Pramina

Chlormadinone acetate 2.00 mg
Ethinylestradiol 0.03 mg

Urufarma

LI-0000-01

Formula:
Each coated tablet contains: Chlormadinone acetate 2.00 mg, Ethinylestradiol 0.03 mg and excipients (q.s.)

Therapeutic effect:
Contraceptive.

Indications:
Preventing pregnancy.
Taking one daily tablet of **Pramina** inhibits ovulation, alters the cervical mucus, induces changes in the endometrium, and alters tubal motility, thus preventing pregnancy.

Posology and method of administration:
Take **Pramina** ("the pill" for short) according to these instructions, no more than 24 hours apart, to achieve the highest contraceptive efficacy.
Starting the treatment: Take the first pill of the pack orally on day 1 of the menstrual cycle - the day when menstrual bleeding starts. Then, take 1 pill per day, always at the same time (preferably at night), for 21 consecutive days.
If you stop the treatment for 7 days when you are bleeding, generally on day 2 or 4, start a new pack on day 8, regardless of whether bleeding has stopped or not. Start each new pack on the same day of the week when you took the first pill of the first pack.
Treatment with **Pramina** should be started as follows, as appropriate:
- *With no prior use of hormonal contraceptives (the previous month).*

If you start taking this medicine exactly on day 1 of menstrual bleeding, no other contraceptive method needs to be added. You can also start taking the pill on days 2 to 5 of bleeding, regardless of whether the bleeding has stopped or not. In this case, use an additional birth control method (barrier contraceptive, such as a condom) during the first 7 days of taking the pill. If the bleeding has started more than 5 days ago, you should wait until the next cycle to start the treatment.
- *If you are changing brands of oral contraceptive (COC)*

Start taking the pill on the next day of the usual break between taking the pills or the day after finishing the dummy pills of the previous COC.
- *If you are changing from a progestogen-only treatment*

Take the first tablet the day after discontinuing the progestogen-only preparation. Take additional contraceptive measures during the first 7 days.
- *If you are switching from an implant or injection of a hormone contraceptive*

You may start taking the pill the day after the implant is removed or the day when the next injection was originally scheduled. Additionally, you must use a barrier contraceptive during the first 7 days.
- *After having a miscarriage or abortion in the first trimester*

You may start taking the pill immediately after an abortion or miscarriage during the first trimester. In this case, other contraceptive methods are unnecessary.
- *After delivery or having a miscarriage or abortion in the first trimester*

Non-breastfeeding users may start taking the pill 21 to 28 days after delivery, in which case, no other contraceptive method is necessary. If dosing starts 28 days after birth, a barrier contraceptive is required during the first 7 days. If you have had sexual intercourse, pregnancy must be ruled out before dosing, and you must wait until your next menstrual period.
Continuing the treatment: You should start the following packs on the same day of the week as the first pill of the first pack, using the same dosage regime: 21 days of treatment, followed by a 7-day break. If for any reason you do not start the next packs on the right day, an additional method must be used (barrier contraceptives: condoms), for at least 10 days. When all 21 tablets are taken correctly, birth-control protection lasts the whole month, including the 7-day break.
What to do if you miss a pill: Missing a pill may expose you to getting pregnant. If you miss a pill, take it as soon as you remember.
You realise you missed a dose within 12 hours of the regular time, take it immediately, and continue the treatment as usual. If more than 12 hours have passed, the efficacy decreases. In this case, take the missed pill as soon as you remember and continue the treatment. This means you may take two pills on the same day. In this case, you must use an additional birth control method (barrier contraceptive), such as condoms, during the following 7 to 10 days. If you forget taking the pills during the week of the cycle and you have had sexual intercourse within 7 days of missing the pills (including the break period between taking the pills), you must consider the possibility that you might be pregnant. The more pills that you have missed and the closer to the break period between taking the pills, the higher the chance of pregnancy.
If the current blister pack contains less than seven pills, you must start the next one as soon as you finish the current one. This means there will be no break period between blister packs. You will probably not have your normal menstrual bleeding until finishing the blister; however, intermenstrual bleeding or spotting may occur frequently. If you do not have your next menstrual bleeding after taking the second blister pack, you must get tested for pregnancy.
Stopping the treatment: If you decide to stop the treatment, finish taking this pack and do not restart the treatment with a new pack. The next cycle may last a few more days than the previous ones. From this month onwards, your ability to bear children is restored. Available statistical data suggest it is best to wait until the third month without treatment before attempting to get pregnant, due to the possibility of twin pregnancy.

