

# Fertilovit® for a new life

Gonadosan Distribution GmbH | Römerstr. 2 | 6900 Bregenz | Österreich  
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A-Bregenz, 27.04.2016

## To Romanian authorities / to whom it may concern

**Gonadosan Distribution GmbH**, Römerstrasse 2, 6900 Bregenz, Austria, hereby informs.

### Fertilovit® F Endo

**Food for special medical purposes for the dietary management of endometriosis in women planning for pregnancy.**

### What is Fertilovit® F Endo?

**Fertilovit® F Endo** is a food for special medical purposes for the dietary management of endometriosis in women planning for pregnancy.

### Endometriosis

Endometriosis is a chronic inflammatory disease in which endometrial tissue is present outside the uterus. It affects an estimated 10-20 % of women during their reproductive years. They often suffer from significant pain and subfertility. This is thought to be caused by a combination of hormonal changes, elevated inflammatory and homocysteine levels, and increased oxidative stress. While the disease itself is not curable, the body can be supported by a healthy diet.

Just like every other woman planning for pregnancy, women with endometriosis ought to make sure they take up sufficient folate. Folate is a B-vitamin and is abundant in green, leafy vegetables. However, due to its sensitivity to light and heat, it is easily destroyed during meal preparation. Therefore, many women do not have a sufficient supply. Low maternal folate status, however, is a risk factor for the development of neural tube defects in the developing foetus. Particularly for women with endometriosis, other micronutrients are important as well. They can contribute to maintenance of a balanced hormone and immune system, homocysteine metabolism, effective energy production, healthy mucosa, and protection from oxidative stress.

**Fertilovit® F Endo** is a dietetic food for special medical purposes tailored to meet the needs of women with endometriosis planning for pregnancy. It contains highly dosed folic acid and N-acetyl-L-cysteine in combination with a comprehensive supply of precious vitamins, minerals and omega-3 fatty acids. These micronutrients help to form the basis for healthy conception and pregnancy.

### Administration form:

Capsules

### Packaging sizes (Net quantity):

60 capsules (30 vitamin/mineral capsules and 30 fish oil capsules) (45.4 g)

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## Supplement facts:

	Daily dose (1 vitamin/mineral capsule and 1 omega 3 capsule)	% NRV*
Vitamin D	10 µg	200
Vitamin E	12 mg	100
Vitamin C	100 mg	126
Thiamin	3 mg	273
Riboflavin	3 mg	214
Niacin	35 mg	219
Vitamin B6	4 mg	286
Folic acid	800 µg	400
Vitamin B12	7 µg	280
Biotin	100 µg	200
Pantothenic acid	12 mg	200
Iron	7,8 mg	56
Zinc	5,3 mg	53
Copper	1 mg	100
Selenium	110 µg	200
Iodine	150 µg	100
Coenzyme Q10	35 mg	-
N-acetyl-L-cysteine	100 mg	-
Lycopene	10 mg	-
Eicosapentaenoic acid (EPA)	90 mg	-
Docosahexaenoic acid (DHA)	60 mg	-

\*Percentage of Nutrition Reference Values (according to regulation 1169/2011/EU)

**Fertilovit® F Endo** contains neither lactose nor gluten.

### Directions:

Please take 1 vitamin/mineral and 1 fish oil capsule daily. Swallow whole with plenty of water. **Fertilovit® F Endo** is a nutritionally incomplete food for special medical purposes. Some of its ingredients exceed defined maximum quantities. The product must be used under medical supervision. Do not exceed the recommended dosage. **Fertilovit® F Endo** cannot and must not replace a healthy lifestyle and a well-balanced diet. Please store out of reach of children.

### Scientifically Proven Effects of the Ingredients

#### Protection from neural tube disorders

Supplemental folate intake increases maternal folate status. Increasing maternal folate status contributes to the reduction of the risk of neural tube disorders. The positive effect is achieved by taking a minimum of 400 µg of supplemental folate for at least one month before and up to three months after conception.

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## **Energy supply**

Vitamins B1, B2, niacin and pantothenic acid support energy metabolism.

## **Homocysteine metabolism**

Vitamins B6, B12 and folic acid contribute to normal homocysteine metabolism.

## **Immune system**

Folic acid, vitamin C, vitamin D, selenium and iron contribute to normal function of the immune system.

## **Inflammation**

Lycopene is a carotenoid featuring excellent antioxidant as well as anti-inflammatory properties. This has a positive effect on latent inflammations of the urogenital tract, reducing oxidative stress.

## **Contra-indications**

Women who suffer from autoimmune thyroiditis, have issues with your iron metabolism or have a known intolerance to any of the ingredients should not consume **Fertilovit® F Endo**.

