

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

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## EDGE™ – P PLUS

(Evening Primrose Oil and Mecobalamin capsule)

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### COMPOSITION

Each soft gelatin capsule contains:

Evening Primrose Oil .....1000 mg  
Mecobalamin J.P. ....750 mcg  
(Methylcobalamin)

Excipients .....Mixed Tocopherol

Approved colours used in capsules shell.

Appropriate overages of vitamin added to compensate for loss on storage.

### DESCRIPTION

Edge P Plus is a formulation that contains Evening primrose oil, the oil from the seed of the evening primrose plant, which contains gammalinolenic acid (GLA) along with methylcobalamin and mixed tocopherols. GLA is known to balance the inflammatory response of the body and relieves the premenstrual engorgement of the breast tissue as well as the symptoms of Fibrocystic breast disease.

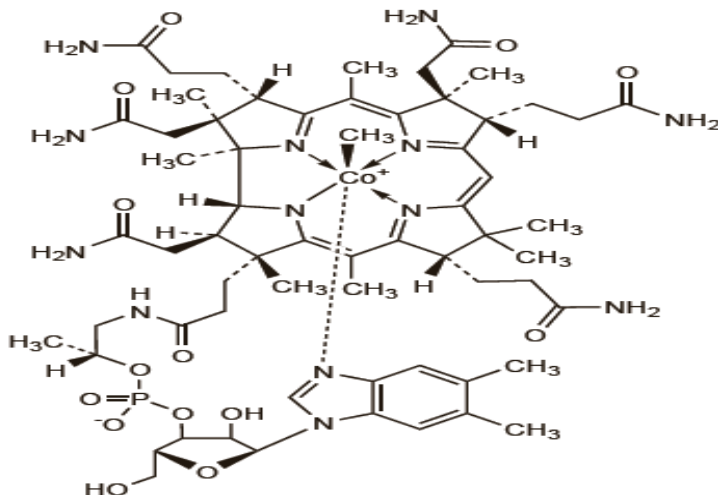
#### *Evening Primrose*

Evening primrose, the aerial parts of *Oenothera biennis* (Onagraceae) and related species of *Oenothera*, is reported to have sedative and astringent properties. It has been used in herbal preparations for respiratory and gastrointestinal disorders.

Evening primrose seed is the source of evening primrose oil (below), which is a source of essential fatty acids.

#### *Mecobalamin*

Chemically it is  $Co\alpha$ -[ $\alpha$ -(5,6-Dimethylbenzimidazolyl)]- $Co\beta$ -methylcobamide. Molecular formula is  $C_{63}H_{91}CoN_{13}O_{14}P$  and empirical formula 1344.4.



## **CLINICAL PHARMACOLOGY**

### ***Evening primrose oil***

Evening primrose oil is a source of linoleic and gamma-linolenic acid which are essential fatty acids of the omega-6 series that act as prostaglandin precursors.

### ***Mecobalamin***

Vitamin B12, a water-soluble vitamin, occurs in the body mainly as methylcobalamin (mecobalamin) and as adenosylcobalamin (cobamamide) and hydroxocobalamin.

Mecobalamin and cobamamide act as coenzymes in nucleic acid synthesis. Mecobalamin is also closely involved with folic acid in several important metabolic pathways.

### **Pharmacokinetics**

#### ***Mecobalamin***

Vitamin B12 substances bind to intrinsic factor, a glycoprotein secreted by the gastric mucosa, and are then actively absorbed from the gastrointestinal tract. Absorption is impaired in patients with an absence of intrinsic factor, with a malabsorption syndrome or with disease or abnormality of the gut, or after gastrectomy.

Absorption from the gastrointestinal tract can also occur by passive diffusion; little of the vitamin present in food is absorbed in this manner although the process becomes increasingly important with larger amounts such as those used therapeutically.

Vitamin B12 is extensively bound to specific plasma proteins called transcobalamins; transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. Vitamin B12 is stored in the liver, excreted in the bile, and undergoes extensive enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours; urinary excretion, however, accounts for only a small fraction in the reduction of total body stores acquired by dietary means. Vitamin B12 diffuses across the placenta and also appears in breast milk.

