Patient package insert according to Pharmacists' Regulations (Preparations) – 1986
This medicine can be sold with a physician's prescription only

FLAME®, Tablets

Each tablet contains Ethinylestradiol 0.02 mg and Gestodene 0.075 mg.

Inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of the medicine".

Read this entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if you think that their medical condition is similar to yours.

1. What is the medicine intended for?

Flame is intended for contraception.
Therapeutic group: Combined contraceptive pills, a combination of estrogen and progestogen.
Each tablet contains two female hormones, estrogen (ethinylestradiol) and progestogen (gestodene).

Several important things to know about combined hormonal contraceptives:

- When taken correctly, combined hormonal contraceptive pills are one of the most reliable reversible contraceptive methods.
- They slightly increase the risk of thrombosis (blood clots) in the veins and arteries, especially during the first year or upon resuming use after stopping for 4 weeks or more.
- Be vigilant and contact the doctor if you are concerned that you suffer from any symptoms of a blood clot (see section 2, "**Flame** and thrombosis (blood clots)").

2. Before using the medicine

Before you start taking **Flame**, you should read the information about thrombosis (blood clots) in section 2. It is especially important to read the part about the symptoms of thrombosis (see in section 2, "**Flame** and thrombosis (blood clots)").

Do not use the medicine if:
You are subject to any of the following conditions. If you have any of the conditions listed below, you must tell your doctor. Your doctor will discuss with you other contraceptive methods that are more suitable for you. If any of these conditions appears for the first time while using **Flame**, you should contact your doctor immediately.

- You are hypersensitive (allergic) to the active ingredients (ethinylestradiol or gestodene) or to any of the other ingredients this medicine contains (see section 6).
- You have (or have ever had) a blood clot in a blood vessel in the leg (deep vein thrombosis, DVT), lung (pulmonary embolism, PE), eyes or any other organ (see "**Flame** and thrombosis (blood clots)").
- You know that you suffer from a blood coagulation disorder, for example, protein C deficiency, protein S deficiency, antithrombin III deficiency, factor V Leiden mutation or presence of anti-phospholipid antibodies.
- You are going to have an operation or if you are expected to be in a situation of prolonged immobility (see "**Flame** and thrombosis (blood clots)").
- You have ever had a heart attack or stroke (CVA).

- You have (or have ever had) a type of migraine called "migraine with aura" (with an unusual sensation, such as flashes of light).
- You suffer from heart valve disorders or heart rhythm disorders.
- You have (or have ever had) angina pectoris (a condition that causes severe chest pain and can be an initial sign of a heart attack) or a transient ischemic attack (TIA -temporary stroke symptoms).
- You have one of the following diseases, which may increase the risk of a blood clot formation in the arteries:
    - Severe diabetes with blood vessel damage
    - Very high blood pressure
    - High levels of blood fats (cholesterol and triglycerides)
    - A condition known as hyperhomocysteinaemia
- You have (or have ever had) known or suspected breast, uterus or liver cancer (see "Contraceptive pills and cancer").
- You have severe liver disease – and your liver function is not back to normal yet.
- You have unexplained vaginal bleeding.
- You are pregnant or think you may be pregnant.
- You have or have ever had inflammation of the pancreas, which has been linked to a severe increase in the level of lipids in the blood.

Do not use **Flame** if you have hepatitis C (viral liver inflammation) and are taking medicines containing ombitasvir/paritaprevir/ritonavir, dasabuvir, glecaprevir/pibrentasvir or sofosbuvir/velpatasvir/voxilaprevir (see also "Drug interactions").

Special warnings regarding the use of the medicine

<u>Seek immediate medical attention</u>:
If you notice possible symptoms of a blood clot, which could indicate that you have a blood clot in a leg (i.e., deep vein thrombosis), a blood clot in a lung (pulmonary embolism), a heart attack or stroke (see "Flame and thrombosis (blood clots)").
For information about the symptoms of these serious side effects, see section 2 "How to recognize symptoms of a blood clot".

