Package leaflet: Information for the user

Zafrilla 2 mg tablets

dienogest

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Zafrilla is and what it is used for

Zafrilla is a preparation for the treatment of endometriosis (painful symptoms due to displaced tissue of the lining of the womb). Zafrilla contains a hormone, the progestogen dienogest.

2. What you need to know before you take Zafrilla

Do not take Zafrilla:
- if you are suffering from a **blood clot** (thromboembolic disorder) in your veins. This may occur, for example, in the blood vessels of the legs (deep vein thrombosis) or the lungs (pulmonary embolism). See also *"Zafrilla and venous blood clots"* below;
- if you have or have ever had a **severe arterial disease**, including cardiovascular disease, such as a **heart attack**, **stroke** or **heart disease** which causes a reduced blood supply (angina pectoris). See also "*Zafrilla and arterial blood clots"* below;
- if you have **diabetes** with blood vessel damage;
- if you have or have ever had **severe liver disease** (and your liver function values have not returned to normal). Symptoms of liver disease may be yellowing of the skin and/or itching of the whole body;
- if you have or have ever had a **benign or malignant liver tumour**;
- if you suffer or have ever suffered, or if it is suspected that you suffer from a **malignant** sex-hormone dependent tumour such as cancer of the breast or the genital organs;
- if you have any unexplained **vaginal bleeding**;
- if you are **allergic (hypersensitive)** to dienogest or any of the other ingredients of this medicine (listed is section 6).

If any of these conditions appear for the first time while using Zafrilla, stop taking it at once and consult your doctor.

Warnings and precautions
Talk to your doctor or pharmacist before taking Zafrilla.

You must not use hormonal contraceptives of any form (tablet, patch, intrauterine system) while taking Zafrilla.

Zafrilla is **not** a contraceptive. If you want to prevent pregnancy, you should use condoms or other non-hormonal contraceptive precautions.

In some situations you need to take special care while using Zafrilla, and your doctor may need to examine you regularly. Tell your doctor if any of the following conditions applies to you:
If you:
- have ever had a **blood clot** (venous thromboembolism) or anyone in your immediate family has had a blood clot at a relatively early age;
- have a close relative who has had **breast cancer**;
- have ever suffered from **depression**;
- have **high blood pressure** or develop high blood pressure while taking Zafrilla;
- develop a **liver disease** while taking Zafrilla. Symptoms may include yellowing of the skin or eyes or itching all over your body. Inform your doctor also if such symptoms occurred during a previous pregnancy;
- have diabetes or had **diabetes** temporarily during previous pregnancy;
- have ever had **chloasma** (golden-brown patches on the skin, particularly of the face); if so, avoid too much exposure to the sun or ultraviolet radiation;
- suffer from **pain in your lower abdomen** while taking Zafrilla.

While taking Zafrilla your chance of becoming pregnant is reduced because Zafrilla may affect ovulation.

If you become pregnant while taking Zafrilla you are at **a slightly increased risk** of having an extrauterine pregnancy (the embryo develops outside the womb). Tell your doctor before you start taking Zafrilla, if you had an extrauterine pregnancy in the past or have an impaired function of the Fallopian tubes.

Zafrilla and serious uterine bleeding
Uterine bleeding, for example in women with a condition where the mucous membrane of your uterus (endometrium) grows into the muscle layer of your uterus, called adenomyosis uteri or **benign tumours of the womb** sometimes called uterine fibroids (uterine leiomyomata), may become worse with the use of Zafrilla. If bleeding is heavy and continuous over time, this may lead to low red blood cell levels (anemia), which may be severe in some cases. In the event of anemia, you should discuss with your doctor if you should stop taking Zafrilla.

Zafrilla and changes in bleeding pattern
Most women treated with Zafrilla experience changes in their menstrual bleeding pattern (see section 4, Possible side effects).

Zafrilla and venous blood clots
Some studies indicate that there may be a slight, but not statistically significant, increased risk of a **blood clot in the legs (venous thromboembolism)** associated with the use of preparations with progestagens like Zafrilla. Very rarely, blood clots may cause serious permanent disabilities or may even be fatal.

