Vitamin supplementation is now recognized as an important part of prenatal nutrition. Prenatal vitamins are indicated as a supplement to improve the nutritional status of women throughout pregnancy and in the postnatal period. Research has suggested that prenatal supplementation can help reduce the risk of various pregnancy complications such as pre-eclampsia, maternal anemia, and congenital malformations.

Pregnant women have increased nutrient requirements to support adequate nutrition for fetal growth and development in addition to maternal metabolism. Table 1 provides a summary of dietary reference intakes during pregnancy recommended by the Food and Nutrition Board, Institute of Medicine (IOM), and the National Academy of Sciences. Since it can be more difficult for pregnant women to choose a diet that meets the increased nutrient requirements, vitamins are often recommended as a supplement.

Prenatal supplements contain a variety of vitamins and minerals. According to the IOM and the American College of Obstetricians and Gynecologists (ACOG), specific focus should be placed on adequate supplementation of the following:

- **Folic Acid**: Folic acid helps to produce and maintain new cells, and it is important during the embryonic and fetal periods when rapid cell division and growth are occurring. Research and clinical studies have demonstrated that increasing folic acid concentrations pre-conception and during pregnancy can reduce birth defects such as neural tube defects (e.g., spina bifida) and possibly other congenital abnormalities. The first 28 days after conception pose the highest risk for the development of neural tube defect. Therefore, it is imperative that folic acid supplementation be initiated prior to conception. The IOM recommends that women consume 400 mcg/day of folic acid at least three months before conception. Supplementation should increase to 600 mcg/day once the woman is pregnant. According to ACOG, women who have a family history or who have had a child with a neural defect should consume higher doses of folic acid. Since they have an increased risk of having a child with this problem up to 4 mg/day of folic acid is recommended. Supplementation of up to 4 mg/day should begin one month before conception and during the first three months of pregnancy.

- **Iron**: Iron deficiency anemia is a common complication in pregnancy. Sufficient iron helps both the mother and baby’s blood carry oxygen. Research suggests iron supplementation can decrease the risk of preterm delivery and low birth weight infants.
• The IOM and ACOG recommend a daily allowance of 27 mg of iron. Iron has various dietary sources, but it is very inefficiently absorbed in the gut. Therefore, in most cases well balanced diets do not provide sufficient iron, and supplementation is required to maintain the recommended daily allowance.

• Calcium: Calcium is the main mineral necessary for bone health. Increased levels of calcium are required during pregnancy for the construction of fetal tissues and the maintenance of the maternal bone density. Most prenatal vitamins only contain 200-300 mg of the 1000 mg/day of elemental calcium suggested by the IOM and ACOG. Vitamin supplements contain less than the recommended amount due to the constipating effects of calcium. The IOM and ACOG suggest the remaining calcium be provided through a well balanced diet. Docosahexaenoic acid (DHA) is a long chain omega-3 fatty acid. Suggested health benefits of DHA supplementation include increased birth weight, prevention of preterm birth, and decreased risk of pre-eclampsia. Benefit outcomes of DHA in clinical trials and research are conflicting. Therefore, there is limited scientific evidence supporting maternal DHA supplementation.

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### Nutritional Recommendations

**Nutrient** | **Benefit** | **Natural Sources** | **IOM Nutritional Recommendations**
--- | --- | --- | ---
Vitamin A† | Maintenance of visual function | Green leafy vegetables and yellow-orange vegetables. | 770 mcg/day (Note: Doses greater than 15,000 IU/day are associated with an increased risk for birth defects, although most prenatal vitamins contain alpha carotene, a vitamin A precursor that is not teratogenic.)

