



comida **MSUD**^A formula

This practical guide is an introduction for the use of **comida-MSUD A formula**, an amino acid based isoleucine, leucine and valine free* formula from birth to 12 months of age.



*No added isoleucine, leucine and valine.



Enhancing Lives Together



Important information

PURPOSE

This practical guide is for the use of **comida-MSUD A formula** in the dietary management of an infant with Maple Syrup Urine Disease (MSUD).

INTENDED USERS

This practical guide is:

- for use by **healthcare professionals** working with infants diagnosed with MSUD.
- **not** for use by parents/caregivers of patients with MSUD or patients themselves.
- for **general information** only and must not be used as a substitute for professional medical advice.

TARGET POPULATION

This practical guide is for use in infants with diagnosed/proven MSUD.

PRODUCT INFORMATION

comida-MSUD A formula is a food for special medical purposes.

Any product information contained in this practical guide, although accurate at the time of publication, is subject to change. The most current product information may be obtained by referring to product labels and **www.comidamed.com**. Please refer to these sources for information regarding allergens.

DISCLAIMER

The information contained in the practical guide is for general information purposes only and **does not** constitute medical advice. The practical guide is not a substitute for medical advice or care provided by a licensed and qualified healthcare professional and Vitaflo does not, in the absence of negligence on Vitaflo's part, accept any liability arising from reliance on information contained in this guide and or the incorrect use of **comida-MSUD A formula** product.

This practical guide should be read in conjunction with local, national and international guidelines and best practice for the dietary management of Maple Syrup Urine Disease. Information contained within the guide is based on the most recent scientific evidence available on the management of / use of Maple Syrup Urine Disease as of date of publication.

COLLABORATORS

Vitaflo dietitians in collaboration with: Taelor Mellor, MS, RD, LDN, Children's Hospital of Philadelphia, Philadelphia, PA

Introducing and adjusting **comida-MSUD A formula** is dependent on the individual patient. Practical examples are given in this guide; however, it is the responsibility of the managing healthcare professional to use clinical judgement to introduce and adjust **comida-MSUD A formula** in the most appropriate way for individual patients and it may not always be appropriate to use the practical guide.

IMPORTANT NOTICE

- **comida-MSUD A formula** must only be used under medical supervision.
- Suitable from birth to 12 months of age.
- Not suitable for use as a sole source of nutrition.
- **comida-MSUD A formula** must only be consumed by infants with proven Maple Syrup Urine Disease.
- **comida-MSUD A formula** must be used in conjunction with breast milk or infant formula to provide the isoleucine, leucine, valine, fluid and general nutritional requirements of the infant in quantities as advised by a metabolic healthcare professional.
- For enteral use only.

This practical guide does not establish or specify particular standards of medical care for the treatment of any conditions referred to in this practical guide.

Vitaflo International Limited **does not** recommend or endorse any specific tests, procedures, opinions, clinicians or other information that may be included or referenced in this practical guide.

Symbols and Abbreviations

Symbol	Abbreviation	Definition
	HM	Human milk
	BF	Breastfeed
	HCP	Healthcare Professional
	MSUD	Maple Syrup Urine Disease
	BCAA	Branched-chain amino acid
	LEU	Leucine
	BCAA-free formula	BCAA-free formula (comida-MSUD A formula)
	SIF	Standard infant formula

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Features of comida-MSUD A formula

comida MSUD^A formula

comida-MSUD A formula is an isoleucine, leucine and valine free* amino acid based powdered formula containing essential and non-essential amino acids, carbohydrate, fat, vitamins, minerals, trace elements, arachidonic acid (ARA) and docosahexaenoic acid (DHA).

comida-MSUD A formula provides all the essential nutrients required by an infant, except isoleucine, leucine and valine.

comida-MSUD A formula is for use in the dietary management of Maple Syrup Urine Disease (MSUD) from birth to 12 months of age.



*No added isoleucine, leucine and valine.

Overview of feeding an infant with MSUD

Newly diagnosed infants with MSUD are prescribed a BCAA-free formula (**comida-MSUD A formula**) as soon as diagnosis is confirmed and as medically appropriate pending the clinical status of the infant. The branched-chain amino acids (BCAAs – offending amino acids) consist of leucine, isoleucine, and valine.

