MATERNAL PHENYLKETONURIA

A quick guide and practical tips for healthcare professionals
Preface

For details on the nutritional management of maternal PKU, please refer to the resources in the back of this booklet. Feel free to use the notes pages at the end of the booklet to document your takeaways from the GMDI breakfast symposium.

We hope you find this booklet useful. Please reach out to our Nutrition Services department at NutritionServices@Nutricia.com for further questions or if you would like to be connected to our Metabolic Hotline, staffed by an experienced metabolic RD. Thank you for allowing Nutricia to continue to be your trusted partner.

Sincerely,
The Nutricia Metabolic Team
What is Maternal PKU?

Since the start of newborn screening over 50 years ago, patients with phenylketonuria (PKU) have been managed successfully and outcome has been overwhelmingly positive, resulting in an increasing number of PKU patients choosing to become pregnant. These patients, referred to as maternal PKU patients, are especially vulnerable: high plasma phenylalanine (PHE) levels throughout pregnancy can not only lead to an increased risk of miscarriages\(^1\) for the expectant mother, but are also teratogenic for the unborn child. Studies in maternal PKU (MPKU) patients have shown that uncontrolled plasma PHE levels during pregnancy can cause the following clinical outcomes\(^1\)\(^-\)\(^4\) for the baby:

- Microcephaly
- Intellectual disability
- Behavioral issues / Lower IQ
- Congenital heart defects (CHD)
- Low birth weight and reduced length for age

Control of plasma PHE levels during pregnancy is critical, with control prior to conception being ideal. Women are encouraged to plan their pregnancies and maintain close contact with their metabolic center.

This booklet provides a summary of important recommendations for metabolic healthcare professionals involved in the care of maternal PKU patients.

KEY GOALS FOR THE NUTRITIONAL MANAGEMENT OF MPKU
Key Goals of Nutrition Management

- Appropriate nutrition
  - Support fetal growth with sufficient amounts of protein (a combination of PKU formula and foods containing intact protein), tyrosine (TYR), energy, fat, vitamins and minerals (especially vitamin B12, folate and iron).
  - PHE tolerance will vary depending on the trimester; adjust intake of intact protein accordingly.
  - Monitor nutrient intake to help prevent deficiencies and support normal fetal outcome.

- Target plasma PHE levels between 120 – 360 µmol/L (2-6 mg/dL) prior to conception and throughout pregnancy.
- Reduce PHE levels within target range as soon as possible if pregnancy is unplanned.
  - Continued elevations of plasma PHE after the first 8 to 10 weeks of gestation are associated with a higher risk for fetal congenital heart defects and poor fetal growth.

The following are tables and references for calculating the maternal PKU diet, as well as for monitoring throughout pregnancy. For extensive guidelines, case calculations and resources on the nutrition management for pregnancy, lactation, and postpartum, please visit www.gmdi.org.

Select Recommended Nutrient Intake During Pre-Conception, Trimesters and Lactation

<table>
<thead>
<tr>
<th>Age</th>
<th>PHE (mg/day)</th>
<th>TYR (mg/day)</th>
<th>Protein (g/day)</th>
<th>Energy (Kcal/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-conception</td>
<td>200 – 1,100</td>
<td>4,000 – 6,000</td>
<td>120 – 140% DRI for age</td>
<td>DRI for age</td>
</tr>
<tr>
<td>1st Trimester</td>
<td>265 – 770</td>
<td>6,000 – 7,600</td>
<td>≥70</td>
<td>2,000 – 3,500</td>
</tr>
<tr>
<td>2nd Trimester</td>
<td>400 – 1,650</td>
<td>6,000 – 7,600</td>
<td>≥70</td>
<td>2,000 – 3,500</td>
</tr>
<tr>
<td>3rd Trimester</td>
<td>700 – 2,275</td>
<td>6,000 – 7,600</td>
<td>≥70</td>
<td>2,000 – 3,500</td>
</tr>
<tr>
<td>Lactation</td>
<td>700 – 2,275</td>
<td>6,000 – 7,600</td>
<td>≥70</td>
<td>2,000 – 3,500</td>
</tr>
</tbody>
</table>