Vitamin B-1 (Thiamine) † | Involved in the release of energy from cells. | Milk and raw grains. | 1.4 mg/day

Vitamin B-2† (Riboflavin) | Involved in the release of energy from cells. | Green vegetables, milk, eggs, cheese, and fish. | 1.4 mg/day

Vitamin B-6† (Pyridoxine) | Important in protein, carbohydrate, and lipid metabolism. | Found mostly in vegetables. | 1.9 mcg/day

Vitamin B-12† | Essential for DNA synthesis and cell division. | Found in animal proteins. B-12 deficiency most commonly occurs secondary to intestinal malfunction and in strict vegan diets. | 2.6 mcg/day

Vitamin C† (Ascorbic acid) | Reduces free radicals and assists in procollagen formation. | Found in fruits and vegetables. | 85 mcg/day

Vitamin D† | Assists in the development of tooth enamel. | Found in fortified milk. Exposure to ultraviolet light is necessary for vitamin conversion. | 5 mcg/day

Vitamin E† | Provides antioxidant properties. | Found in animal protein and fats. | 15 mcg/day

Vitamin K† | Required for synthesis of clotting factors VII, IX, and X. | Found in green leafy vegetables, tomatoes, dairy products, and eggs. | 90 mcg/day

(continued on page 3)
Safety Alerts:

Ongoing Safety Review for Singular®:
The FDA is investigating the possible link between the use of Singular® and behavior/mood changes, suicidal thoughts/behavior, and suicide. This investigation may take the FDA up to nine months to complete before providing the public any conclusions and recommendations. Singular is indicated to treat asthma, the symptoms of allergic rhinitis, and to prevent exercise-induced asthma. Over the last year the makers of Singular have updated the package insert to include information on the following adverse events seen in post-marketing reports: tremors, depression, suicidality, and anxiety. Patients are advised not to stop taking Singular over the last year the makers of Singular have updated the package insert to include information on the following adverse events seen in post-marketing reports: tremors, depression, suicidality, and anxiety. Patients are advised not to stop taking Singular before talking to their doctors concerning any questions they might have. In addition, health care professionals and caregivers should monitor any patients on Singular for any changes in behavior, mood, or the development of suicidal thoughts/behavior.

Revised Product Labeling for Prezista®:
The manufacturer of Prezista® has updated the package insert in conjunction with the FDA’s updated package insert and added to the warning section information concerning the risk of hepatotoxicity. There have been reports from clinical trials and post-marketing experience of drug-induced hepatitis in patients who are receiving Prezista in combination with ritonavir. Those patients who seem to be at an increased risk for hepatotoxicity are those with pre-existing liver dysfunction, including chronic active hepatitis B or C. The updated package insert now reads in part that “If there is evidence of new or worsening liver dysfunction in patients on Prezista and ritonavir, interruption or discontinuation of treatment may be considered.” In response, it is recommended to conduct appropriate laboratory tests prior to initiating therapy with Prezista/ritonavir, and patients should have continued monitoring during treatment. Patients with underlying chronic hepatitis, cirrhosis, or in patients who have pretreatment elevations of transaminases should have increased AST/ALT monitoring during the first several months of treatment. In addition, both the adverse reaction section and the patient medication information have been updated to include this new information.

Tysabri® Label Revision:
The manufacturer of Tysabri® has updated the Tysabri® Label Revision: The manufacturer of Tysabri® has updated the warning section concerning the possible link between use of Tysabri® and behavior/mood changes, suicidal thoughts/behavior, and suicide. This investigation may take the FDA up to nine months to complete before providing the public any conclusions and recommendations. Tysabri is indicated to treat MS, and is used to prevent attacks and recommendations. Tysabri is indicated to treat MS, and is used to prevent attacks and to slow the progression of disease in patients with relapsing-remitting MS who have active disease at the time of treatment, and in patients who have had one or more attacks in the previous two years. In addition, health care professionals and caregivers should monitor any patients on Tysabri for any changes in behavior, mood, or the development of suicidal thoughts/behavior. Patients are advised not to stop taking Tysabri before talking to their doctors concerning any questions they might have. In addition, health care professionals and caregivers should monitor any patients on Tysabri for any changes in behavior, mood, or the development of suicidal thoughts/behavior.

A Recall Issued for Neupro®:
The manufacturer of Neupro® began recalling the product at the end of April 2008. It is no longer available in the United States. Neupro is being recalled due to the formation of crystals in the patches. The formation of these crystals causes less of the drug to be available for absorption through the skin which could possibly affect the efficacy of the medication. Patients currently taking Neupro should not be immediately taken off of the medications, but begin a gradual down-titration per the package insert. The manufacturer of Neupro requests that no new patients begin treatment with Neupro.

