emily

Estradiol Valerate
Dienogest

CONTRACEPTIVES
Urufarma

Formula:
Each pale-yellow tablet contains: Estradiol valerate 3 mg and excipients (q.s.) Each pale pink tablet contains: Estradiol valerate 2 mg, Dienogest 2 mg and excipients (q.s.) Each Estradiol valerate 2 mg, Dienogest 3 mg and excipients (q.s.) Each dark pink tablet contains: Estradiol valerate 1 mg and excipients (q.s.) Each white coated tablet contains: excipients (q.s.)

Therapeutic effect:
Contraceptive.

Indications:
Preventing pregnancy. Treatment of heavy menstrual bleeding in women without any organ pathology who wishes to use oral contraception.

Posology and method of administration:
Take one tablet daily for 28 consecutive days, in the order indicated on the pack, at approximately the same time, with a little liquid if necessary. The tablets are taken continuously. Each new pack is started the day after the last tablet of the previous pack is finished. Menstrual bleeding usually starts while taking last tablets in the pack and may have not stopped before the next pack is started. In some women, bleeding starts after taking the first tablets from the new pack.
Take the tablets in the following order: 2 pale yellow tablets, 5 pale pink tablets, 17 cream-coloured tablets, 2 dark pink tablets, and: finally, 2 white tablets.
Treatment with Emily should be started as follows, as appropriate:
Without prior use of hormonal contraceptives, the previous month.
Start taking the tablets on day 1 of the natural female cycle, that is, the first day of menstrual bleeding.
• *Changing from a combined oral contraceptive (COC), vaginal ring or transdermal patch.*
Start after taking the last active tablet (last tablet containing the drug substances) of the previous COC. In case of a vaginal ring or transdermal patch, start taking Emily the day the device is removed.
• *Changing from a gestagen-only method (progestogen-only tablet, injection, implant) or an progestogen-releasing intrauterine system (IUS).*
Progestogen-only tablets alone can be replaced any day. In the case of an implant or IUS, replace treatments on the day of removal and in the case of an injectable, on the day of the next injection. In all these cases, a barrier method should be used in addition during the first 9 days of taking the tablets.
- *After abortion or miscarriage in the first trimester.*
You can start taking this medicine right away. In this case, other contraceptive methods are unnecessary.
- *After childbirth, abortion, or miscarriage in the second trimester.*
Administration in non-lactating women can begin 21 to 28 days after delivery or second-trimester abortion or miscarriage. If you start later, you should additionally use a barrier method during the first 9 days of taking the tablets. If you have had sexual intercourse already, rule out pregnancy before starting administration, or wait for the first menstrual period.

What to do if you miss a tablet: Missing a dummy tablet (white) will not have any consequences. Nevertheless, these tablets must be discarded to avoid inadvertently prolonging the interval between taking the active tablets.
The following advise applies only to missing active tablets:
If less than 12 hours have passed since you missed a tablet, contraceptive protection is not reduced. You should take the tablet as soon as you remember and continue to take the next tablets at the usual time.
If more than 12 hours have passed since you missed a tablet, contraceptive protection may be reduced. Take the last forgotten tablet as soon as you remember, even if this means taking two tablets at the same time. Afterwards, you will continue to take the tablets at the usual time.
Depending on the day of the cycle on which you forgot to take the tablet, you should use additional contraceptive measures (e.g., a barrier method such as a condom), as described in the outline below. Do not take more than two tablets per day.
If you forget to start a new pack or if you forget to take one or more tablets on days 3 to 9, consider the possibility that you might be pregnant (if you have had sexual intercourse within 7 days of forgetting). The more tablets (containing both active ingredients, days 3 to 24) you have missed and the closer you are to the dummy medication (white tablets) phase, the higher the risk of pregnancy.
If you forget to take several tablets and subsequently have no withdrawal bleeding at the end of the pack/beginning of the new pack, consider the possibility of pregnancy.

