Chapter 2: Treatment and Diet Overview

The PKU Clinic Team

The phenylketonuria (PKU) clinic team consists of a group of healthcare professionals trained to support individuals with PKU. You will see them on your regular clinic visits. These visits are extremely important to monitor your PKU and to adjust your diet if required.

- The physician oversees PKU treatment which includes monitoring Phe levels and other labs, growth and developmental progress, prescribing medication such as Kuvan and monitoring routine childhood medical concerns.

- The registered dietitian works closely with you to plan nutritious dietary choices with formula and low protein foods as well as to monitor blood Phe levels and growth.

- The genetic counselor provides education regarding the genetics of PKU and assists the physician with monitoring PKU treatment. Some clinics also have nurses to assist the physician with monitoring PKU treatment.

- The social worker organizes group and individual discussion sessions with patients and parents to support those affected by PKU.

- Some clinics have a psychologist that performs neurological and psychometric assessments at certain ages to ensure children with PKU are developing at an appropriate rate.

Diet Essentials

Formula: Defining Medical Foods

For people with PKU, medical food is vital to treat PKU and ensure good health. Medical foods include medical formula and foods modified to be low in protein. Because protein intake is restricted, medical formula provides all the essential amino acids found in protein except for Phe. It also provides tyrosine, vitamins, minerals and trace elements that most people who do not have PKU would get from their diet.

Your PKU clinic physician will provide a prescription for medical foods. Taking the prescribed amount of medical formula each day is essential. Low protein medical formulas are made to suit the nutritional needs of people with PKU at different ages, and are available in a variety of forms and flavors to suit different lifestyles and preferences. Your dietitian will assess your nutritional needs and provide a recommended formula to meet these.

Medical formula helps to:
- give energy throughout the day
- build muscle
- increase strength
- maintain brain function and analytical thinking
- keep your Phe levels in control and keep you healthy.

Why is the PKU diet different for different people?
The amount of Phe needed and tolerated by each person with PKU can be different depending on the severity of their PKU. Your PKU dietitian will help you create a specialized diet based on your need. In addition, your PKU team will adjust your diet according to your blood Phe levels, which means that your prescribed diet may vary from time to time.
Foods modified to be low in protein are defined as manufactured products that will deliver no more than one gram of protein per serving. Low protein food products supply needed additional calories without supplying additional phenylalanine containing protein. This helps prevent catabolism (the breakdown of protein in the body i.e., muscle) which in itself can cause Phe levels to rise. Use of low-protein products, especially when used consistently, greatly improves adherence to the treatment.

Types of medical foods:

- **The Drink**: Formula in the form of a powdered drink mix. This is the traditional and most common type of PKU formula.

- **The Low Fat Formula**: A reduced fat version of the traditional formula for adults.

- **The Bar**: Convenient PKU medical food in the form of a bar that can be eaten on the go.

- **The Fortifier**: Concentrated amino acid formulas that can be added to any low protein food or beverage you already enjoy. It can also be added to traditional formula to increase the protein content without added volume.

- **The Tablet**: You can supplement your diet with liquid formula or take multiple tablets daily to meet your formula needs. Just remember to meet your daily fluid requirements to ward off dehydration.

- **Ready to Drink**: These convenient formulas are prepared in advance, ready for you to drink wherever you are. These prepared drinks have the protein you need with the essential amino acids and nutrients you’re used to getting from your formulas. You can find a variety of flavors, and some are even freezable for hot days when you need a cool alternative for your formula needs.

- **Glycomacropeptide (GMP) foods**: GMP is used to make formulas (including some ready-to-drink formulas) as well as some PKU-friendly food. This whey-based protein is produced when making cheese. It is the only known dietary protein that contains a minimal amount of Phe. GMP foods have also been found to significantly lower Phe levels in blood. Foods made with GMP provide an alternative to the amino acid medical foods currently required in the PKU diet.

