Revised: January 2012 (12th version)

Standard Commodity Classification No. of Japan
873959

- Egg-white lysozyme preparation -

Neuzym® Tablets 10mg
Neuzym® Tablets 30mg
Neuzym® Tablets 90mg
Neuzym® Granules 10%
Neuzym® Fine Granules 20%

	Tablets 10 mg	Tablets 30 mg	Tablets 90 mg	Granules 10 %	Fine granules 20 %
Approval No.	13900AZZ05050000	14100AZZ05449000	15200AMZ00724000	21300AMZ00534000	15400AMZ00920000
Date of listing in the NHI reimbursement price	Dec 1965	Oct 1967	Apr 1978	Sep 2001	Sep 1981
Date of initial marketing in Japan	Dec 1964	Aug 1967	Apr 1978	Jan 1968	Sep 1981
Date of indication for second reevaluation (reevaluation of drug efficacy)	Jan 2012				

Storage
NEUZYM should be stored at room temperature. Press-through packages of Neuzym should be protected from moisture after opening transparent bag. Packet packages of Neuzym should be protected from moisture after opening aluminum bag. Neuzym in bottle package should be protected from light and moisture after opening the cap of bottle.

Expiration date
NEUZYM should be used before the expiration date indicated on the package or label.

CONTRAINDICATIONS (NEUZYM is contraindicated in the following patients.)

1. Patients with a history of hypersensitivity to any ingredients of NEUZYM
2. Patients with allergy to egg-white
   [The active ingredient of NEUZYM is a protein derived from egg-white. It has been reported that hypersensitivity symptoms including anaphylactic shock may occur in patients with allergy to egg-white.]

DESCRIPTION

1. Composition

Tablets 10 mg:

Each white, plain tablet contains 10 mg (potency) of lysozyme hydrochloride.

It also contains calcium stearate, hydroxypropylcellulose and D-mannitol as inactive ingredients.

Tablets 30 mg:

Each white, plain tablet contains 30 mg (potency) of lysozyme hydrochloride.

It also contains calcium stearate, hydroxypropylcellulose and D-mannitol as inactive ingredients.

Tablets 90 mg:

Each white plain tablet contains 90 mg (potency) of lysozyme hydrochloride.

It also contains calcium stearate, hydroxypropylcellulose and D-mannitol as inactive ingredients.

Granules 10%:

Each 1 g of white granules contains 100 mg (potency) of lysozyme hydrochloride.

It also contains corn starch, povidone and D-mannitol as inactive ingredients.

Fine granules 20%:

Each 1 g of white fine granules contains 200 mg (potency) of lysozyme hydrochloride.

It also contains D-mannitol as an inactive ingredient.

2. Product description

Brand name	Dosage form and identification code	Appearance			Description
		Face	Reverse	Lateral	
NEUZYM Tablets 10mg	Plain tablets				White
	EISAI NZ010	Diameter (mm) 6.1	Weight (mg) 80	Thickness (mm) 2.2	
NEUZYM Tablets 30mg	Plain tablets				White
	EISAI NZ030	Diameter (mm) 7.1	Weight (mg) 120	Thickness (mm) 2.5	
NEUZYM Tablets 90mg	Plain tablets				White
	EISAI NZ090	Diameter (mm) 8.0	Weight (mg) 170	Thickness (mm) 2.8	
NEUZYM Granules 10%	Granules				White
NEUZYM Fine granules 20%	Fine granules				White

INDICATIONS

Remission of swelling in the following diseases:

Chronic sinusitis

Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent expectoration:

Bronchitis, bronchial asthma and bronchiectasis

DOSAGE AND ADMINISTRATION

The usual adult dosage for oral use is 60-270 mg (potency) of lysozyme hydrochloride daily divided into three doses.

NEUZYM should not be administered aimlessly, because the internal action mechanism of lysozyme has not been completely elucidated nor have the relationships between dose and effect been clearly revealed.

PRECAUTIONS

1. Careful Administration (NEUZYM should be administered with care in the following patients.)

(1) Patients with an allergic predisposition manifested as atopic dermatitis, bronchial asthma, drug allergy or food allergy, etc.
[Patients with a predisposition to allergies are liable to be sensitized by various allergens including drugs. Anaphylactoid reactions may occur in such patients.]

(2) Patients with a family history of allergy
[If an allergic predisposition has been inherited, allergy may occur.]

2. Adverse Reactions

Adverse reactions were reported in 42 of 8,653 pateints. (0.49%) [1] (Postmarketing clinical investigation)

(1) Clinically significant adverse reactions (incidence unknown)

1) **Shock and anaphylactoid reactions**
Shock or anaphylactoid reactions may occur. Patients should be carefully observed, treatment discontinued and appropriate measures taken, in the event of symptoms such as facial pallor, feeling of coldness in the extremities, decrease in blood pressure, cyanosis, unconsciousness, flushing, urticaria, facial edema, laryngeal edema or dyspnea, etc.