Feeding an infant with MSUD is a balance between providing BCAA-free infant formula alongside adequate amounts of BCAA from human milk (HM)/ standard infant formula (SIF), with the goal of keeping leucine (LEU) levels within target therapeutic range. The goal range for leucine is 75–200 $\mu\text{mol/L}$ for infants and children less than 5 years of age, and 75–300 $\mu\text{mol/L}$ for those greater than 5 years of age¹. LEU is the offending amino acid that is tightly controlled because it has proven toxicity to the brain, whereas the other two BCAAs, isoleucine (ISO) and valine (VAL), have not been proven acutely dangerous at higher plasma levels. ISO and VAL, are usually supplemented outside of formula to maintain target plasma levels. Given that MSUD involves an inability to break down all three BCAAs, it is safer to omit them from formula to control their levels and use additional supplementation as needed. This balance can be achieved with HM or SIF as the source of BCAAs; a family should be supported to make the appropriate choice for their family and their infant, with relevant healthcare professionals' input as appropriate.

comida-MSUD A formula may be used from diagnosis in combination with HM/SIF or as a sole source of nutrition for a brief period known as an "emergency regimen" or "sick day diet" in order to achieve a rapid reduction in blood LEU levels. An emergency regimen should only be used by the metabolic healthcare provider, if diagnostic blood LEU levels are found to be significantly elevated on laboratory results, or if presenting symptomatically and there is concern for significant LEU elevation. It is important that blood BCAA levels are monitored very closely to prevent BCAA deficiency. Once blood LEU levels approach target therapeutic range as determined by the metabolic healthcare provider, a source of BCAA, either HM or SIF, is reintroduced and given in combination with **comida-MSUD A formula**.

Another example in which an emergency regimen may be used is during illness, however, in this instance family/carers should contact their metabolic healthcare provider. Illness is treated/managed by, or supported by, the metabolic healthcare provider in an urgent and individual way so will not be discussed in this practical guide.

Breast fed infants

Healthcare providers should support a family's decision to BF or provide HM as the intact protein source for an infant with MSUD whenever possible. **comida-MSUD A formula** combined with bottle-fed HM or feeding at the breast is able to maintain satisfactory blood LEU control provided there is adequate HM available for the infant and blood BCAA levels can be closely monitored^{1,2}. Feeding at the breast may not always be possible with MSUD. Families should discuss what is best for them and their infant with their metabolic healthcare provider. HM offers nutritional benefits including higher long chain polyunsaturated fatty acid concentrations and a lower LEU content (104 mg/100 ml in HM³ compared with approximately 154 mg/100 ml in SIF⁴).

Breastfeeding an infant with MSUD is based on the principle of giving a measured volume of **comida-MSUD A formula** to offset the infant's appetite for breastfeeds.

Feeding a measured amount of **comida-MSUD A formula** alongside each breastfeed, or alternating measured feeds of **comida-MSUD A formula** with breastfeeds, decreases the total amount of HM consumed and therefore decreases total BCAA intake. Infants can still feed on demand, varying the quantity of feeds from day to day provided that the prescribed quantity of **comida-MSUD A formula** is given throughout the day². Successful MSUD management with breastfeeding is achieved via close monitoring of blood BCAA levels and adjustment of the prescribed volume of **comida-MSUD A formula** by the metabolic healthcare professional in order to maintain blood BCAA control. See sections 1.1–1.4 for more details.

SIF fed infant

There are various options for feeding an infant with SIF and **comida-MSUD A formula**. With the help of healthcare providers, including the metabolic healthcare professional, families may choose a SIF supplemented with DHA and ARA that is best for their infant and family circumstances. SIF and **comida-MSUD A formula** may be given in separate or mixed bottles pending specific clinic protocol and preference, with a variety of feeding approaches capable of optimizing blood BCAA control and catering to a family's individual circumstances. See Sections 1.1 – 1.4 for more details.