Ongoing Safety Review for Botulinum Toxin Type A:
The FDA released an early communication about an “ongoing safety review” for Botox and Botox Cosmetic (Botulinum toxins types A and Myobloc (Botulinum toxins type B). The release stated that reports of been received of adverse reactions following the use of both Botulinum toxins type A and B for both FDA-approved and non-FDA approved indications. The reported reactions are suggestive of botulism, which can occur after the botulinum toxin is given and spreads throughout the body beyond the site of injection. In the most serious cases patients have been hospitalized and/or died. These occurred mostly in children treated for cerebral palsy associated limb spasticity. However these serious adverse reactions also have been reported following treatment of patients with a wide variety of conditions using a wide variety of doses. Until the review is completed by the FDA, health care professionals using a botulinum toxin product are advised to:
1. Understand that the potency determinations expressed in “Units” or “U” are different among the botulinum toxin. The clinical doses expressed in units are not comparable between botulinum toxin products.

Folic Acid†: Important for DNA synthesis and cell replication. Found in fortified grains, dried beans, and leafy greens. 600 mcg/day
Niacin†: Involved in the release of energy from cells. Found in poultry, fish, and nuts. 18 mg/day
Iron†: Essential to the production of hemoglobin. Dietary sources include animal protein, dried beans, fortified grains, and any food cooked in cast iron cookware. 27 mg/day
Calcium†: Construction of fetal tissues, especially in the third trimester. Found in dairy products and leafy green vegetables such as collard, kale, turnip, and mustard greens. Vitamin D is required for calcium absorption. 1,000 mg/day
Phosphorous†: Required for bone formation. Well balanced diet. 700 mg/day
Zinc†: Involved in nucleic acid and protein metabolism. Well balanced diet. 11 mg/day

* Recommendations may vary for different subgroups (e.g. vegetarians, teen age mothers, and low income mothers).
† A well balanced diet can provide the recommended daily allowance.
‡ The average diet does not provide sufficient levels and therefore vitamin supplementation is recommended. Although most women are advised to start a prenatal vitamin when they become pregnant and to continue during the postpartum period, prenatal vitamins are not a substitute for lifestyle changes. Women should stop smoking, stop alcohol use, and change bad eating habits prior to conception. Proper prenatal nutrition (diet and prenatal vitamins) and lifestyle modifications (altering eating habits and starting a low impact exercise regimen) can decrease the risk of complications during pregnancy and promote overall good health for the mother and the baby.

References

(continued on page 7)
# Formulary Update: Additions to the Keystone Mercy Drug Formulary

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<tr>
<th>Drug</th>
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<tr>
<td>Allegra® Oral Suspension (Step Therapy Requirement)</td>
<td>Relief of seasonal allergic rhinitis symptoms in children 2 to 11 years old.</td>
<td>30 mg twice daily (Refer to package insert for specific dosing recommendations for children less than 2 years old and for renal impairment.)</td>
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<td>Cetirizine OTC Chewable Tablets</td>
<td>Relief of indoor and outdoor allergy symptoms in children ≥ 6 years old and adults.</td>
<td>1 tablet twice daily (Refer to package insert for oral and hepatic impairment listing recommendations)</td>
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<td>Cetirizine HCl/ pseudoephedrine 12 Hour OTC</td>
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<td>200 mg twice daily following a meal.</td>
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<td>Lotrimin Ultra® (OTC)</td>
<td>Treatment of fungal infections in children &gt; 12 years old and adults.</td>
<td>Tina Caps/Tina Cruns: Apply topically once daily for 2 weeks.</td>
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<td>Tina Pedis: Apply topically to affected area twice daily for 1 week or once daily for 4 weeks</td>
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<td>Renuvela®</td>
<td>For the control of serum phosphorus in patients with chronic renal disease on dialysis.</td>
<td>1-2 tablets three times daily with meals.</td>
<td>800 mg</td>
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<td>30 mg once daily in the morning for patients either starting treatment for the first time or switching from another medication.</td>
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**Product Updates:**

Please be aware the information discussed in this section is to provide the reader with product updates only. It is not indicative of what is currently or will be on Keystone Mercy’s formulary.