Warnings:
Analyse the complete case history (including family history) and rule out pregnancy before starting or restarting dosing of **Pramina**. Measure the blood pressure and perform a complete physical examination.
Episodes of vomiting and severe diarrhoea within 4 hours of taking the pill may reduce contraceptive efficacy, as absorption may be incomplete. It is advisable to use an additional non-hormonal, barrier method, such as a condom, and to follow the instructions under "What to do if you miss a pill".
Women taking oral contraceptives should be advised to quit smoking because of the increased risk of cardiovascular adverse events. The use of oral contraceptives is associated with an increased risk of certain diseases such as myocardial infarction, thromboembolism, stroke, hepatic neoplasms. Some studies indicate that long-term use of hormonal contraceptives is a risk factor for the development of cervical cancer in women infected with human papillomavirus (HPV).
Since breast cancer is rare in women under 40 years of age, the excess number of breast cancer diagnoses in current and recent users of combined oral contraceptives is small relative to the overall risk of breast cancer.
In case of severe abdominal pain that does not resolve spontaneously, hepatomegaly, or signs of intra-abdominal haemorrhage, the possibility of a liver tumour should be considered, and treatment should be discontinued.
The relationship between the use of hormonal contraception and clinical hypertension has not been confirmed. If your blood pressure rises significantly during treatment, consult your doctor.
In patients with a history of gestational herpes in a previous pregnancy, herpes may recur during hormonal contraceptive use.
The use of combined contraceptives is associated with an increased risk of developing venous thromboembolism (VTE), compared to not using them. The risk of VTE is highest during the first year of use and there is evidence that the risk increases when the treatment is restarted after a break of 4 weeks or more. Venous thromboembolism can be fatal in 1 to 2% of cases.
Epidemiological studies have also associated the use of hormonal contraceptives with an increased risk of arterial thromboembolism (myocardial infarction) or stroke (e.g., transient ischaemic attack, stroke). Arterial thromboembolic events can be fatal.
It should be noted that the risk of thrombosis may be synergistically increased in women with a combination of risk factors or an individual risk factor of increased severity. This increased risk may be greater than a mere cumulative risk of the factors. COCs should not be prescribed in case of a negative benefit-risk balance.

The risk of venous thromboembolic events increases with: age, family history of this condition (any case of venous thromboembolism, 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 case of scheduled surgery, at least four weeks in advance) and not to resume use until two weeks after full recovery of mobility, and antithrombotic treatment should be considered if **Pramina** has not been discontinued in advance), and obesity (body mass index greater than 30 kg/m^2). 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.
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.
If symptoms occur, seek medical assistance and tell the healthcare provider that you are taking a COC. 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.
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.
Hormonal contraceptives do not protect against HIV infection (AIDS) or any other sexually transmitted diseases.

Precautions:
Patients suffering from epilepsy, multiple sclerosis, tetany, migraine, asthma, heart or kidney failure, chorea minor, diabetes mellitus, liver disease, dyslipoproteinaemia, autoimmune diseases (including systemic lupus erythematosus), obesity, hypertension, endometriosis, varicose veins, phlebitis, blood coagulation disorders, mastopathy, uterine myoma, gestational herpes, depression, chronic inflammatory bowel disease such as Crohn's disease or ulcerative colitis should be carefully monitored.
If patients develop symptoms of depression while taking oral contraceptives, the medication should be discontinued, and an alternative method of contraception should be used in order to determine if the depression is drug-related. In women with a personal or family history of hypertriglyceridaemia, the risk of pancreatitis is increased during the use of oral contraceptives. In case of acute or chronic disturbances of liver function it may be necessary to discontinue use until liver function values return to normal. In case of recurrence of cholestatic jaundice during pregnancy or before the use of sex hormones, discontinuation of treatment is recommended.
In case of suspected or confirmed VTE or ATE, **Pramina** should be discontinued.
Peripheral insulin resistance or glucose tolerance may be affected, so diabetic patients should be carefully monitored while taking hormonal contraceptives.
Chloasma may occur infrequently, especially in women with a history of gestational chloasma. Therefore, sun exposure and ultraviolet radiation should be avoided during treatment.
Particularly during the first few months of administration, irregular vaginal bleeding (intermenstrual bleeding or spotting) may occur. If bleeding persists or occurs after an adjustment period of approximately 3 cycles, or recurs after several regular previous consecutive cycles, talk to your doctor.
<u>*Breastfeeding:*</u> Combined oral contraceptives may affect breastfeeding by reducing the quantity of breast milk and changing its composition. Therefore, the use of **Pramina** is not recommended until finishing breastfeeding. During the use of combined oral contraceptives (COCs), small amounts of contraceptive steroids and/or their metabolites may be excreted in the milk, which may affect the breastfeeding baby.
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.
Patients with hepatitis C virus infection treated with medicines containing ombitasvir/paritaprevir/ritonavir and dasabuvir, with or without ribavirin, may experience increased in transaminase (ALT) levels.