Overview of feeding an infant with MSUD

Blood LEU Level Monitoring

Blood LEU levels are used to determine whether the volume of **comida-MSUD A formula** and HM/SIF should be adjusted; as discussed earlier, LEU is the most dangerous BCAA to the brain. Expect to adjust the feeding plan weekly, especially during the first two months of life. Blood BCAA levels should be checked at least weekly throughout infancy¹. The quantity of LEU tolerated by infants will vary and be guided by blood LEU levels. Individual LEU tolerance will vary significantly throughout infancy with changes in growth and development. It is vital to investigate all the possible causes for changes in LEU level before adjusting the feeding plan. Consider waiting for two consecutive blood BCAA levels to indicate the need for a feeding plan adjustment, unless the blood LEU level is very low or very high.

Progression

A combination of HM/SIF and **comida-MSUD A formula** and may continue to provide 100% of the infant's nutrition requirements until the age of 6 months, or when the infant is developmentally ready for the introduction of solids. Complementary feeding should be supported by the metabolic healthcare provider.

IMPORTANT NOTICE

Breastfeeding can continue for as long as the mother and infant wish, provided that growth and blood LEU levels are satisfactory. SIF should be introduced if there is inadequate HM to provide enough BCAA or liquid nutrition volume for age, in combination with **comida-MSUD A formula**. If the mother wishes to wean the infant from HM, then a gradual approach is recommended, if possible.

Overview of feeding an infant with MSUD

PRINCIPLES OF INITIATING NUTRITION MANAGEMENT

If LEU levels > 200 $\mu\text{mol/L}$ and if medically appropriate given clinical status after diagnosis, implement use of **comida-MSUD A formula**.

Depending on diagnostic BCAA levels and clinical circumstances, the metabolic team may consider the following strategies for initiating.

comida-MSUD A formula:

- Temporarily stop HM/SIF and use **comida-MSUD A formula** as sole nutrition source for ≤ 48 hours.
- Introduce **comida-MSUD A formula** in combination with HM/SIF.

Once LEU levels approach the target therapeutic range, if HM/SIF has been stopped, reintroduce to tolerance.

Intact protein intake is adjusted based on individual blood LEU levels.

For breastfed infants, **comida-MSUD A formula** volumes will be adjusted with the intended effect of modifying the infant's appetite for HM.

Continue to give a combination of **comida-MSUD A formula** + HM/SIF to provide 100% of the infant's requirements and to achieve optimal growth and LEU levels.

HM/SIF and **comida-MSUD A formula** should provide 100% of the infants' nutrition needs until approximately the age of 6 months when solids are introduced or when the infant is developmentally ready for the introduction of solids².

Monitor blood BCAA levels weekly or more frequently as needed to achieve stability in blood LEU; treatment range of 75-200 $\mu\text{mol/L}$ for infants and children less than or equal to 5 years of age¹.

- **comida-MSUD A formula** and BCAA source should be given together at each feed, or at alternating feeds to ensure nutrient availability throughout the day.
- If the prescribed volume of **comida-MSUD A formula** is not taken, it may cause a rise in blood LEU levels, which is very dangerous for the infant.
- Blood LEU levels are used to determine whether **comida-MSUD A formula**, SIF/HM prescription should be adjusted.
- The infant should be weighed at each clinic visit.

Nutrition prescription using comida-MSUD A formula at diagnosis

THE AIM IS TO ACHIEVE A RAPID REDUCTION IN BLOOD LEU LEVELS

If temporarily stopping intact protein and using **comida-MSUD A formula** alone to lower very high blood LEU levels, a two-step method is used:

Step 1 - Introduction of comida-MSUD A formula

- Use **comida-MSUD A formula** as a sole source of nutrition for 24-48 hours or until blood LEU level approaches target range as directed by metabolic medical team.
- **comida-MSUD A formula** should be offered on demand to the infant if medically appropriate to do so.

Feeding plan and considerations:

- Mix desired amount of **comida-MSUD A formula** per feed (see example feeding plans which follow).
A 1–2 week-old infant will typically take 45-90 ml (1.5-3 fl oz) per feed.
- Encourage family to track number of wet and soiled diapers to ensure intake adequacy.
- Feeding frequency may need to be higher for infants who have not yet regained their birth weight.
 - Family should consult with their metabolic healthcare professional.
- Encourage mothers breastfeeding to express breast milk when the infant feeds to establish and protect breast milk supply during the emergency regimen.
- Maternal-infant skin-to-skin contact and/or a small number of short duration breastfeeds (if approved by metabolic healthcare provider), may be continued to help promote breast milk supply and bonding during the period when breastfeeding is stopped.

