



Proferrin[®] Forte

(HEME IRON POLYPEPTIDE WITH FOLIC ACID)
Medical Food

Each tablet contains 12 mg elemental iron
as heme iron polypeptide and 1 mg folic acid

Proferrin Forte 90 Tablet Bottles (NDC 67181-216-90)

Low Side Effects³
High Absorption⁶
More Convenient^{5,6}

Product Form:

Proferrin[®] Forte is a solid oral tablet containing 12 mg of elemental iron from heme iron polypeptide and 1 mg of folic acid, with the balance of the tablet containing polypeptides of varying molecular weights, porphyrin rings, and inactive excipients.

Description:

Proferrin[®] Forte is manufactured as oblong tablets approximately 2 cm in length and approximately 0.5 cm in both diameter and thickness. The tablets are coated red, and have a bisect line on the center of the tablet. If broken in half, the interior consists of material with a black appearance. These tablets are formulated for oral ingestion only.

Proferrin[®] Forte is derived from bovine hemoglobin. Peptides and amino acids are cleaved during processing to increase the concentration of the bioavailable form of heme iron polypeptide. The heme moiety remains covalently bound to the polypeptide chain, enhancing solubility in aqueous solutions at a wide range of pH levels; pH less than 3 and pH greater than 6 (data on file).

Physiological Mechanisms

Mechanism of Absorption:

Heme Iron Polypeptide is absorbed over several hours after oral administration. Available evidence suggests that heme attaches to the apical brush border of the absorptive enterocyte. At this point the heme moiety binds to HCP1 (heme carrier protein 1). HCP1 carries the Heme Iron Polypeptide across the brush border into the cytosol intact.^{1,9} This absorption mechanism is unique to heme iron and is not shared by ionic iron forms, such as iron salts, iron chelates and iron saccharides.

Metabolism:

Peak change in serum iron from a single dose is seen in two to four hours and gently slopes thereafter for up to ten hours.⁸

Physiological Activity:

Upon transport into the brush border cells of the intestine, the iron atom is stripped from the heme ring by heme oxygenase. The iron atom is then reduced by the mobilferrin/paraferritin complex with NADPH. The iron ion is then carried by mobilferrin to the vascular side of the cell where it is attached to either apotransferrin or apoferritin. These iron transport/storage proteins then carry the iron through the vascular system to storage sites or the site of erythropoiesis in the marrow.¹⁰

Usage:

Proferrin[®] Forte is a unique product for dietary management of iron deficiency. GI tolerability is comparable to IV iron, and reduced GI distress is reported in comparison to traditional oral ionic iron.^{4,6} Proferrin[®] Forte is ideal for individuals seeking an alternative to traditional iron therapy.

Recommended use of Proferrin[®] Forte is one tablet up to three times daily, with or without meals. Consult a health care provider for your recommended intake.

Contraindications:

Folic acid in consumption above 1 mg daily may obscure pernicious anemia in that hematologic remission can occur while neurological manifestations remain progressive. Pernicious anemia should be ruled out before using this product since folic acid may mask the symptoms of pernicious anemia.

Individuals with known allergies to meat products or any ingredients of Proferrin[®] Forte should not consume Proferrin[®] Forte.

Patients with hereditary hemochromatosis or other conditions of iron overloading should not consume Proferrin[®] Forte.

Proferrin[®] Forte is derived from bovine hemoglobin. Vegetarians or those who object to consumption of animal products should be informed of its origin.

Warning: Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately.

General

Pregnancy:

Heme iron polypeptide has been shown to be safe for use by pregnant women. It has been shown to maintain hematocrit and hemoglobin levels during the third trimester of pregnancy with consumption as low as 6.5 mg elemental iron (as heme iron polypeptide) per day.¹¹

Adverse Reactions:

A minor incidence of side effects with the use of Proferrin[®] ES has been reported, including gas, diarrhea, and constipation. No clear pattern of adverse gastrointestinal side effects has been established.³

Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

Over Consumption or Abusive Use:

Heme iron polypeptide is the primary component in Proferrin[®] Forte. In vivo LD₅₀ studies in mice indicate an LD₅₀ of 20g/kg of HIP (data on file). Ingestion of large amounts is not life threatening but can cause vomiting or gastrointestinal discomfort.²

Large amounts containing greater than 60 mg elemental iron (equal to approximately 5 tablets) from Proferrin[®] Forte at one time may result in darkened stool and result in only modest or no incremental gains in serum iron (data on file).

Folic acid is a water soluble vitamin with low toxicity. In vivo LD₅₀ studies in mice indicate an LD₅₀ of 10,000mg/kg.

Other Considerations:

Proferrin[®] Forte can be expected to cause false positive reactions to occult stool testing and should be discontinued from use for at least 5 days prior to occult stool testing.⁷

Additional Information:

Proferrin[®] Forte does not contain corn, dairy, soy, or gluten products.

Active Ingredients: Heme Iron Polypeptide, Folic Acid.

Other Ingredients: Cellulose, Croscarmellose Sodium, Coating (Polyvinyl Alcohol, PEG3350Peg 3350, Talc, FD&C Yellow #5, FD&C Blue #2Red #40, Titanium Dioxide, FD&C Blue #1), Sucrose, Povidone, Protease (denatured), Hydrogenated Vegetable Oil, Calcium Stearate, Silicone Dioxide.

Footnotes:

1. Andrews, N. C., *New England Journal of Medicine*, 2005. Vol. 353(23):2508-9.
2. Biology Technology Laboratories Co. Ltd., Data On File.
3. Ghaddar, S., and Moore, G.M., *Abstract presented at National Kidney Foundation*, April 7, 2003, Dallas, TX.
4. Hallberg et al., *American Journal of Clinical Nutrition*, 1997, Vol. 66, 347-356.
5. Lynch, S.R., *Nutrition Reviews*, 1997. 55(4):102-10.
6. Nissenson, A. R., et al., *American Journal of Kidney Disease*, 2003. 42(2):325-30.
7. Ostrow, J.D. "Tests for Fecal Occult Blood" in *Clinical Methods: The History, Physical, and Laboratory Examinations*. Walker, H.K., et al, ed. Stoneham, MA: Butterworth Publishers; 1990: 489-91.
8. Seligman, P.A., et al., *Nutrition Research*, 2000. 20(9):1279-86.
9. Shayeghi, M., et al., *Cell*, 2005. 122(5):789-801.
10. Uzel, C., and Conrad, M. E., *Seminars in Hematology*, 1998. 35(1):27-34.
11. Suzuki et al., *Obstetrics and Gynecology World*, 42(10):32-43.