Contraindications:
Hypersensitivity to any of the components of the formula.
Pramina should not be administered in case of pregnancy or suspected pregnancy, uncontrolled diabetes mellitus; uncontrolled hypertension or significant increase in blood pressure (values consistently above 140/90 mmHg); presence or risk of venous thromboembolism (VTE) or arterial thromboembolism (ATE), presence or history of liver tumours (benign or malignant), or undiagnosed vaginal bleeding. This medicine is contraindicated in patients with breast or uterus cancer, whether known or suspected, or any other oestrogen-dependent malignancy.
Pramina is contraindicated in patients with hepatitis, jaundice, and liver function disorders until liver values return to normal; generalised pruritus, cholestasis, especially during a previous pregnancy or oestrogen therapy; Dubin-Johnson syndrome, Rotor syndrome, bile flow disorders; severe epigastric pain, hepatomegaly or symptoms of intra-abdominal bleeding; first case or recurrence of porphyria (in its three forms, in particular acquired porphyria); severe lipid metabolism disorders; pancreatitis or history of pancreatitis, if associated with severe hypertriglyceridaemia; first symptoms of migraine headaches or more frequent episodes of unusual severe headaches; acute sensory disturbances (e.g., visual or auditory disturbances); motor disturbances (particularly paresis); increased epileptic seizures; severe depression; deteriorating otosclerosis during previous pregnancies; amenorrhoea of unknown cause; endometrial hyperplasia.
The risk of venous thromboembolism (VTE) may be caused by: 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 or existence of several risk factors.
The risk of arterial thromboembolism (ATE) may be caused by: current ATE; history of thromboembolism (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 arterial thromboembolism due to multiple risk factors or the presence of a severe risk factor (diabetes mellitus with vascular symptoms, severe hypertension, severe dyslipoproteinaemia). **Pramina** is contraindicated in case of concomitant use with medicines that contain ombitasvir/paritaprevir/ritonavir and dasabuvir.
Drug-drug interactions:
Interactions with medicines that induce microsomal enzymes may occur. This may result in increased clearance of sex hormones, which can lead to breakthrough 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 tablets in the blister, the next pack should be started disregarding the usual break from taking the tablets.
In case of long-term treatment with liver enzyme-inducing drug substances, it is recommended to use another reliable non-hormonal method of contraception.
When coadministered with oral contraceptives, many HIV y hepatitis C virus (HCV) protease inhibitors and non-nucleoside reverse transcriptase inhibitors, may increase or decrease plasma concentrations of oestrogens or progestogens. Use of an additional barrier method (e.g., condom) is recommended.
Medicines that function as competitive sulphation inhibitors in the gastrointestinal tract, such as ascorbic acid or paracetamol, may increase the bioavailability of ethinylestradiol. Atorvastatin and enzyme inhibitors such as imidazole-derived antifungals (e.g., fluconazole), indinavir, or troleandomycin may also increase the serum concentration of ethinylestradiol.
Concurrent use with enzyme inducers may decrease contraceptive efficacy: barbiturates, bosentan, carbamazepine, barbexaclone, phenytoin, primidone, modafinil, rifampicin, rifabutin, ritonavir, nevirapine, efavirenz, felbamate, griseofulvin, oxcarbazepine, topiramate, and products containing St. John's Wort (*Hypericum perforatum*).
Serum concentrations of ethinylestradiol may be reduced when administered with metoclopramide, which increases gastrointestinal motility, or with activated charcoal, which affects absorption.
The use of oral contraceptives may affect the efficacy of the following medicines: cyclosporine, lamotrigine, theophylline, diazepam, and other benzodiazepines, prednisolone, clofibrate, paracetamol, morphine, and lorazepam.
The requirement for insulin or oral antidiabetics may be altered as a consequence of effects on glucose tolerance.

Side effects:
Nausea, vomiting, vaginal discharge, dysmenorrhoea, amenorrhoea, lower abdominal pain, depressive episodes, nervousness, irritability, vertigo, migraine (and/or worsening of migraine), visual disturbances, acne, leaden paralysis, fatigue, oedema, weight gain, or increased blood pressure may occur exceptionally and infrequently. Vaginal candidiasis, vulvovaginitis, breast fibroadenoma, hypersensitivity to the medicine including allergic skin reactions, blood lipid changes including hypertriglyceridaemia, increased appetite, decreased libido, conjunctivitis, intolerance to wearing contact lenses, sudden hearing loss, tinnitus, hypertension, hypotension, circulatory failure, varicose veins, venous thrombosis, venous or arterial thromboembolism, abdominal pain, abdominal distension, diarrhoea, pigmentation disorders, chloasma, alopecia, dry skin, hyperhidrosis, urticaria, eczema, erythema, pruritus, worsening of psoriasis, hypertrichosis, erythema nodosum, back pain, muscle disorders, galactorrhoea, breast enlargement, menorrhagia, premenstrual syndrome, and changes in blood lipids, including hypertriglyceridaemia, have been reported in rare cases.

Presentation:
Calendar pack containing 21 coated tablets.
Keep at room temperature (15 - 30°C).
In case of poisoning, seek medical assistance immediately.

Keep out of the reach of children.

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