2) **Toxic Epidermal Necrolysis (TEN) and oculo-muco-cutaneous syndrome (Stevens-Johnson syndrome)**
Toxic epidermal necrolysis and oculo-muco-cutaneous syndrome may occur. Patients should be carefully observed, treatment discontinued and appropriate measures taken, in the event of symptoms such as fever, erythema, itching, ocular congestion or stomatitis, etc.

(2) Other adverse reactions

	5% > ≥0.1%	<0.1%	Incidence unknown
Hypersensitivity note)	Rash/redness		
Gastrointestinal		Diarrhea, stomach discomfort, nausea / vomiting and anorexia	Stomatitis
Hepatic		Hepatic function disorders (elevation of AST (GOT), ALT (GPT), Al-P, γ-GTP or LDH, etc.)	
Others			Dizziness

Note) In the event of such symptoms, treatment should be discontinued.

3. Use in the Elderly

Since the elderly often have a physiological hypofunction, it is advisable to take measures, such as reduction in dosage under careful supervision.

4. Precautions Concerning Use

Caution in handing over drug (tablets)
For drugs that are dispensed in a press-through package (PTP), instruct the patient to remove the drug from the package prior to use. [It has been reported that, if the PTP sheet is swallowed, the sharp corners of the sheet may puncture the esophageal mucosa, causing perforation and resulting in serious complications such as mediastinitis.]

PHARMACOKINETICS

Blood concentration

Among 10 healthy adult male volunteers, five received a 90mg tablet of NEUZYM after fasting overnight and five served as the control and received no treatment.
Upon measuring the serum lysozyme concentration over time by the two-site enzyme immunoassay for the subjects who received NEUZYM, the lysozyme concentration peaked at 1,700pg/mL within 1h and decreased to a non-detectable level by 48h. Lysozyme was not detected in the control subjects.[2]

CLINICAL STUDIES

Clinical efficacy

Clinical trials including double blind studies showed the efficacy of NEUZYM for chronic sinusitis and bronchitis accompanying difficulty of expectoration as the chief complaint, etc. [1, 3, 4]

PHARMACOLOGY

1. Dissolution and expectoration of mucopus

In an *in vitro* study, lysozyme hydrochloride decomposes the nasal discharge of sinusitis patients and decreases its viscosity. It has further been demonstrated that lysozyme hydrochloride significantly increases ciliary movement in ciliary cells collected from human nasal mucosa. [5, 6]

2. Promotion of tissue restoration in the presence of inflammation.

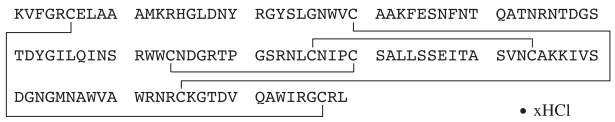
When lysozyme hydrochloride was added to cultures of fibroblasts isolated from the heart of chick embryo, human nasal mucosa and rat subcutaneous tissue, their growth was greatly promoted. [7)]

PHYSICOCHEMISTRY

Nonproprietary name: Lysozyme Hydrochloride (JAN)

Molecular formula: $C_{616}H_{963}N_{193}O_{182}S_{10}$·$x$HCl

Structural formula:



Description:

Lysozyme hydrochloride occurs as white crystals, crystalline powder or amorphous powder. It is soluble in water and practically insoluble in ethanol (99.5). It is hygroscopic.

The pH of an aqueous solution (3 in 200) is 3.0 to 5.0.

PACKAGING

NEUZYM Tablets 10 mg:
Boxes of 100 in press-through packages

NEUZYM Tablets 30 mg:
Boxes of 100 and 500 in press-through packages

NEUZYM Tablets 90 mg:
Boxes of 100 and 500 in press-through packages, and bottles of 500

NEUZYM Granules 10%:
Bottles of 100g and Boxes of 540 g (0.9 g packet × 3 × 200)

NEUZYM Fine granules 20%:
Bottles of 100 g

REFERENCES

1) Aoki K. et al.: Clin. Report, **20,** 517, 1986.
2) Hashida S. et al.: Clin. Exp. Pharmacol. Physiol., **29**, 79 (2002)
3) Takahashi R. et al.: Oto-Rhino-Laryngol. Tokyo, **17,** 731, 1974.
4) Mibe S. et al.: Med. Consult. New Remed., **14,** 1837, 1997.
5) Imamura T. et al.: Pract. Otol. (Kyoto), **61,** 748, 1968.
6) Hisamatsu K. et al.: Acta Otolaryngol., **101**, 290, 1986.
7) Takaoka T. et al.: Jpn. J. Exp. Med., **42**, 221, 1972.

REQUESTS FOR LITERATURE AND PRODUCT INFORMATION SHOULD BE MADE TO:

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