**Intalence™ (etravirine)** is a human immunodeficiency virus type 1 (HIV-1) specific, non-nucleoside reverse transcriptase inhibitor (NNRTI). It is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced adult patients, who have evidence of viral replication and HIV-1 strains resistant to a NNRTI and other antiretroviral agents. The safety and efficacy of Intalence has not been established in treatment-naive or pediatric patients. Intalence should not be prescribed in patients who have experienced virologic failure on a regimen containing a NNRTI. It also should not be used in combination with only nucleotide reverse transcriptase inhibitors (NtRTIs). Refer to package insert for a complete list of drug interactions and/or appropriate dosing changes. Dosing of Intalence does not need to be adjusted due to renal or mild to moderate hepatic impairment (Child Pugh Class A and B).

The recommended dose of Intalence is 200 mg (two 100 mg tablets) taken twice daily following a meal. For patients who have difficulty swallowing, Intalence tablets are dispersible in water. The most commonly reported adverse effects (>10%) during clinical trials were rash and nausea. Intalence is available in 100 mg tablets.

**Pristiq® (desvenlafaxine)** is an extended release serotonin-norepinephrine reuptake inhibitor (SNRI). It is the major active metabolite of the antidepressant venlafaxine. It is indicated for the treatment of major depressive disorder (MDD) in adults. The recommended dose is 50 mg once daily without food. There is no evidence that doses above 50 mg/day provided any additional benefit. Please refer to full prescribing information for dose adjustments due to moderate or severe renal impairment (CrCl < 30 – 50 ml/min). No dose adjustment is necessary in patients with hepatic impairment. Pristiq is not approved for use in pediatric patients. This medication does have a black box warning regarding increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants for MDD and other psychiatric disorders. Common side effects (>5%) reported in clinical trials were nausea, dizziness, insomnia, hyperhidrosis, constipation, somnolence, decreased appetite, anxiety and specific male sexual function disorders. Pristiq can also cause some serious side effects such as hypertension, abnormal bleeding, glaucoma, hyponatraemia, and cholesterol and triglyceride elevations. Pristiq is used concomitantly with a monoamine oxidase inhibitor (MAOI) or within 14 days of stopping a MAOI is contraindicated due to risk of serious drug interactions. The Medication Guide for Pristiq must be provided to patients with each prescription. Pristiq is available in 50 mg and 100 mg tablets.

**Rotarix®** is an oral live-attenuated human rotavirus vaccine. Rotarix is indicated for the prevention of rotavirus gastroenteritis caused by G1 and non-G1 types (G3, G4, and G9). It is administered as a two-dose series in infants beginning at six weeks of age and should be completed by 24 weeks of age. Refer to the package insert for complete administration schedule. Rotarix is contraindicated in patients with a history of uncorrected congenital malformation of the gastrointestinal tract (such as Meckel’s diverticulum) that would predispose the infant to intussusception. Administration of Rotarix should be delayed in infants suffering from acute diarrhea or vomiting. In clinical trials, co-administration with other vaccines (e.g. Pediarix® and U.S. licensed Hib conjugate vaccine) showed no evidence of interference to any of the antigens as compared with separate administration. Immunosuppressive therapies may reduce response to Rotarix. The most common side effects (>5%) reported during the first week of receiving the vaccine were fussiness, irritability, cough, runny nose, fever, loss of appetite, and vomiting. Rotarix is available as a vial of lyophilized vaccine to be reconstituted with a liquid diluent in a prefilled oral applicator. The dropper used to administer the vaccine contains latex.

