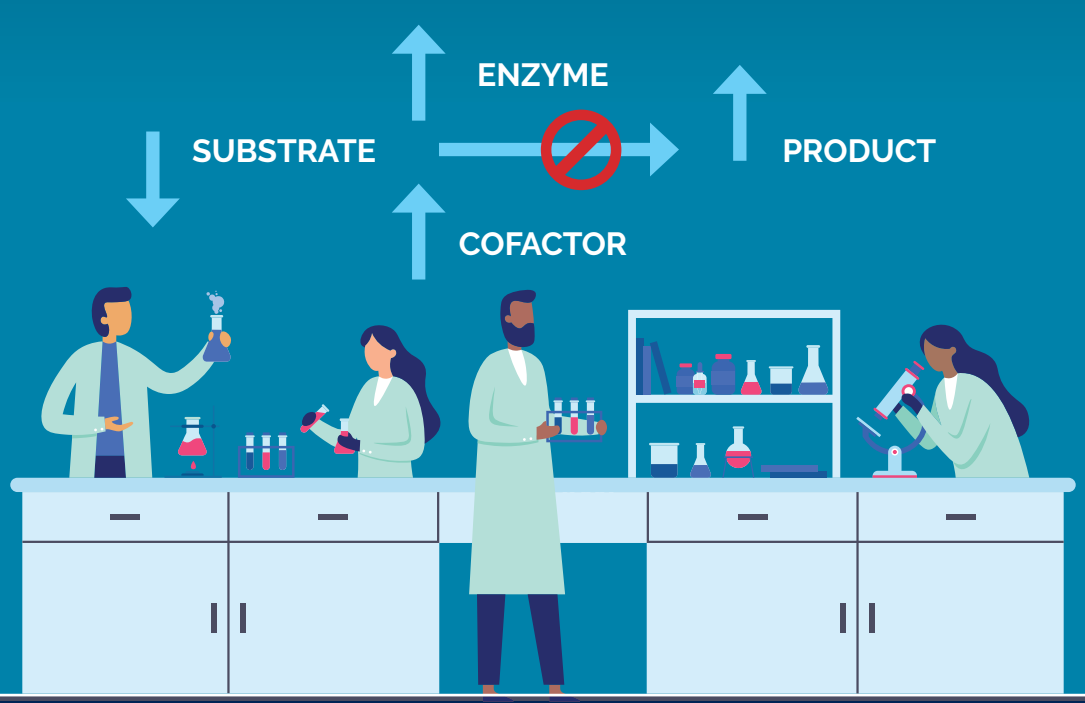
Established and Emerging Treatments for Patients With

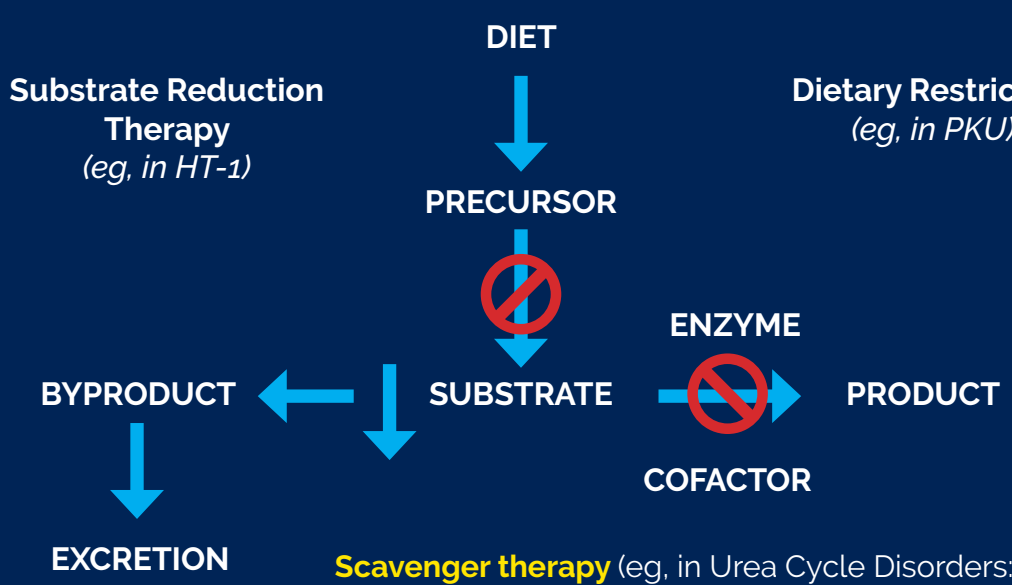
INBORN ERRORS OF METABOLISM

Three Main Approaches to Management

- Decrease Substrate and Remove Toxic Metabolites
- Provide Product That Is Deficient
- Enhance Conversion of Substrate to Product Via Enzyme or Cofactor Replacement

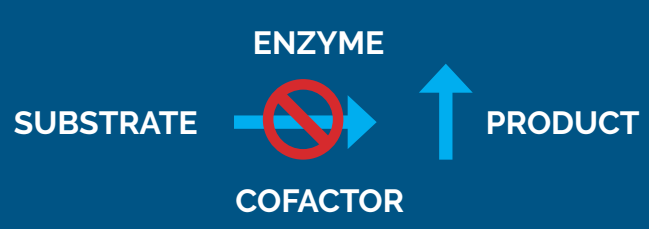


1 Decreasing Substrate



Scavenger therapy (eg, in Urea Cycle Disorders: Na benzoate, Na phenylbutyrate, glycerol phenylbutyrate)

2 Provide Product That Is Deficient



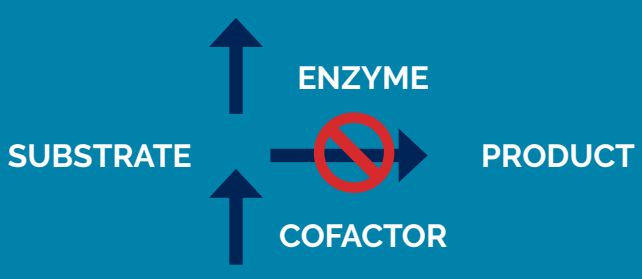
Examples:

Tyrosine in PKU

Arginine or Citrulline in Urea Cycle Disorders

MCTs or Triheptanoin in VLCAD

3 Enhance Conversion of Substrate to Product



Cofactor Therapy: eg, B12 in methylmalonic acidemia, Sapropterin in PKU

Enzyme Replacement Therapy: eg, in Lysosomal storage diseases, Pegvaliase for PKU

Hematopoietic Stem Cell Transplantation: eg, in IEM with neurologic manifestations (Krabbe's disease, X-linked adrenoleukodystrophy)

Liver Transplantation and Human Heterologous Liver Cell Transplant: eg, in OTC deficiency and Maple Syrup Urine disease

Gene Therapy: Using adenoviral and lentiviral vectors

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PKU: Phenylketonuria
HT-1: Hereditary Tyrosinemia type 1
MCTs: Medium Chain Triglycerides

VLCAD: Very Long-Chain Acyl-Coenzyme A Dehydrogenase Deficiency
IEM: Inborn Errors of Metabolism
OTC: Ornithine Transcarbamylase

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Infographic made by: Krithika Lingappan, MD, MS, PhD

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