



Indiana Medicaid Therapeutics Committee **Therapeutic Class Review Summary**

Therapeutic Class:

Prenatal Vitamins

Overview:

Prenatal Vitamins are specially formulated supplements containing numerous vitamins and minerals including folic acid, iron, and calcium. Prenatal vitamins are recommended during pregnancy to supplement any nutritional deficiencies in the diet of the mother, as deficiencies of specific supplements can lead to birth defects, preterm delivery, and low birth rate. Additionally, there is increasing evidence that maternal under nutrition in pregnancy can lead to developmental delays and behavioral disturbances, as well as other health consequences in adult life. In 1973, the United States Food and Drug Administration (FDA) established recommended daily allowances (RDA) to be used as a reference for use in nutritional labeling, and to provide a standard for amounts of specific vitamins and minerals that are needed each day.

Folic acid, also known as Vitamin B9, is important in preventing neural tube defects (NTD), which develop in the first 28 days after conception, and should ideally be taken during the month before conception, and for the first month of pregnancy. Available evidence indicates that 0.4mg (400mcg) per day of folic acid will reduce the number of cases of NTDs, and as a result, the United States Public Health Service recommends that all women of childbearing age including women who have had a previous NTD-affected pregnancy should consume 0.4mg of folic acid per day for the purpose of reducing their risk. Because the effects of high intakes of folic acid are not well known but include complicating the diagnosis of vitamin B12 deficiency, total folate consumption should be $\leq 1\text{mg}$ per day, except under the supervision of a physician. Prenatal vitamins containing 1mg of folic acid are available by prescription only whereas those containing $\leq 0.8\text{mg}$ are available over-the-counter (OTC).

Iron deficiency is the most common known form of nutritional deficiency; particularly in women of childbearing age and during pregnancy. In pregnant women, iron deficiency increases the risk of preterm delivery, low birth weight, and perinatal mortality, and in children can lead to development delays and behavioral disturbances. There also may be an association between maternal iron deficiency anemia and postpartum depression. The recommended daily allowance (RDA) of iron is 27mg per day, but the typical diet and endogenous iron stores are insufficient sources for the increased iron requirements during pregnancy. Both the American College of Obstetricians and Gynecologists (ACOG) and The Centers for Disease Control (CDC) recommend universal iron supplementation to meet the iron requirements of pregnancy.

Calcium needs also increase during pregnancy, and numerous studies have shown that calcium supplementation can reduce the incidence of pregnancy induced hypertension. A recent analysis in the *Journal of the American Medical Association (JAMA)* reports that calcium supplements lower the risk of hypertension caused by pregnancy by 70%, as well as the risk of preeclampsia by over 60%. Women typically consume less than 600mg/day of calcium in their diet, and it is recommended that during pregnancy they ingest at least 1500 mg/day. Unfortunately, most prenatal vitamin formulations only contain 200 to 300mg of calcium; therefore, additional supplementation would be needed.

Other vitamins and minerals often requiring supplementation during pregnancy include vitamin A, vitamin B6, vitamin B12, vitamin D, choline, iodine, magnesium, selenium, and zinc. Vitamin A is an essential nutrient for normal cellular function including reproduction and development, but taken in excess before or during pregnancy may increase the risk of congenital abnormalities, except in the form of beta-carotene, which has not been associated with toxicity in animals or humans. Vitamin B6 (pyridoxine) is important for the production of protein for new cells, bolstering the immune system, and participating in red blood cell formation. Pyridoxine has also demonstrated both significantly lower nausea scores and fewer vomiting episodes in clinical trials of women with severe pregnancy-induced nausea. Vitamin B12 (cyanocobalamin) assists in red blood cell production and helps the body use fat and carbohydrates for energy. Vitamin D promotes calcium absorption from food and its deposition into the bones and teeth of the mother and the fetus. Studies have shown that vitamin D deficiency during pregnancy may adversely effect fetal growth, bone ossification, tooth enamel formation, and neonatal calcium homeostasis. Choline helps prevent neural tube defects and enhances brain development. Iodine is an essential mineral needed for proper thyroid function, and a maternal iodine deficiency can cause significant irreversible mental retardation in the fetus. Magnesium levels decrease during pregnancy, and there is evidence of magnesium disturbance in women who later develop pre-eclampsia. Newborns from a selenium deficient mother can suffer from muscular weakness, and selenium deficiency in humans has also been implicated as a risk factor for pregnancy loss. Zinc is essential for cell growth and repair, energy production, and brain development, and low maternal levels have been associated with low birth weights.

