REVIEW ARTICLE

Therapeutic Enteral Formulas in Children

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Purpose: A variety of enteral formulas for various diseases have become available in India in the last few years. Awareness among pediatricians about the availability and indications for these therapeutic formulas is low. **Methods:** A literature search was conducted in PUBMED and relevant data collected from all English language publications available. Data on the commercial preparations was sourced from the individual companies, the Diet 4 life initiative as well as FSSAI (Food safety and standards authority of India). **Conclusions:** Therapeutic enteral formulas, which are indicated in various disease states belong to four categories - lactose modified, hydrolyzed, MCT based and metabolic disease specific formulas. Lactose modified formulas which are used in temporary or permanent lactose intolerance and Galactosemia are either casein or soy protein based. Hydrolyzed formulas could be partially hydrolyzed, extensively hydrolyzed or amino acid based. Only extensively hydrolyzed formula should be recommended in milk protein allergy. Amino acid (elemental) formulas are mainly indicated in patients with diffuse intestinal mucosal disease. MCT formulas are used in chronic liver disease with cholestasis, and have 30 to 80% MCT. Formulas for inborn errors of metabolism are free of specific carbohydrate, amino acid or fatty acid. Proprietary formulas presently available in India with their specifications have been listed.

Keywords: *Elemental formula, Hydrolyzed formula, Lactose intolerance, MCT based formula, Therapeutic enteral formula*.

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Therapeutic enteral formulas are those that are indicated in specific situations of disease or need and are not substitutes for breast milk. They can be divided into the following broad categories - lactose modified formulas, hydrolyzed formulas, medium chain triglyceride (MCT) based formulas and disease-specific enteral formulas, which include those for various inborn errors of metabolism and specific clinical settings such as liver or renal disease. A thorough understanding of the underlying nutritional requirement in each disease state as well as the ingredients present in each formula is important to ensure their optimum use. Literature search was conducted in Medline through PUBMED, using MeSH terms. Data on the commercial preparations was sourced from the individual companies, the Diet 4 life initiative, as well as FSSAI (Food safety and standards authority of India). Copies of the FSSAI license for each product were also obtained from the companies. Authors have taken extreme care in reviewing the proprietary food products. This review article provides guidance regarding the various categories of enteral formulas and their indications, so that pediatricians can use them rationally in clinical practice.

AVAILABLE FORMULAS

Lactose Modified Formulas

Lactose, the carbohydrate component of milk is not only a source of energy, but also supports linear growth and neuro-development of the growing infant. Lactose is broken down into glucose and galactose in the small intestine by the action of the enzyme lactase, present at the tip of the microvilli of enterocytes. Mild lactose malabsorption is desirable in early infancy since lactose acts as a prebiotic in the colon facilitating growth of bifidobacterium rich fecal microbiota. When the lactase enzyme activity is critically reduced or absent, either temporarily (secondary lactase deficiency following small bowel disease like acute diarrhea, persistent diarrhea, giardiasis, celiac disease, crohn's disease etc) or permanently (primary lactase deficiency attributed to a relative absence of lactase in childhood, which is common in many racial groups including Indians), a reduced or lactose-free diet is necessary. Lactose-free diet is also indicated in galactosemia; an autosomal recessive disease, where patients cannot metabolize galactose due to a congenital enzyme defect.

Diarrhea as a manifestation of lactose intolerance occurs mainly in infants and young children, since they lack the ability to compensate by colonic reabsorption. In older children, colonic reabsorption of fermentation products (e.g. short chain fatty acids, lactate) results in less osmotic diarrhea, but more abdominal bloating from the hydrogen produced [1]. Most patients with acute gastroenteritis do not have lactose intolerance and recover well with continued intake of breast or standard milk. Routine use of lactose-free formula is not recommended in acute diarrhea, since it neither results in faster recovery nor prevents complications [2]. However, in persistent diarrhea, a lactose modified diet is indicated [3]. Unlike cow milk protein allergy, lactose intolerance is quantity-related and most patients with secondary lactose intolerance require reduced amounts of lactose rather than a totally lactose-free diet. Low lactose formula may be used in young infants with temporary lactose intolerance that are not breast-fed. Studies do not support the use of lactose-free diet to improve crying or fussy infant behaviour [4]. Lactose-free formulas are either milk protein-or soy protein-based.

