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Eisai Co., Ltd.

EISAI SUBMITS APPLICATIONS FOR REEVALUATION OF EFFICACY AND PARTIAL CHANGE TO LABEL OF EGG WHITE LYSOZYME PREPARATION NEUZYM® BASED ON RESULTS OF REEVALUATION STUDIES

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that its pharmaceutical manufacturing and marketing subsidiary Sannova Co., Ltd. (Headquarters: Gunma Prefecture, President: Toru Takekawa, "Sannova") has submitted an application for reevaluation of the indication of bronchitis, bronchial asthma and bronchiectasis for egg white lysozyme preparation Neuzym® (lysozyme hydrochloride, "lysozyme"). At the same time, Sannova has also submitted an application for a partial label change to remove chronic sinusitis as an approved indication for Neuzym. The Neuzym series consists of six products －Neuzym Tablets (10 mg, 30 mg, 90 mg), Neuzym Granules (10%), Neuzym Fine Granules (20%) and Neuzym Syrup (0.5%). While Sannova is the manufacturing and marketing authorization holder of Neuzym, Eisai is responsible for marketing the products.

After receiving a designation to reevaluate lysozyme preparations including Neuzym in January 2012, Eisai, Sannova and three other companies*[1] handling lysozyme have been jointly carrying out post-marketing clinical studies (double blind, placebo-controlled comparative studies) to verify efficacy of these drugs for chronic sinusitis, bronchitis, bronchial asthma, and bronchiectasis.

Among the studies on the lower respiratory tract diseases bronchitis, bronchial asthma and bronchiectasis, the clinical pharmacology study on chronic obstructive pulmonary disease (COPD)*[2] and asthma with sputum symptom (Study LYS-003) suggested that lysozyme has efficacy as an add-on to standard treatment in patients with COPD. In the study to assess the efficacy of lysozyme as an add-on to standard treatment in preventing exacerbation in patients with COPD (Study LYS-002), a statistically significant improvement over placebo in the study's primary endpoint could not be verified. However, in the study's secondary endpoints, lysozyme showed a trend of greater improvement over placebo across the treatment period. The results from both studies suggested that lysozyme has efficacy in improving difficulty of expectoration compared to placebo. Since there are also many cases of hypersecretion and difficulty expectorating in lower respiratory tract diseases such as COPD, it is believed that lysozyme, which eases the ejection of sputum, makes a significant clinical difference, and therefore an application has been submitted for reevaluation of the indication of bronchitis, bronchial asthma and bronchiectasis.

Meanwhile, in the study on chronic sinusitis (Study LYS-001), the efficacy of lysozyme as an add-on to the current standard treatment of clarithromycin could not be verified and an application for a partial label change has been submitted to remove the indication of chronic sinusitis for Neuzym. With the approval of the partial label change, Neuzym will no longer able to be used for the indication of "chronic sinusitis." Eisai and Sannova will strive to ensure that information is provided to healthcare professionals in order to avoid confusion either in the medical setting or amongst patients taking Neuzym.

*1 ASKA Pharmaceutical Co., Ltd., Nippon Shinyaku Co., Ltd., Sioe Pharmaceutical Co., Ltd.
*2 Chronic obstructive pulmonary disease (COPD) is primarily encompasses chronic bronchitis and pulmonary emphysema, and sputum is a symptom of both conditions

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[Notes to editors]

1. Proposed changes to the Neuzym® label (application seeks to remove underlined parts)

1) Neuzym Tablets 10 mg, Neuzym Tablets 30 mg, Neuzym Tablets 90 mg, Neuzym Granules 10%, Neuzym Fine Granules 20%

Label Prior to Revision	Revised Label (Proposed)
【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	【Indications】 Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent expectoration: Bronchitis, bronchial asthma and bronchiectasis

2) Neuzym Syrup 0.5%

Label Prior to Revision	Revised Label (Proposed)
【Indications】 Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent expectoration: Bronchitis, bronchial asthma and bronchiectasis Remission of swelling in the following diseases: Chronic sinusitis	【Indications】 Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent expectoration: Bronchitis, bronchial asthma and bronchiectasis

2. About the reevaluation studies

1) Post-marketing study on patients with chronic sinusitis

Title of Study	A double blind, randomized, placebo-controlled comparative study to evaluate the efficacy of lysozyme hydrochloride (LYS) in chronic sinusitis (Study LYS-001)
Study Design	Multicenter, placebo-controlled, randomized, double-blind, parallel-group study
Number of Subjects	260
Study Treatments	Investigational drug: clarithromycin 200 mg/day + LYS 270 mg/day Reference therapy: clarithromycin 200 mg/day + placebo
Objectives	Primary Objective: Scoring assessment of total change in shadows on a standard x-ray of the maxillary sinuses after 12 weeks of treatment Secondary Objective: Subjective and objective symptoms after 12 weeks of treatment

2) Post-marketing studies on patients with bronchitis, bronchial asthma and bronchiectasis

Title of Study	A double blind, randomized, placebo-controlled comparative study to evaluate the efficacy of lysozyme hydrochloride (LYS) in preventing exacerbation of chronic obstructive pulmonary disease (COPD) (Study LYS-002)
Study Design	Multicenter, placebo-controlled, randomized, double-blind, parallel-group study
Number of Subjects	400
Study Treatments	Investigational drug: standard treatment*[1] + LYS 270 mg/day Reference therapy: standard treatment*[1] + placebo
Objectives	Primary Objective: Acute exacerbation of COPD after 52 weeks of treatment Secondary Objective: Spirometry*[2] during 52 weeks (FEV_1)*[3] and QOL (quality of life) assessed by CAT*[4] (COPD assessment test)

Title of Study	Pharmacological effect of lysozyme for chronic obstructive pulmonary disease and asthma with sputum symptom: a randomized, placebo-controlled, double-blind study (Study LYS-003)
Study Design	Single-center, placebo-controlled, randomized, double-blind, two-period/two-treatment crossover study
Number of Subjects	24 COPD patients, 24 patients with bronchial asthma
Study Treatments	Treatment duration: First treatment period: 28 days, Second treatment period: 28 days Investigational drug: standard treatment*[1] + LYS 270 mg/day Reference therapy: standard treatment*[1] + placebo
Objectives	Breathing resistance measured by spirometry and IOS*[5] (Impulse Oscillometry System), CAT (COPD Assessment Test) and other tests

*[1] Standard treatment: Bronchodilator agents (beta-agonists, anticholinergic drugs, xanthine derivatives), inhaled corticosteroids, or a combination of both

*[2] Spirometry: Respiratory function test that uses instruments to measure lung capacity

*[3] FEV_1: Volume of air that has been exhaled at the end of the first second of forced expiration

*[4] CAT: A tool to analyze what kind of impact COPD has on health and lifestyle based on how patients score on a specialized questionnaire.

*[5] IOS: A method of measuring breathing resistance that can obtain stable values through quiet breathing, without requiring effort in breathing from the patient