EMPYNASE®-P
EMPYNASE®-PD Tablets

<Pronase Preparations>

CONTRAINDICATIONS (EMPYNASE®-P, EMPY- NASE®-PD is contraindicated in the following patients.)

Patients with a history of hypersensitivity to this product

DESCRIPTION

1. Composition
EMPYNASE®-P (Capsules): Each capsule contains 9,000 units of pronase.
The capsule itself contains sodium lauryl sulfate, Red No.3 (Erythrocin) and Blue No.1 (Brilliant Blue-FCF) as inactive ingredients.
EMPYNASE®-PD Tablets: Each tablet contains 18,000 units of pronase.

2. Product description
EMPYNASE®-P Capsules are hard capsules with a white body and a blue cap. The content is composed of white granules (lactose) and light brown granules (pronase). It has a slight peculiar odor and taste. The light brown granules are soluble in the intestine.

EMPYNASE®-PD TABLETS are white to grey-white odorless film-coated enteric tablets.

INDICATIONS
Remission of swelling in the following diseases or symptoms:
after operation and trauma, and chronic sinusitis
Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent hawking:
bronchitis, bronchial asthma and pulmonary tuberculosis

DOSAGE AND ADMINISTRATION
Usually, for adults, administer orally 27,000 to 54,000 units daily (3 to 6 EMPYNASE®-P Capsules or 3 EMPYNASE®-PD TABLETS) in three divided doses.
Overindulgent administration of EMPYNASE® should be avoided because much remains unknown about its mechanisms of action and the dose-response relationship is not necessarily clear.

PRECAUTIONS
1. Careful Administration (EMPYNASE®-P, EMPY- NASE®-PD should be administered with care in the following patients.)
   (1) Patients with a history of hypersensitivity to drugs
   (2) Patients with abnormal blood coagulation
   (3) Patients with serious hepatic or renal dysfunction

2. Drug Interactions
Caution during coadministration. (Empynase®-P, Empynase®-PD should be coadministered with the following drugs with caution).
3. Adverse Reactions
During clinical trials, of the total number of 12,211 subjects, 80 (0.66%) experienced 109 separate cases of adverse reactions. The major adverse reactions were anorexia (25 events, 0.20%), skin eruption (18 events, 0.15%), gastric discomfort (13 events, 0.11%) and nausea-vomiting (12 events, 0.10%).

(At the time of completion of re-examination)

- discontinue administration if symptoms occur

4. Use in the Elderly
Since the elderly often have a physiological hypofunction. It is advisable to take such measures as the reduction in the dose under careful supervision.

5. Precautions concerning use
(1) Taking Empynase
1) If the capsule lodges in the esophagus it may rarely cause ulceration. Hence capsules should be consumed with much water and particular care should be taken when consuming directly before sleep.
2) Instruct that the capsule should not be chewed when it is taken.

(2) Packaging
Instruct that the capsules, which are packaged in PTP, are to be removed from the PTP sheet before consumption. (It has been reported that when mistakenly ingested, the sharp edges of PTP sheet can cut the esophageal mucosa and lead to serious complications such as perforation and mediastinitis.

PHARMACOKINETICS
<Reference> Absorption in animals

When both mice and rats where administered the drug by intraduodenal injection, the maximum concentration of pronase in mouse plasma and rat lymph was observed 1 hour after administration.

CLINICAL STUDIES
1. This product has been found to be effective for edema and swelling after surgery and trauma in various fields and improve symptoms such as pain, redness and feeling of warmth.

2. This product improves nasal obstruction, rhinorrhea, changes in nasal membrane, amount of nasal mucus, pus viscosity, etc. in patients with chronic sinusitis.

3. This product improves the amount and nature of phlegm, frequency of coughing, looseness of phlegm, etc. in the presence of poor expectoration in patients with bronchitis, bronchial asthma and pulmonary tuberculosis.

PHARMACOLOGY
1. Proteolytic action
This product affects almost all peptide bonds and exerts potent proteolytic activity (in vitro).

2. Decomposition of inflammatory polypeptides
This product decomposes bradykinin, an inflammatory polypeptide, and suppresses its activity (in vitro).

3. Dissolution of viscous substances
This product shows potent mucinolytic effects and reduces the viscosity of sputum, pus, etc. (humans and in vitro).

4. Fibrinolytic action
This product shows potent fibrinolytic action on fibrin formed and accumulated in inflammatory foci (in vitro).

5. Anti-inflammatory and anti-swelling action
This product inhibited acute inflammatory edema induced by carrageenin, dextran, formalin, ovalbumin, etc (rats). It showed similar inhibitory action on inflammatory reactions (Arthus reaction) on the rat skin induced by rat and rabbit antisera.
In chronic inflammation models produced by the croton oil and adjuvant pouch methods, this product cleared altered tissues and promoted regeneration of connective tissues (rats).

PHYSICOCHEMISTRY
Pronase is a proteolytic enzyme produced by the actinomycetes Streptomyces griseus.
Description:
Pronase is a white to light-brown powder with a slight characteristic odor and a slight bitter taste. It is soluble in water but is practically insoluble in ethanol and ether.
PpH in water (1→100): 6.7-8.3
PACKAGING
EMPYNASE®-P Capsules: Boxes of 100, 500, 1,000, 2,000 and 5,000 in press-through package, and bottles of 1,000.
EMPYNASE®-PD TABLETS: Boxes of 100, 500, 1,000, 2,100 and 3,000 in press-through package, and bottles of 1,000.

REFERENCES
1) Uda K. et al.: In-house data of Kaken Pharmaceutical Co., Ltd.
2) Kajino G. et al.: Shinryo-to Shinyaku (Medical Consultation and New Remedies), 13, 2187-2202, 1976.
10) Matsuo T. et al.: In-house data of Kaken Pharmaceutical Co., Ltd.
14) Yamamura Y. et al.: Sogoh Rinsho (Clinic All-round), 16, 1772-1777, 1967.

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