

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

**CHYMORAL/ CHYMORAL FORTE/ CHYMORAL FORTE – DS
(TRYPSIN-CHYMOTRYPSIN TABLETS)**

COMPOSITION

CHYMORAL

Each enteric-coated tablet contains:

50,000 Armour Units of Enzymatic Activity*

*Supplied by a Purified Concentrate which has Specific Trypsin and Chymotrypsin Activity in a Ratio of Approximately Six to One.

Colours: Lake of Sunset Yellow FCF and Titanium Dioxide I.P.

CHYMORAL FORTE

Each enteric-coated tablet contains:

1,00,000 Armour Units of Enzymatic Activity*

*Supplied by a Purified Concentrate which has Specific Trypsin and Chymotrypsin Activity in a Ratio of Approximately Six to One.

Colours: Ponceau 4R and Sunset Yellow FCF

CHYMORAL FORTE – DS

Each enteric-coated tablet contains:

2,00,000 Armour Units of Enzymatic Activity*

*Supplied by a Purified Concentrate which has Specific Trypsin and Chymotrypsin Activity in a Ratio of Approximately Six to One.

Colours: Lake of Erythrosine and Titanium Dioxide I.P.

DESCRIPTION

Trypsin

A proteolytic enzyme crystallised from an extract of the pancreas of healthy bovine or porcine animals, or both. It contains not less than 2500 USP units in each mg, calculated on the dried basis. A white to yellowish-white, odourless, crystalline or amorphous powder. Store in airtight containers at temperature not exceeding 40°C.

Chymotrypsin

A proteolytic enzyme crystallised from an extract of the pancreas gland of the ox, *Bos taurus* (Bovidae). It contains not less than 1000 USP units in each mg, calculated on the dried basis. A white to yellowish-white, crystalline or amorphous, odourless powder. An amount equivalent to 100 000 USP units is soluble in 10 mL of water and in 10 mL of sodium chloride 0.9%. Store in airtight containers at a temperature not exceeding 40°C.

CLINICAL PHARMACOLOGY

Pharmacodynamics

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 blood stream or the intestines where they are excreted or are converted by process of proteolysis into the active enzymes that aid digestion. When taking 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 reducing inflammation and fighting infection.

Combination of Trypsin-Chymotrypsin enzyme consist of purified proteolytic enzyme concentrate providing 50,000/1,00,000/2,00,000 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.

Fibrinolytic 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:

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 Trypsin-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.

PHARMACOKINETICS

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 ^[13]labeled 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.

INDICATIONS

- Acute or chronic osteoarthritis, rheumatoid arthritis and spondyloarthritis, spondylosis and other ortho-degenerative disorders, pain management.
- Surgery: Post-operative wounds, Oedema and Haematoma, Prevention of inflammation of the stitching
- Gynecology: Pelvic Inflammatory Disease, Caesarean section, Episiotomy and Hysterectomy
- Dentistry: Tooth Extraction, Peri apical abscess, Maxillofacial surgery
- Ophthalmology: Ocular Trauma such as Macular edema, Black eye, Hyphema, Uveal tract inflammation, Subconjunctival hemorrhage,
- ENT: Auricular Septal hematoma, Nasal fractures, Parapharyngeal abscess
- Orthopedics: Post-traumatic edema, soft tissue injury, Fractures & dislocation, Sports injury, Sprains & Strains, Intervertebral disc herniation (sciatica or PID)
- Ophthalmology: Ocular Trauma such as Macular oedema, Black eye, Hyphema, Uveal tract inflammation, Subconjunctival haemorrhage, Extra-ocular trauma

DOSAGE AND ADMINISTRATION

As directed by the Physician.

The dose and dose frequency of Chymoral, Chymoral Forte, Chymoral Forte DS will be decided under the supervision of qualified physician

CONTRAINDICATIONS

- Adjunctive therapy in management of inflammatory edema due to injury, surgery, infection or dental procedures
- Hypersensitivity to Chymoral ingredients or enzymes
- Chymoral is contraindicated in patients with severe liver, kidney impairment, peptic ulcer, high vitreous pressure, and hypersensitivity.

WARNING AND PRECAUTION

Chymotrypsin is safe when used in the eye by a healthcare professional. It can cause side effects when used in the eye, including an increase in pressure in the eye and other eye conditions such as uveitis, paralysis of the iris, and keratitis.

Chymotrypsin also seems to be safe for most people when taken by mouth to reduce redness and swelling following surgery or injury, and when applied directly to the skin for burns.

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 be employed in patients with severe hepatic insufficiency or renal damage or irregularities of blood clotting mechanism.

Trypsin and Chymotrypsin should not be employed in patients with severe hepatic insufficiency and should be given cautiously to patient with renal damage or irregularities of blood clotting mechanism. It should be used for a week after pulmonary hemorrhage.

After many years of wide spread clinical use, there is no reason to believe that Trypsin and Chymotrypsin is, or may be teratogenic in humans. However it its sound medical principle to exercise precaution in prescribing any medications during the first three months of pregnancy.

Severe hepatic or renal disease. To be used with caution during Lactation, or in the elderly, children, pregnancy (use only, if clearly indicated) and patients with irregularities of blood clotting mechanism.

Pregnancy

Not enough is known about the use of trypsin and chymotrypsin during pregnancy. Stay on the safe side and avoid use.

Lactation

Not enough is known about the use of trypsin and chymotrypsin during breastfeeding. Stay on the safe side and avoid use.

DRUG INTERACTIONS

When certain medications are taken together with Trypsin drug interactions could occur that may affect the efficacy of the medicines. It can even increase your risk for side effects. Trypsin can interact with other medicines such as vitamins, minerals, herbal products, and drugs prescribed by other doctors resulting in side effects or altered effectiveness of Trypsin.

Drug- drug interactions

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

Antibiotics

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

Chymotrypsin is known to interact with chloramphenicol.

Anticoagulants

Trypsin chymotrypsin combination should not be administered concurrently with anti-coagulants such as Coumadin, Heparin and clopidogrel.

ADVERSE EFFECTS

Hepatic damage and necrosis may precipitate arrhythmias, shivering during recovery.

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.

OVERDOSAGE

No data available.

Swallow whole tablet, do not crush or chew

EXPIRY DATE

Three years from the date of manufacturing.

STORAGE

Store in dry place below 25° C.

PRESENTATION

Chymoral is available in blister pack of 10 tablets.

Chymoral Forte is available in blister pack of 20 tablets.

Chymoral Forte - DS is available in blister pack of 10 tablets.

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

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