### Total Pregnancy Weight Gain

<table>
<thead>
<tr>
<th>Underweight (BMI &lt;18.5)</th>
<th>13 – 18 kg (28 – 40 lbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight (BMI 18.5 – 24.9)</td>
<td>11 – 16 kg (25 – 35 lbs)</td>
</tr>
<tr>
<td>Overweight (BMI 25 – 29.9)</td>
<td>7 – 11 kg (15 – 25 lbs)</td>
</tr>
<tr>
<td>Obese (BMI &gt;30)</td>
<td>5 – 9 kg (11 – 20 lbs)</td>
</tr>
</tbody>
</table>


### Monitoring*

<table>
<thead>
<tr>
<th>Nutrition visit in clinic</th>
<th>Monthly to per trimester</th>
<th>At 6 weeks postpartum, then every 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interim nutrition contact</td>
<td>Once to twice weekly</td>
<td>Weekly to monthly</td>
</tr>
<tr>
<td>Anthropometrics</td>
<td>Every clinic visit</td>
<td>Every clinic visit</td>
</tr>
<tr>
<td>PHE</td>
<td>Once to twice weekly</td>
<td>Weekly to monthly</td>
</tr>
<tr>
<td>TYR</td>
<td>Once to twice weekly</td>
<td>Weekly to monthly</td>
</tr>
<tr>
<td>Complete AA Profile</td>
<td>Weekly to monthly</td>
<td>Yearly or as indicated</td>
</tr>
<tr>
<td>Prealbumin</td>
<td>Monthly to per trimester</td>
<td>Yearly or as indicated</td>
</tr>
<tr>
<td>Albumin or total protein</td>
<td>Per trimester</td>
<td>Yearly or as indicated</td>
</tr>
<tr>
<td>CBC</td>
<td>Per trimester</td>
<td>Yearly or as indicated</td>
</tr>
<tr>
<td>Ferritin</td>
<td>Per trimester</td>
<td>Yearly or as indicated</td>
</tr>
<tr>
<td>Prealbumin</td>
<td>Per trimester</td>
<td>Yearly or as indicated</td>
</tr>
<tr>
<td>Vitamin D 25-OH</td>
<td>Per trimester</td>
<td>Yearly or as indicated</td>
</tr>
<tr>
<td>Comprehensive metabolic panel, serum Vit B12, erythrocyte folate, zinc, copper, essential fatty acids</td>
<td>First visit and then as indicated</td>
<td>Yearly or as indicated</td>
</tr>
</tbody>
</table>

*These are guidelines provided to help support healthcare professionals involved in the dietary management of maternal PKU patients. Practices may vary from clinic to clinic, and this booklet should serve as guidance, not as strict protocol. Monitoring should be individualized per patient.

Unplanned Pregnancy

It is crucial to achieve plasma PHE levels within target range as soon as possible for a patient presenting with unplanned pregnancy. Best clinical outcome for the fetus is typically seen when plasma PHE levels are in target range within the first 8 to 10 weeks of gestation. In some cases, inpatient admission may be necessary to achieve PHE levels in target range. If your patient is unable to consume her prescribed PKU formula then placement of nasogastric tube (NGT) should be considered.

Suggestions for decreasing plasma PHE levels until target range is met:

- Consider a washout period:
  - Only PKU formula, fruits, low-PHE vegetables and low protein foods to reduce PHE levels faster.
  - If PHE tolerance unknown, start with 250-300 mg of PHE/day.
- Consider an inpatient admission to:
  - Provide an opportunity to quickly reduce PHE concentrations into the goal range.
  - Provide intensive education about diet management, including PKU formula preparation and appropriate food options.
  - Sample a variety of PKU formulas with patient until right one is found.
  - Start NGT feeds if patient is unable to take PKU formula.
PHE Levels Remain Elevated:
- Evaluate PKU formula intake
  - Make sure protein intake from PKU formula and intact protein is adequate.
- Make sure she is consuming adequate amounts of energy:
  - Is she gaining appropriate weight?
- Assess PHE intake:
  - Is she counting correctly?
  - Is she eating non-allowed foods?
- Assess if mom has been sick
- Evaluate need for social support at home