## **Representative bibliography**

### **Fertilovit® F Endo**

- For **Fertilovit® F Endo**, an observational study is planned for this year.

### **Omega-3-PUFAs (EPA, DHA)**

- Omega-3-PUFAs contribute to down-regulation of inflammation mediators. Increased consumption of Omega-3-PUFAs has been associated with a decreased risk of endometriosis (Hansen und Knudsen, 2013)

### **N-acetyl-L-cysteine (NAC)**

- NAC has been identified as an effective and safe treatment option in women with endometriosis (Porpora et al, 2013)

### **Vitamins B6, B12 and folic acid**

- Studies have shown increase in homocysteine levels in endometriosis patients (Aidrus et al. 2013)

### **Vitamins D, E and selenium**

- The Vitamins D and alpha tocopheryl succinate and the trace element selenium contribute to down-regulation of survivin-mediated escape from apoptosis in ectopic endometrial tissue (Chun et al, 2007, Pactasil et al, 2012)

### **Antioxidants**

- In a placebo controlled trial, the vitamins E and C reduced chronic pelvic pain in women with endometriosis and inflammatory markers in the peritoneal fluid (Santanam et al 2013).

### **Vitamin C**

- Contributes to normal energy metabolism: EFSA 2009; 7(9):1226 ; 2010;8(10):1815

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- Contributes to normal function of the immune system: EFSA 2009; 7(9):1226 ; 2010;8(10):1815
- Contributes to protecting cells from oxidative stress: EFSA 2009; 7(9):1226 ; 2010;8(10):1815
- Contributes to collagen formation
- Vital for iron metabolism (transferrin -> ferritin)
- Henmi et al showed 2003 in a controlled randomized study that women taking 750 mg ascorbic acid per day had higher progesterone levels and higher pregnancy rates
- Antioxidants like vitamin C are particularly important for active and passive smokers (Alberg et al, 2002, Dietrich et al, 2003).
- Women with total vitamin C intakes of <10th percentile preconceptionally have twice the risk of preterm delivery because of premature rupture of the membranes (Siega-Riz et al, 2003)
- In patients with a luteal phase defect supplementation of vitamin C leads to higher pregnancy rates (Henmi et al, 2003)

### Vitamin E

- Contributes to protecting cells from oxidative stress: EFSA 2010;8(10):1816
- „ particularly folic acid, vitamin B6, vitamin C, vitamin D, vitamin E, iodine, selenium, iron, ... might have a positive impact on infertility treatment“ (Buhling and Graejecki, 2013)

### Vitamin D

- vitamin D deficiency has been linked to infertility and pregnancy loss (Lerchbaum et al, 2012)
- Contributes to normal function of the immune system: EFSA 2010; 8(2):1468
- Has a role in cell division: EFSA 2009; 7(9):1227

### Vitamin B1 (Thiamine)

- Contributes to normal energy metabolism: EFSA 2009; 7(9):1222
- Contributes to normal heart action: EFSA 2009; 7(9):1222

### Vitamin B2 (Riboflavin)

- Contributes to normal energy metabolism: EFSA 2010;8(10):1814
- Contributes to maintenance of normal red blood cells: EFSA 2010;8(10):1814
- Contributes to protecting cells from oxidative stress: EFSA 2010;8(10):1814
- Riboflavin contributes to the maintenance of normal mucous membranes: EFSA 2010;8(10):1814

### Vitamin B3 (Niacin)

- Contributes to normal energy metabolism: EFSA 2009; 7(9):1224; 2010;8(10):1757
- Niacin contributes to the maintenance of normal mucous membranes: EFSA 2009; 7(9):1224

### Vitamin B5 (Pantothenic acid)

- Contributes to normal energy metabolism: EFSA 2009; 7(9):1218
- Contributes to normal synthesis and metabolism of steroid hormones, vitamin D and some neurotransmitters: EFSA 2009; 7(9):1218

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### Vitamin B6 (Pyridoxine)

- Contributes to normal energy metabolism: EFSA 2010;8(10):1759
- Contributes to normal homocysteine metabolism: EFSA 2010;8(10):1759
- Contributes to normal red blood cell formation: EFSA 2009; 7(9):1225
- Contributes to normal function of the immune system: EFSA 2009; 7(9):1225
- Contributes to regulation of hormone action: EFSA 2009; 7(9):1225
- Used in traditional medicine for relief of premenstrual syndrome, menopausal symptoms and for fertility improvement.
- Deficiency of vitamin B6 has been linked to decreased conception rates and an increased risk of early miscarriage (Ronnenberg et al, 2007)