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- Important for DNA synthesis and cell replication.
- Found in fortified grains, dried beans, and leafy greens.
- 600 mcg/day

**Niacin**
- Involved in the release of energy from cells.
- Found in poultry, fish, and nuts.
- 18 mg/day

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- Essential to the production of hemoglobin.
- Dietary sources include animal protein, dried beans, fortified grains, and any food cooked in cast iron cookware.
- 27 mg/day

**Calcium**
- Construction of fetal tissues, especially in the third trimester.
- Found in dairy products and leafy green vegetables such as collard, kale, turnip, and mustard greens. Vitamin D is required for calcium absorption.
- 1,000 mg/day

**Phosphorus**
- Required for bone formation.
- Well balanced diet.
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- Involved in nucleic acid and protein metabolism.
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† A well balanced diet can provide the recommended daily allowance.
‡ The average diet does not provide sufficient levels and therefore vitamin supplementation is recommended.

Although most women are advised to start a prenatal vitamin when they become pregnant and to continue during the postpartum period, prenatal vitamins are not a substitute for lifestyle changes. Women should stop smoking, stop alcohol use, and change bad eating habits prior to conception. Proper prenatal nutrition (diet and prenatal vitamins) and lifestyle modifications (altering eating habits and starting a low impact exercise regimen) can decrease the risk of complications during pregnancy and promote overall good health for the mother and the baby.
prenatal vitamin DHA supplementation. Therefore, the IOM, the ACOG and the National Research Council do not recommend DHA supplementation. Women can get DHA from various natural food sources (e.g. salmon, DHA enriched eggs, walnuts, and canola oil). Therefore, the IOM, the ACOG and the National Research Council do not recommend prenatal vitamin DHA supplementation.

Docosahexaenoic acid (DHA) is a long chain omega-3 fatty acid. Suggested health benefits of DHA supplementation include increased birth weight, prevention of preterm birth, and decreased risk of pre-eclampsia. Benefit outcomes of DHA in clinical trials and research are conflicting. Therefore, there is limited scientific evidence supporting maternal DHA supplementation. Women can get DHA from various natural food sources (e.g. salmon, DHA enriched eggs, walnuts, and canola oil). Therefore, the IOM, the ACOG and the National Research Council do not recommend prenatal vitamin DHA supplementation.

Highlights:
2. Be aware of the possibility of serious systemic adverse reactions following treatment with a botulinum toxin product. These systemic adverse events include: dysphagia, dysphonia, weakness, dyspnoea, and/or respiratory distress.
3. Understand that serious adverse effects can occur anywhere from one day to several weeks after treatment with a botulinum toxin product.
4. Provide the patient and/or caregiver information they will need to identify the signs or symptoms of an adverse reaction to a botulinum toxin product.
5. Inform the patient and/or caregiver at any point if he/she is having worsening or unexpected difficulty swallowing or talking, trouble breathing, or muscle weakness to immediately seek medical attention.

References

Mandatory “90-Day Supply” Generic Drug Program

This program requires that participating network pharmacies dispense a 90 day supply of specifically identified generic drugs. The drugs included in this program have been identified as chronic/maintenance drugs that are safe and more cost-effective when dispensed in larger quantities.