Day	Colour Estradiol valerate (EV) /Dienogest (D) content	Principios a seguir si olvida tomar un comprimido y han pasado más de 12 horas:
1-2	Pale yellow tablets (3.0 mg of EV)	- Take the tablet that you missed immediately and take the next tablet as usual (this may mean that you take two tablets on the same day). - Keep taking the tablets as usual. - Use an additional contraceptive method for the following 9 days.
3-7	Pale pink tablets (2.0 mg of EV/2.0 mg of D)	
8-17	Cream coloured tablets (2.0 mg of EV/3.0 mg of D)	
18-24	Cream coloured tablets (2.0 mg of EV/3.0 mg of D)	- Discard the current pack and immediately take the first tablet of the new pack. - Keep taking the tablets as usual. - Use an additional contraceptive method for the following 9 days.
25-26	Dark pink tablets (1.0 mg of EV)	- Take the pill that you missed immediately and take the next pill as usual (this may mean that you take two pills on the same day). - No additional contraceptive method is required.
27-28	White tablets (dummy medication)	- Discard the missed tablet and keep taking the tablets as usual. - No additional contraceptive method is required.

Contraindications
Combined oral contraceptives should not be used in the presence of any of the conditions listed below. If any of these conditions appear for the first time during use, treatment should be discontinued immediately.

- Presence or risk venous thromboembolism (VTE).
current VTE (with anticoagulants) or history of VTE (e.g., deep vein thrombosis (DVT) or pulmonary embolism (PE)); known hereditary or acquired predisposition to venous thromboembolism (VTE), such as activated protein C (APC) resistance (including factor V Leiden), antithrombin III deficiency, protein C deficiency, protein deficiency; major surgery with prolonged immobilisation; elevated risk of VTE due to the presence of several risk factors.
- Presence or risk of arterial thromboembolism (ATE).
current arterial thromboembolism (ATE), history of ATE (e.g., myocardial infarction) or prodromal condition (e.g., angina pectoris); cerebrovascular disease (current stroke, history of stroke, or prodromal condition such as transient ischaemic attack, TIA); known hereditary or acquired predisposition to arterial thromboembolism (ATE), such as hyperhomocysteinemia and antiphospholipid antibodies (anticardiolipin antibodies, lupus anticoagulant); History of migraine with focal neurological symptoms, elevated risk of ATE due to multiple risk factors or the presence of a severe risk factor (diabetes mellitus with vascular symptoms, severe hypertension, severe dyslipoproteinaemia).
- existence or history of severe liver disease, provided that the values of liver function tests have not returned to normal
- Existence or history of liver tumours (benign or malignant)
- Known or suspected sex hormone-dependent malignancies (e.g., of genital organs or breasts)
- Undiagnosed vaginal bleeding
- Pregnancy (known or suspected)
- Hypersensitivity to the drug substances or any of the other components of the formula.

Data on special populations:
Children and teenagers: No data on use in teenagers under 18 years of age are available.
Geriatric patients: This medicine is not indicated after menopause.
Patients with liver failure: This medicine is contraindicated in women with severe liver disease.
Patients with renal impairment: This medicinal product has not been specifically studied in patients with renal impairment.