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Treatment and Diet Overview

The Low-Protein Diet

People with PKU get most of the protein they need from medical formula, the backbone of the PKU diet. The remaining protein – which includes the essential amount of Phe the body needs for growth and functioning – comes from food. The PKU diet consists of low protein foods such as:

- Fruits
- Vegetables
- Foods modified to be low in protein, including low-protein pasta, rice and breads
- Fats and sugar

Foods such as red meat, chicken, fish, eggs, milk, yogurt, cheese, nuts, soybeans and beans are too high in protein to include in a PKU diet, except when the dietary restriction required is minimal. Foods such as regular pasta, bread, rice and starchy vegetables (potatoes, peas, corn etc) will likely be limited in your diet as well. Your dietitian will instruct you as to which foods and how much you or your child can eat.

Even low protein foods cannot be eaten in unlimited quantities. All foods must be measured to make sure that Phe intake stays within the daily limit.

It is helpful to incorporate the PKU diet into the family meal. This can be done by basing your child’s PKU meal on the vegetables or grains the rest of the family will be eating. For example, if your family is having pasta with meat sauce for dinner, you can prepare low protein pasta with tomato sauce for you or your child with PKU.

Counting Phe/Protein

One study shows that the more mothers know about counting Phe, the better their child’s dietary compliance is based on the child’s blood Phe levels^{10}. It is important for all individuals with PKU to count the protein in foods for meal planning and tracking Phe intake. There are many different ways and styles to keep track of Phe in food. Your dietitian will counsel you on the system the clinic uses and which method may work best for you. They will also inform you on how much protein, Phe, or exchanges is needed each day and provide you with a food reference guide.

What is a food reference guide?
A food reference guide shows how much protein and Phe common foods contain, which helps you figure out and plan how much protein and phe you will eat at each meal or snack. It also lists ‘free foods’, i.e. foods that contain little or no protein, which do not need to be counted. The dietitian at your PKU clinic may give you a reference guide and help you use it.
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The most accurate way to measure serving sizes is to use a food scale.

How to measure formula or food using a scale
1. Make sure the scale is on a level surface.
2. Turn on the scale. The scale should read “0 g” which means that the scale is “zeroed”. If it reads something other than “0 g”, push the “On/Off Zero” button once and the scale should read “0 g”.
3. When the scale reads “0 g”, place the container to measure the powder or food on the scale. Once it has read the weight press the “On/Off Zero” button to zero the scale. The screen should read “0 g” again.
4. You can then start adding the food or formula powder to measure the grams needed. Repeat the above instructions each time you need to measure formula or food.

You can also measure formula and foods using measuring cups, although this method is not as accurate as using a scale. Your food reference guide lists both gram weights and cup measurements for many common foods.

This section provides three methods for keeping track of Phe. The common factor between each method is to know your portion size and measure what you eat.

Method 1: Counting Milligrams (mg) of Phe

Counting milligrams is the most accurate method of keeping track of how much Phe is consumed. When using this method to keep track of Phe, it is helpful to have a food reference guide that tells you how much Phe is contained in the food and beverages being consumed (see the Chapter 15 Resources for recommended food reference guides). If the food you are preparing is in the reference guide with the amount that you plan on serving, you just need to record the amount listed in the guide. It is also important to pay attention to the brand name of the product. Different brands of a similar item may not have the same amount of Phe due to the ingredients and amounts used.

Measuring using weight

You will need your kitchen scale and a calculator.
1. Weigh the food you are going to serve.
2. Multiple the gram weight of the food by the number in the “Mg Phe/Gm Food” for that food in the reference guide.
For example, if you are serving 9 grams of a particular cereal, find the amount of Phe in 1 gram from the “mg Phe/gm food” column in your reference guide. If the amount is 3.5 mg Phe/gm of food, you would have:

9 grams of this cereal x 3.5 = 31.5 grams of Phe

How do I convert grams of protein into milligrams of Phe?
To convert grams of protein into milligrams of PHE, always multiply the number of grams by 50. So, for example, if a serving size has 1.5 grams of protein, you can do the following calculation:

1.5g protein x 50 = 75mg Phe

Use a calculator, if you need to, to make sure you are getting an accurate count every time.