## **INDICATIONS**

Indicated for:

- Fibrocystic Breast Disease,
- Mastalgia

## **CONTRAINDICATION**

Hypersensitivity to any of the ingredients

## **WARNINGS AND PRECAUTIONS**

### ***Evening primrose oil***

*Effects on the nervous system:* Temporal lobe epilepsy was diagnosed after treatment with evening primrose oil in 3 patients who had previously been diagnosed as schizophrenic. Tonic clonic (grand mal) seizures occurred in 2 additional schizophrenic

patients during treatment with evening primrose oil. All of these patients had received or were taking phenothiazine antipsychotics.

Gamolenic and linoleic acids from evening primrose oil, and presumably other sources, can produce minor gastrointestinal disturbances and headache. They can precipitate symptoms of undiagnosed temporal lobe epilepsy, and should be used with caution in patients with a history of epilepsy or those taking epileptogenic drugs, in particular phenothiazines. Hypersensitivity reactions may also occur.

*Bleeding disorders:* There is a concern that evening primrose oil might increase the chance of bruising and bleeding.

*Schizophrenia:* Seizures have been reported in people with schizophrenia treated with phenothiazine drugs, GLA (a chemical found in evening primrose oil), and vitamin E.

*Surgery:* Evening primrose oil might increase the chance of bleeding during or after surgery.

### ***Mecobalamin***

Cyanocobalamin or hydroxocobalamin should, if possible, not be given to patients with suspected vitamin B12 deficiency without first confirming the diagnosis.

Regular monitoring of the blood is advisable. Use of doses greater than 10 micrograms daily may produce a haematological response in patients with folate deficiency; indiscriminate use may mask the precise diagnosis.

Conversely, folate may mask vitamin B12 deficiency.

Cyanocobalamin should not be used for Leber's disease or tobacco amblyopia since these optic neuropathies may degenerate further.

## **DRUG INTERACTION**

### ***Mecobalamin***

Absorption of vitamin B12 from the gastrointestinal tract may be reduced by neomycin, aminosalicic acid, histamine H<sub>2</sub>-antagonists, omeprazole, and colchicine. Serum concentrations may be decreased by use of oral contraceptives. Many of these interactions are unlikely to be of clinical significance but should be taken into account when performing assays for blood concentrations.

Reduced effects in anaemia with parenteral chloramphenicol.

### ***Evening primrose oil***

Evening primrose oil with phenytoin and other anticonvulsant medications, as the oil may lower the threshold for seizures. No other significant drug interactions have been reported.

*Medications that slow blood clotting (Anticoagulant / Antiplatelet drugs):*

Evening primrose oil contains GLA (gamma-linolenic acid), which might slow blood clotting. Taking evening primrose oil along with medications that also slow clotting might increase the chances of bruising and bleeding.

Some medications that slow blood clotting include aspirin, clopidogrel, nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac, ibuprofen, naproxen, dalteparin, enoxaparin, heparin, warfarin, and others.

*Phenothiazines:*

Taking evening primrose oil with phenothiazines might increase the risk of having a seizure in some people.

## **ADVERSE EFFECTS**

### ***Mecobalamin***

*Hypersensitivity:* allergic skin reactions; reactions were defined as being generalized morbilliform exanthems, urticaria, or generalised pruritus only.

In a patient with a generalised pruritic reaction to hydroxocobalamin (with subsequent urticaria, bronchospasm, and oropharyngeal angioedema), cyanocobalamin was relatively well-tolerated, with only one episode of delayed urticaria.

Oral: Anorexia, nausea, vomiting and diarrhoea.

### ***Evening primrose oil***

Evening primrose oil has not been reported as having toxic or severe side effects. Some patients, however, have reported nausea, headache, and softening of the stools.

Reports of side effects from using evening primrose oil in topical preparations for sunburn and other skin problems are the same as with any EFA supplement. Bruising due to damage of the blood platelet function is possible.

## **DOSAGES AND ADMINISTRATION**

1-2 Soft Gelatin CAPS per day for 3-6 months.

Dose may be increased, if necessary according to physician's discretion.

## **USE IN PREGNANCY AND NURSING MOTHER**

### ***Mecobalamin***

*Pregnancy & breast feeding:* Vitamin B12 is distributed into breast milk.

### ***Evening primrose oil***

*Pregnancy and breast-feeding:* Taking evening primrose oil is possibly unsafe during pregnancy. It might increase the chance of having complications. Don't use it if you are pregnant.

**EXPIRY DATE**

18 Months from the date of manufacturing.

**STORAGE**

Store in a cool, dry place. Protect from direct sunlight.

**PRESENTATION**

Blister pack of 10 Capsules

**MARKETED BY**

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