Precautions and warnings
Before starting or resuming treatment with Emily, a complete history should be assessed (including family history) and pregnancy should be ruled out. Blood pressure should be measured, and a complete physical examination should be performed.
In case of severe gastrointestinal disturbances (e.g., vomiting or diarrhoea), absorption may not be complete and additional contraceptive measures should be taken. If you vomit within 3 to 4 hours of taking the active tablet, take the next tablet as soon as possible, no later than 12 hours after the usual time when you take the tablets. If more than 12 hours have passed, follow the instructions under "What to do if you miss a dose".
The use of any combined hormonal contraceptive (CHC) increases the risk of venous thromboembolism (VTE) compared to non-use. Medicines containing levonorgestrel, norgestimate, or norethisterone are associated with the lowest risk of VTE. Limited available data suggest that Emily might have a similar VTE risk. The risk of VTE is highest during the first year of use and there is evidence that the risk increases when the CHC treatment is resumed after a break of 4 weeks or more. VTE can be fatal in 1 to 2% of cases.
The risk of venous thromboembolic complications may increase substantially in women with additional risk factors, particularly if they have several risk factors. This medicine is contraindicated in women who have several risk factors that put them at elevated risk of venous thrombosis. COCs should not be prescribed in case of a negative benefit-risk balance.
The risk of VTE increases when: age, obesity (body mass index greater than 30 kg/m^2), positive family history (a case of venous thromboembolism in a sibling or parent at a relatively young age), prolonged immobilisation, major surgery, any surgery of the legs or pelvis, neurosurgery or severe trauma (under these circumstances it is advisable to discontinue use (in the case of scheduled surgery, at least four weeks in advance) and not resume use until two weeks after full recovery of mobility and antithrombotic treatment should be considered if use of Emily has not been discontinued already. Temporary immobilisation, including air travel longer than 4 hours, may also be a risk factor for VTE, especially in women with other risk factors.
Other diseases that have been associated with VTE include cancer, systemic lupus erythematosus, haemolytic-uraemic syndrome, chronic inflammatory bowel disease (e.g., Crohn's disease or ulcerative colitis), and sickle cell disease.
Symptoms of deep vein thrombosis (DVT) may include: unilateral swelling of the leg and/or foot or along a vein in the leg; pain or tenderness in the leg, which may only be noticed when standing or walking; raised temperature of the compromised leg; redness or discolouration of the skin on the leg. Symptoms of pulmonary embolism (PE) may include: sudden onset of shortness of breath or rapid breathing without a cause, sudden cough that may be associated with haemoptysis, severe chest pain, severe light-headedness, or dizziness, rapid or irregular heartbeat. Other signs of vascular occlusion may include: sudden pain, swelling and slight blue discolouration of a limb.
If the occlusion occurs in the eye, symptoms can range from painless blurred vision, which can progress to loss of vision. Sometimes vision loss can occur almost immediately.
Epidemiological studies have associated the use of CHCs with an increased risk of arterial thromboembolism (myocardial infarction) or stroke (e.g., transient ischaemic attack, ictus). Arterial thromboembolic episodes can be fatal.
The risk of developing arterial thromboembolic complications or stroke is increased by: age, smoking, obesity (body mass index over 30 kg/m^2), high blood pressure, migraine, or a family history of this condition (a case of arterial thromboembolism in a sibling or parent at a relatively young age). Other diseases that have been associated with adverse vascular events include diabetes mellitus, hyperhomocysteinemia, valvular heart disease and atrial fibrillation, dyslipoproteinaemia and systemic lupus erythematosus.
Symptoms of a stroke include: sudden numbness or weakness of the face, arm or leg, especially on one side of the body; sudden difficulty walking, dizziness, loss of balance or coordination; sudden confusion, difficulty in speaking or understanding; sudden difficulty in eye-sight, in one or both eyes; sudden, intense and prolonged headaches, without known causes; loss of consciousness or fainting, with or without convulsions. Symptoms of myocardial infarction (MI) may include: pain, discomfort, pressure, leaden paralysis, tightness or fullness in the chest, arm or under the breastbone; discomfort that spreads to the back, jaw, throat, arm, or stomach; feeling of fullness, indigestion or choking; sweating, nausea, vomiting or dizziness; extreme weakness, anxiety or shortness of breath; rapid or irregular heartbeat.
Some epidemiological studies have reported an increased risk of cervical cancer in long-term COC users (greater than 5 years).
Epidemiological studies have shown a slightly increased relative risk (RR = 1.24) of breast cancer diagnosis in women taking COCs. This increased risk gradually disappears within 10 years of stopping COCs. Since breast cancer is rare in women under the age of 40, the increase in diagnosed cases of breast cancer in current and recent COCs users is small relative to the overall risk of breast cancer.
In rare cases, benign liver tumours (and even more rarely, malignant tumours) have been reported in COC users. In isolated cases, these tumours have resulted in life-threatening intra-abdominal haemorrhages. Existence of a liver tumour should be considered during the differential diagnosis of women taking COCs with severe upper abdominal pain, liver enlargement, or signs of intra-abdominal bleeding.
In case of acute or chronic disturbances of liver function it may be necessary to discontinue use until liver function values return to normal. Recurrence of cholestatic jaundice that first appeared during pregnancy, or during previous use of sex steroids requires discontinuation of treatment.
In women with a personal or family history of hypertriglyceridemia, the risk of pancreatitis is increased during oral contraceptive use.
Small increases in blood pressure have been reported during COC use, but clinically relevant increases are rare. However, if clinically significant and sustained hypertension occurs during COC use, consult your doctor.
The following conditions have been reported to occur or worsen during both pregnancy and COC use, but the evidence for their association with COCs is inconclusive: jaundice and/or pruritus related to cholestasis, gallstones, porphyria, systemic lupus erythematosus, haemolytic uraemic syndrome, Sydenham's chorea, herpes gravidarum, otosclerosis-related hearing loss.
In women with hereditary angioedema, exogenous oestrogens may induce or exacerbate angioedema symptoms.
Peripheral insulin resistance or glucose tolerance may be affected; therefore, diabetic patients should be carefully monitored while taking hormonal contraceptives.
Worsening of endogenous depression, epilepsy, Crohn's disease, and ulcerative colitis has been reported during COC use.
Depressed mood and depression are recognised adverse reactions to the use of hormonal contraceptives. Depression can be severe and is a recognised risk factor associated with suicidal behaviour and suicide. Consult your doctor if you experience mood swings and depressive symptoms, even if they appear shortly after starting treatment.
Chloasma may occur infrequently, especially in women with a history of gestational chloasma. Therefore, sun exposure and ultraviolet radiation should be avoided during treatment.
Oestrogens may cause fluid retention, hence, patients with impaired heart or kidney function should be carefully monitored. Patients with end-stage renal failure should be closely monitored as the level of circulating oestrogens may increase with administration of Emily.
All COCs may cause irregular bleeding (spotting or intermenstrual bleeding), especially during the first few months of use. Therefore, the assessment of any irregular bleeding is only meaningful after an adaptation interval of about 3 cycles.
Patients may experience amenorrhoea without being pregnant. According to studies, amenorrhoea occurs in about 15 % of cycles.
If you have taken Emily as instructed, it is unlikely that you are pregnant. If you have not taken it according to these instructions before the first missing a period, or if there is no bleeding in two consecutive cycles, you must rule out the possibility of pregnancy before continuing use. If bleeding irregularities persist or occur after previously regular cycles, talk to your doctor.
This medicine contains lactose. Patients with hereditary intolerance to galactose, Lapp lactase insufficiency, or poor absorption of glucose or galactose should not take this medicine.
Hormonal contraceptives do not protect against HIV infection (AIDS) or any other sexually transmitted diseases.
Breastfeeding: COCs may affect breastfeeding by reducing the quantity of breast milk and changing its composition. Therefore, the use of Emily is not recommended until finishing breastfeeding. During the use of COCs, small amounts of contraceptive steroids and/or their metabolites may be excreted in the milk, which may affect the breastfeeding baby.

