1.4 PRODUCT INFORMATION

1.4.1 Summary of Product Characteristics (SmPC)

1. Name of the Medicinal Product

Trypsin-Chymotrypsin Tablets

Trypsin-Chymotrypsin 50,000 Armour Units of Enzymatic Activity

2. Qualitative and Quantitative Composition

Each Enteric Coated Tablet Contains:

Trypsin-Chymotrypsin in the ration of approximately (6:1)

Equivalent to 50,000 Armour Units of Enzymatic Activity.

Excipients……..……..…QS

Colour: Ponceau 4 R & Titanium Dioxide

3. Pharmaceutical Form

Enteric coated tablet.

Red colored, biconvex, round shaped, enteric coated tablet having both side plain.

4. Clinical Particulars

4.1 Therapeutic Indications

Trypsin-Chymotrypsin 50,000 Armour Units of Enzymatic Activity, Tablet is used for acute or chronic osteoarthritis, rheumatoid arthritis and spindly arthritis, spondylosis and other ortho-degenerative disorders, pain management.

4.2 Posology and Method of Administration

Dose: The daily recommended dose is as directed by the Physician.

Method of administration

Trypsin-Chymotrypsin 50,000 armour units of enzymatic activity tablets should be administered orally. Do not crush or chew the tablet. Swallow as a whole.

4.3 Contraindications

- Hypersensitivity to trypsin-chymotrypsin any of the other constituents.
- Severe liver problems, kidney impairment, peptic ulcer, high vitreous pressure, and hypersensitivity.
- Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- 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.
- 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.
- Trypsin-Chymotrypsin 50,000 armour units of enzymatic activity 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.

4.4 Special Warnings and Precautions for Use

- Rarely, chymotrypsin might cause an allergic reaction when taken by mouth.
- Symptoms include itching, shortness of breath, swelling of the lips or throat, shock, loss of consciousness, and death.
- Not to be used in patients with severe hepatic impairment or renal damage or irregularities of the blood clotting mechanism.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Herbal Supplements/Alcohol

Systemic proteases may increase the effectiveness of herbal supplements. Chymotrypsin is also known to interact with alcohol.

Antibiotics

Administration of the trypsin-chymotrypsin combination (intramuscularly) has been found to increase the levels of orally administered semi-synthetic penicillin antibiotics in the blood serum and organs of rats.

Chymotrypsin is known to interact with chloramphenicol.

Anticoagulants

The trypsin-chymotrypsin combination should not be administered concurrently with anticoagulants such as coumadin, heparin and clopidogrel.

4.6 Pregnancy and Lactation

Pregnancy

Not enough is known about the use of trypsin and chymotrypsin during pregnancy.

Breastfeeding

Not enough is known about the use of trypsin and chymotrypsin during breastfeeding.

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 Trypsin Chymotrypsin 50,000 armour units of enzymatic activity. If affected, patients should not drive or operate machinery.

4.8 Undesirable Effects

Rarely, chymotrypsin might cause an allergic reaction when taken by mouth. Symptoms include itching, shortness of breath, swelling of the lips or throat, shock, loss of consciousness, and death.

Occasional gastric disturbance may also occur.

4.9 Overdose

No data available

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic Group: A proteolytic enzyme.

Mechanism of action

The cells in the pancreas synthesize and produce digestive enzymes that breakdown fats (lipases), starches (amylases) and proteins (proteases). Pancreatic proteases can be divided into several families of enzymes that differ in structure and catalytic effect in how they interact with the peptide bonds of proteins. Trypsin and chymotrypsin are two types of proteases originally synthesized in the pancreas in the inactive form of zymogen precursors (trypsinogen and chymotrypsinogen) for the purpose of stopping unnecessary cellular activity and controlling when and where enzyme activity occurs. Zymogens are then carried either into the bloodstream or the intestines where they are excreted or are converted by the process of proteolysis into the active enzymes that aid digestion. When taking the trypsin chymotrypsin combination, the active proteolytic enzymes are being ingested and used in addition to the inactive forms the body naturally produces. Trypsin and chymotrypsin give the body the extra boost it might need for smoother digestion of proteins as well as for reducing inflammation and fighting infection.

Pharmacodynamic properties:

Combination of Trypsin-Chymotrypsin enzyme consist of purified proteolytic enzyme concentrate providing 50,000 armour units of Trypsin and Chymotrypsin activity in the ratio 6.1. It is essential to use a combination of both enzymes because trypsin hydrolysis peptide linkage involving the carboxyl group of agrinine and lysine whereas Chymotrypsin acts on peptide linkages involving phenylalanine, tyrosine and tryptophan.

Therefore complete proteolytic spectrum is achieved only with the combination of Trypsin and Chymotrypsin.

The anti-inflammatory properties in the following ways.