Milk Protein- based Lactose-free Formulas

Milk protein based lactose free formula has malt dextrin as the carbohydrate. Even though the calorie content is the same, they have very little iron, and lower fat than standard formula. They should be used only when lactose intolerance is strongly suspected or proven. In temporary lactose intolerance, they should be used only for a few weeks, since recovery of the mucosa and lactase enzyme activity occurs by then.

Soy-based Lactose-free Formulas

Soy-based lactose-free formulas are made of proteins extracted from soybean. The source of carbohydrate is corn malt dextrin, corn syrup solids and sucrose and it is completely lactose free. It contains essential fatty acids which can be easily absorbed, and is fortified with methionine, carnitine and taurine. Being a vegetable protein, the bioavailability is lower and so the overall protein content is higher than in milk-based formula [5]. Soy protein is heat stable and nutritionally optimum even after heating. There are concerns regarding use of soya protein below 6 months of age due to high concentration of aluminum (600-1,300 ng/mL *vs*. 4-65 ng/mL in human milk) and excess of phytoestrogens [6]. Since calcium absorption is sub-optimal in lactose free formula, all soy-based formulas contain 20% more calcium and phosphorus than standard cow's milk-based formulas. In addition, because soy phytates bind iron and zinc, they are fortified with these minerals. [7]. Soy formulas contain very small amounts of galactose, but they are considered safe for use in classic galactosemia [8].

Soy formula is used in clinically significant secondary lactose intolerance as well as primary lactose intolerance [9]. A soy formula may also be considered in infants with cow milk protein allergy (CMPA), if the extensively hydrolyzed formula is not available/ affordable/acceptable/ tolerable or if there is a strong parental preference for a vegan diet [10]. About 15-20 % of infants with CMPA also may have soy protein allergy.

The various lactose free formulas available in India are shown in ***Table* I**.

Hydrolyzed Formulas

Hydrolyzed formulas were originally developed to enhance tolerability and reduce allergenicity, compared with intact cows' milk protein formula. It was therefore believed to have the potential to decrease the incidence of atopic diseases as well as management of cow milk protein allergy (CMPA). Milk proteins are hydrolyzed by enzymes, heat pressure and /or ultrafiltration. Currently they are classified based on the degree of hydrolysis and accordingly there are partially hydrolyzed formulas (pHF), extensively hydrolyzed formulas (eHF), and amino acid formulas. While amino acid formulas are referred to as elemental formulas, eHF and pHF are called semi-elemental formulas. The lesser the degree of intact protein, enhanced is the immunologic tolerability; however, more the degree of protein hydrolysis, worse is the taste of the formula. In general, pHFs have peptides which are 5-10 kDa, whereas in eHFs they are <3 kDa [11] while amino acid-based formulas contain only free amino acids and are devoid of any peptides (***Table* II**). Both casein and whey hydrolyzed formula products exist worldwide. ***Table* I** shows the hydrolyzed formulas available in India.

In the past, the term 'hypoallergenic' has been used to refer to any formula that is used in cow milk protein allergy. Therefore, both pHF and eHF were referred to as hypoallergenic. However, recent literature prefer to avoid this terminology as it is potentially misleading. Presently its use is restricted to individual eHF that have clinical studies documenting therapeutic hypoallergenic effect in cow milk protein allergy.

Partially Hydrolyzed Formulas

They are made by hydrolyzing the intact milk protein. The average peptide size in pHF varies from 3-10 kDa (mean 5) and they retain some antigenicity of the milk protein. These are therefore beneficial as an alternative to intact cow milk protein formula for tolerance induction in infants [12,13]. Tolerance induction is; however, not an accepted practice in international management protocols on CMPA. pHF should not be used for patients with

TABLE I Lactose Modified, Hydrolyzed and MCT-based Formulas Currently Available in India

