing no clinical effect. Thiocolchicoside and its metabolites exert aneugenic activity at different concentration levels, which is a risk factor for impairment of human fertility.

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, vertigo, drowsiness, fatigue, visual disturbances or other central nervous system disorders are possible after taking NSAIDs. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Aceclofenac:

Exceptionally, occurrence of serious cutaneous and soft tissues infections complications during varicella has been reported in association with NSAID treatment. Aceclofenac is both structurally related and metabolised to Diclofenac for which a greater amount of clinical and epidemiological data consistently point towards an increased risk of general arterial thrombotic events (myocardial infarction or stroke, particularly at high doses and in long treatment). Epidemiological data has also found an increased risk of acute coronary syndrome and myocardial infarction associated with the use of aceclofenac.

Gastrointestinal:

The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, 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 reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Cardiovascular:

Oedema, hypertension 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 (for example myocardial infarction or stroke.

Other adverse reactions reported less commonly include:

Renal:

Nephrotoxicity in various forms, including interstitial nephritis, nephritic syndrome and renal failure.

Hepatic: Abnormal liver function, hepatitis and jaundice. Neurological and special senses: Visual disturbances, optic neuritis, headaches, paraesthesia, 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, depression, confusion, hallucinations, tinnitus, vertigo, dizziness, malaise, fatigue and drowsiness.

Haematological:
Thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia.

Dermatological:
Bullous reactions including Stevens Johnson Syndrome and Toxic Epidermal Necrolysis (very rare).

Thiocolchicoside:
Thiocolchcoside has shown some side effects like anaphylactic reactions, such as pruritus, urticaria, angioneurotic oedema, anaphylactic shock, following intramuscular injection; diarrhea, gastralgia, nausea, vomiting & allergic skin reaction & phototoxicity.

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

5. Pharmacological properties

5.1 Pharmacodynamic properties

Aceclofenac is a non-steroidal agent with marked anti-inflammatory and analgesic properties. ATC code: M01A B16
The mode of action of aceclofenac is largely based on the inhibition to prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins.

Thiocolchicoside:

A semisynthetic derivative of the naturally occurring compound colchicoside with a relaxant effect on the skeletal muscle, has been found to displace both [3H]gamma- amino

butyric([3H]GABA) and [3H]strychnine binding, suggesting an interaction with both GABA and strychnine-sensistive glycine receptors.

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 L.

The mean plasma elimination half-life is around 4 hours. Aceclofenac is highly protein- bound (>99%). Aceclofenac circulates mainly as unchanged drug. 4'-hydroxyaceclofenac is the main metabolite detected in plasma. 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

After oral administration, no thiocolchicoside is detected in plasma. Only two metabolites are observed:

The pharmacologically active metabolite SL18.0740 and an inactive metabolite SL59.0955. For both metabolites, maximum plasma concentrations occur 1hour after thiocolchicoside administration. After a single oral dose of 8 mg of thiocolchicoside the Cmax and AUC of SL18.0740 are about 60 ng/mL and 130 ng.h/mL respectively. For SL59.0955 these values are much lower: Cmax around 13 ng/mL and AUC ranging from 15.5 ng.h/mL (until 3h) to 39.7 ng.h/mL (until 24h).

Distribution

The apparent volume of distribution of thiocolchicoside is estimated around 42.7 L after an IM administration of 8 mg. No data are available for both metabolites.

Metabolism

After oral administration, thiocolchicoside is first metabolized in the aglycon 3-demethyltiocolchicine or SL59.0955. This step mainly occurs by intestinal metabolism explaining the lack of circulating unchanged thiocolchicoside by this route of administration.

SL59.0955 is then glucuroconjugated into SL18.0740 which has equipotent pharmacological activity to thiocolchicoside and thus supports the pharmacological activity after oral administration of thiocolchicoside. SL59.0955 is also demethylated into didemethyl-thiocolchicine.

Elimination

After oral administration, total radioactivity is mainly excreted in feces (79%) while urinary excretion represents only 20%. No unchanged thiocolchicoside is excreted either in urine or feces. SL18.0740 and SL59.0955 are found in urine and feces while the didemethyl-thiocolchicine is only recovered in feces.

After oral administration of Thiocolchicoside, the SL18.0740 metabolite is eliminated with an apparent t1/2 ranging from 3.2 to 7 hours and the metabolite SL59.0955 has a t1/2 averaging 0.8h.

5.3Preclinical safety data

The results from preclinical studies conducted with aceclofenac are consistent with those expected for NSAIDs. The principal target organ was the gastro-intestinal tract.

No unexpected findings were recorded.

Aceclofenac was not considered to have any mutagenic activity in three *in vitro* studies and an *in vivo* study in the mouse.

Aceclofenac was not found to be carcinogenic in either the mouse or rat.

Animal studies indicate that there was no evidence of teratogenesis in rats although the systemic exposure was low and in rabbits, treatment with aceclofenac (10 mg/kg/day) resulted in a series of morphological changes in some fetuses.