If you have one or more of the following conditions, consult your doctor before taking Flame.
You should also consult your doctor if any of the following conditions develop or get worse while you are taking **Flame**.

- If you smoke (especially if you are over the age of 35), see "**Flame** and thrombosis (blood clots)"
- If someone in your immediate family has had a disease caused by blood clots, such as deep vein thrombosis, pulmonary embolism, heart attack or stroke, see "**Flame** and thrombosis (blood clots)"
- If you are overweight, see "**Flame** and thrombosis (blood clots)"
- If you suffer from migraines
- If you have (or have ever had) one or more cysts in the breast and someone in your immediate family has had breast cancer
- If you have uterine fibroids (a benign non-cancerous growth)
- If you have a disease of the liver or gallbladder (gallstones)
- If you have had a biliary disorder while taking contraceptive tablet or during pregnancy
- If you suffer from a hypersensitivity reaction called angioedema
- If you suffer or have suffered from severe depression
- If you have (or have ever had) chloasma (brown spots on the skin called a "mask of pregnancy", particularly on the face). In such a case, you should avoid excessive exposure to the sun or UV rays

- If you suffer from Crohn's disease or ulcerative colitis (chronic inflammatory bowel diseases)
- If you suffer from systemic lupus erythematosus (SLE - a disease affecting the immune system)
- If you suffer from hemolytic uremic syndrome (HUS - a blood clotting disorder which may cause kidney failure)
- If you suffer from sickle-cell anemia (a hereditary disease of the red blood cells)
- If you suffer from high levels of fats in the blood (hypertriglyceridemia) or have a family history of this condition. Hypertriglyceridemia has been linked to an increased risk of pancreatitis (inflammation of the pancreas)
- If you have given birth several weeks ago, or if you had an abortion or miscarriage in the second trimester of pregnancy, you are at an increased risk of blood clot formation. You should ask your doctor how soon you can start using **Flame** after giving birth or after a second trimester abortion or miscarriage
- If you suffer from an inflammation in the veins under the skin (superficial thrombophlebitis)
- If you have varicose veins

Pay attention to certain conditions which may worsen while taking the pills, such as asthma, epilepsy, herpes occurring during pregnancy (herpes gestationis), hyperprolactinemia, a condition called chorea or "Saint Vitus' Dance" (a disease characterized by rapid, body movements, uncoordinated jerking movements primarily affecting the face, feet and hands) and otosclerosis (a disease of the inner ear).

If you experience symptoms of angioedema, such as swollen face, tongue and/or throat and/or difficulty swallowing or rash (hives) potentially with difficulty breathing, contact a doctor immediately. Products containing estrogens may cause or worsen the symptoms of hereditary or acquired angioedema.

Flame, like other contraceptive pills, does not prevent contracting the HIV infection (AIDS) or other sexually transmitted diseases.

Psychiatric disorders
Some women have reported depression or a depressed mood while using hormonal contraceptives including **Flame**. Depression can be severe and can sometimes lead to suicidal thoughts. If you experience mood changes and depressive symptoms, contact your doctor as soon as possible for further medical advice.

Flame and thrombosis (blood clots)
Using combined hormonal contraceptives such as **Flame** increases the risk of developing blood clots compared to the risk in women not using such contraceptives. In rare cases, a blood clot can block blood vessels and cause serious problems.

Blood clots can develop:
- in the veins [venous thrombosis, venous thromboembolism (VTE)].
- in the arteries [arterial thrombosis, arterial thromboembolism (ATE)] .

Full recovery is not always achieved following a blood clot. In rare cases, they can cause serious and lasting damage, and in very rare cases they can be fatal.
It is important to remember that the overall risk of a blood clot due to the use of Flame is small.

How to recognize symptoms of a blood clot
Contact your doctor urgently if you notice one or more of the following symptoms.

