Sapropterin (Kuvan®)

Sapropterin is a co-factor for PAH and in some individuals residual enzymatic activity can be increased by co-factor supplementation. The mechanism by which cofactor therapy increases PAH activity in the PAH deficient individual may be due to pathogenic variants that affect PAH interaction with pterin, and in some cases it is understood that sapropterin acts as a chaperon, stabilizing the abnormal PAH protein [Camp et al 2014]. Genotyping may help to predict which individuals will respond to sapropterin supplementation and the level of the response.

Large neutral amino acids (LNAA) transporters

At the blood-brain barrier, phenylalanine shares a transporter with other large neutral amino acids (LNAA). Some individuals exclude excess phenylalanine, more or less efficiently, because they show evidence of variation in the high-capacity/high $K_m$ component of phenylalanine transport across the blood-brain barrier [Weglage et al 2002]. LNAA supplementation has reduced brain phenylalanine concentration despite consistently high serum concentrations of phenylalanine by competition at this transporter [Pietz et al 1999, Moats et al 2003].

References