Category	*Brand*	*Manufacturer*	*Remarks*
Lactose modified formulas			
Low lactose	NAN lo Lac	Nestle	5 g lactose /100gm
Milk protein-based	Nusobee Casein	Nutricia	Lactose *and* sucrose free.
	Zerolac Casein	Raptakos Brett	Lactose *and* sucrose free.
	Simyl MCT	FDC Ltd.	Lactose *and* sucrose free. MCT only 7.4%.
Soy protein-based	Isomil	Abbott	Lactose free. Has sucrose (10gm/100gm powder)
	Nusobee Soy	Nutricia by Danone	Lactose, sucrose free
	Zerolac	Raptakos Brett	Lactose, sucrose free.
Hydrolyzed formulas			
Partially hydrolyzed	Peptamen Jr	Nestle	Lactose free LF). Age 2-10 yrs
	Similac total comfort	Abbott	Has lactose.100% Whey. Age < 2 yrs
Extensively hydrolysed	Alimentum	Abbott	L F. Casein based Age < 2 yrs
	Nutramigen LGG	Mead Johnson	L F. Has Lactobacillus GG
	Althera	Nestle	Has lactose. 100% whey
	Alfare	Nestle	L F.100 % whey
Amino acid-based	Neocate LCP	Nutricia	Age < 1 yr
	Alfamino	Nestle	Age < 1 yr
	EleCare Infant	Abbott	Age < 1 yr
	EleCare Jr	Abbott	Age 1 – 2yrs
Medium chain triglyceride based formulas			
For infants/children	Monogen	Nutricia	420 kcal, Protein: 12.5g, Fat: 11g, MCT 84%
For infants	Pregestimil	Mead Johnson	500kcal, Protein: 14g, Fat: 28g.MCT 55%, Lactose free. Extensively hydrolyzed.
For infants/children	Metanutrition LD	Pristine Organics	462 kcal, Protein: 12.5g, Fat: 20g, MCT 80%.
> 2 years of age	PediaGold plus	Hexagon Nutrition	475 kcal, Protein: 14.25g (whey peptide) Fat: 18.5g, MCT 70%, Gluten *and* lactose free.

TABLE II Comparison of Extensively Hydrolyzed and Partially Hydrolyzed Formula

*Contents**	*Extensively hydrolyzed*	*Partially hydrolyzed*
Energy (kcal)	70	70
Protein (g)	1.8	1.3
Maximum MW	<1.2 kDa peptide	<10 kDa peptide
Carbohydrate (g)	#7.8 (as Dextrin, starch, sugar)	8.7 (as Dextrin, Lactose)
Fat (g)	3.5	3.3
LCT (%)	75	83.0
MCT (%)	25.0	17.0

**Per 100 g; Protein source for both formulas is casein hydrolysate*; *LCT*: *Long chain triglycerides*; MCT: *Medium chain triglycerides*; MW: *Molecular weight*; #*some are lactose free*.

documented CMPA. While pHF are safe and are allowed by the USFDA (United States Foods and Drugs Authority) and EFSA (European Food Safety Agency) as an alternate protein source for all babies, there are limited studies evaluating the allergy-prevention role in the healthy population. While some studies in high-risk infants with an individual formula have shown benefit, these benefits have not been universally reproduced with other pHFs [14,15]. It is therefore important to evaluate the clinical evidence of each pHF from an allergy prevention perspective. pHF contain lactose and so cannot be used in galactosemia or lactose intolerance. Their taste is not comparable to standard infant formula, but is not as unpleasant as the extensively hydrolyzed formula.

Extensively Hydrolyzed Formulas

eHF is made by hydrolyzing milk protein to a peptide size

that does not usually elicit an immune response [16]. Most eHF are lactose-free and the main source of carbohydrate is malt dextrin, with the remainder being, sugar, starch and corn syrup. Vegetable oil or MCT oil is the source of fat, which is easily absorbed, and also contains essential fatty acids. The formula has a relatively high osmolality, and can sometimes cause osmotic diarrhea. They are recommended in the treatment of cow's milk and soy protein allergy. However, since antigenicity has not been totally eliminated, a few children with severe disease may not respond [17]. eHF can also be used in those with serious malabsorption due to intestine failure, short bowel syndrome, as well as, Crohn disease and pancreatic disease. Those eHF that do not contain lactose can be used for galactosemia or lactose intolerance. The role of these formulas in prevention of allergies and autoimmune diseases is controversial [17]. Few studies are available which report some benefit in adding the probiotic lactobacillus GG in eHF to enhance the immune regulatory mechanism and lead to earlier immune tolerance [18,19]. However, evidence is insufficient to recommend addition of probiotics in eHF. Palatability is an issue, but eHF taste better than amino acid-based formula.

Amino Acid-based Formulas

Amino acid-based formula has no peptide at all and the protein is in the form of free amino acids. It is lactose free and the source of fat is MCT oil. In children with milk or soy protein allergy, this formula can be used in the small minority of patients who do not respond to eHF [20,21]. It can also be used as an enteral nutrition therapy for individuals with Crohn disease (polymeric formulas are equally good) as well as in children with severe malabsorption from diffuse intestinal mucosal disease; who do not respond to eHF.

