

EnBrace® HR

with DeltaFolate™

[1 NF Units] [15 mg DFE Folate]

ANTI-ANEMIA PREPARATION as extrinsic/intrinsic factor concentrate plus folate.

Prescription Prenatal/Vitamin Drug For Therapeutic Use

Multi-phasic Capsules (30ct bottle)

NDC 64661-650-30

R_x Only [DRUG]

GLUTEN-FREE

DESCRIPTION:

EnBrace® HR is an orally administered **prescription prenatal/vitamin drug** for therapeutic use formulated for female macrocytic anemia patients that are in need of treatment, and are under specific direction and monitoring of vitamin B₁₂ and vitamin B₉ status by a physician. EnBrace® HR is intended for women of childbearing age who are – or desire to become, pregnant regardless of lactation status. EnBrace® HR may be prescribed for women at risk of depression as a result of folate or cobalamin deficiency - including folate-induced postpartum depression, or are at risk of folate-induced birth defects such as may be found with spina bifida and other neural tube defects (NTDs).

INGREDIENTS:

Cobalamin intrinsic factor complex

1 NF Units*

*National Formulary Units ("NF UNITS") equivalent to 50 mcg of active coenzyme cobalamin (as cobamamide concentrate with intrinsic factor)

ALSO CONTAINS:

Folinic acid (B₉-vitamer)

2.5 mg¹

Control-release, citrated folic acid, DHF⁺ (B₉-Provitamin)

1 mg¹

Levomefolic acid (B₉ & B₁₂- cofactor)

5.23 mg²

¹6 mg DFE folate (vitamin B₉)

²9 mg DFE l-methylfolate magnesium (molar equivalent).

FUNCTIONAL EXCIPIENTS: 13.6 mg FeGC as ferrous glycine cysteinate (1.5 mg elemental iron³) [colorant], 25 mg ascorbates^{3,4} (24 mg magnesium l-ascorbate, 1 mg zinc l-ascorbate) [antioxidant], at least 23.33 mg phospholipid-omega3 complex⁵ [marine lipids], 500 mcg betaine (trimethylglycine) [acidifier], 1 mg magnesium l-threonate [stabilizer].

OTHER EXCIPIENTS: Annatto [colorant], citrates (citric, sodium) [stabilizers], flavin adenine dinucleotide⁶ (FAD), gelatin (bovine), glycerine, plant lipids (sunflower) [lecithin], natural orange flavor [masking], nicotinamide adenine dinucleotide hydride⁶ (NADH), pyridoxal 5' phosphate⁶ (P5P), piperine [bioavailability enhancer], purified water, thiamine pyrophosphate⁶, ubiquinol [antioxidant], yellow beeswax.

³ 20% daily value (DV) of VITAMIN C, and 5% DV IRON.

⁴ NOT a significant source of magnesium and zinc.

⁵ Contains at least 12 mg phosphatidylserine (PS) – of which approximately 6.4 mg as PS-DHA-Ca, and less than 1% EPA (<800 mcg PS-EPA-Ca)

⁶ Contains less than 2% (<25 mcg/each) of vitamins B₁, B₂, B₃ and B₆.

CONTAINS FISH/KRILL/SOY.

Certified 3rd-party **GLUTEN-FREE**. No artificial colorants. No dairy, wheat, sugar or egg.

MECHANISM OF ACTION:

Vitamin B₁₂ [treatment]; Vitamin B₉ [prevention]; Intrinsic Factor [facilitator].

[Vitamin B₁₂]

Vitamin B₁₂ deficiency results in megaloblastic anemia, GI lesions, and neurological damage that begins with an inability to produce myelin and is followed by gradual degeneration of the axon and nerve head. *Vitamin B₁₂ has hematopoietic activity apparently identical to that of the anti-anemia factor in purified liver extract.*

[Vitamin B₁₂] / [Intrinsic factor]

Gastrointestinal absorption of cobalamin depends on the presence of sufficient intrinsic factor. Intrinsic factor deficiency causes pernicious anemia - which may be associated with subacute combined degeneration of the spinal cord.

[Vitamin B₉]

Vitamin B₉ deficiency results in megaloblastic anemia. Vitamin B₉ stimulates specifically the production of red blood cells, white blood cells, and platelets in persons suffering from certain megaloblastic anemias.

Folic acid, folinic acid and l-methylfolate metabolism results in the creation of tetrahydrofolic acid by different pathways. Both folinic acid and levomefolic acid do not require dihydrofolate reductase (DHR), however folic acid does.

[Vitamin B₉] / [Vitamin B₁₂]

Vitamin B₁₂ is essential for the synthesis of methionine from homocysteine - a reaction which also requires folate. In the absence of Vitamin B₁₂, tetrahydrofolate cannot be regenerated from 5-methyltetrahydrofolate, and a functional Vitamin B₉ deficiency occurs (ie, "methyl trap hypothesis").

Inborn errors of metabolism (IEMs) - such as methyltetrahydrofolate reductase (MTHFR), may also inhibited cobalamin intracellular conversion due to impaired ability to metabolize folic acid.