Highlights:
✓ The member will not be given a 90-day supply when a medication is initially prescribed. The member will continue to receive a 30-day supply, or less if prescribed by the physician, initially in order to insure that the drug is tolerated and effective.
✓ The network pharmacy will be required to dispense a 90-day supply of the specified generic maintenance medications.
✓ Medications included on the list are drugs that can easily, safely, and cost effectively be dispensed in 90-day quantities.
✓ Controlled Substances will not be included in this program.
✓ The member will receive the 90-day supply of the specified generic drugs for a single co-payment if applicable.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Benefit</th>
<th>Natural Sources</th>
<th>IOM Nutritional Recommendations*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A†</td>
<td>Maintenance of visual function.</td>
<td>Green leafy vegetables and yellow/orange vegetables.</td>
<td>770 mcg/day Note: Doses greater than 15,000 IU/day are associated with an increased risk for birth defects, although most prenatal vitamins contain alpha carotene, a vitamin A precursor that is not teratogenic.</td>
</tr>
<tr>
<td>Vitamin B-1 (Thiamine) †</td>
<td>Involved in the release of energy from cells.</td>
<td>Milk and raw grains.</td>
<td>1.4 mg/day</td>
</tr>
<tr>
<td>Vitamin B-2† (Riboflavin)</td>
<td>Involved in the release of energy from cells.</td>
<td>Green vegetables, milk, eggs, cheese, and fish.</td>
<td>1.4 mg/day</td>
</tr>
<tr>
<td>Vitamin B-6† (Pyridoxine)</td>
<td>Important in protein, carbohydrate, and lipid metabolism.</td>
<td>Found mostly in vegetables.</td>
<td>1.9 mcg/day</td>
</tr>
<tr>
<td>Vitamin B-12‡</td>
<td>Essential for DNA synthesis and cell division.</td>
<td>Found in animal proteins. B-12 deficiency most commonly occurs secondary to intestinal malabsorption and in strict vegan diets.</td>
<td>2.6 mcg/day</td>
</tr>
<tr>
<td>Vitamin C† (Ascorbic acid)</td>
<td>Reduces free radicals and assists in procollagen formation.</td>
<td>Found in fruits and vegetables.</td>
<td>85 mg/day</td>
</tr>
<tr>
<td>Vitamin D†</td>
<td>Assists in the development of tooth enamel.</td>
<td>Found in fortified milk. Exposure to ultraviolet light is necessary for vitamin conversion.</td>
<td>5 mcg/day</td>
</tr>
<tr>
<td>Vitamin E†</td>
<td>Provides antioxidant properties.</td>
<td>Found in animal protein and fats.</td>
<td>15 mcg/day</td>
</tr>
<tr>
<td>Vitamin K†</td>
<td>Required for synthesis of clotting factors VII, IX, and X.</td>
<td>Found in green leafy vegetables, tomatoes, dairy products, and eggs.</td>
<td>90 mcg/day</td>
</tr>
</tbody>
</table>

(continued on page 3)
Prenatal Vitamin Supplementation

Vitamin supplementation is now recognized as an important part of prenatal nutrition. Prenatal vitamins are indicated as a supplement to improve the nutritional status of women throughout pregnancy and in the postnatal period. Research has suggested that prenatal supplementation can help reduce the risk of various pregnancy complications such as pre-eclampsia, maternal anemia, and congenital malformations.

Pregnant women have increased nutrient requirements to support adequate nutrition for fetal growth and development in addition to maternal metabolism. Table 1 provides a summary of dietary reference intakes during pregnancy recommended by the Food and Nutrition Board, Institute of Medicine (IOM), and the National Academy of Sciences. Since it can be more difficult for pregnant women to choose a diet that meets the increased nutrient requirements, vitamins are often recommended as a supplement.

Prenatal supplements contain a variety of vitamins and minerals. According to the IOM and the American College of Obstetricians and Gynecologists (ACOG), specific focus should be placed on adequate supplementation of the following:

- **Folic Acid:** Folic acid helps to produce and maintain new cells, and it is important during the embryonic and fetal periods when rapid cell division and growth are occurring. Research and clinical studies have demonstrated that increasing folic acid concentrations pre-conception and during pregnancy can reduce birth defects such as neural tube defects (e.g., spina bifida) and possibly other congenital abnormalities. The first 28 days after conception pose the highest risk for the development of neural tube defect. Therefore, it is imperative that folic acid supplementation be initiated prior to conception. The IOM recommends that women consume 400 mcg/day of folic acid at least three months before conception. Supplementation should increase to 600 mcg/day once the woman is pregnant. According to ACOG, women who have a family history or who have had a child with a neural defect should consume higher doses of folic acid. Since they have an increased risk of having a child with this problem up to 4 mg/day of folic acid is recommended. Supplementation of up to 4 mg/day should begin one month before conception and during the first three months of pregnancy.

- **Iron:** Iron deficiency anemia is a common complication in pregnancy. Sufficient iron helps both the mother and baby’s blood carry oxygen. Research suggests iron supplementation can decrease the risk of preterm delivery and low birth weight infants.

(continued on page 2)