Medium-chain Triglycerides-based Formulas

MCTs are triglycerides whose fatty acids have an aliphatic chain of 6–12 carbon atoms. They passively diffuse from the GI tract to the portal system without emulsification, unlike long-chain fatty acids (LCTs) or very-long-chain fatty acids. Thus they are not dependent on bile salts or lipase for absorption. The energy-enhancing properties of MCTs are attributed to the fact that they cross the double mitochondrial membrane rapidly, and do not require the presence of carnitine, unlike LCTs [22].

There is no clear guideline regarding the percentage of MCT that needs to be in a formula for it to be classified as MCT formula. Most commercially available preparations have between 30% and 80% MCT. ***Table* I** gives the various MCT formulas presently available in India. MCTs provide about 10% fewer calories than LCTs (8.3 calories/g for MCTs vs 9 calories/g for LCTs); thus, it should be supplemented. All MCT formulas have relatively higher osmolality, and hence should be introduced at lower concentrations [22]. Their use should be strictly limited to specified medical indications, and these are not recommended to complement standard formulas for healthy children.

The common indications of MCT–based formulas are given in ***Box* I** [23].

Liver disease: Growth failure and malnutrition are important components that need to be addressed in patients with liver disease. Nutritional need depends on the type of liver disease (cholestatic or hepatocellular, acute or chronic), severity of the disease as well as age of the patient. In patients with chronic liver disease (CLD) malnutrition and negative nitrogen balance are negative prognostic indicators for overall survival [24].

Estimated energy requirement (EER) in children with CLD can be up to 140% nutrient reference value for age or 120-150 kcal/kg/day initially [25]. MCT-based diets are the standard in CLD, particularly when there is significant cholestasis. It is recommended that between 30% and 50% of the fat requirement should be provided as MCT. In children with cholestatic CLD, long chain poly-unsaturated fatty acid (LCPUFA) metabolism is disturbed and therefore more than 10% of total energy should be provided as PUFA [26]. In older children, LCPUFA containing foods like Canola, sunflower, soybean oils, walnut oil, fish oil and egg yolk can be added to the diet. Children with CLD have deranged amino acid metabolism, with lower levels of branched-chain amino acids (BCAA) and elevated aromatic amino

Box I Indications for Medium-chain Triglyceride Formulas

- Liver disease, particularly cholestatic liver disease
- Malabsorption with steatorrhoea
- Malnutrition (Preoperative and postoperative)
- Primary intestinal lymphangiectasia
- Chylothorax
- Long chain acyl-CoA dehydrogenase (LCHAD) deficiency
- Carnitine palmitoyl transferase deficiency (CPTD)
- Primary and secondary lipoprotein lipase deficiency· Short bowel syndrome
- Inflammatory bowel disease
- Cystic fibrosis

acids. Some studies have shown that adding BCAA to feeds can improve nitrogen retention, reduce protein catabolism and increase protein synthesis [27]. CLD patients have deranged gluco-neogenesis as well as delayed insulin catabolism and so are at increased risk for hypoglycemia in fasting state. Hence, adequate amount of simple carbohydrate need to be provided in the formula or diet.

Specific formulas for Inborn Errors of Metabolism (IEM)

These are a group of genetic disorders where a specific enzyme deficiency causes block in a metabolic pathway leading to clinically significant consequences [28]. The disease state is a consequence of any of the following

- The block can lead on to non-availability of essential substrates that are required for normal metabolism *e.g.* glucose production from glycogen is affected in GSD leading to non-availability of glucose
- The intermediary product that builds up due to the block can be toxic e.g. build up of leucine in maple syrup urine disease.
- The intermediary product is converted to a toxic by product causing clinical manifestation *e.g.* succinylacetone in tyrosinemia
- The intermediary product that builds up in sub-cellular level impacts the cellular physiology (lysosomal/ peroxisomal storage disorders e.g. lysosomal acid lipase deficiency)

Management of these patients aims to remove the offending substance from diet and/or to supplement the end product that is essential for metabolism. Disease-specific proprietary foods are now available with absent specific carbohydrate, amino acids or fatty acids [29]. However, it needs to be stressed that diet plan has to be individualized even when patients have the same disease. Essential amino acids as the name suggests are required for anabolism. Therefore children with metabolic defects involving essential amino acids require their supplementation at minimum daily requirements. Their total avoidance could result not only in relevant symptoms but also in poor growth, while any excess would lead to metabolic decompensation. This is the concept of 'metabolic paradox'.

