



## Phenylketonuria

### Fact Sheet

#### **About Phenylketonuria (PKU)**

- Phenylketonuria (PKU) is a rare, inherited, brain-threatening metabolic disorder found in approximately 1 in 12,000 to 15,000 infants born in Canada <sup>i</sup>
- PKU is observed when the body is unable to process phenylalanine, or “Phe,” an essential amino acid found in dietary protein <sup>ii</sup>
- In people with PKU, more than 500 mutations have been identified in the phenylalanine hydroxylase (PAH) gene, which is responsible for processing Phe in the liver <sup>iii</sup>
- These mutations cause a deficiency in the PAH enzyme, resulting in an accumulation in the blood and brain of toxic levels of Phe <sup>iii</sup>
- If left untreated, symptoms of PKU can range from mild cognitive impairment to severe mental retardation and epilepsy <sup>iv</sup>

#### **Diagnosis**

- PKU is recognized as the first condition widely tested for through newborn screening – a simple procedure conducted through bloodspot collection
- Bloodspot collection involves pricking the heel of a newborn baby to collect blood samples, which are sent to a specialized laboratory to test for certain rare disorders <sup>v</sup>
- All provinces and territories offer newborn screening to determine if a child is born with PKU <sup>vi</sup>
- Once PKU is diagnosed, it is critical to the child’s brain development and function that the appropriate treatment is initiated immediately and maintained throughout life

#### **Treatment**

- For decades, the only treatment for this brain-threatening condition has been lifelong adherence to a severely restrictive low-Phe diet reliant on synthetic formulas and medical foods <sup>vii</sup>
- The PKU diet is vegan with severe restrictions on natural protein foods that are high in Phe, therefore most people with PKU cannot eat foods such as meat, eggs, nuts, beans, milk and cheese <sup>ii</sup>
- Patients treated with a restrictive low-Phe diet alone can see clinical benefits, but evidence indicates that a significant burden of illness still exists <sup>viii</sup>
- Adherence to the lifelong medical food-based low-Phe diet in PKU is extremely challenging, as the planning required to achieve acceptable blood Phe levels is very complex and time consuming, and the food is limited, expensive and unpalatable <sup>ix</sup>
- Those patients who are unable to adequately control their Phe levels often suffer from neurocognitive impairment with psychosocial impacts <sup>x</sup>

- PKU patients must be monitored frequently by specially trained health care providers which can include dietitians, physicians, genetic counselors, psychologists, nurses and social workers
- There is a proven clinical need for non-dietary treatment alternatives to assist in managing PKU, as outcomes with dietary management alone are clinically sub-optimal<sup>xi</sup>
- Approved by Health Canada in April 2010, Kuvan (sapropterin) is the first and only drug therapy proven to reduce blood Phe levels in patients with PKU, when taken in conjunction with a Phe-restricted diet<sup>xii</sup>
- Depending on the province, patient access to publicly-funded treatment for PKU through provincial drug programs is varied

## **Symptoms**

- Depending on the age of the individual, studies have shown that up to 79 per cent of PKU patients could have blood phenylalanine concentrations above recommended limits<sup>xiii</sup>
- Despite being treated early and continuously with diet alone, children and adults with PKU may experience cognitive symptoms, as well as disturbances in emotional and behavioural functioning – including executive function deficits, attention deficits and reduced processing speed<sup>viii</sup>
- Children, adolescents and adults with PKU treated with diet have been reported to demonstrate deficiencies in vitamin B6 and B12, as well as imbalances in bone formation<sup>viii</sup>

## **References**

- 
- <sup>i</sup> Arnold GL. Phenylketonuria. 2009; <http://emedicine.medscape.com/article/947781-print>
- <sup>ii</sup> PKU and the Brain. Canadian PKU and Allied Disorders Inc. 2010. Available at [http://canpku.org/images/pdf/pku-and-the-brain\\_canpku.pdf](http://canpku.org/images/pdf/pku-and-the-brain_canpku.pdf) Accessed May 7, 2012.
- <sup>iii</sup> PAH. Genetics Home Reference. Available at <http://ghr.nlm.nih.gov/gene/PAH> Accessed April 25, 2012
- <sup>iv</sup> Martynyuk A et al., Epilepsy in Phenylketonuria: A Complex Dependence on Serum Phenylalanine Levels. *Epilepsia*. 2007, 48(6):1143-50
- <sup>v</sup> Newborn Bloodspot FAQ's. Save Babies Through Screening Foundation. Available at: <http://www.savebabies.org/questions.html> Accessed March 9, 2012.
- <sup>vi</sup> Canada lags on newborn screening. Canadian Medical Association. Available at <http://www.cmaj.ca/content/173/1/23.1.full>. Accessed on January 18, 2012.
- <sup>vii</sup> MacDonald A, et al., Nutrition in phenylketonuria, *Mol. Genet. Metab.* (2011), doi:10.1016/j.ymgme.2011.08.023
- <sup>viii</sup> Enns G, Koch R, Brumm V et al. Suboptimal outcomes in patients with PKU treated early with diet alone: Revisiting the evidence. *Mol. Genet. Metab.* 2010; 101: 99–109
- <sup>ix</sup> Singh RH, Quirk ME. Using change in plasma phenylalanine concentrations and ability to liberalize diet to classify responsiveness to tetrahydrobiopterin therapy in patients..., *Mol. Genet. Metab.* (2011), doi:10.1016/j.ymgme.2011.09.009
- <sup>x</sup> Brumm VL, Bilder D, Waisbren SE. Psychiatric symptoms and disorders in phenylketonuria. *Mol Genet Metab.* 2010; 99:S59-S63
- <sup>xi</sup> Phenylketonuria: screening and management. National Institutes of Health. Available at: <http://consensus.nih.gov/2000/2000Phenylketonuria113html.htm> Accessed on December 8, 2011.
- <sup>xii</sup> Kuvan [product monograph]. Toronto, ON: BioMarin Pharmaceutical (Canada) Inc.; 2010.
- <sup>xiii</sup> Walter JH, White FJ, Hall SK et al., How practical are recommendations for dietary control in phenylketonuria? *The Lancet*. 2002; 360: 55-57