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Measuring portions

To measure portions using measuring cups or spoons, you will need the cups or spoons and a calculator. This may be slightly more difficult than using weight.

1. First, you will need to convert any fractions to decimals. To do this, divide the number on the top of the fraction by the number on the bottom. For example, for ¼, \( 1 \div 4 = 0.25 \). Or ¾ is \( 3 \div 4 = 0.75 \).
2. Divide the portion size of the serving you are using by the number you will find in the “Measurement” section of your food reference guide.
3. Multiply this number by the number in “Phe mg” column of your food reference guide. This will give you the amount of Phe in the serving you are using.

For example, you want to serve ½ cup of a particular cereal, but the cereal is listed using ¾ cup.

1. \( 1 \div 2 = 0.5 \) is your serving. \( 3 \div 4 = 0.75 \) is the serving size listed.
2. Divide your serving by the serving listed. \( 0.5 \div 0.75 = 0.66 \)
3. Multiply 0.66 by the number in the “Phe mg” from the food reference guide.
   If it is 45 mg Phe, it would be:

\[
0.66 \times 45 = 30 \text{ mg Phe}
\]

If you are unable to obtain the amount of Phe in a food or beverage, it is possible to estimate how much Phe it contains by the serving size and nutrition information on a food label (see example of a food label below). Commit to memory that 1 gram of protein contains about 50 milligrams of Phe. If you multiply the number of grams of protein by 50 you can get a rough estimate of how much Phe is contained in that food or beverage\(^{12}\). Remember, this is only an estimate and is not as exact for calculating Phe content. Sometimes food manufacturing companies may be able to give you additional nutrition information or call your dietitian to see if they are able to find more information on a particular food.

1 gram of protein = 50 mg Phe

For example, if the food has 4 grams of protein, multiply it by 50 to get 200 milligrams Phe.

\[
4 \text{ g of protein} \times 50 \times \text{(number of mg Phe in each g of protein)} = 200 \text{ mg Phe}
\]

Method 2: Counting Exchanges of Phe

Keeping track of Phe intake by counting exchanges was developed to help make the process of calculating your intake easier. Phe exchanges are values assigned to a food item for easy reference. Exchanges can be found in most food reference guides and make use of decimals rather than percentages to make calculations easier. Counting exchanges is not as detailed and accurate as counting Phe by milligrams, but counting by exchanges is based on:

\[ 1 \text{ g protein} = 50 \text{ mg Phe} \]
\[ 1 \text{ exchange} = 15 \text{ mg Phe} \]
\[ 1 \text{ g protein} = 3.5 \text{ exchanges} \]

If you are using the same measurement as in the book you are using, it is easy to just record the number of exchanges listed. If you are not using the same amount, you will need to measure the milligrams of Phe using method 1. For example, if you measure the food and determine that there is 45 mgs of Phe, you would divide 45 mgs of Phe by 15 (the milligrams of Phe in 1 exchange) to determine that the food you are preparing has 3 exchanges.

If you know that you or your child can have 20 exchanges of Phe per day, that means you or your child can have 300 mgs of Phe per day. Rather than counting to 300 every day, you just have to get to 20!

Method 3: Counting Grams (g) of Protein

Counting grams of protein is generally used for people with a higher Phe and protein tolerance. A “Nutrition Facts” label is required for most packaged foods in the United States. For people with PKU, the most important nutrition facts listed are serving size (by grams or pieces) and protein (grams) based on the serving size listed. Before eating any packaged food, check the Nutrition Facts label to see how much protein is in each serving, and weigh or count out your serving to make sure that you are only eating the amount of protein you have planned for that snack or meal.

While this may not be the most accurate way to keep track of the amount of Phe you consume, counting grams of protein might be the easiest way for you to become accustomed to a low protein diet.

Be aware that Nutrition Facts labels aren’t always exact. Due to the food labeling laws, items that say, “Protein 0g” may actually contain up to 0.49 grams of protein per serving. If a label says that one serving of a given food item has 1 gram of protein, it can have anywhere from 0.50 to 1.49 grams of protein. If you do not have a PKU food list or if it is a new product and the label says “Protein 0g”, it is best to assume that it has ½ gram of protein. You can also add 0.50g to any rounded number to come up with the maximum grams of protein in each serving.

