

This product information is intended for physicians and is the entire product information.  
NO OTHER INFORMATION, WHETHER ORAL OR IN WRITING, SHOULD BE RELIED UPON!

NDC 52747-904-60

## Tandem® DHA

FERROUS FUMARATE / POLYSACCHARIDE IRON COMPLEX VITAMIN  
MINERAL COMPLEX PRENATAL CAPSULES WITH DHA

### DESCRIPTION: Each opaque pink capsule contains:

Ferrous Fumarate (Elemental Iron)	15 mg
Polysaccharide Iron Complex (Elemental Iron)	15 mg
(Equivalent to about 30 mg of elemental iron)	
Vitamin C (Sodium Ascorbate)	20 mg
Folic Acid	1 mg
Vitamin B <sub>6</sub> (Pyridoxine HCl)	25 mg
Omega-3 Fatty Acids	310.1 mg
(Derived from 450 mg Fish Oil)	
Docosahexaenoic Acid (DHA)	215.12 mg
Eicosapentaenoic Acid (EPA)	53.46 mg

Inactive Ingredients: Gelatin, Glycerol Monostearate, Mixed Tocopherols, Titanium Dioxide, FD&C Blue 1, FD&C Red 40, FD&C Blue 2, Ethylcellulose, Ammonium Hydroxide, Medium Chain Triglycerides, Oleic Acid, Sodium Alginate, and Purified Stearic Acid.

Tandem® DHA supplies important prenatal vitamin minerals in a formulation that is especially designed to supplement the nutritional needs of pregnant women, before, during and after pregnancy. In Tandem® DHA, patients receive the balanced support of 5 essential vitamins and minerals, including 1 mg of folic acid. Tandem® DHA is unique in that it utilizes two (2) different forms of iron, i.e., Ferrous Fumarate and Polysaccharide Iron Complex (as cell-contracted akaganéite), making available a total of 30 mg of elemental iron per capsule as follows:

Ferrous Fumarate (anhydrous)	15 mg
Polysaccharide Iron Complex (PIC)	15 mg

**Ferrous Fumarate:** Provides about 15 mg of elemental iron per dose. Ferrous Fumarate is an anhydrous salt of a combination of ferrous iron and fumaric acid, containing 33% of iron per weight. The acute toxicity in experimental animals is low and Ferrous Fumarate is well tolerated clinically. As a ferrous salt, it is more efficiently absorbed in the duodenum. Ferrous Fumarate contrasts very favorably with the availability of the 20% of elemental iron of ferrous sulfate, and the 13% of elemental iron of ferrous gluconate.

**Polysaccharide Iron Complex:** Provides about 15 mg elemental iron, as a cell-contracted akaganéite. It is a product of ferric iron complexed to a low molecular weight polysaccharide. This polysaccharide is produced by the extensive hydrolysis of starch and is a dark brown powder that dissolves in water to form a very dark brown solution, which is virtually odorless and tasteless.

The most frequent cause of anemia in pregnant women is iron deficiency. Because of the continuous loss of iron due to monthly menstruation, most women enter pregnancy with less than optimal iron stores. Supplementation of iron must suffice to meet the needs for maternal and fetal erythropoiesis, and account for daily maternal gastrointestinal losses and obligate fetal transfer and growth. Iron requirements during pregnancy usually cannot be met with the average diet. (ACOG technical bulletin (1993): Nutrition during Pregnancy, p.4. Number 179-April 1993: The American College of Obstetricians and Gynecologists, Washington, D.C. 20024-2188).

Tandem® DHA does not contain calcium, as calcium may inhibit iron absorption because of the binding or conversion of ferrous salts by calcium and other minerals. Calcium salts can always be prescribed separately for women at high nutritional risk, including those who do not eat adequate amounts of dairy products. The recommendation of the National Academy of Sciences Tenth Ed. 1989 National Academy Press, Washington, D.C., suggests the supplementation of 1200 mg of calcium for pregnant and lactating women for the prevention of calcium deficiency.

Folic acid is a hematopoietic vitamin and has been used extensively for the prevention of neural tube defects. The need for folic acid in pregnancy, with its increased demands of the fetus, or lactation, is not being met by normal dietary sources.

Tandem® DHA capsules contain 1 mg of folic acid. Neural tube defects (NTDs) are the most common birth defects that result in infant mortality and serious disability. For women with a previous pregnancy that resulted in a child with a neural tube malformation, the use of 4 mg/d of folic acid has been reported to be effective in preventing a recurrence (MRC Vitamin Study Research Group, 1991). However, earlier studies from the United Kingdom suggested that lower daily doses, for example 0.36 mg, might result in a comparable reduction of a recurrence of NTDs. Since neural tube closure is complete by four weeks following conception, beginning folic acid supplementation after that time is not likely to be of any value. It should be noted that a daily 4 mg dose of folic acid did not prevent all NTDs in the MRC study. Patients should be cautioned that folic acid supplementation does not preclude the need for consideration for prenatal testing for NTDs (ACOG Committee Opinion, Number 120, March 1993: The American

College of Obstetricians and Gynecologists, Washington D.C. 20024-2188). The U.S. Public Health Service has recommended that all women of childbearing age in the United States who are capable of becoming pregnant should consume 0.4 mg of folic acid per day for reducing their risk of having a pregnancy affected with spina bifida or other NTD's (Center of Disease Control, 1992). Recommendation for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects: MMWR 1992:41(RR14):1-7).