Do you experience one or more of these signs?	You probably suffer from

• swelling of one leg or along a vein in the leg or foot, especially when accompanied by:
  ○ pain or sensitivity in the leg only manifested when standing or walking
  ○ sensation of warmth in the same leg
  ○ change in color of the skin of the leg, for example turning pale, red or blue
	Deep vein thrombosis

• sudden unexplained shortness of breath or rapid breathing • sudden cough without apparent cause, which may contain blood • sharp chest pain which may increase with deep breathing • sensation of light-headedness or dizziness • rapid or irregular heartbeat • severe stomach pain If you are unsure, contact your doctor as some of these symptoms such as coughing or shortness of breath may be mistaken for a mild condition such as a respiratory infection (for example the common cold).	Pulmonary embolism
signs that usually appear in one eye: • immediate loss of vision or • painless blurring of vision that can progress to loss of vision	Retinal vein thrombosis (blood clot in a blood vessel in the eye)
• pain, discomfort, pressure, heaviness in the chest • sensation of squeezing or fullness in the chest, arm or under the breastbone • fullness, indigestion or choking feeling • upper body discomfort radiating to the back, jaw, throat, arm and stomach • sweating, nausea, vomiting or dizziness • extreme weakness, anxiety or shortness of breath • rapid or irregular heartbeat	Heart attack
• sudden weakness or numbness in the face, arm or leg, especially on one side of the body • sudden confusion, difficulty speaking or understanding • sudden difficulty seeing in one or both eyes • sudden difficulty walking, dizziness, loss of balance or coordination • sudden, severe or prolonged headache with no known cause • loss of consciousness or fainting with or without seizure Sometimes the symptoms of stroke can be brief with an almost immediate full recovery, but you should still seek urgent medical attention, as you may be at risk of another stroke.	Stroke (CVA)
• swelling and slight blue discoloration of an extremity • severe pain in the stomach (acute abdomen)	Blood clots blocking other blood vessels (such as those of the liver, intestines or kidneys)

Blood clots in a vein

What can happen if a blood clot forms in a vein?

- The use of combined hormonal contraceptives is associated with an increased risk of developing blood clots in the veins (venous thrombosis). However, this side effect is rare. It can occur more frequently during the first year of using combined hormonal contraceptives.
- When a blood clot forms in a vein in the leg or foot, it may cause deep vein thrombosis.
- If a blood clot travels from the leg to the lung, it can cause a pulmonary embolism.
- Very rarely, a blood clot may form in a vein in another organ, such as the eye (retinal vein thrombosis).

When is the risk of developing a blood clot in a vein highest?

The risk of developing a blood clot in a vein is highest during the first year of taking a combined hormonal contraceptive for the first time. The risk may also be higher of you restart taking a combined hormonal contraceptive (the same product as before or a different product) after a break of 4 weeks or more.

After the first year, the risk gets smaller but is always slightly higher than if you were not taking a combined hormonal contraceptive. When you stop taking **Flame**, the risk of developing a blood clot returns to normal within a few weeks.

What is the risk of developing a blood clot?

The risk depends on your natural risk of venous thromboembolism and the type of combined hormonal contraceptive you are taking.

The overall risk of a blood clot in a leg or lung (deep vein thrombosis or pulmonary embolism) with **Flame** is small.

- Out of 10,000 women who are not using any combined hormonal contraceptive and are not pregnant, about 2 will develop a blood clot in a year.
- Out of 10,000 women who are using a combined hormonal contraceptive that contains levonorgestrel, norethisterone or norgestimate, about 5-7 will develop a blood clot in a year.
- Out of 10,000 women who are using a combined hormonal contraceptive that contains gestodene, such as **Flame**, about 9-12 will develop a blood clot in a year.
- The risk of a blood clot will vary according to your personal medical history (see "Factors that increase your risk of developing a blood clot in a vein" below).

