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Eisai Co., Ltd.

## **MHLW APPROVES PARTIAL LABEL CHANGE FOR EGG WHITE LYSOZYME PREPARATION NEUZYM<sup>®</sup>, DESIGNATES DRUG FOR REEVALUATION**

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that its pharmaceutical manufacturing and marketing subsidiary Sannova Co., Ltd. (Headquarters: Gunma Prefecture, President & CEO: Toshio Kaneko, "Sannova") received approval from Japan's Ministry of Health, Labour and Welfare (MHLW) on January 20 to remove alveolar pyorrhea and other dental and urologic conditions as approved indications for egg white lysozyme preparation Neuzym<sup>®</sup>. Additionally, the drug was designated for reevaluation for other indications not subject to removal.

The Neuzym<sup>®</sup> Series comprises a total of six products—Neuzym<sup>®</sup> Tablets (10 mg, 30 mg, 90 mg), Neuzym<sup>®</sup> Granules (10%), Neuzym<sup>®</sup> Fine Granules (20%) and Neuzym<sup>®</sup> Syrup (0.5%). While Sannova is the manufacturing and marketing authorization holder of Neuzym<sup>®</sup>, Eisai is responsible for marketing the products.

The reevaluation of efficacy of Neuzym<sup>®</sup> and other anti-inflammatory enzyme preparations has been under consideration by the MHLW Pharmaceutical Affairs and Food Sanitation Council's Special Committee of Drug Efficacy Reevaluation. This approval for partial label change was granted following the submission of an application on December 21, 2011 seeking approval to remove "alveolar pyorrhea (inflammatory type)" and "hemorrhage during or after minor operations (dentistry and urology)" as approved indications from the label and make corresponding changes to dosage and administration for Neuzym<sup>®</sup> after Eisai and Sannova determined that it would not be feasible to conduct any further studies for the these indications.

Neuzym<sup>®</sup> and other anti-inflammatory enzyme preparations were designated as drugs for which efficacy must be reconfirmed based on a decision reached by the aforementioned reevaluation committee at a meeting held on December 22, 2011. This means that the five companies\* handling lysozyme hydrochloride will have to carry out post-marketing studies (double blind, placebo-controlled comparative studies) for chronic sinusitis, bronchitis, bronchial asthma, and bronchiectasis.

With the approval of the partial label change, Neuzym<sup>®</sup> is no longer able to be used in the treatment of "alveolar pyorrhea (inflammatory type)" and "hemorrhage during or after minor operations (dentistry and urology)." 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<sup>®</sup>, and will work to reconfirm the efficacy of the preparation in the treatment of chronic sinusitis, bronchitis, bronchial asthma, and bronchiectasis.

\*Eisai Co., Ltd., Sannova Co., Ltd., Nippon Shinyaku Co., Ltd., Sioe Pharmaceutical Co., Ltd., ASKA Pharmaceutical Co., Ltd.

**[Please refer to the following notes for further information on changes to the Neuzym<sup>®</sup> label]**

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**[Notes to editors]**

1. Changes to the Neuzym<sup>®</sup> label (underlined parts have been deleted)

1) Neuzym<sup>®</sup> Tablets 10 mg

Label Prior to Revision	Revised Label
<p><b>【Indications】</b>  Remission of swelling in the following diseases:  Chronic sinusitis  Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent hawking:  Bronchitis, bronchial asthma and bronchiectasis  <u>Hemorrhage during or after minor operations (dentistry and urology)</u></p>	<p><b>【Indications】</b>  Remission of swelling in the following diseases:  Chronic sinusitis  Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent hawking:  Bronchitis, bronchial asthma and bronchiectasis</p>

※No changes have been made to the dosage and administration information contained in the Neuzym<sup>®</sup> Tablets 10 mg package insert.

2) Neuzym<sup>®</sup> Tablets 30 mg, Neuzym<sup>®</sup> Tablets 90 mg, Neuzym<sup>®</sup> Granules 10%, Neuzym<sup>®</sup> Fine Granules 20%

Label Prior to Revision	Revised Label
<p><b>【Indications】</b>  Remission of swelling in the following diseases:  Chronic sinusitis <u>and alveolar pyorrhea (inflammatory)</u>  Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent hawking:  Bronchitis, bronchial asthma and bronchiectasis  <u>Hemorrhage during or after minor operations (dentistry and urology)</u></p>	<p><b>【Indications】</b>  Remission of swelling in the following diseases:  Chronic sinusitis  Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent hawking:  Bronchitis, bronchial asthma and bronchiectasis</p>
<p><b>【Dosage and Administration】</b>  <u>For remission of swelling in chronic sinusitis, difficulty in expectoration in bronchitis, bronchial asthma and bronchiectasis with hard-to-eliminate sputum and frequent hawking, and hemorrhage during or after minor operations (dentistry and urology):</u>  The usual adult dosage for oral use is 60-270 mg (potency) of lysozyme hydrochloride daily divided into three doses.  <u>For remission of swelling of alveolar pyorrhea (inflammatory type):</u>  <u>The usual adult dosage for oral use is 180-270 mg (potency) of lysozyme hydrochloride daily divided into three doses. Depending on the severity of symptoms, local treatment (e.g. removal of dental</u></p>	<p><b>【Dosage and Administration】</b>    The usual adult dosage for oral use is 60-270 mg (potency) of lysozyme hydrochloride daily divided into three doses.</p>

<p><u>calculus, mouth rinses or topical application of appropriate remedies to the affected area) may be advisable before or during administration.</u></p> <p>Neuzym should not be administered aimlessly, since the mechanism of action of lysozyme has not been completely elucidated nor have dose-effect relationships been clearly established.</p>	<p>Neuzym should not be administered aimlessly, since the mechanism of action of lysozyme has not been completely elucidated nor have dose-effect relationships been clearly established.</p>
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3) Neuzym<sup>®</sup> Syrup 0.5%

Label Prior to Revision	Revised Label
<p><b>【Indications】</b>            Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent hawking:                Bronchitis, bronchial asthma and bronchiectasis            Remission of swelling in the following diseases:                Chronic sinusitis  <u>Hemorrhage during or after minor operations</u>  <u>(dentistry and urology)</u></p>	<p><b>【Indications】</b>            Difficulty of expectoration in the following diseases with hard-to-eliminate sputum and frequent hawking:                Bronchitis, bronchial asthma and bronchiectasis            Remission of swelling in the following diseases:                Chronic sinusitis</p>

※No changes have been made to the dosage and administration information contained in the Neuzym<sup>®</sup> Syrup 0.5% package insert.