Drug-drug interactions
- *Effects of other medicines on Emily*
Interactions with medicines that induce microsomal enzymes may occur. This may result in increased clearance of sex hormones and may lead to intermenstrual bleeding and/or contraceptive failure. During short-term treatment with enzyme-inducing medicines, a barrier method (e.g., condom) or another birth control method should be used temporarily in addition to the COCs. The barrier method should be used for the duration of concomitant administration of this medicine and for 28 days after discontinuation. If the drug treatment extends beyond the end of the active tablets in the blister, the dummy tablets should be discarded, and a new pack should be started.
In case of long-term treatment with liver enzyme-inducing active substances, another reliable non-hormonal method of contraception should be used.
Concurrent use with enzyme inducers may decrease contraceptive efficacy: barbiturates, carbamazepine, phenytoin, primidone, rifampicin, HIV medicines, ritonavir, nevirapine, efavirenz, and possibly also felbamate, griseofulvin, oxcarbazepine, topiramate, as well as products containing St. John's Wort (*Hypericum perforatum*).
When coadministered with oral contraceptives, many HIV protease inhibitors and non-nucleoside reverse transcriptase inhibitors, including combinations with HCV inhibitors, may increase or decrease plasma concentrations of oestrogens or progestogens. The net effect of these changes may be clinically relevant in some cases. In case of doubt, use an additional barrier method (e.g., condom). Dienogest is a substrate of CYP3A4.
The clinical relevance of potential interactions with enzyme inhibitors is unknown.
Concomitant administration of potent CYP3A4 inhibitors may increase plasma concentrations of dienogest, estradiol, or both.
Coadministration with ketoconazole, a potent CYP3A4 inhibitor, resulted in a 2.9-fold and 1.6-fold increase in steady-state AUC (0-24 h) for Dienogest and Estradiol, respectively. Concomitant administration with erythromycin, a moderate inhibitor, resulted in a 1.6-fold and 1.3-fold increase in the steady-state AUC (0-24 h) for dienogest and estradiol, respectively.
- *Effects of Emily on other medicines*
Oral contraceptives may affect the metabolism of other drugs. Consequently, plasma and tissue levels may increase (like cyclosporine) or decrease (like lamotrigine).
- *Laboratory tests*
The use of oral contraceptives may affect the results of certain laboratory tests, such as biochemical parameters of liver, thyroid, adrenal and renal function, plasma levels of transport proteins (e.g., corticosteroid transporting globulin, and lipid/lipid-protein fractions), parameters of carbohydrate metabolism, and parameters of coagulation, and fibrinolysis. Generally, changes remain within the normal limits.