Fibrinolysis activity:

When fibrin clots have stopped bleeding, body's own fibrinolytic agent – plasmin breaks the fibrin barrier. Liver, in response to trauma, releases APR's (Acute Phase

Reactants) that inhibits Plasmin (and its fibrinolytic action). Chymotrypsin and trypsin together breaks down the fibrin barrier thus improving and restoring circulation, resolving edema, hematoma and pain, promoting phagocytosis to remove the debris an accelerate recovery.

There are reports suggesting that chymotrypsin trypsin combination helps modulate the process of inflammation. Thus, trypsin and chymotrypsin combination reduces the proinflammatory mediators and fastens the healing process.

The protein bound fraction of the drug exerts a direct fibrinolytic activity at the site of inflammation thus improving microcirculation and dispersion of tissue fluid.

Reduction in Plasmin Inhibitor levels:

In reported studies have been done measure the levels of plasma inhibitors post-surgery with and without the postoperative administration of trypsin - chymotrypsin enzyme. It was found that there was a reversal in the initial rise of plasma inhibitors during the three-to-five day post-operative period as compared to that in the placebo group where these levels were maintained over a longer period. This action is seen because the plasmin inhibitors (alpha 1 antitrypsin and alpha 2 macroglobulin) have greater propensity to bind elastase and cathepsins as compared to Trypsin Chymotrypsin but more affinity to bind Tryosin Chymotrypsin as compared to plasma to plasmin. Therefore the inhibition of damaging phagocytic proteases by elastases and cathepsins continues while the plasmin inhibiting action is prevented.

Release of Intestinal Plasminogen activators:

Studies have shown that Trypsin-Chymotrypsin brings about release of Plasminogen activators from the intestinal mucosa. Those are absorbed into the systemic circulation along with Trypsin-Chymotrypsin and contribute further to bringing about fibrinolysis. Therefore Trypsin–Chymotrypsin enhances fibrinolysis by a triple mechanism, thereby increasing tissue circulation and decreasing edema.

Increased Microcirculation:

This not only reduces tissue edema but also decreases the contact time of damaged tissue with various inflammatory mediators like leucocytes, immunoglobulins and Plasma complement factors etc.

Smoothens process of digestion:

Trypsin helps to break down large protein molecules by cutting protein chains at specific sites. The large protein molecule is actually a chain of smaller units called amino acids which are linked, end to end, in chains hundreds. There are 20 different amino acids from which these protein chains are made. The specific site along the protein chain where trypsin is active is one with the amino acids lysine and arginine, two of the smaller amino acids.

The enzyme chymotrypsin also cuts the larger protein chain but at different sites from where trypsin cuts. Chymotrypsin makes its cut at positions along the protein chain that contain very large amino acids such as phenylalanine, tyrosine and tryptophan. Otherwise, it is very similar to trypsin.

In some individuals, the production of these digestive enzymes is deficient, resulting in the inability to completely digest food. This can result in abdominal pain, indigestion, gas and malnutrition. This condition is treatable with trypsin chymotrypsin enzyme supplements.

5.2 Pharmacokinetic Properties

Trypsin and Chymotrypsin are related and absorbed in the small intestines. This mode of administration protects the enzymes from being destroyed by acids or other enzymes in the stomach and promotes intestinal absorption. Higher the dosage, higher is the plasma peak levels, but whatever may be the dosage, plasma peak levels are reached in 2-3 hours and return to base level in 8 hours. Therefore the dosage should be repeated every 6 hours. Proof of absorption is provided by the fact that when labelled. Trypsin or Chymotrypsin is administered to animals, radioactivity can be detected in plasma. In human volunteers, active esterase levels have been found in the plasma after administration of Trypsin and Chymotrypsin, maximum esterase levels are proportional to the dosage used. Rapid and significant elevation of blood esterase levels are obtained following oral administration.

5.3 Preclinical Safety Data

Not Applicable

6. Pharmaceutical Particulars

6.1 List of Excipients

Microcrystalline Cellulose 102, Lactose, Maize Starch Powder, Butylated Hydroxy Toluene, Cross Povidone XL-10, Purified Talcum, Colloidal Silicon Dioxide (Aerosil), Cross Carmellose Sodium, Magnesium Stearate, Iso-Propyl Alcohol, Methylene Chloride & DR Coat MB-S.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Do no store above 30°C. Protect from light and moisture.

6.5 Nature and Contents of Container

10 Tablets are packed in an Alu-Alu Blister. Such 3 Blisters are packed in one inner carton along with package insert

6.6 Special Precautions for Disposal

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

7. APPLICANT/SUPPLIER

CHRISNELB PHARMACEUTICAL NIG. LTD. House
1GH Close Festac Town, Lagos State

8. MANUFACTURER

CLAROID PHARMACEUTICALS LIMITED
Survey No. 217/P Opp. Gurukul English Medium School Kamod, Satpanth Mandir Pirana Rd, TA, Ahmedabad- 382425, Gujarat, India.

9. DATE OF PREQUALIFICATION/RENEWAL OF PREQUALIFICATION

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10. Date of Revision of the Text

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