The risk of a **venous blood clot** increases:
- with increasing age;
- if you are overweight;
- if you or one of your close relatives had a blood clot in the leg (thrombosis), lung (pulmonary embolism), or other organ at a young age;
- if you must have surgery, if you have had a serious accident or if you are immobilized for a long time. It is important to tell your doctor in advance that you are using Zafrilla as the treatment may have to be stopped. Your doctor will tell you when to start Zafrilla again. This is usually about two weeks after you are back on your feet.

Zafrilla and arterial blood clots
There is little evidence for an association between preparations with progestagens like Zafrilla and an increased risk of a blood clot in, for example, the bloodvessels of the heart (heart attack) or the brain (stroke). In women with hypertension the risk of stroke may be slightly enhanced by these preparations.

The risk of an **arterial blood clot** increases:
- **if you smoke. You are strongly advised to stop smoking when you use Zafrilla, especially if you are older than 35 years.**
- if you are overweight;
- if one of your close relatives had a heart attack or stroke at a young age;
- if you have high blood pressure.

Talk to your doctor before taking Zafrilla **Stop taking Zafrilla and contact your doctor immediately if you notice possible signs of a blood clot, such as:**
- severe pain and/or swelling in one of your legs;
- sudden severe pain in the chest which may reach the left arm;
- sudden breathlessness;
- sudden cough without an obvious cause;
- any unusual, severe or long-lasting headache or worsening of migraine;
- partial or complete blindness or double vision;
- difficulty in speaking or inability to speak;
- giddiness or fainting;
- weakness, strange feeling, or numbness in any part of the body.

Zafrilla and cancer
It is not clear from the data currently available whether or not Zafrilla increases the risk of breast cancer. Breast cancer has been observed slightly more often in women taking hormones compared to those not taking hormones, but it is not known whether this is caused by the treatment. For example, it may be that more tumours are detected and detected earlier in women taking hormones because they are examined by their doctor more often. The occurrence of breast tumours becomes gradually less after stopping the hormone treatment. **It is important to regularly check your breasts** and you should contact your doctor if you feel any lump.
In rare cases, benign liver tumours, and in even fewer cases malignant liver tumours have been reported in women taking hormones. Contact your doctor if you have unusually severe stomach pain.

Zafrilla and osteoporosis
Changes in bone mineral density (BMD)
The use of Zafrilla may affect the strength of the bone of adolescents (12 to under 18 years). If you are under 18 your doctor will, therefore, carefully weigh the benefits and risks of using Zafrilla for you as an individual patient, taking into account possible risk factors for bone loss (osteoporosis).

If you use Zafrilla, it will help your bones if you have an adequate intake of calcium and vitamin D either via your food or via supplements.

If you have an increased risk of getting osteoporosis (weakening of bones due to loss of bone minerals), your doctor will carefully weigh the risks and benefits of treatment with Zafrilla because Zafrilla has a moderate suppressing effect on the production of oestrogen (another type of female hormone) by your body.

Children and adolescents
Zafrilla is not for use in girls before menarche (first menstrual bleeding).
The use of Zafrilla may affect the strength of the bone of adolescents (12 to under 18 years). If you are under 18 your doctor will, therefore, carefully weigh the benefits and risks of using Zafrilla for you as an individual patient, taking into account possible risk factors for bone loss (osteoporosis).

Other medicines and Zafrilla
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
Some medicines can have an influence on the blood levels of Zafrilla and can make it less effective, or can cause undesirable effects.
These include:
- medicines used for the treatment of
  - **epilepsy** (e.g. phenytoin, barbiturates, primidone, carbamazepine, oxcarbazepine, topiramate, felbamate);
  - **tuberculosis** (e.g. rifampicin);
  - **HIV and Hepatitis C Virus infections** (so-called protease inhibitors and non-nucleoside reverse transcriptase inhibitors such as ritonavir, nevirapine, efavirenz);
  - **fungal infections** (griseofulvin, ketoconazole).
- the herbal remedy **St. John's** wort.

Ask your doctor or pharmacist for advice before taking any medicine.

Zafrilla with food and drink
During Zafrilla treatment, you should avoid drinking grapefruit juice, because this may increase the levels of Zafrilla in your blood. This may increase the risk of getting side effects.

Laboratory tests
If you need a blood test, tell your doctor or the laboratory staff that you are taking Zafrilla, because Zafrilla can affect the results of some tests.

Pregnancy, breast-feeding and fertility
Do not take Zafrilla if you are pregnant or breast-feeding.