Details of individual IEMs are beyond the purview of this paper and readers are advised to refer to standard textbooks. ***Web Tables*** **I, II and III** give the various formulas currently available for disorders of carbohydrate, protein and lipid metabolism, respectively.

CONCLUSIONS

The four basic categories of formulas available in India are the lactose modified, hydrolyzed, MCT-based and metabolic-disease specific formulas. Lactose modified formulas are either casein- or soy protein-based. Most children with acute diarrhea do not need a lactose free diet, though some may need a low lactose diet. Soy protein formulas, are best avoided below 6 months of age. Hydrolyzed formulas are either partially or extensively hydrolyzed or amino acid-based. Extensively hydrolyzed formula should be the first choice in milk protein allergy. Amino acid formula, also called elemental formula, are needed only in a minority of children with cow's milk protein allergy or diffuse intestinal disease, who do not respond to eHF. MCT formulas are used in chronic liver disease particularly with cholestasis. Formulas for inborn errors of metabolism are free of the specific carbohydrate, amino acid or fatty acid. Choice of such formula and diet for metabolic diseases should be individualized and made in consultation with a specialist.

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Disclaimer: This paper does not claim to enumerate all the products available in market, and the purpose is to give only an overview. Although authors have taken extreme care in reviewing the proprietary food products, we strongly recommend checking product information resources. The FSSAI licenses are for a limited period and companies are expected to renew it at the appropriate time. It is also advisable to consult the appropriate specialists if necessary, before disease-specific formulas are used.

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WEB TABLE I Formulas for Carbohydrate Metabolism Disorders

Metabolic disease and Dietary intervention	*Products and age recommended*	*Company*	*Remarks (Nutrients/100 gm)*
Galactosemia diet - Galactose free	Galactomin 17	Nutricia	514 kcal, Protein Eq: 10.3g, Fat: 27.3g, CHO: 57.1g.
	Milupa basic; Infants/toddlers	Nutricia	645 kcal, Protein: 28.3g, Fat: 58g, CHO: <0.1g
	Metanutrition GLC Infants/Children	Pristine Organics	528 kcal, Protein Eq: 14.4g, Fat: 30g, CHO: 50g
	Pregestimil; Infants	Mead Johnson	500 kcal, Protein: 14g, Fat: 28g, CHO: 51g. MCT 55%, Lactose free Extensively hydrolysed casein.
	Nutramigen LGG Infants	Mead Johnson	Same as pregestimil, but fat: 26g, CHO: 55 g.
Other carbohydrate metabolism disorders diet - Free/Low carbohydrate	Milupa basic-ch; Infants/toddlers	Nutricia	Details under galactosemia. Also suitable for Ketogenic diet
	RCF (Ross Carbohydrate free); Infants	Abbott Healthcare	Per100ml. 81 kcal, Protein: 4g, Fat:7.2g,CHO:0.07g.Soy base. Gluten free. Ketogenic diet.
	Metanutrition CMD; Infants/Children	Pristine Organics	538 kcal, Protein Eq: 22g, Fat: 50g, No CHO
	Metanutrition GTD (Glucose transport defect); Infants/Children	Pristine Organics	720 kcal, Protein Eq: 14.4g, Fat: 70g, CHO: 8g. Ideal for Glucose transport defect (Glut 1 def)

*** All lactose free soy formulas can be used in galactosemia; ** Other CMD disorders include Sucrase/ Isomaltase deficiency, Fructosemia, Glucose transport defect (Glut 1 def), Glucose-Galactose malabsorption etc. Formula for these should be individualized and chosen in consultation with a specialist; ** All the above free/low carbohydrate diet contains essential/non-essential amino acids, fats, vitamins and minerals.*