Filling Out a Diet Record

Keeping a diet record, or food log, helps you track the amount of Phe being consumed each day so that Phe intake stays within the daily limit. (A blank diet record can be found in the resources in Chapter 14). Tracking intake of food, drinks and formula will help you maintain the PKU diet and help your dietitian determine how to adjust you or your child’s diet when necessary. Your PKU team will typically ask for a diet record when you send in a blood Phe sample.

You will need to keep track of the information below. It may be helpful to add up the Phe as you go so you can see the total that has been consumed so far for that day. This will help you figure out how much more Phe can still be eaten that day to stay within the limit:

- **Date/Time:** Record Date and time the food/drink was consumed.
- **Food or Liquid Consumed:** Record the name of the food or liquid (including formula) and be specific as possible (apple vs. fruit, include brand names if possible).
- **Measured Amount Eaten:** Record specific measurements like grams, tablespoons, tea spoons, cups. If a few bites were eaten, record as “3 bites”. The amount is just as important as the type of food eaten.
- **Milligrams of Phe:** Look up the amount of Phe in your food reference guide and record the amount of Phe that is accurate to the amount of the food eaten.
- **Grams of Protein and Calories:** This is to record the amount of protein and calories that are in foods. This is to be recorded if this information is available.
- **Daily Totals:** Record the total Phe, Protein and Calories (when available) consumed that day.

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<table>
<thead>
<tr>
<th>DATE/TIME</th>
<th>FOOD OR LIQUID OFFERED</th>
<th>MEASURED AMOUNT EATEN</th>
<th>MG PHE</th>
<th>GRAMS PROTEIN</th>
<th>CALORIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/4/11 PM</td>
<td>Trix cereal 2 phenex 2</td>
<td>20 grams</td>
<td>46</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Fruit loop 1</td>
<td>1 container (1/2)</td>
<td>7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5/5 AM</td>
<td>Easy Mac n cheese</td>
<td>1 slice</td>
<td>7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>buns</td>
<td>1 tablespoon</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Lay’s chips</td>
<td>1 oz</td>
<td>93</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>apple sandwich</td>
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<td>1</td>
<td>17</td>
<td>-</td>
</tr>
<tr>
<td>5/6 AM</td>
<td>Phenex 2</td>
<td>1 ounce</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5/6 AM</td>
<td>Hot tea (nil)</td>
<td>1 cup (dry)</td>
<td>19</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Huntsmanina</td>
<td>1/4 cup</td>
<td>20</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Seeding lettuce</td>
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<tr>
<td></td>
<td>phenex 2</td>
<td>1 ounce</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**247 phe**

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New Jersey : Applied Nutrition Corp. 2007:16
Treatment and Diet Overview

Diet and Treatment During Illness

Illness such as high fevers and stomach distress, surgery, and injuries such as bone fractures will affect Phe levels. The most important steps when this happens are:

1. Treat your or your child’s illness like you normally would.
2. Formula should be continued as tolerated.
3. Continue the diet if you or your child are able to tolerate food.
4. Stay in contact with your PKU team if you have questions about the diet as it may need to be adjusted during illness.

When a person is sick, energy needs increase and the person may not take in enough calories. When this happens, the body dips into muscles for nutrients, which is called being “catabolic.” Your muscles are made up of protein, therefore they contain Phe. When you are catabolic, you break down muscle which releases Phe into your blood, causing your Phe levels to go up. This is why it is important for a person with PKU to continue to consume formula on a daily basis at regular intervals. The nutrition provided by formula will help give you or your child the energy to fight off illness and disease. It is also important to stay hydrated and consume enough calories while sick.

Frequency of Phe monitoring may also need to increase during times of illness to ensure Phe levels are not too high or too low. Call your PKU team with any questions about Phe levels when sick.