Step 2 - Reintroduction of HM/SIF

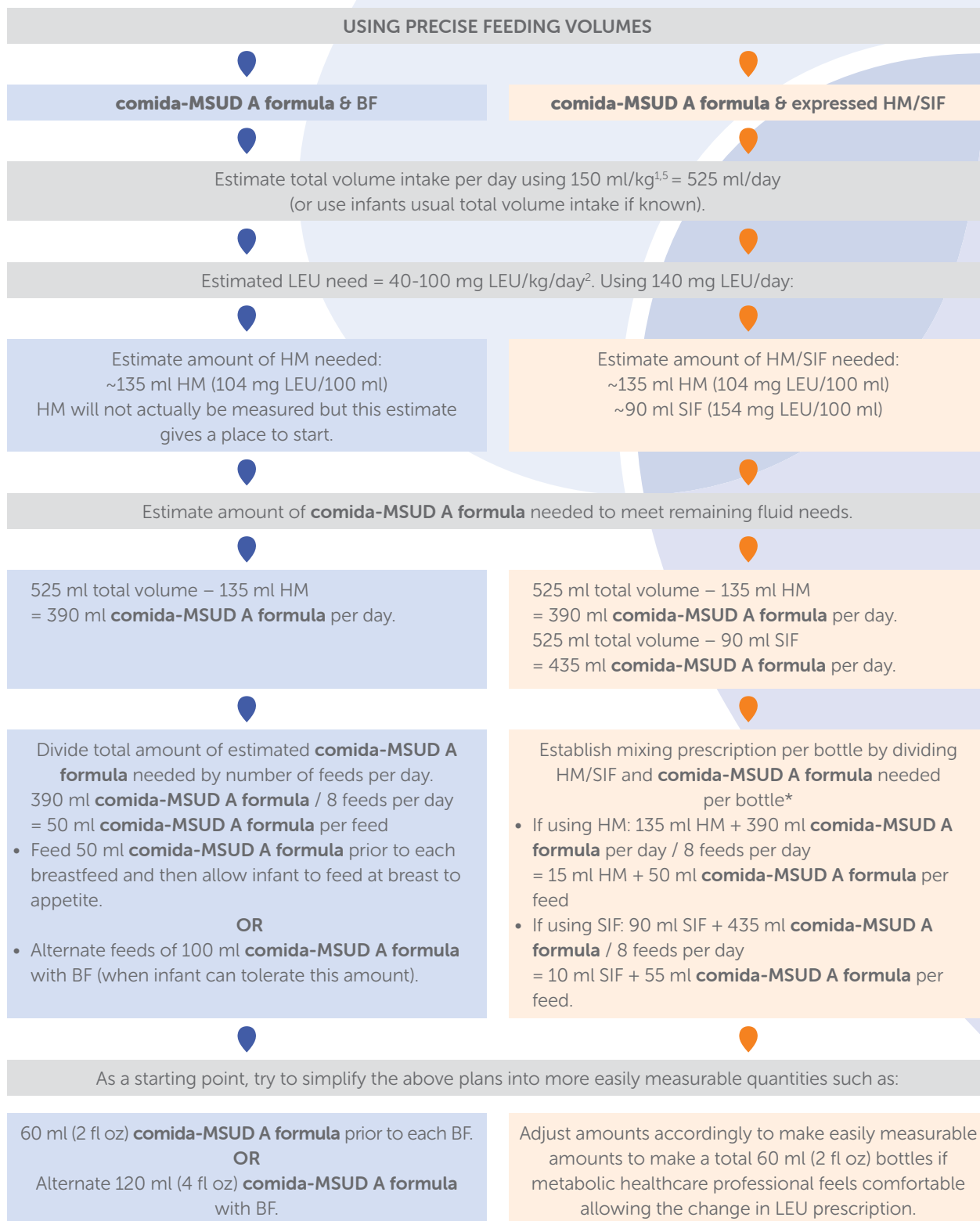
- When blood levels are in the therapeutic target range.

Example feeding plans

If an emergency regimen is not required or reintroducing intact protein source, the following feeding plans illustrate 2 methods for calculating the feeding plan whether breastfeeding or bottle feeding with expressed HM or SIF.