WEB TABLE II FORMULAS FOR PROTEIN/AMINO ACID METABOLISM DISORDERS

Metabolic disease / Dietary intervention	*Products/ Age recommended*	*Company*	*Remarks (Nutrients/100 gm)*
Urea cycle disorders (UCD) Diet: Low in Non-essential amino acids. High in essential AA	Milupa UCD- 1 (Mixt) Anamix; Infant UCD (Form); below 1	Nutricia	Milupa UCD 1: 280 kcal, Protein Eq: 50 g, Fat: 0 g, CHO: 19.9 g (After 1 y: Milupa UCD 2 - Prima Mixt)
	Cyclinex-1; Infants/toddlers	Abbott	Cyclinex 1 (Per 100 ml): 77 kcal Protein : 1 g, Fat: 4 g, CHO: 9 g (Children/adults**:** Cyclinex – 2)
	Metanutrition UCD-1; below 3 y	Pristine Organics	483 kcal, Protein E q: 12.5 g, Fat: 25 g, CHO: 52 g (>3 y: Metanutrition UCD-2)
	UCD Trio; above 1 y	Nestle (Vitaflo)	393 kcal, Protein Eq: 15 g, Fat: 14.3 g, CHO: 51 g.
Phenyl ketonuria (PKU) Diet – Phenylalanine free	Milupa PKU-1 (Mixture) Anamix Infant PKU (Form) Below 1 y	Nutricia Intl	Milupa PKU-1: 302 kcal, Protein: 50 g, Fat: 0 g, CHO: 25.6 g (After 1 y**:** Milupa PKU 2 - Prima Mixt)
	Phenex 1; Infants/toddlers	Abbott Healthcare	Phenex 1 (Per 100 mL): 72 kcal, Protein Eq: 2 g, Fat: 3 g, CHO: 8 g. (After 3 y: Phenex 2)
	Phenyl-Free-1; For infants	Mead Johnson	500 kcal, Protein: 16.2 g, Fat: 26 g, CHO: 51 g. Iron fortified.
	Metanutrition PKU-1; below 3 y	Pristine Organics	483 kcal, Protein: 12.5 g, Fat: 25 g, CHO: 52 g(Above 3 y**:** Metanutrition PKU-2/3)
	PKU Gel; 6 mo to 10 y PKU Trio; From 1 y PKU Express; From 3 y	Nestle (Vitaflo)	339 kcal, Protein Eq: 41.7 g, Fat: 0.05 g, CHO: 42.9 g405 kcal, Protein: 30 g, Fat: 14.3 g, CHO: 38.9 g. Contains milk *and* soya.297 kcal, Protein : 60 g, Fat: 0.2 g, CHO: 13.7 g. Contains soya.
Tyrosinemia (TYR) Diet – Phenylalanine and Tyrosine free	Milupa TYR-1 (Mixture) Anamix Infant TYR (Form); Below 1 y	Nutricia	Milupa TYR -1: 302 kcal, Protein: 50 g, Fat: 0 g, CHO: 25.6 g (Above 1 y: Milupa TYR 2 - Prima Mixt)
	Tyrex- 1; Infants/toddlers	Abbott	Tyrex 1 (Per 100 mL): 72 kcal, Protein: 2.25g, Fat: 3.25g, CHO: 7.95g, has L-carnitine *and* taurine (Children/adults: Tyrex-2)
		Tyros 1 for infants	Mead Johnson 500 kcal, Protein: 16.7g, Fat: 26g, CHO: 51g. Iron fortified
	Metanutrition Tyros-1; below 3 y	Pristine Organics Metanutrition	483 kcal, Protein: 12.5g, Fat: 25g, CHO: 52g (Above 3 y: Tyros-2)
	TYR Gel; 6 mo to 10 y TYR Express; above 3 y	Nestle (Vitaflo)	TYR gel : 339 kcal, Protein: 41.7 g, Fat: 0.05 g, CHO: 42.9 g297 kcal, Protein: 60 g, Fat: 0.2 g, CHO: 13.7 g. Contains soya.

Contd....