All Tandem® products include a unique patented source of iron, e.g. Ferrous Fumarate and Polysaccharide Iron Complex (U.S. Patent No: 11/243,043 Pending). The patent is entitled: IMPROVED TOLERATION IRON SUPPLEMENT COMPOSITIONS. It incorporates the research study performed on August 2005 by Liesa M. Diehl (see below). The Abstract of the Patent states that "...the (patent) relates to compositions and methods for the treatment or prophylaxis of iron deficiency, and in particular of iron deficiency anemia, by administering a composition containing an effective amount of a pharmaceutically acceptable ferrous iron salt; and an effective amount of Polysaccharide Iron Complex", and that "the increase in tolerability observed with the (patented formulation) is believed to occur as the result of distributing the total iron content in the composition among compounds that provide iron to the patient's blood stream via two different mechanisms. The ferrous salts are readily absorbed in the upper gut, by direct dissolution and absorption of the ferrous iron by the bloodstream. However, the iron available from PIC is absorbed in the lower gut, via an active protein transport mechanism".

The Tandem® DHA formulation supplies additional important prenatal vitamins and minerals, which supplement the nutritional needs of pregnant women, before, during and after pregnancy. Deficiencies of these ingredients are common during pregnancy and lactation. The recommended daily allowance for DHA is between 200 and 300 mg per day for pregnant or lactating women. However, studies show that American women only consume an average of 60-80 mg per day (Benisek D, et al. Dietary intake of polyunsaturated fatty acids by pregnant or lactating women in the United States. Obstet Gynecol, 2000.). Studies have shown that infants born to mothers with higher blood levels of DHA and omega-3 fatty acids had more advanced levels of attention spans than those born to mothers with lower levels of DHA and omega-3 fatty acids. The infants were also shown to have higher IQ scores at the age of 18 months than those receiving lower amounts (Child Development, July/ August 2000).

**Clinical Studies:** The licensee U.S. Pharmaceutical Corporation and JLM Pharmatech, Inc. had jointly sponsored new research pertaining to this formulation (Liesa M. Diehl August 2005: A 14-Day Comparative Pharmacokinetic Study of Ferrous Fumarate and Ferrous Fumarate-Polysaccharide Iron Complex Administered by the Oral (Gavage) Route to Rats, Charles River Laboratories, Preclinical Services: Spencerville, OH). (Personal Communication, Study number NEM00001, August 2005). Because Ferrous Fumarate is an organic complex, it contains no free ions, either ferric or ferrous. Polysaccharide Iron Complex is clinically non-toxic. Prior studies in rats demonstrated that Polysaccharide Iron Complex (PIC), administered as a single oral dose to Sprague Dawley rats did not produce evidence of toxicity at a dosage level of 5000 mg iron/kg: (An Acute Oral Toxicity Study in Rats with Polysaccharide-Iron Complex. T.N.Merriman, M. Aikman and R.E. Rush, Springborn Laboratories, Inc. Spencerville, Ohio Study No. 3340.1 March - April 1994). Other clinical studies had demonstrated that Polysaccharide Iron gives a good hematopoietic response with an almost complete absence of the side effects usually associated with oral iron therapy. Picinni and Ricciotti suggested in 1982, that "the therapeutic effectiveness of Polysaccharide Iron Complex when compared with iron fumarate in the treatment of iron deficiency anemia, appears to be as active as the iron fumarate and as well tolerated, however, it exerted a greater influence on the level of hemoglobin and on the number of red cells..." and that, "it has been exceptionally well tolerated by all patients" (Picinni, L.-Ricciotti, M. 1982. Therapeutic effectiveness of an iron-polysaccharide complex in comparison with iron fumarate in the treatment of iron deficiency anemias): PANMINERVA MEDICA-EUROPA MEDICA, Vol. 24, No. 3, pp. 213-220 (July - September 1982).

As mentioned above, the patented source of iron used in Tandem® DHA (Ferrous Fumarate and Polysaccharide Iron Complex) provides a high level of elemental iron with a low incidence of gastric distress.

The Liesa Diehl study maintains that, "the oral combination of Ferrous Fumarate and Polysaccharide Iron Complex was better tolerated than the oral administration of Ferrous Fumarate alone." Overall, greater statistically and toxicologically significant effects in hematology and clinical chemistry parameters were observed in Group 2 animals (Ferrous Fumarate only) than were observed in Group 3 animals (Ferrous Fumarate and PIC) as compared to controls.