6. Pharmaceutical Particulars

6.1 List of Excipients

MCCP
Maize
starch
Maize
Starch
Copovidon
e
Sod. Methyl
Hydroxybenzoate Sod.
Propyl Hydroxybenzoate
Purified Water
Colloidal anhydrous silica
Purified Talc
Magnesium
Stearate
F.C.Titanium
Dioxide
Colour yellow oxide of Iron
Isopropyl Alcohol
Dichloromethane

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months from the date of manufacture.

6.4 Special precautions for storage

Store in the original packaging in order to protect from moisture

This medicinal product does not require any special temperature storage conditions

6.5 Nature and contents of container

Alu – Alu blister pack of 1 x 10 Tablets, packed in an outer carton along with package insert.

6.6 Special precautions for disposal and other handling

No special requirements

7. Marketing authorization holder

-Name: PHARMWEB CHEMIST

-Address: Nairobi, Kenya

8. Marketing authorization number(s)

H2022/CTD9456/21911

9. Date of first authorization/renewal of the authorization

NA

10. Date of revision of the text

21/08/2026

1.17.2 Patient information leaflet (For All Products not subject to Medical Prescription)

Attached

1. **Product Name :**
ACLORAX T4 TABLETS
Generic Name or INN
Aceclofenac 100 mg & Thiocolchicoside 4 mg Tablets

2- **Name and Strength of the active Ingredient (s)**
Each film coated tablet Contains :
Aceclofenac BP 100 mg.
Thiocolchicoside BP 4 mg.
Excipients q. s.
Colors: Yellow Oxide of Iron

3- **Product Description Physical properties**
Yellow color, round, Biconvex, film coated tablet without break line.

4- **Pharmacodynamics/ Pharmacokinetics**
Aceclofenac is a non-steroidal agent with marked anti-inflammatory and analgesic properties. ATC code: M01A B16
The mode of action of aceclofenac is largely based on the inhibition to prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins.
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A semisynthetic derivative of the naturally occurring compound colchicoside with a relaxant effect on the skeletal muscle, has been found to displace both [3H]gamma- amino butyric([3H]GABA) and [3H]strychnine binding, suggesting an interaction with both GABA and strychnine-sensistive glycine receptors.

Pharmacokinetics
Aceclofenac

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No changes in the pharmacokinetics of aceclofenac have been detected in the elderly. Thiocolchicoside:
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metabolite SL59.0955. For both metabolites, maximum plasma concentrations occur 1hour after thiocolchicoside administration. After a single oral dose of 8 mg of thiocolchicoside the Cmax and AUC of SL18.0740 are about 60 ng/mL and 130 ng.h/mL respectively. For SL59.0955 these values are much lower: Cmax around 13 ng/mL and AUC ranging from 15.5 ng.h/mL (until 3h) to 39.7 ng.h/mL (until 24h).

Distribution

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Elimination

After oral administration, total radioactivity is mainly excreted in feces (79%) while urinary excretion represents only 20%. No unchanged thiocolchicoside is excreted either in urine or feces. SL18.0740 and SL59.0955 are found in urine and feces while the didemethyl-thiocolchicine is only recovered in feces.

After oral administration of Thiocolchicoside, the SL18.0740 metabolite is eliminated with an apparent t1/2 ranging from 3.2 to 7 hours and the metabolite SL59.0955 has a t1/2 averaging 0.8h.

5- **Indication**

Aceclofenac & Thiocolchicoside tablet is a medicine that is used for the treatment of muscle stiffness in spine, muscle stiffness in muscle diseases, muscle stiffness in the joint diseases, Lumbago, muscle stiffness in nerve diseases, Pain caused by nonarticular rheumatism and other diseases.

6- **Recommended Dose**

Aceclofenac

Adults

The recommended dose is 200 mg daily, taken as two divided doses. Paediatric population

There are no clinical data on the use of Aceclofenac in children and therefore it is not recommended for use in children under 18 years of age.

Elderly

The elderly, who are more likely to be suffering from impaired renal, cardiovascular or hepatic function and receiving concomitant medication, are at increased risk of serious consequences of adverse reactions.

If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

The pharmacokinetics of Aceclofenac are not altered in elderly patients, therefore it is not considered necessary to modify the dose or dose frequency.

Renal insufficiency

There is no evidence that the dosage of Aceclofenac needs to be modified in patients with mild renal impairment, but as with other NSAIDs caution should be exercised.

Hepatic insufficiency

There is some evidence that the dose of Aceclofenac should be reduced in patients with hepatic impairment and it is suggested that an initial daily dose of 100 mg be used.

Thiocolchicoside:

For the oral form 8 mg:

The recommended and maximal dose is 8 mg every 12 hours (i.e. 16 mg per day). The treatment duration is limited to 7 consecutive days.

Both for oral and for IM:

Doses exceeding recommended doses or long-term use should be avoided. Pediatric population

Aceclofenac & Thiocolchicoside tablets should not be used in children and adolescents under 16 years of age because of safety concerns

7. Recommended route of administration:

For oral administration.