Nausea and Vomiting
- Encourage foods she enjoys
- Cold foods are sometimes better tolerated than hot foods
- Avoid empty stomach
  - Encourage small frequent snacks every 2 hours during the day.
- Change to a lower volume PKU formula, if appropriate
- Divide current PKU formula into small frequent portions throughout the day
- Change to a PKU formula with less of a smell
  - Or drink current PKU formula through a straw in a container with a cover to prevent smelling PKU formula while drinking.
- Avoid taking any vitamin/mineral supplement on an empty stomach

Increasing Calories
- Mix oil or non-dairy margarine into low protein pasta or rice
- Change from low calorie PKU formula to a higher calorie PKU formula containing fat
- Dip low protein bread in olive oil
- Add avocado to salads or sandwiches
- Add sweets to teas, coffees, muffins and smoothies
  - Maple syrup, honey, agave nectar, sugar
- Consider adding Duocal® to any liquid or semi-solid food

Heartburn
- Avoid - caffeine, peppermint or spearmint, sodas, spicy foods and acidic foods
- Avoid large meals
  - Try small frequent meals spread throughout the day
- Limit meals close to bedtime
- Sleep with head at elevated angle
- Consider ginger candy or tea

Refer to her OB/GYN specialist for anti-emetics if vomiting persists and consider need for hospitalization.
Hunger

If your patient is consistently hungry she may benefit from preparing portioned out low-PHE snacks for the week:

- Make single-serving bags of low protein pretzels, popcorn, cereal and sliced vegetables
  - Consider gluten-free* items
- Fruit leathers or fresh fruit
- Sliced vegetables such as cucumbers, peppers, zucchini, etc.
- Portioned out cherry or grape tomatoes or baby carrots
- Prepare ahead and freeze bulk items such as low protein breads, biscuits, muffins, cookies and soups

*Be sure to read labels and check serving sizes when planning a snack. PHE content varies by brand. Not all gluten-free foods are low in protein. For more on finding the PHE content in common foods, check out www.HowMuchPHE.org
PKU Formulas for Maternal PKU Patients

Every patient is different and has different needs – especially during pregnancy. Taste, smell and volume may be a challenge at times. Nutricia provides an extensive selection of PKU formulas to help your patient follow the PKU diet during this critical time and beyond. We also provide a selection of low protein foods.

Request samples from:
(US) Your sales representative, MedicalFood.com or by calling 800-605-0410
(Canada) Your sales representative or by calling 877-636-2283

All PKU formulas should be used only under medical supervision and managed by a healthcare professional.

Visit www.medicalfood.com for more information.

Looking for a higher calorie PKU formula?
Here are our higher calorie options:

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Description</th>
</tr>
</thead>
</table>
| PhenylAde® GMP Drink Mix | • 2 flavors (Original and Vanilla)  
                           • GMP-based  
                           • Added DHA  
                           • 10 g PE (15.3 mg PHE) / 132 kcal (180 mL, 6 fl oz) |
| PhenylAde® Essential Drink Mix | • 5 flavors (Unflavored, Vanilla, Chocolate, Orange Creme and Strawberry)  
                                • 10 g PE / 157 kcal (240 mL, 8 fl oz) |
| Periflex® LQ          | • 2 flavors (Orange Creme and Berry Creme)  
                           • Ready to drink  
                           • 10 g PE / 107 kcal (15 g PE & 160 kcal per 250 mL, 8.5 fl oz container) |
| Periflex® Advance     | • 2 flavors (Unflavored and Orange)  
                           • 10 g PE / 110 kcal |
| Duocal®               | • Protein-free energy source  
                           • Provides carbohydrate and fat to increase calories  
                           • 1 Tbsp delivers 42 kcal |
### Looking for a lower volume PKU formula?