Web Table II continued

Metabolic disease / Dietary intervention	*Products/ Age recommended*	*Company*	*Remarks (Nutrients/100 gm)*
Homocystinuria (HCU)	Milupa HOM-1 Mixt Anamix infant HCU Form; below 1 y	Nutricia	Milupa HOM-1: 302 kcal, Protein: 50 g, Fat: 0 g, CHO: 25.6 g (Above 1 y**:** Milupa HOM 2-prima Mixt)
Diet – Methionine free	Hominex-1; below 3 y	Abbott Healthcare	Hominex-1 (Per 100 mL): 72 kcal, Protein: 2 g, Fat: 3 g, CHO: 8 g. (Above 3 y: Hominex-2)
	Metanutrition HCY-1; Below 3 y	Pristine Organics	483 kcal, Protein Eq: 12.5g, Fat: 25 g, CHO: 52 g (Above 3 y: Metanutrition HCY 2)
	HCU Gel; Above 3 y 6 mo to 10 y: HCU Express	Nestle (Vitaflo)	339 kcal, Protein Eq: 41.7 g, Fat: 0.05 g, CHO: 42.9 g297 kcal, Protein: 60 g, Fat: 0.2 g, CHO: 13.7 g. Contains soya.
Maple syrup urine disease (MSUD)	Milupa MSUD-1 Mixt Anamix Infant MSUD Form; below 1 y	Nutricia	Milupa MSUD-1: 302 kcal, Protein: 50 g, Fat: 0 g, CHO: 25.6 g (Above 1 y**:** Milupa MSUD-2 prima Mixt)
Diet – Leucine, Isoleucine *and* Valine free	Ketonex-1 Below 3 y	Abbott	Ketonex-1 (Per 100ml): 72 kcal, Protein: 2 g, Fat: 3 g, CHO: 8 g (above 3 y: Ketonex-2)
	BCAD-1, below 1 y Metanutrition MSUD-1 below 3 y	Mead Johnson Pristine Organics	500 kcal, Protein: 16.2 g, Fat: 26 g, CHO: 51 g. Iron fortified 483 kcal, Protein: 12.5 g, Fat: 25 g, CHO: 52 g (above 3 y Metanutrition MSUD-2)
	MSUD Gel ; 6 mo to 10 yrs MSUD Express; above 3 y	Nestle (Vitaflo)	339 kcal, Protein: 41.7 g, Fat: 0.05 g, CHO: 42.9 g297 kcal, Protein Eq: 60 g, Fat: 0.2 g, CHO: 13.7 g. Contains soya.
Methylmalonic acidemia *and* Propionic acidemia (MMA/PA)	Milupa OS-1 Mixt Anamix Infant MMA/PPA; below 1 y	Nutricia	Milupa OS-1: 286 kcal, Protein Eq: 50 g, Fat: 0 g, CHO: 21.5 g (above 1 y**:** Milupa OS 2 - Prima Mixt)
Diet – Methionine *and* Valine - Free and Isoleucine *and* Threonine -Low/free	OA 1; below 1 y Metanutrition MMA/PA-1; below 3 y	Mead Johnson Pristine Organics	500 kcal, Protein: 15.7 g, Fat: 26 g, CHO: 51 g. 483 kcal, Protein: 12.5 g, Fat: 25 g, CHO: 52 g **(**above 3 y**:** Metanutrition MMA/PA-2)
	MMA/PA Gel; 6 mo to 10 y MMA/PAExpress above 3 y	Nestle (Vitaflo)	339 kcal, Protein Eq: 41.7 g, Fat: 0.05 g, CHO: 42.9 g297 kcal, Protein Eq: 60 g, Fat: 0.2 g, CHO: 13.7 g. Contains soya
Isovaleric acidemia (IVA)	Milupa LEU-1 Mixt. Anamix infant IVA Form; below 1 y	Nutricia	Milupa LEU-1: 286 kcal, Protein : 50 g, Fat: 0 g, CHO: 21.5 g **(**Above 1 y**:** Milupa LEU 2-prima Mixt)
Diet – Leucine free	I-Valex-1; below 3 y	Abbott	I-Valex-1 (Per 100 mL): 72 kcal, Protein: 2 g, Fat: 3 g, CHO: 8 g. (above 3 y: I-Valex-2)
	Metanutrition IVA-1; below 3 y	Pristine Organics	483 kcal, Protein: 12.5 g, Fat: 25 g, CHO: 52 g (Above 3 y: Metanutrition IVA-2)
Glutaric acidemia Type 1 (GA 1)	Milupa GA-1 Mixt Anamix infant GA1 Form; below 1 y	Nutricia	Milupa GA-1: 290 kcal, Protein: 50 g, Fat: 0 g, CHO: 22.4 g (above 1 y**:** Milupa GA2-prima Mixt)

Contd....