Docosahexaenoic acid (DHA), a long chain omega-3 fatty acid accrues rapidly in the human brain from about 26 weeks gestation until the age of 2 years, and is also a component of the retina. The mother is the primary source of DHA for the fetus, and epidemiologic evidence suggests consumption of DHA during pregnancy increases birth weight, prevents preterm birth, and decreases risk of pre-eclampsia. Despite this evidence, randomized clinical trials do not support DHA for this use; however, they do show a correlation between newborn DHA levels and newborn brain maturity and infant visual maturation. There is not enough scientific evidence to determine an RDA for DHA in pregnancy, but 300mg per day is assumed to meet or exceed needs.

Prenatal vitamins are indicated for use in improving the nutritional status of women throughout pregnancy and in the post-natal period for both lactating and nonlactating

mothers. Prenatal vitamins are also beneficial in improving the nutritional status of women prior to conception. Numerous prenatal vitamins are commercially available with varying amounts and combinations of vitamins, minerals, and other agents to meet the needs of individual women. Premesis Rx, CombiRx, and Folbecal include 75mg of pyridoxine as a sustained-release preparation and have the additional indication for use in conjunction with a physician prescribed regimen to minimize pregnancy-related nausea. Neevo and Neevo DHA contain L-methylfolate, the biologically active isomer of folate, and have additional indications for patients with high risk pregnancies, older OB patients, and patients unable to fully metabolize folic acid. Several products, including Duet DHA, CitraNatal DHA, and Primacare contain DHA, or DHA plus eicosapentanoic acid (EPA). Products such as Poly-Iron 150 Forte, Prenatal U, and Vinate GT contain more than the recommended 27mg of iron. A number of products including Prenacare, Prenatal AD, Vinate Calcium, and Vinate GT contain the stool softener docusate sodium. The vast majority of prenatal vitamin formulations contain vitamins B1, B2, B6, B12, C, D, and E, calcium, folic acid, niacinamide, and zinc.

Name	Rx / OTC	Generic/Brand	Manufacturer
A-Free Prenatal	OTC	G	Freedra
Advanced Care Plus	Rx	G	Trigen
Aminate Fe	Rx	G	Amide
Cavan Prenatal	Rx	G	Seton
CitraNatal [®] 90 DHA	Rx	G	Mission
CitraNatal [®] Assure	Rx	G	Mission
CitraNatal [®] DHA	Rx	G	Mission
CitraNatal [®] Rx	Rx	G	Mission
Complete-RF Prenatal	Rx	G	Trigen
CompleteNate Chewable	Rx	G	Trigen
Duet [®]	Rx	B	Xanodyne
Duet [®] Chewable	Rx	B	Xanodyne
Duet [®] DHA	Rx	B	Xanodyne
Duet [®] DHA EC	Rx	B	Xanodyne
Duet [®] Stuart Prenatal	OTC	B	Xanodyne
Fe C Plus	Rx	G	Boca
Femtabs [®]	Rx	B	Azur/Pharmelle
Finest Prenatal Complete	OTC	G	Walgreens
Folbecal	Rx	G	Breckenridge
Foltabs Prenatal	Rx	G	Midlothian
Foltabs Prenatal Plus DHA	Rx	G	Midlothian
Foltabs 90 Plus DHA	Rx	G	Midlothian
Gesticare	Rx	B	Azur/Pharmelle
Gesticare DHA	Rx	B	Azur/Pharmelle
Gold Seal Prenatal	OTC	G	Walgreens
iNatal Advance Tablet	Rx	G	Nnodum
ICAR-C Plus SR	Rx	G	Hawthorn
KPN Prenatal	OTC	G	Freedra
Lactocal-F	Rx	B	Laser
NataChew [™]	Rx	G	Warner-Chilcott
Natafort	Rx	B	Warner-Chilcott