INDICATIONS:

EnBrace® HR is indicated in the treatment of macrocytic anemias before, during or after pregnancy - including pernicious anemia and megaloblastic anemia, and the prevention of folic acid deficiency.

Requirements of vitamin B₁₂ and/or vitamin B₉ in excess of normal (due to pregnancy, thyrotoxicosis, hemolytic anemia, hemorrhage, malignancy, hepatic and renal disease) can usually be met with oral supplementation.

WARNINGS:

1. **USE OF THIS PRODUCT WITHOUT DIRECT SUPERVISION OF A PHYSICIAN IS DANGEROUS.**
2. *Some patients afflicted with pernicious anemia may or not respond to the orally ingested vitamin B₁₂, and there is no*

known way to predict which patients may respond and which patients may cease to respond.

3. **Periodic examination and laboratory studies of pernicious anemia patients are essential and recommended.**
4. The parenteral administration of (*cyano*)cobalamin – or vitamin B₁₂, is generally recognized as a fully effective treatment of pernicious anemia. Parenteral *alkyl*-cobalamin preparations have not been and are not authorized for use except by or on the prescription of a physician.

PRECAUTIONS:

GENERAL:

0.1 mg or more of folic acid daily may obscure pernicious anemia in that the hematological remission may occur while neurological manifestations remain progressive. The safe tolerable limit for folic acid (*in preparations*) is 1 mg [emphasis added].

Folic acid is not a substitute for vitamin B₁₂ - although it may improve vitamin B₁₂-deficient megaloblastic anemia. Exclusive use of folic acid in treating vitamin B₁₂-deficient megaloblastic anemia could result in progressive and irreversible neurologic damage. Specifically, vitamin B₁₂ deficiency allowed to progress over 3 months may produce permanent degenerative lesions of the spinal cord - as observed when folate therapy is used as the only hematopoietic agent.

Doses of vitamin B₁₂ exceeding 10 mcg daily may produce hematologic response in patients with folate deficiency. Indiscriminate administration may mask the true diagnosis.

A dietary deficiency of only vitamin B₁₂ is rare; multiple vitamin deficiency is expected in any dietary deficiency. No single regimen fits all cases, and the status of the patient observed in follow-up is the final criterion for adequacy of therapy.

DRUG INTERACTIONS:

Colchicine, para-aminosalicylic acid, and heavy alcohol intake for longer than 2 weeks may produce malabsorption of vitamin B₁₂.

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY:

There is no evidence from long-term use in patients with pernicious anemia that vitamin B₁₂ or folate is carcinogenic. Pernicious anemia is associated with increased incidence of carcinoma of the stomach, but this is believed to be related to the underlying pathology and not to treatment with vitamin B₁₂.

PREGNANCY, NURSING MOTHERS, PEDIATRIC USE:

Vitamin B₁₂ and vitamin B₉ are essential vitamins and requirements are increased during pregnancy. Amounts of vitamin B₁₂ and vitamin B₉ that are recommended by the Food and

Nutrition Board, National Academy of Science - National Research Council for lactating women should be consumed during pregnancy.

Vitamin B₁₂ and vitamin B₉ appear in the milk of nursing mothers in concentrations which approximate the mother's vitamin B₁₂ and vitamin B₉ blood level. Amounts of vitamin B₁₂ that are recommended by the Food and Nutrition Board, National Academies of Science - National Research Council for lactating women should be consumed during lactation.

Intake in pediatric patients should be in the amount recommended by the Food and Nutrition Board, National Academy of Science - National Research Council.

ADVERSE REACTIONS:

Mild transient diarrhea, polycythemia vera, itching, transitory exanthema, feeling of swelling of entire body may occur with administration of vitamin B₁₂.

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

DOSAGE AND ADMINISTRATION:

The adult dose is one capsule daily *preferably on an empty stomach*.

As a general rule - in patients with Addisonian Pernicious Anemia, treatment will be required for the remainder of the patient's life. Reticulocyte plasma count, vitamin B₁₂ and folate must be obtained prior to treatment.

Do not exceed recommended dose. Call your medical practitioner about side effects. You may report side effects by calling 337.662-5962.

HOW SUPPLIED:

Oval, brownish-orange softgel capsule with "ENL"⁷ on one side, in bottles of 30 with NDC 64661-650-30.

STORAGE:

Store at 20°-25°C (68°-77°F). *Protect from light and moisture as contact with moisture may produce surface discoloration and/or erosion.*

Rx Only [DRUG]

Caution: **Federal law prohibits dispensing without a prescription.**

KEEP OUT OF THE REACH OF CHILDREN.

Tamper Evident: Do not use if seal is broken or missing.

⁷ Upper case.

MANUFACTURED FOR:

JayMac Pharmaceuticals, LLC; Sunset, LA 70584.

MANUFACTURED AND/OR PACKAGED IN USA/CANADA.

PATENTS:

US Patent No 7,935,365; *and other patent applications pending.*

TRADEMARKS:

EnBrace® HR is a registered mark of JayMac Pharmaceuticals. DeltaFolate™ is a use-trademark of JayMac Pharmaceuticals.

Revision 3 (*November 14, 2018*)