

February 26, 2019

**Launch of Demser[®] Capsule 250 mg,
a Tyrosine Hydroxylase Inhibitor in Japan**

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President, Representative Director, Gyo Sagara; “ONO”) announced today that it has launched Demser[®] Capsule 250 mg (generic name: metyrosine, “Demser”), a tyrosine hydroxylase inhibitor, in Japan for the improvement of status of catecholamine excess secretion in pheochromocytoma.

Pheochromocytoma (PC) is a neuroendocrine tumor deriving from the adrenal medulla or the extra-adrenal gland ganglion with 2,920 patients estimated in Japan*. Catecholamine excessively secreted from PC causes various symptoms, such as tachycardia, headache, palpitation, sweating, constipation, including hypertension. Sympatholytic drugs, α -blocker and β -blocker, for control of blood pressure and heart rate have been usually used to improve these symptoms. As there are many cases where surgical removal of tumors is not applicable in patients with locally invasive or metastatic malignant PC, a long-term therapy, such as radiotherapy and chemotherapy is required. The chronic continuation of catecholamine excess secretion may increase a risk of causing cardiovascular-related adverse events such as heart failure or fatal arrhythmia.

Demser inhibits tyrosine hydroxylase related to the production of catecholamine, reduces catecholamine extremely secreted from PC, and alleviates symptoms due to catecholamine excess secretion. Demser is a promising drug with an efficacy in the improvement of the symptoms in patients who are not able to sufficiently control the symptoms with sympatholytic drugs.

Demser is a product for which development companies were recruited in Japan at the “Review Committee on Unapproved or Off-label Drugs with High Medical Needs”, established by the Ministry of Health, Labour and Welfare (MHLW), and ONO has been developing this product. In May 2015, the product was designated for the orphan drug by the MHLW.

ONO obtained exclusive rights to develop and commercialize metyrosine in Japan for the treatment of PC (and conditions and symptoms related thereto), in accordance with the license agreement concluded in October 2013 with Valeant Pharmaceuticals North America LLC, an affiliate of Valeant Pharmaceuticals International, Inc. (In July 2018, the company name was changed to Bausch Health Companies Inc., “Bausch Health”). In the US, Bausch Health markets the product under the tradename of “Demser[®]” in the indication of PC.

*: “Actual condition survey and preparation of medical guideline of pheochromocytoma” Research Report 2009, Research Project on Overcoming Intractable Diseases Project being conducted by the Ministry of Health, Labour and Welfare

Overview of Demser® Capsule 250 mg

Product Name	Demser® Capsule 250 mg
Generic name	Metyrosine
Indication	Improvement of status of catecholamine excess secretion in pheochromocytoma
Dosage and administration	Usually, for adults and children 12 years of age and older, start to administer 500 mg of metyrosine orally daily. When the effect is insufficient, titrate the dose by 250 mg or 500 mg daily at intervals of 3 days or more by monitoring the clinical course closely, and dosage should be adjusted under adequate observation of urinary catecholamine amount and symptoms of the patient. However, the maximum daily dose is 4,000 mg with the highest dose of 1,000 mg per dose at intervals of 4 hours or longer. The daily dose of 500 mg is divided twice a day, 750 mg three times a day and 1,000 mg or more four times a day.
Package	100 capsules
Approval date	January 8, 2019
NHI price listing date	February 26, 2019
NHI drug price	¥5,853.50
Launch date	February 26, 2019
Manufacturer/distributor	Ono Pharmaceutical Co., Ltd.

Product photograph



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