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*Therapeutics Class Review Summary of
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Name	Rx / OTC	Generic/Brand	Manufacturer
Natelle®	Rx	B	Azur/Pharmelle
Natelle® -C	Rx	B	Azur/Pharmelle
Natelle® -EZ	Rx	B	Azur/Pharmelle
Natelle® Plus	Rx	B	Azur/Pharmelle
Natelle® Prefer	Rx	B	Azur/Pharmelle
Neevo®	Rx	G	Pamlab
Neevo® DHA	Rx	G	Pamlab
Novanatal™	Rx	B	Pharmelle
Novastart™	Rx	B	Azur/Pharmelle
OB Complete	Rx	B	Vertical
OB Complete w/DHA	Rx	B	Vertical
OB-Natal® ONE	Rx	G	Lannett
Obtrex DHA	Rx	B	Pronova
O-Cal Prenatal	Rx	G	Pharmics
Poly-Iron 150 Forte	Rx	G	Cypress
Precare Chewables	Rx	B	Ther-Rx
Precare Conceive	Rx	B	Ther-Rx
Precare Premier	Rx	B	Ther-Rx
Prefera OB	Rx	G	Alaven
Premesis Rx	Rx	B	Ther-Rx
PrenaCare	Rx	G	Cypress
Prenafirst	Rx	G	Cypress
PrenaPlus	Rx	G	Cypress
Prenatabs FA	Rx	G	Cypress
Prenatabs Rx	Rx	G	Cypress
Prenatal 19	Rx	G	Cypress
Prenatal 19 Chewable	Rx	G	Cypress
Prenatal AD	Rx	G	Cypress
Prenatal Plus	Rx	G	Amneal
Prenatal S	OTC	G	Ivax
Prenatal Tablet	OTC	G	Major
Prenatal U	Rx	G	Cypress
Prenate DHA	Rx	B	Sciele
Prenate Elite	Rx	B	Sciele
Prenavite	OTC	G	Rugby
Prenavite Protein	OTC	G	Rugby
PreNexa	Rx	G	Upsher-Smith
Primacare	Rx	B	Ther-Rx
Primacare Advantage	Rx	B	Ther-Rx
Primacare One	Rx	B	Ther-Rx
RE OB + DHA Prenatal	Rx	G	Rivers Edge
RE OB 90 + DHA Prenatal	Rx	G	Rivers Edge
Renate DHA	Rx	G	Rivers Edge
Renate DHA 430	Rx	G	Rivers Edge
Renate DHA Extra	Rx	G	Rivers Edge
Renate Prenatal	Rx	G	Rivers Edge
RightStep Prenatal Vitamins	OTC	B	TriMarc
Se-care Chewable	Rx	G	Seton
Se-care Conceive	Rx	G	Seton
Select OB	Rx	G	Everett



Name	Rx / OTC	Generic/Brand	Manufacturer
Tandem OB	Rx	G	US Pharmaceuticals
Taron Prenatal w/DHA	Rx	G	Trigen
Taron A Prenatal w/DHA	Rx	G	Trigen
Trifera OB	Rx	G	Trigen
Trinate	Rx	G	Cypress
UltimateCare Advantage	Rx	G	Trigen
Vinatal Forte	Rx	G	Breckenridge
Vinate AZ	Rx	G	Breckenridge
Vinate AZ Extra	Rx	G	Breckenridge
Vinate Calcium	Rx	G	Breckenridge
Vinate GT	Rx	G	Breckenridge
Vinate II	Rx	G	Breckenridge
Vinate III	Rx	G	Breckenridge
Vinate One	Rx	G	Breckenridge
Vinate Ultra	Rx	G	Breckenridge
Vinate-M	Rx	G	Breckenridge
Vitafof OB	Rx	G	Everett
Vitafof OB + DHA	Rx	G	Everett
VitaPhil + DHA 90	Rx	G	Rivers Edge
VitaPhil AiDE	Rx	G	Rivers Edge
VitaPhil Caplet	Rx	G	Rivers Edge

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