Also note, many factors can affect blood BCAA levels. Always check for causes of high or low blood BCAA level before making a change to the nutrition prescription.

Example using a 6-day old infant diagnosed with MSUD, weight 3.5 kg.



* Infants should be fed to appetite when hungry and total liquid volume per day should not be limited to establish BCAA level formula control. If the estimated volume intake does not satisfy the infant, then additional feeds either **comida-MSUD A formula** alone or mixed **comida-MSUD A formula** + HM/SIF can be given depending on what is clinically appropriate.

Check list for blood LEU monitoring

Many factors can affect blood LEU levels. Always check for causes of high or low blood LEU level before making a change to the nutrition prescription.

Considerations for high blood LEU levels:

POSSIBLE CAUSE	ACTION
Excess intake of intact protein (HM/SIF)	• Confirm feeding preparation and provision is consistent with prescription. • Review mixing and measuring of feeds/formula. • Adjust prescription of HM/SIF and comida-MSUD A formula to meet infant's LEU tolerance.
Inadequate intake of comida-MSUD A formula	• Ensure that adequate comida-MSUD A formula supply is available. • Address symptoms that may affect tolerance such as colic, constipation, or reflux by seeking appropriate medical advice. • Determine presence of short-term symptoms affecting intake such as illness, pain, teething, or vaccination. • Monitor weight and increase comida-MSUD A formula prescription as needed.
Catabolism or slow weight gain	• Monitor weights frequently to better understand growth trajectory. • Rule out illness or infection and encourage appropriate medical treatment. • Encourage optimal total volume intake and adjust feeding intervals and frequency as needed to achieve goals. • Cross-check BCAA and calorie intake to ensure infant is meeting requirements.
Change in blood monitoring routine	Encourage consistent timing of blood LEU level within family's and infant's specific circumstances.
Individual amino acid supplements	Inadequate provision of other BCAAs (isoleucine and valine) can contribute to catabolism and inadequate LEU utilization. Maintain isoleucine and valine levels 200-400 µmol/L¹.

Check list for blood LEU monitoring

Considerations for low blood LEU levels:

POSSIBLE CAUSE	ACTION
Inadequate intake of intact protein (HM/SIF) or Excessive intake of comida-MSUD A formula	• Confirm feeding preparation and provision is consistent with prescription. • Review mixing and measuring of feeds/formula. • Ensure adequate HM available if applicable, supplement SIF as needed. • Adjust prescription of HM/SIF and comida-MSUD A formula to meet infant's LEU tolerance.
Anabolism or rapid growth phase	• Monitor weight frequently to better understand growth trajectory. • Increase BCAA source if blood LEU level is very low; consider continuing prescription and repeating level if blood LEU level is in an acceptable low range.
Change in blood monitoring routine	• Encourage consistent timing of blood BCAA level over the day within family's and infant's specific circumstances

MONITORING TIPS

For all infants, frequent monitoring of BCAA levels is key, but try not to make changes to a feeding plan too frequently.

Consider:

Many factors affect BCAA levels; review all causes in this section.

- Monitor BCAA level trends
 - Unless LEU level is very low or very high consider:
 - Continuation of the current plan
 - Awaiting 2 consecutive LEU levels before adjusting prescription
- In general, do not make more than 1 change to the plan in 1 week