Adverse reactions
The most frequently reported adverse reactions in women without any organ pathology are acne, breast discomfort, headache, intermenstrual bleeding, nausea, and weight gain.
The most serious adverse reactions associated with COC use are arterial and venous thromboembolism, which are described in *Precautions and Warnings*. The adverse reactions listed below are classified according to their frequency of occurrence according to the following criteria:
Common: >1/100 to <1/10
Uncommon: >1/1.000 to < 1/100
Rare: >1/10.000 to < 1/1.000
Infections and infestations
Uncommon: fungal infection, vulvovaginal fungal infection, vaginal infection. *Rare:* candidiasis, oral herpes, pelvic inflammatory disease, suspected ocular histoplasmosis syndrome, tinea versicolor, urinary tract infection, bacterial vaginitis.
Metabolic and nutrition disorders.
Uncommon: weight gain. *Rare:* fluid retention, hypertriglyceridemia.
Psychiatric disorders
Uncommon: depression or depressed mood, emotional disorders, insomnia, decreased libido, mental disorder, mood swings. *Rare:* aggression, anxiety, dysphoria, increased libido, nervousness, nightmares, unease, sleep disorders, stress.
Nervous system disorders
Common: headache. *Uncommon:* dizziness, migraine. Rare: decreased attention, paraesthesia, vertigo.
Eye disorders
Rare: intolerance to wearing contact lenses, dry eye, eye swelling.
Heart disorders
Rare: myocardial infarction, palpitations.
Vascular disorders
Uncommon: hot flushes, hypertension. *Rare:* varicose vein bleeding, venous thromboembolism (VTE), and arterial thromboembolism (ATE), hypotension, superficial phlebitis, venous pain.
Gastrointestinal tract disorders
Common: nausea, abdominal pain. *Uncommon:* vomiting, diarrhoea. *Rare:* constipation, dry mouth, dyspepsia, gastro-oesophageal reflux disease.
Hepatobiliary disorders
Uncommon: increased liver enzymes. *Rare:* Focal nodular hyperplasia of the liver, chronic cholecystitis.
Skin and connective tissue disorders
Common: Acne *Uncommon:* alopecia, hyperhidrosis, pruritus, rash. *Rare:* allergic skin reaction, chloasma, dermatitis, hirsutism, hypertrichosis, neurodermatitis, pigmentation disorder, seborrhoea, skin disorder.
Musculoskeletal and connective tissue disorders
Uncommon: muscle spasms. Rare: back pain, jaw pain, leaden paralysis.
Kidney and urinary disorders
Rare: urinary tract pain.
Reproductive and breast disorders
Common: amenorrhoea, breast discomfort, dysmenorrhoea, intermenstrual bleeding (metrorrhagia). *Uncommon*: breast enlargement, breast mass, cervical dysplasia, functional metrorrhagia, dyspareunia, fibrocystic breast disease, menorrhagia, menstrual disorder, ovarian cyst, pelvic pain, premenstrual syndrome, uterine leiomyoma, uterine spasm, uterine/vaginal bleeding including spotting, vaginal discharge, vulvovaginal dryness. Rare: abnormal withdrawal bleeding, benign breast neoplasia, *in situ* breast cancer, breast cyst, breast discharge, cervical polyp, cervical erythema, coital bleeding, galactorrhoea, genital discharge, hypomenorrhea, delayed menstruation, ovarian cyst rupture, vaginal odour, vulvovaginal burning sensation, vulvovaginal discomfort.
Blood and lymphatic system disorders
Rare: lymphadenopathy.
Respiratory, thoracic, and mediastinal disorders
Rare: asthma, dyspnoea, epitaxy.
General disorders
Uncommon: fatigue, irritability, oedema. *Rare:* chest pain, malaise, pyrexia.
Complementary exams
Common: weight gain. *Uncommon:* weight loss, changes in blood pressure.
Rare: abnormal cervical smear.

Presentation:
Calendar pack containing 28 tablets (2 pale yellow tablets, 5 pale pink tablets, 17 cream-coloured tablets, 2 dark pink tablets and 2 white coated tablets).

Keep at room temperature (15 to 30°C).

In case of poisoning, seek medical assistance immediately.

Keep out of the reach of children.

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