For Immediate Release

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Daiichi Sankyo Launches Natural Tetrahydrobiopterin Agent Biopten® Granules 10%

Tokyo, Japan (November 29, 2013) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that today it launched natural tetrahydrobiopterin agent Biopten® Granules 10% (generic name: sapropterin hydrochloride; approved for manufacture and marketing in Japan: August 20, 2013; Listing in the National Health Insurance drug price list: November 29, 2013).

Biopten is a highly pure, chemically synthesized form of natural tetrahydrobiopterin (hereafter, BH_4) that occurs naturally in the human body. It is used to treat patients with atypical hyperphenylalaninemia (hereafter, HPA; approved in March, 1992) and those with BH_4-responsive HPA (approved in July, 2008) by maintaining an appropriate phenylalanine level.

As Biopten® Granules 2.5% was administered to infants based on their body weight, or one sachet per kilogram, to treat BH_4-responsive HPA, it became evident that an extremely large amount of sachets would be necessary each day for growing infants; consequently, an improved formulation was badly needed. In order to meet this need while improving patient adherence and lessening the physical burden, Daiichi Sankyo developed high content Biopten® Granules 10% containing 100mg of sapropterin hydrochloride per sachet (1g). Today's launch of the new formulation follows approval by the Japanese authorities in August 2013.

About hyperphenylalaninemia

Hyperphenylalaninemia is a medical condition characterized by elevated levels of the essential amino acid phenylalanine in the blood due to metabolic disorder. The condition is genetic and if left untreated after birth can lead to irreversible neurological disorder, such as mental retardation.

There are two main causes of the condition. One is lack at birth of a substance (BH_4) which promotes the mechanism of an enzyme that metabolizes phenylalanine (atypical HPA). The other is when the enzyme that metabolizes phenylalanine is abnormal. In patients with the former, elevating levels of BH_4 in the body can restore the metabolic function (referred to as BH_4-responsive HPA).

Hyperphenylalaninemia is a rare disease with an incidence rate of 1 in 80,000 in Japan. Since mass screening of newborns was started in 1977, a total of 600 have been diagnosed with the condition.

Biopten has been designated as an orphan disease drug for its use in treating BH_4-responsive HPA.

For reference

Overview of the new Biopten® Granules 10% and existing product Biopten® Granules 2.5%

Drug name	Biopten® Granules 10%	Biopten® Granules 2.5%
Generic name (JAN)	Sapropterin hydrochloride	
Indications and usage	1. To reduce blood phenylalanine levels in patients with dihydrobiopterin synthetase deficiency and dihydropteridine reductase deficiency in patients with hyperphenylalaninemia (HPA) 2. To reduce blood phenylalanine levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin-responsive phenylalanine hydroxylase deficiency	
Dosage and administration	1. Atypical hyperphenylalaninemia Under normal circumstances, sapropterin hydrochloride can be administered orally between one and three times daily at a rate of 2 - 5 mg/kg, but the maintenance dose can be established when blood phenylalanine levels become steady. 2. Tetrahydrobiopterin-responsive phenylalanine hydroxylase deficiency Under normal circumstances, start administration of sapropterin hydrochloride at a rate of 10mg/kg daily (between one and three times, orally) while observing clinical symptoms and establish the maintenance dose corresponding to the patient's age when blood phenylalanine levels become steady.	
Packaging	10% granules: 1g sachets (100mg sapropterin hydrochloride per sachet)	2.5% granules: 0.4g sachets (10mg sapropterin hydrochloride per sachet)
NHI drug price	35,875.00 yen/sachet	3,587.50 yen/sachet
Daily dosage	For indication #2 above with patient body weight of 30kg: 3 - 6 sachets (3 - 6g)	For indication #2 above with patient body weight of 30kg: 30 - 60 sachets (24g)