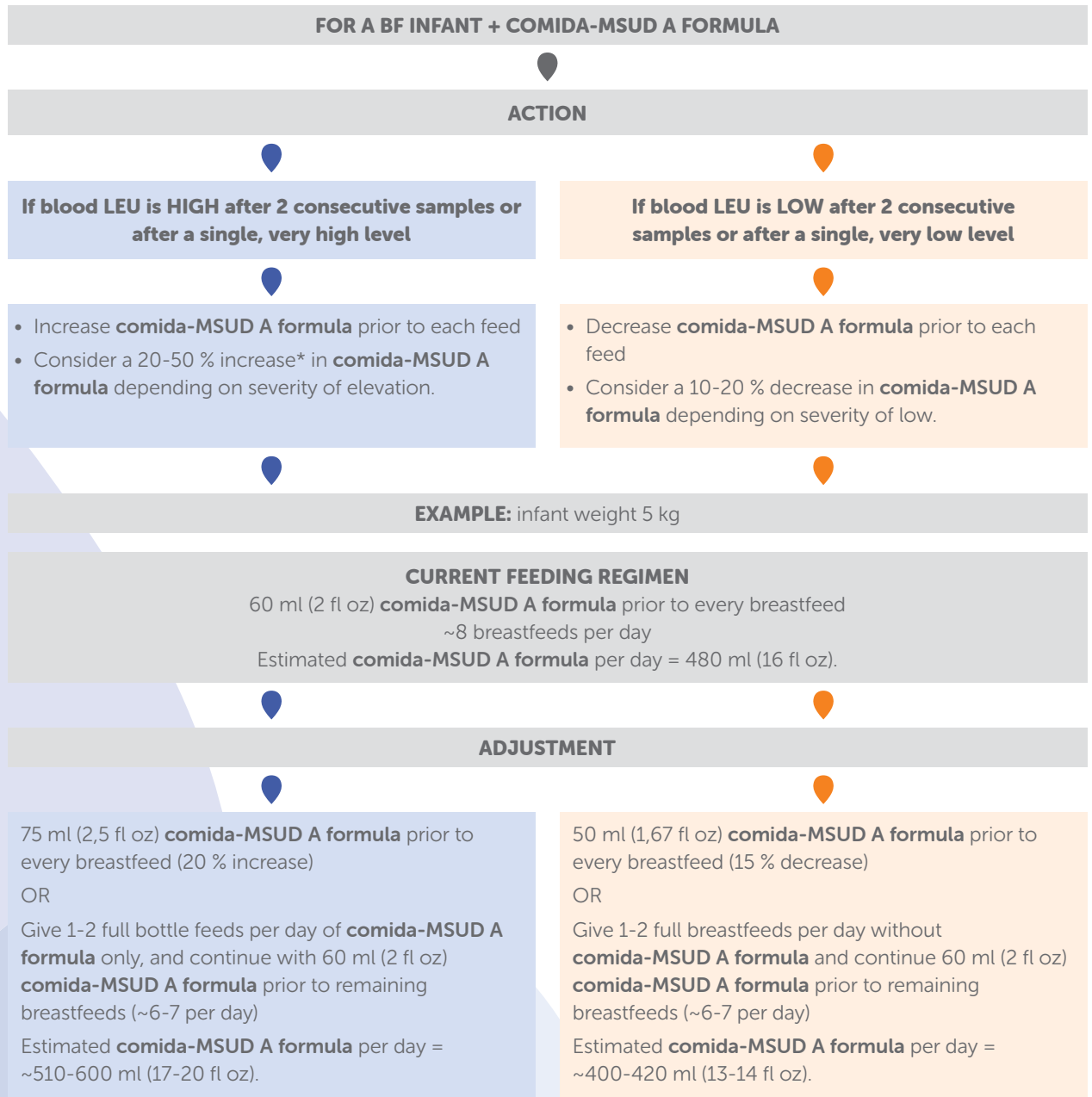
For LEU levels that ARE very low or very high:

- Consider repeating blood LEU level sooner than 1 week to guide interventions or other intervention as recommended by metabolic healthcare professional.

ILLNESS MANAGEMENT:

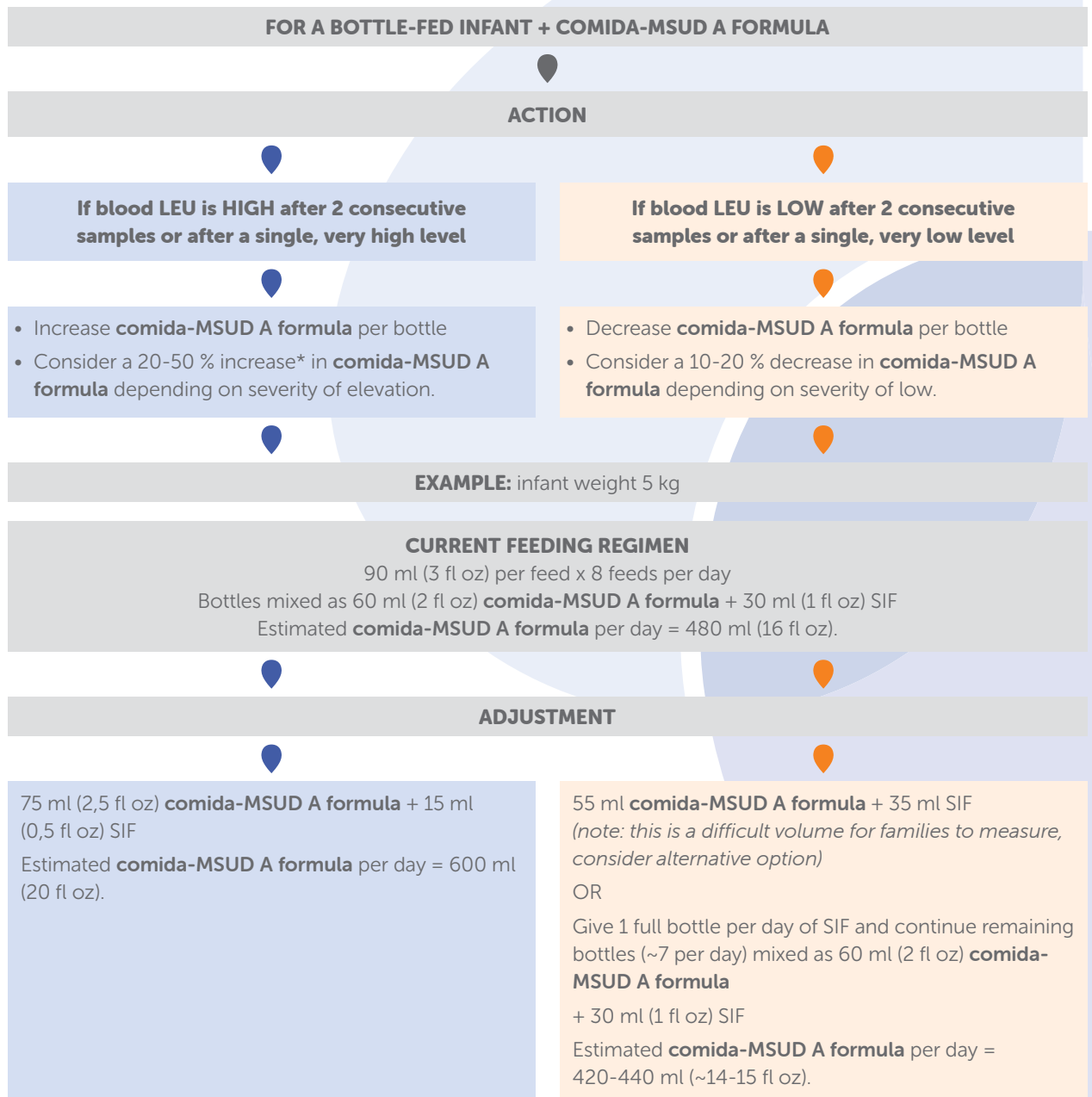
There is a risk of metabolic decompensation during trauma, surgery, illness or inappropriate dietary intake¹. Emergency regimes are individually prescribed to prevent catabolism and promote anabolism, with close monitoring of biochemical and clinical status. Refer to local and international guidelines for further information¹.

Fine-tuning the nutrition prescription



* Although a 50% increase seems high, it often coincides with a simultaneous increase in total infant feeding volume per day.

Fine-tuning the nutrition prescription



* If the infant is still hungry after the feed, there are different approaches that may be used to achieve satiety for the infant while maintaining blood LEU control (infants should always be fed to appetite, and total feeding volume should not be restricted to achieve LEU level control):

- 1) Offer additional **comida-MSUD A formula** to achieve satiety.
- 2) Offer additional mixed bottle of SIF/HM + **comida-MSUD A formula** where clinically appropriate to achieve satiety.

Practical feeding strategies to use with caregivers



Be prepared with feeding supplies. It is important for HCPs to know what supplies the family/caregivers have on-hand and to ensure they can get proper supplies when needed.