Other Treatment Options for PKU

KUVAN®

KUVAN (sapropterin, sapropterin dihydrochloride) is an FDA-approved medication that is used as a treatment method for patients with PKU who respond to sapropterin. KUVAN works by helping the phenylalanine hydroxylase (PAH) enzyme work more effectively to break down Phe in the body.

How KUVAN Works
KUVAN is the pharmaceutical form of a naturally occurring substance in the body called BH4. BH4 is a cofactor, or helper, of the PAH enzyme; it aids the PAH enzyme in the breakdown of Phe. As a medication, KUVAN supplies more BH4 to the body, which helps the PAH enzyme break down more Phe and lower Phe levels. KUVAN is not a cure, but a treatment method that, when combined with diet, can help keep Phe levels under better control.

Determining Responsiveness to KUVAN

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While KUVAN works for many, not every person with PKU is responsive to this form of treatment. This means KUVAN may not lower Phe levels for some people with PKU. When first starting KUVAN, there is a trial phase to determine responsiveness; this can last two to four weeks. The trial phase requires more frequent blood sampling, a record of dietary intake, and taking KUVAN consistently every day.

When determining whether an individual responds to KUVAN, there are a few criteria that are used, along with a physician’s clinical judgment. These include a significant decrease in Phe levels; an increase in Phe tolerance; and or changes in behavior or mood.

There is no age limit for using KUVAN in the United States. Research has shown that KUVAN reduces Phe levels in KUVAN-responsive patients from infancy through to adulthood (Burton BK, 2011, Mar). The most common side effects of KUVAN are headache, diarrhea, nausea, and abdominal pain. These listed side effects are mild and will usually resolve after a short time.

Starting KUVAN
Ask your PKU team if you or your child would like to start KUVAN. See Chapter 14 Resources for more information about beginning KUVAN responsiveness trials.

Large Neutral Amino Acids (LNAA)

Large Neutral Amino Acids (LNAA) are a treatment option that is mostly used for adults who have difficulty in maintaining the recommended Phe levels. LNAA are considered a medical food product, and come in a powder or pill form containing certain essential amino acids (not including Phe) referred to as large neutral amino acids. LNAA mixtures contain amino acids similar to those that are found in PKU formulas, but in more concentrated amounts.

How LNAA Works
When a person with PKU consumes protein-rich foods, his or her body cannot break down most of the Phe. As a result, the bloodstream is flooded with excess Phe that is carried to the brain by “transporter cells.”

LNAA pills or powder have high concentrations of specific amino acids that compete with Phe to latch on to the transporter cells. LNAA are taken with food so that the amino acids are digested along with consumed proteins and enter the bloodstream at the same time as Phe from foods. As LNAA flood the bloodstream with a large number of “safe” amino acids, more of these non-harmful nutrients enter the brain, blocking much of the Phe from being transported into the brain. This process reduces the amount of Phe transported to the brain,
Treatment and Diet Overview

helping reduce the neurocognitive effects of high blood Phe levels.

The purpose of LNAA is to decrease Phe levels in the brain; patients may not necessarily see a decrease in blood Phe levels, although some do. LNAA are used in treating patients that are struggling with the PKU diet or are off diet. LNAA must be taken with each meal and protein-containing snack.

Future of PKU Research and Treatment

Over the last five years, there have been many great strides to improve treatment for PKU. Below is a brief synopsis of work being done by leading researchers to improve PKU treatment options.

Enzyme Substitution

Researchers discovered an alternate enzyme phenylalanine ammonia lyase or ‘PAL’ found in plants and bacteria that can break down Phe. On its own, this enzyme is destroyed very quickly in the body. To work, a protector (PEG), or “coater” needs to be placed around PAL to slow down the speed with which it breaks down in the body and to protect it from the body’s immune response. The result is PEG-PAL, an injectable medicine that has been shown to lower Phe levels in PKU mice. The first study of PEG-PAL in human patients with PKU began in 2008, and hopes to show a decrease in Phe levels in PKU patients. Successful Phase 1 results were reported in June 2009.