### Biotin

- Contributes to normal energy metabolism: EFSA 2009; 7(9):1209
- Biotin contributes to the maintenance of normal mucous membranes: EFSA 2009; 7(9):1209

### Folic acid

- Contributes to growth of maternal tissue during pregnancy: EFSA 2009; 7(9):1213
- Contributes to normal blood formation: EFSA 2009; 7(9):1213
- Contributes to normal homocysteine metabolism: EFSA 2009; 7(9):1213
- Contributes to normal function of the immune system: EFSA 2009; 7(9):1213
- Has a role in cell division: EFSA : 2009; 7(9):1213 ; 2010;8(10):1760
- A diet high in synthetic folate may be associated with increased progesterone levels and lower risk of sporadic anovulation (Gaskins et al, 2012)
- Important for healthy neural tube development
- Supplementation during fertility treatment improves oocyte quality (Szymanski et al, 2003)

### Vitamin B12 (Cobalamin)

- Contributes to normal energy metabolism: EFSA 2009; 7(9):1223
- Contributes to normal homocysteine metabolism: EFSA 2010;8(10):4114
- Contributes to normal formation of red blood cells: EFSA 2009; 7(9):1223
- Contributes to normal function of the immune system: EFSA 2009; 7(9):1223
- Has a role in cell division: EFSA 2009; 7(9):1223; 2010;8(10):1756
- Deficiencies are frequently found in vegetarians
- In 2001, Bennet et al found that patients (n=14) with vitamin B12 deficiency often suffer from subfertility and miscarriage. Supplementing the vitamin resulted in a rise in pregnancy rate and a fall in miscarriage rate
- Molloy et al (2008) showed that low B12 levels in early pregnancy are linked to an increased risk of spina bifida (split spine)

### Zinc

- Contributes to normal DNA-synthesis: EFSA 2010;8(10):1819
- Contributes to normal fertility and reproduction: EFSA 2009; 7(9):1229
- Contributes to normal function of the immune system: EFSA 2009; 7(9):1229
- Contributes to protecting cells from oxidative stress: EFSA 2009; 7(9):1229
- Has a role in cell division: EFSA 2009; 7(9):1229

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### Magnesium

- Contributes to normal energy metabolism: EFSA 2009; 7(9):1216
- Has a role in cell division: EFSA 2009; 7(9):1216
- Pregnancy is associated with an increased risk for deficiency due to an increased demand and an increase of up to 25 % in excretion
- Deficiency symptoms include muscular hyperexcitability , which in pregnancy might lead to premature labor
- Therefore supplementation of magnesium is recommended from 16 gestational week
- Dose is important: Studies show (e.g.Fine et al, 1991) that only 35 % from 120 mg are resorbed by the body and when taking a higher dose of 360 mg this is even reduced to 18 %

### Iron

- Contributes to normal energy metabolism: EFSA 2009; 7(9):1215; 2010;8(10):1740
- Contributes to normal to normal hemoglobin and red blood cell formation: EFSA 2009; 7(9):1215; 2010;8(10):1740
- Contributes to normal transport of oxygen in the human body: EFSA 2009; 7(9):1215; 2010;8(10):1740
- Contributes to normal function of the immune system: EFSA 2009; 7(9):1215
- Contributes to reduction of tiredness: EFSA 2010;8(10):1740
- Has a role in cell division: EFSA 2009; 7(9):1215
- Consumption of iron supplements and nonheme iron from other sources may decrease the risk of ovulatory infertility (Chavarro et al 2006)
- During pregnancy demand doubles from 15 mg to 30 mg
- Women with iron deficiency have decreased fertility (Rushton et al, 1991)

### Coenzyme Q10

- Antioxidant
- Tissue concentration is 5 – 10 x higher than vitamin E (Bentinger et al, 2007)
- Important for ATP-synthesis in the mitochondria (Mitchell, 1975, Santos-Ocana, 2002)
- Effective ATP production is required for oocyte maturation and early stages of embryonic development (Jansen et al, 1998)
- Tissue concentration of coenzyme Q10 declines with age (Pignatti et al, 1980)
- When supplementing coenzyme Q10, the majority is detected in adrenal gland and ovary ( Bentiger et al, 2008)

### Iodine

- Contributes to normal energy metabolism: EFSA 2009; 7(9):1214; 2010;8(10):1800
- Contributes to normal thyroid function and normal thyroid hormone synthesis: EFSA 2009; 7(9):1214; 2010;8(10):1800
- Mothers to be are recommended to have full stores, as the child will cause an increased demand

Dr. Daniel Matthes, Regulatory Affairs

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