

News Release

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Merck Serono Initiates KAMPER, The First Pan-European Registry for Patients Under Kuvan[®] Therapy

Geneva, Switzerland, December 10, 2009 – Merck Serono, the pharmaceutical division of Merck KGaA, Darmstadt, Germany, today announced the enrollment of the first patient in KAMPER, the Kuvan Addult Maternal Pediatric European Registry. KAMPER is the first Pan-European registry for patients suffering from hyperphenylalaninaemia (HPA), due to phenylketonuria (PKU) or tetrahydrobiopterin (BH4) deficiency, and treated with Kuvan[®] (sapropterin dihydrochloride).

The registry aims to follow 625 patients over a period of up to 15 years in order to document the long-term treatment outcomes of Kuvan[®]. Kuvan[®] was granted with an Orphan Drug designation by the European Commission and received a marketing authorization in December 2008.

“The purpose of the KAMPER registry is to collect additional information on the benefits and long-term safety of therapy with Kuvan. Beyond this objective, Merck Serono’s goal is to help improve the clinical care of patients with PKU or BH4 deficiency. The KAMPER registry represents a significant commitment in this direction”, said Bernhard Kirschbaum, Executive Vice President Research and Development at Merck Serono.

The KAMPER registry is a multi-center observational registry which will be conducted in specialist clinics across 11 European countries. Patients over the age of 4 suffering from PKU and all patients with BH4 deficiency, treated with Kuvan[®] are eligible to participate. A maternal sub-registry will also be open to collect additional data from

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pregnant patients under Kuvan[®]. An assessment of patients will be performed on a regular basis according to local practice. Interim analyses of the data collected will be published over the 15 years of the registry.

About hyperphenylalaninemia (HPA)

Disorders of phenylalanine (Phe) metabolism can lead to abnormal elevations of blood Phe levels, also called hyperphenylalaninemia (HPA). Two inborn errors of metabolism, phenylketonuria (PKU) and tetrahydrobiopterin (BH4) deficiency, account for the majority of cases of HPA.

About phenylketonuria (PKU)

PKU, a genetic disorder affecting approximately 50,000 diagnosed patients in the developed world, is caused by a deficiency of the enzyme phenylalanine hydroxylase (PAH). PAH is required for the metabolism of phenylalanine (Phe), an essential amino acid found in all protein-containing foods. If the active enzyme is not present in sufficient quantities, Phe accumulates to abnormally high levels in the blood and brain, resulting in a variety of complications including severe mental retardation and brain damage, mental illness, seizures and tremors, and cognitive problems. As a result of global newborn screening efforts implemented in the 1960s and early 1970s, virtually all PKU patients in developed countries are diagnosed at birth.

About tetrahydrobiopterin (BH4) deficiency

BH4 deficiency is a very rare inborn error of metabolism, and is estimated to account for 1–2 % of cases of HPA. BH4 deficiency is an autosomal recessive genetic condition and can result from deficiencies of any of the five different enzymes involved in BH4 synthesis and regeneration. BH4 is a necessary co-factor for PAH. Therefore, BH4 deficiency impairs PAH activity leading to a biochemical situation similar to PKU, with HPA resulting from deficient conversion of Phe to tyrosine. In addition, since BH4 is also a necessary co-factor for both tyrosine hydroxylase and tryptophan hydroxylase, BH4 deficiency causes deficiencies in the downstream neurotransmitter products of these amino acids including catecholamines and serotonin. Dietary limitation of whole protein or Phe intake is often not necessary with BH4 treatment. However, since BH4 does not cross the blood brain barrier, concomitant therapy with neurotransmitter precursors, i. e. levodopa and 5-hydroxytryptophan, may be necessary to boost central nervous system substrate levels for catecholamine and serotonin synthesis, respectively.

About Kuvan[®]

Developed by Merck Serono and BioMarin Pharmaceutical Inc. (Nasdaq and SWX: BMRN), Kuvan (sapropterin dihydrochloride), is an oral therapeutic and the first treatment indicated in Europe for the treatment of hyperphenylalaninemia (HPA) due to phenylketonuria (PKU) in patients over the age of 4, or due to tetrahydrobiopterin (BH4) deficiency. Kuvan is the synthetic form of 6R-BH4, a naturally occurring enzyme cofactor that works in conjunction with the enzyme phenylalanine hydroxylase (PAH) to metabolize phenylalanine (Phe). Clinical data show that Kuvan produces significant reductions in blood Phe levels in the subset of patients who are BH4-responsive.

Most common side effects reported with the use of Kuvan include headache, runny nose, diarrhea, vomiting, sore throat, cough, abdominal pain, stuffy nose and low levels of phenylalanine in the blood.

Kuvan is approved in 32 countries, including member states of the European Union and the USA. Under the terms of the agreement with BioMarin, Merck Serono has exclusive rights to market Kuvan in all territories outside the USA, Canada and Japan.



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About Merck Serono

Merck Serono is the division for innovative prescription pharmaceuticals of Merck KGaA, Darmstadt, Germany, a global pharmaceutical and chemical company. Headquartered in Geneva, Switzerland, Merck Serono discovers, develops, manufactures and markets innovative small molecules and biopharmaceuticals to help patients with unmet medical needs. In the United States and Canada, EMD Serono operates through separately incorporated affiliates.

Merck Serono has leading brands serving patients with cancer (Erbix®[®], cetuximab), multiple sclerosis (Rebif®[®], interferon beta-1a), infertility (Gonal-f®[®], follitropin alpha), endocrine and metabolic disorders (Saizen®[®] and Serostim®[®], somatropin), (Kuvan®[®], sapropterin dihydrochloride) as well as cardiometabolic diseases (Glucophage®[®], metformin), (Concor®[®], bisoprolol), (Euthyrox®[®], levothyroxine). Not all products are available in all markets.

With an annual R&D expenditure of around € 1bn, Merck Serono is committed to growing its business in specialist-focused therapeutic areas including neurodegenerative diseases, oncology, fertility and endocrinology, as well as new areas potentially arising out of research and development in autoimmune and inflammatory diseases.

About Merck

Merck is a global pharmaceutical and chemical company with total revenues of € 7.6 billion in 2008, a history that began in 1668, and a future shaped by approximately 33,000 employees in 60 countries. Its success is characterized by innovations from entrepreneurial employees. Merck's operating activities come under the umbrella of Merck KGaA, in which the Merck family holds an approximately 70% interest and free shareholders own the remaining approximately 30%. In 1917 the U.S. subsidiary Merck & Co. was expropriated and has been an independent company ever since.

For more information, please visit www.merckserono.com or www.merck.de