8- **Contraindications**

Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

NSAIDS are contraindicated in patients who have previously shown hypersensitivity reactions (eg. Asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin, or other non-steroidal anti-

inflammatory drugs.
Hepatic failure and renal failure
Patients with established congestive heart failure (NYHA II-IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.
History of gastrointestinal bleeding or perforation, related to previous NSAIDS therapy. Active bleedings or bleeding disorders.
Aceclofenac should not be prescribed during pregnancy, especially during the last trimester of pregnancy, unless there are compelling reasons for doing so. The lowest effective dosage should be used

9- **Warnings and Precautions**

Before using Aceclofenac & Thiocolchicoside tablet inform your doctor of the current medications over the counter products (e.g. vitamins, herbal supplements, etc), allergies, pre-existing dieases and current health conditions (e.g., pregnancy, upcoming surgery etc),. Some health conditions make you more susceptible to the side effects of the drug.

Important counselling points include: Avoid driving and operate dangerous machinery, Gastro-intestinal disorders History of gastroulceration, Limit alcoholic beverages, Patients recovering after a surgery, Severe cardiac impairment, Severe renal impairment, Severe hepatic impairment, Usage of diuretics

10- **Fertility, Pregnancy and Lactation**

Aceclofenac:

Pregnancy:

There is no information on the use of Aceclofenac during pregnancy. Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development. Data from epidemiological studies suggest an increased risk of miscarriage, cardiac malformation or gastroschisis after use of prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, Aceclofenac should not be given unless clearly necessary. If Aceclofenac is used by a women attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to: Cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension); renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;

the mother and the neonate, at the end of pregnancy, to:

Possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses. Inhibition of uterine contractions resulting in delayed or prolonged labour .

Consequently, aceclofenac is contraindicated during the third trimester of pregnancy Lactation:

There is no information on the secretion of Aceclofenac to breast milk, there was however no notable transfer of radio labelled (14C) Aceclofenac to the milk of lactating rats.

The use of Aceclofenac Tablets should therefore be avoided in pregnancy and lactation unless the potential benefits to the other outweigh the possible risks to the foetus.

Fertility;

The use of Aceclofenac tablets may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility withdrawal of Aceclofenac tablets should be considered .

Thiocolchicoside:

Pregnancy:

There are limited data on the use of thiocolchicoside in pregnant women. Therefore, the potential hazards for the embryo and foetus are unknown.

Studies in animals have shown teratogenic effects. Lactation

Since it passes into the mother's milk, the use of Thiocolchicoside is contraindicated during breastfeeding. Fertility:
In a fertility study performed in rats, no impairment of fertility was seen at doses up to
12 mg/kg, i.e. at dose levels inducing no clinical effect. Thiocolchicoside and its metabolites exert aneugenic activity at different concentration levels, which is a risk factor for impairment of human fertility.

11- Undesirable Effects

Aceclofenac:
Exceptionally, occurrence of serious cutaneous and soft tissues infections complications during varicella has been reported in association with NSAID treatment. Aceclofenac is both structurally related and metabolised to Diclofenac for which a greater amount of clinical and epidemiological data consistently point towards an increased risk of general arterial thrombotic events (myocardial infarction or stroke, particularly at high doses and in long treatment). Epidemiological data has also found an increased risk of acute coronary syndrome and myocardial infarction associated with the use of aceclofenac.

Gastrointestinal:
The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, 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 reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated

asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Cardiovascular:
Oedema, hypertension 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 (for example myocardial infarction or stroke.

Other adverse reactions reported less commonly include:
Renal:
Nephrotoxicity in various forms, including interstitial nephritis, nephritic syndrome and renal failure. Hepatic: Abnormal liver function, hepatitis and jaundice. Neurological and special senses: Visual disturbances, optic neuritis, headaches, paraesthesia, 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, depression, confusion, hallucinations, tinnitus, vertigo, dizziness, malaise, fatigue and drowsiness.

Haematological:
Thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia.

Dermatological:
Bullous reactions including Stevens Johnson Syndrome and Toxic Epidermal Necrolysis (very rare).

Thiocolchicoside:
Thiocolchcoside has shown some side effects like anaphylactic reactions, such as pruritus, urticaria, angioneurotic oedema, anaphylactic shock, following intramuscular injection; diarrhea, gastralgia, nausea, vomiting & allergic skin reaction & phototoxicity

12- **Overdose and Treatment**

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 Rabeprazole+ Domperidone Tablets, 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 over dosage.

Please consult your physician or pharmacist or product package for more information

13- Packaging and storage condition

Alu –Alu Blister pack of 1 x 10 Tablets, packed in an outer carton along with package insert. Store below 30°C in a dry place. Protect from light**.**

14- Name and Address of Manufacturer

Name : Ethicare Pharmaceuticals Pvt Ltd

Address : 307, G.I.D.C Por Ramanagamdi, Opposite to Forest Office, Vadodara - 391243 Gujarat

15- Date of Revision of Package Insert

Not Applicable.