Driving and using machines
No effects on the ability to drive and use machines have been observed in users of Zafrilla.

Zafrilla contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Zafrilla

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

For adults, the usual dose is 1 tablet per day.

The following statements apply to Zafrilla unless otherwise prescribed by your doctor. Please follow these instructions, otherwise you will not fully benefit from Zafrilla.

You can start treatment with Zafrilla on any day of your natural cycle.

Adults: take one tablet every day, preferably at the same time with some liquid as needed. When a pack is finished the next one should be started without interruption. Continue to take the tablets also on days of menstrual bleeding.

There is no experience with Zafrilla treatment >15 months in patients with endometriosis.

If you take more Zafrilla than you should

There have been no reports of serious harmful effects from taking too many Zafrilla tablets at one time. However, if you are concerned, contact your doctor.

If you forget to take Zafrilla or suffer from vomiting or diarrhoea
Zafrilla will be less effective if you miss a tablet. If you miss one or more tablets, take one tablet only as soon as you remember, and then continue next day taking the tablet at your usual time.

If you vomit within 3-4 hours of taking Zafrilla or you have severe diarrhoea, there is a risk that the active substance in the tablet will not be taken up by your body. The situation is almost the same as forgetting a tablet. After vomiting or diarrhoea within 3-4 hours of taking Zafrilla, you should take another tablet as soon as possible.

Do not take a double dose to make up for a forgotten tablet.

If you stop taking Zafrilla
If you stop taking Zafrilla, your original endometriosis symptoms may return.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. These effects are more common during the first months after start of intake of Zafrilla and usually disappear with continued use. You may also experience changes in your bleeding pattern, such as spotting, irregular bleeding or your periods may stop completely.

Common (may affect up to 1 in 10 people)
- weight gain;
- depressed mood, problems sleeping, nervousness, loss of interest in sex, or changed mood;
- headache or migraine;
- nausea, abdominal pain, wind, swollen tummy or vomiting;
- acne or hair loss;
- back pain;
- breast discomfort, ovarian cyst or hot flushes;
- uterine/vaginal bleeding including spotting;
- weakness or irritability.

Uncommon (may affect up to 1 in 100 people)
- low red blood cell count (anaemia);
- weight loss or increase in appetite;
- anxiety, depression or mood swings;
- imbalance in the autonomic nervous system (controls unconscious bodily functions, e.g. perspiration) or disturbed attention;
- dry eye;
- ringing in the ears (tinnitus);
- unspecific circulatory problems or uncommon palpitations;
- low blood pressure;
- shortness of breath;
- diarrhoea, constipation, abdominal discomfort, inflammation of the stomach and intestines (gastrointestinal inflammation), inflammation of the gums (gingivitis);
- dry skin, excessive sweating, severe itching of the whole body, male pattern hair growth (hirsutism), brittle nails, dandruff, dermatitis, abnormal hair growth, hypersensitive response to light or problems with skin pigmentation;
- pains in your bones, muscle spasms, pains and/or a sensation of heaviness in your arms and hands or legs and feet;
- urinary tract infection;

- vaginal thrush, dryness of the genital area, vaginal discharge, pelvic pain, atrophic inflammation of the genitals with discharge (atrophic vulvovaginitis), or a lump or lumps in the breast;
- swelling due to fluid retention.

Additional side effects in adolescents (12 to under 18 years): loss of bone density.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Zafrilla

Keep this medicine out of the sight and reach of children.

Store in the original package in order to protect from light.
This medicine does not require any special temperature storage conditions.

Do not use this medicine after the expiry date which is stated on the outer packaging and blister after "EXP". The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Zafrilla contains
The active substance is dienogest. Each tablet contains 2 mg dienogest.

The other ingredients are lactose monohydrate, pregelatinised maize starch, microcrystalline cellulose, povidone K-25, crospovidone (type A), talc, magnesium stearate.

What Zafrilla looks like and contents of the pack
Zafrilla 2 mg tablets are white or almost white, round, flat, bevelled-edge tablets, engraved with "G 93" on one side and with "RG" on the other side. The diameter of the tablets is 7 mm.

28, 84, 168 Zafrilla 2 mg tablets are packaged in green, hard PVC//Al calendar blisters in folded carton box.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Gedeon Richter Plc.
Gyömrői út 19-21
1103 Budapest
Hungary

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