These Include:

Feeding bottles with necessary measurement markings (demarcation) for infant's recipe

- Appropriately staged nipples for infant feeding
- Adequate supply of **comida-MSUD A formula**
- HM pump and supplies if needed to express
- Adequate supply of SIF (if using)

FORMULA MIXING INSTRUCTIONS: REVIEW

- Use **comida-MSUD A formula** scoop (or gram scale) to mix **comida-MSUD A formula**. Do not use scoops from other formula containers to mix **comida-MSUD A formula**
- Ensure family has access to a safe water source for formula mixing
- Inquire about the most effective written method for family to receive new recipes and mixing instructions. Review mixing at every visit

Confirm family/caregivers are able to procure more **comida-MSUD A formula** and SIF (if using) when supplies are low. Consider providing written guidance on where families can obtain these formulas. Direct families to appropriate agencies and services if needed to obtain SIF at low-cost or for free.

Practical points for effective communication between HCPs and caregivers

ESTABLISH LINES OF COMMUNICATION BETWEEN HCP AND CAREGIVER/FAMILY

Phone calls, e-mail, text and/or the medical record portal may all be used. Ensure caregivers/families are comfortable using communication method.

KEEP INFORMATION SIMPLE AND PRACTICAL AND CHECK FAMILY/CAREGIVER UNDERSTANDING OF INFORMATION.

Allow time for questions and encourage questions between visits.

Consider written feeding plans.

ENCOURAGE QUESTIONS

Caregivers should be encouraged to ask questions and speak up whenever they do not understand. Effective and open lines of communication as well as appropriate teaching methods are critical for caregiver success.

EDUCATE ALL CAREGIVERS

Let primary caregiver(s) know that anyone taking care of the infant is welcome at clinic visits and education pieces may be provided for all caregivers depending on their needs.

ESTABLISH FREQUENCY OF REVIEWING BCAA LEVELS AND CLINIC VISITS

Ensure caregivers understand what communication method will be used to report results and adjust the diet between visit.

INFORM OTHER HCPS, INCLUDING THE PRIMARY CARE PHYSICIAN, OF THE MANAGEMENT PLAN

DIRECT CAREGIVERS TO APPROPRIATE PATIENT/FAMILY SUPPORT GROUPS AND APPROPRIATE INFORMATION PLATFORMS

REMEMBER THAT DIFFERENT PATIENTS/FAMILIES SUCCEED WITH DIFFERENT COMMUNICATION METHODS;

Be as adaptable as you can within your clinic's capabilities.

Directions for preparation, use, and storage of comida-MSUD A formula

PREPARATION GUIDELINES

Follow the instructions exactly and feed immediately. Incorrect preparation can make your infant ill.

- 1  Wash hands well.
- 2  Sterilise bottle, teat and cap by boiling in water for five minutes. Leave covered until use.
- 3  Boil drinking water for five minutes. Allow to cool to lukewarm drinking temperature, i.e., water that feels warm on the wrist but not hot.
- 4  Pour exact amount of lukewarm water into the bottle.
- 5  Using the scoop provided, add the prescribed number of scoops of **comida-MSUD A formula** to the water, levelling each scoop off with the back of a clean dry knife. Do not press the powder into the scoop.
- 6  Shake well until the powder is fully dissolved.
- 7  Always test the temperature before feeding by shaking a few drops onto the inside of your wrist - the feed should feel warm but not hot.

It is important for caregivers to carefully follow the instructions for the preparation, use and storage of **comida-MSUD A formula**. Use only the scoop provided in the can or a gram scale for greatest accuracy.

- Any formula remaining in the bottle after 1 hour should be discarded.
- Do not reheat **comida-MSUD A formula**.
- Do not heat **comida-MSUD A formula** in a microwave as uneven heating may occur and could cause scalding.
- Do not boil **comida-MSUD A formula**.
- Infants should be supervised at all times when feeding.
- Regular teeth cleaning is recommended.

Preparation Guidelines				
Water (ml)	comida-MSUD A formula no. scoops	comida-MSUD A formula (g)	Drinking volume (ml)	Protein equivalent (g)
30	1	4,7	35	0,67
90	3	14,1	100	2
180	6	28,2	200	4

STORAGE

UNOPENED: **comida-MSUD A formula** should be stored in a cool, dry place.

OPENED: Use within 3 weeks.

Always replace container lid after use.

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All information correct at the time of publication.