Here are some of our lower volume options:

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhenylAde® 60 Drink Mix</td>
<td>• 2 flavors (Unflavored and Vanilla)</td>
</tr>
<tr>
<td></td>
<td>• 10 g PE / 49 kcal (90 mL, 3 fl oz)</td>
</tr>
<tr>
<td>Lophlex® LQ</td>
<td>• 3 flavors (Juicy Orange, Mixed Berry Blast, Juicy Tropical)</td>
</tr>
<tr>
<td></td>
<td>• Juice-based</td>
</tr>
<tr>
<td></td>
<td>• Added DHA</td>
</tr>
<tr>
<td></td>
<td>• 10 g PE / 60 kcal (20 g PE &amp; 120 kcal per 125 mL, 4.2 fl oz pouch)</td>
</tr>
<tr>
<td>XPhe Maximum®</td>
<td>• 2 flavors (Unflavored and Orange)</td>
</tr>
<tr>
<td></td>
<td>• 10 g PE / 76 kcal (120 mL, 4 fl oz)</td>
</tr>
</tbody>
</table>

### Is the smell or taste of the PKU formula a problem?

Consider these:

<table>
<thead>
<tr>
<th>Product Name</th>
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</tr>
</thead>
<tbody>
<tr>
<td>PhenylAde® GMP Mix-In</td>
<td>• Mix into any liquid or semi-solid food without significant flavor change</td>
</tr>
<tr>
<td></td>
<td>• GMP-based</td>
</tr>
<tr>
<td></td>
<td>• 10 g PE (15.3 mg PHE) / 42 kcal*</td>
</tr>
<tr>
<td>PhenylAde® Amino Acid Blends (MTE)</td>
<td>• Mixes into any flavored liquid (except water)</td>
</tr>
<tr>
<td></td>
<td>• 10 g PE / 40 kcal*</td>
</tr>
</tbody>
</table>

Please note when recommending these products sufficient fat and energy intake from other sources are essential; these products must be combined with an appropriate vitamin & mineral supplement when taken as the sole source of PKU formula.

*When mixed with water, other drinks may alter caloric and PHE content*
Is drinking PKU formula an issue?

Consider tablets:

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phlexy-10® Tablets*</td>
<td>12 tablets = 10 g PE &amp; 49 kcal</td>
</tr>
</tbody>
</table>

Please note when recommending this product sufficient fat and energy intake from other sources are essential; this product must be combined with an appropriate vitamin & mineral supplement when taken as the sole source of PKU medical food.

*Available in the US only
One-on-one support to obtain PKU formula coverage at no cost to your patient!*

Your patient won’t face the challenges of insurance coverage alone. Through the Nutricia Connect program, our formula coverage specialists are here to help through each step to get PKU formula coverage. Our experts will:

- Provide PKU formula free of charge while working to obtain coverage
- Complete pre-determinations, prior authorizations, medical necessity reviews and help find in-network suppliers to fulfill orders
- Verify eligibility and benefits for PKU formula through pharmacy or other medical plans
- Work with families and their employers to find a coverage exception in order to accommodate Nutricia PKU formulas
- Assist in appealing denials for coverage and help resolve billing discrepancies...

...And much, much more!

*Available in the US only

To learn more visit MedicalFood.com/Reimbursement or call 1-800-605-0410 Monday–Friday 8:30a.m. – 5:00p.m. ET.

Talk to a Nutricia Formula Coverage Specialist
Coverage@Nutricia.com

Resources

- Genetic Metabolic Dietitians International (GMDI) – gmdi.org (members only resources)
- National PKU Alliance – adultswithpku.org/Mentor-Programs
- New England Consortium of Metabolic Programs – newenglandconsortium.org

NUTRICIA IS HERE TO LEND A HELPING HAND

MedicalFood.com/Reimbursement or call 1-800-605-0410

Talk to a Nutricia Formula Coverage Specialist
Coverage@Nutricia.com

9 out of 10 people obtain formula coverage

...And much, much more!

*Available in the US only
References

Notes