Gene and Cell Therapy

Gene therapy is an ideal treatment for PKU because it would provide functional PAH enzyme in the liver cells which could break down Phe. Unfortunately, the challenge in gene therapy has been the body’s immune response, which mounts an attack on the transferred enzymes, like it would attack a virus. While gene therapy has worked in curing PKU in mice, immunosuppressant medications have also been needed to maintain the correction. Some new techniques have shown promise though, to cause less immune response and maintain a longer correction and be safer.
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**Therapeutic Liver Repopulation**

Since liver cells in PKU patients are deficient in phenylalanine hydroxylase (PAH), therapeutic liver repopulation aims to replace the cells that are deficient in PAH (PAH negative cells) with cells that are not PAH-deficient (PAH positive cells). PAH positive cells would then restore function of the liver, curing PKU.

One of the challenges of liver repopulation is that the cells that have PAH do not grow any faster than the cells that do not have PAH. In order for this therapy to work, a method needs to be developed to make the cells with PAH grow faster. If this happens, it may be possible to increase the level of Phe breakdown to normal for individuals with PKU.\(^\text{17}\)

**Special Considerations**

**Aspartame**

"Phenylketonurics: Contains Phenylalanine" means this is likely a product a person with PKU cannot eat or drink.

People with PKU in general should not eat or drink any food or beverages containing aspartame. Aspartame is an artificial sweetener that contains Phe; it is commonly known as NutraSweet\(^\text{TM}\) and is found in diet sodas and some reduced-sugar foods and beverages. A warning for people with PKU is listed on products that contain aspartame, but you must look carefully as the warning is often printed in small type. Some sugarless gums contain aspartame in small amounts. Based on the small amount of Phe in these products some individuals are able to include this in their diet (See chapter 10 for more details on sugarless gum).

**Medications**

Sweeteners such as aspartame and aspartame-acesulphame are used in some medications, especially for children. Ask your pharmacist to make sure that medications prescribed for your child do not contain these sweeteners. In some situations it is not possible to prescribe an alternative. If you have been prescribed a medication with added aspartame or aspartame-acesulphame, you should call your pharmacist to find out how much Phe is in the medication. The amount of Phe in the medication should be counted in the daily Phe intake. Contact your PKU team if you have questions about blood testing and diet adjustments.

Other medications, including capsules made of gelatin, can be a source of Phe. When buying over-the-counter medications or picking up a prescription, always check labels or ask a pharmacist if the product contains aspartame, aspartame-acesulphame or gelatin.

**Exercise**

Regular physical activity is an important part of a healthy lifestyle. PKU does not limit the ability to participate in exercise or sports. Regular exercise may even improve the ability

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to tolerate Phe. During exercise, you can drink extra formula to keep yourself hydrated and maintain your energy level. After exercise, your body needs fluids, carbohydrate and protein to recover. Drink plenty of fluids, especially water, and eat some foods with carbohydrates, like low protein bread or pasta.

People with PKU should not consume any protein powders or supplements that promise muscle or weight gain. These supplements contain high levels of protein and will increase your blood Phe levels. Your formula acts as a “protein shake”. If you feel you may need more protein your diet, ask your dietitian to see if adjustments to your formula need to be made.

Dental Care

People with PKU may be more likely to have some tooth decay and dental erosion (when strong acids in food break down the outer layer of teeth) because their diets are more likely to include sugary foods and acidic drinks. As children with PKU do not get much protein from foods, they eat more carbohydrates and fats to give them energy and may snack more often throughout the day. In addition, medical formulas are acidic and sweetened, which means that sweet and acidic foods are coming in frequent contact with a child’s teeth.

To help prevent dental problems, you or your child can:
- Take a sip of water to rinse the mouth after drinking medical formula.
- Offer water instead of juice throughout the day.
- Use a toothpaste containing fluoride.
- Brush teeth twice each day, especially as the last thing before bed at night (avoid snacks or drinks after brushing).
- Schedule regular check-ups with a dentist from an early age, and let the dentist know about you or your child’s PKU.