Web Table II continued

Metabolic disease / Dietary intervention	*Products/Age recommended*	*Company*	*Remarks (Nutrients/100 gm)*
Diet – Lysine free and Tryptophan - Low/free	Glutarex-1; below 3 y	Abbott Healthcare	Glutarex (Per100 mL): 72 kcal, Protein: 2 g, Fat: 3 g, CHO: 8 g, (above 3 y**:** Glutarex-2)
	Metanutrition GA-1; below 3 y	Pristine Organics	483 kcal Protein: 12.5 g,Fat: 25g, CHO: 52 g. (Above 3 y: Metanutrition GA-2**)**
	GA 1 Gel 6; mo to 10 y GA 1 Express; above 3 y	Nestle (Vitaflo)	339 kcal, Protein: 41.7 g, Fat: 0.05 g, CHO: 42.9 g 297 kcal, Protein: 60 g, Fat: 0.2 g, CHO: 13.7 g. Contains soya
Hyperlysinemia Diet – Lysine free	Milupa LYS-1 Mixt; below 1 y	Nutricia	290 kcal, Protein : 50g, Fat: 0 g, CHO: 22.4 g May use in pyridoxine dependent epiliepsy in infants (Above 1 y: Milupa LYS 2-prima Mixt)
Non-ketotic hyper glycinemia (Glycine encephalopathy);	Milupa Basic – p; Infants Metanutrition HLP; Any age Pro-Phree; Infants/toddlers	Nutricia Pristine Organics Abbott Healthcare	536 kcal Protein Eq: 0g, Fat: 32 g, CHO: 62 g 535 kcal, Protein: 0 g, Fat: 25 g, CHO: 70 g Per 100 mL: 77 kcal, Protein Eq: 0 g, Fat: 4 g, CHO: 10 g.
Diet – Protein free, dietary intervention limited role			
*Protein and Aminoacid (AA) free formulas	Milupa Basic-p; infants Pro-Phree; infants/toddlers PFD; toddler young children Metanutrition AAMD-1; below 3 y	Nutricia Abbott Healthcare Mead Johnson Pristine Organics	536 kcal Protein Eq: 0 g Fat: 32 g, CHO: 62 g Per 100 mL: 77 kcal, Protein: 0 g, Fat: 4 g, CHO: 10 g. 530 kcal, Protein: 0 g, Fat: 32 g, CHO: 60 g. Metanutrition AAMD-1: 385 kcal, Protein: 0 g, Fat: 5 g, CHO: 85 g (above 3 y Metanutrition AAMD-2)

*CHO: Carbohydrate; AA: Aminoacids; Gel (Vitaflo, Nestle) - Concentrated powdered protein which when mixed up with water is easily made to a smooth, semisolid consistency. Available as pre-measured sachet, 10 gm Protein Eq per sachet. Suitable from 6 months to 10 years of age. Available for PKU, TYR, MSUD, HCU, MMA/PA and GA 1; Trio (Vitaflo, Nestle) – Powdered protein substitute. Contains milk and soya. Suitable from 1 year of age. Available for UCD and PKU; Express (Vitaflo, Nestle) – Powdered protein substitute. Available as pre-weighed sachets , 15 gm protein equivalent. Contains soya. Suitable from 3 years of age. Available for PKU, TYR, MSUD, HCU, MMA/PA and GA 1; Gel, Trio and Express contain essential and non-essential aminoacids (but excluding the offending aminoacids), carbohydrate, vitamins, minerals and trace element; Mixtures (Mixt) should be taken mixed with calculated amount of food or drink. Formula (Form) can be used as a supplementary feed upto 3 yrs; *Recommended as emergency regimen in sick patients with suspected Amino acidemias, Organic acidurias, Urea cycle disorders.*

WEB TABLE III Formulas for Lipid Metabolism Disorders

Diseases/Diet intervention	*Products*	*Company*	*Remarks (Nutrients/100 g)*
Lipid Metabolism disorders (LMD)/ diet: Low fat	Milupa Basic-f Infants/toddlers	Nutricia	374 kcal, Protein: 14 g, Fat: <0.5 g, CHO: 79 g.
	Monogen Infants/ children	Nutricia	420 kcal, Protein:12.5 g (Whey based), Fat:11 g, (MCT 84%), CHO: 68 g.
	ProViMin Infants/ children	Abbott	Per 100 mL: 62.6 kcal, Protein: 14.6 g (Casein based), Fat: 0.3 g, CHO: 0.4 g.
	Metanutrition LD (Lipid disorders) Infants/children	Pristine Organics	462 kcal, Protein Eq: 12.5 g, Fat: 20 g, CHO: 58 g. MCT 80%.
	Metanutrition LCHAD (Long chain hydroxyacyl-CoA dehydrogenase) Infants/children	Pristine Organics	520 kcal, Protein: 12.5 g, Fat: 30 g, CHO: 50 g. Long chain triglycerides (LCT) free. Indicated in LCHAD deficiency

******** *LMD include Fatty acid oxidation disorder, Severe cholestais, Intestinal lymphangiectasia, Abeta/Hypobetalipoproteinemia, Chylothorax, Malabsorption and Maldigestion of fats. Formula for these should be individualized and chosen in consultation with a specialist.*