**CONCLUSION:** Based on the results of this study, the oral combination of Ferrous Fumarate and Polysaccharide Iron Complex was better tolerated and safer than the oral administration of Ferrous Fumarate alone. The conclusion of this research stated, "that both compositions provide equivalent efficacy at increasing serum iron levels, but that the Group 3 material (i.e., the composition named in the patent), is significantly better tolerated than is Ferrous Fumarate alone, although the concentration of Ferrous Fumarate is the same in both compositions." In other words, the results support the conclusion that the addition of PIC to Ferrous Fumarate surprisingly allows the same concentration of Ferrous Fumarate to be better tolerated than the Ferrous Fumarate alone.

**INDICATIONS:** Tandem® DHA is a prescription prenatal vitamin-mineral preparation containing omega-3 fatty acid supplements designed to supply nutritional supplementation for women throughout pregnancy and during the postnatal period to lactating and non-lactating mothers. Tandem® DHA may also be used to improve the nutritional status of women before conception.

**CONTRAINDICATIONS:** Tandem® DHA is contraindicated in patients with known hypersensitivity to any of its ingredients, including fish or fish oil; also, all iron compounds are contraindicated in patients with hemosiderosis, hemochromatosis, or hemolytic anemias. Pernicious anemia is a contraindication, as folic acid may obscure its signs and symptoms.

**WARNING:** Accidental overdose of iron-containing products is the leading cause of fatal poisoning in children under six. Keep this and all drugs out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately.

**WARNING:** Ingestion of more than 3 grams of omega-3 fatty acids from fish oils per day may have potential antithrombotic effects, including an increased bleeding time and INR (international normalized ratio). DHA should be avoided in patients with inherited or acquired bleeding diatheses, including those taking anticoagulants.

**WARNING:** Folic acid alone is improper therapy in the treatment for pernicious anemia and other megaloblastic anemias where Vitamin B<sub>12</sub> is deficient.

**PRECAUTIONS:** General: Folic acid in doses above 0.1 mg -0.4 mg daily may obscure pernicious anemia, in that hematological remission can occur while neurological manifestations remain progressive.

**Pediatric Use:** Safety and effectiveness of this product have not been established in pediatric patients.

**Geriatric Use:** No clinical studies have been performed in patients age 65 and over to determine whether older persons respond differently from younger persons. Dosage should always begin at the low end of the dosage scale and should consider that elderly persons may have decreased hepatic, renal, or cardiac function and or concomitant diseases.

**Adverse Reactions:** Folic Acid: Allergic sensitizations have been reported following both oral and parenteral administration of folic acid.

**Ferrous Fumarate:** Gastrointestinal disturbances (anorexia, nausea, diarrhea, constipation) occur occasionally, but are usually mild and may subside with continuation of therapy. Although the absorption of iron is best when taken between meals, giving Tandem® DHA after meals may control occasional G.I. disturbances. Tandem® DHA is best absorbed when taken at bedtime.

**OVERDOSE:** Iron: Signs and Symptoms: Iron is toxic. Acute overdosage of iron may cause nausea and vomiting and, in severe cases, cardiovascular collapse and death. Other symptoms include pallor and cyanosis, melena, shock, drowsiness and coma. The estimated overdose of orally ingested iron is 300-mg/kg body weight. When overdoses are ingested by children, severe reactions, including fatalities, have resulted. Tandem® DHA should be stored beyond the reach of children to prevent against accidental iron poisoning. Keep this and all other drugs out of the reach of children.

**Treatment:** For specific therapy, exchange transfusion and chelating agents should be used. For general management, perform gastric lavage with sodium bicarbonate solution or milk. Administer intravenous fluids and electrolytes and use oxygen.

**DOSAGE AND ADMINISTRATION:** Adults (persons over 12 years of age), one (1) capsule daily, orally, between meals, or as prescribed by a physician. Do not exceed recommended dosage. Do not administer to children under the age of 12.

**HOW SUPPLIED:** Tandem® DHA are opaque pink capsules imprinted "Tandem® DHA": Child resistant bottles of 90 capsules NDC# 52747-904-60. Dispense in a tight, light-resistant container as defined in the USP/NF with a child resistant closure. Store at controlled room temperature 15° to 30°C (59° to 86° F). Keep in a cool, dry place. Capsules are not USP.

**CAUTION: Rx only.**

**RESERVED FOR PROFESSIONAL RECOMMENDATION.** Made in the USA exclusively for U.S. Pharmaceutical Corporation, Decatur, GA, 30035 USA. All rights reserved. The appearance and the name of Tandem® DHA and the appearance of the ferrous fumarate/polysaccharide iron complex combination are registered trademarks of U.S. Pharmaceutical Corporation. The Tandem® DHA exclusive formula has been manufactured under one or several exclusive United States patents. In addition, the appearance, design and Tandem® DHA product literature and any statement therein, has been protected by U.S. and International Trademark Laws. Legal action will be taken against all violators. The use of the product information pamphlet is expressly prohibited without prior consent.

Rev. 10/07



**US Pharmaceutical Corporation**  
Products designed with the patient in mind.™