Factors that increase your risk of a blood clot in a vein:

The risk of a blood clot with **Flame** is small, but some conditions will increase the risk. The risk is higher:

- if you are very overweight (BMI over 30 kg/m^2).
- if a member of your immediate family has had a blood clot in the leg, lung or other organ at a relatively young age (before the age of 50). In this case, you may have a hereditary blood coagulation disorder.
- if you need to have an operation, or if you are in a situation of prolonged immobility due to an injury or illness, or at least one of your legs is immobilized (for example in a cast). It may be necessary to stop using **Flame** several weeks before surgery or while your mobility is reduced. If you need to stop using **Flame**, ask your doctor when you can start taking **Flame** again.
- with age (particularly over the age of 35).
- if you have given birth or if you had an abortion or miscarriage in the second trimester of pregnancy several weeks ago.

The risk of developing a blood clot increases the more conditions you have.

Air travel (over 4 hours) may temporarily increase your risk of a blood clot, particularly if you have other conditions that increase the risk.

It is important to tell your doctor if one of the above conditions applies to you, even if you are unsure. Your doctor may decide that you should stop taking **Flame**.

If any of these conditions change while using **Flame**, for example if one of your immediate family members develops thrombosis for an unknown reason or if you gain a lot of weight, tell your doctor.

Blood clots in an artery

What can happen if a blood clot forms in an artery?
Like a blood clot in a vein, a blood clot in an artery may cause serious problems. For example, it may cause a heart attack or a stroke.

Factors that increase your risk of a blood clot in an artery:
It is important to note that the risk of a heart attack or stroke from using **Flame** is very small, but may increase:

- with increasing age (especially over the age of 35).
- **if you smoke.** When using a combined hormonal contraceptive like **Flame**, you are advised to stop smoking. If you are unable to stop smoking and are older than 35, your doctor may advise you to use a different type of contraceptive.
- if you are overweight.
- if you have high blood pressure.
- if a member of your immediate family had a heart attack or stroke at a relatively young age (under the age of 50). In this case, the risk of a heart attack or stroke may be higher for you.
- if you, or a member of your immediate family, have a high level of fat in the blood (cholesterol or triglycerides).
- if you suffer from migraines, especially migraines with aura.
- if you have a heart problem (valve disorders, arrhythmia called atrial fibrillation).
- if you have diabetes.

If you have more than one of these conditions or if one of them is particularly severe, the risk of developing a blood clot may be even higher.
If any of the above conditions change while using **Flame**, for example, if you start smoking, if a close family member experiences a thrombosis for an unknown reason or if you gain a lot of weight, tell your doctor.

Contraceptive pills and cancer
Established risk factors for the development of breast cancer include age, family history, obesity, no childbirth in the past and first pregnancy and childbirth at an older age.

Breast cancer has been diagnosed at a slightly higher incidence in women taking pills compared to women of the same age not taking pills. This moderate increase in the number of breast cancer diagnoses gradually disappears 10 years after discontinuing the pill. It is not known if this difference is caused by the use of the pill. It is possible that women taking pills are examined more carefully and more often, so that breast cancer is detected at an earlier stage. Taking the pill may also increase the risk of cervical cancer, but this has not been scientifically proven.

In rare cases, benign liver tumors, and even more rarely, malignant liver tumors have been reported in women taking the pill. The risk of developing such tumors increases with the duration of taking the pill, but remains low nevertheless.

When should you contact your doctor?

Tests and follow up

Your doctor will instruct you to arrive for regular medical examinations. In general, the frequency and nature of these examinations will depend on individual medical factors. Your doctor will assess the information obtained and provide you with the necessary explanations.

Contact your doctor immediately in the following cases:

- if you experience any signs of thrombosis (see "How to recognize symptoms of a blood clot" above)
- if you feel a lump in or near the breast
- contact your doctor at least 4 weeks in advance if you are going to have an operation or if you are expected to be in a situation of prolonged immobility (see "**Flame** and thrombosis (blood clots)")
- if you have given birth or if you had an abortion or miscarriage in the second trimester of pregnancy several weeks ago (see "**Flame** and thrombosis (blood clots)")
- if you experience unusual heavy vaginal bleeding
- if you think you may be pregnant
- if your period does not start during the week after stopping the pill

Drug interactions

If you are taking or have recently taken any other medicines, **including non-prescription medicines and nutritional supplements, tell your doctor or pharmacist**.

When your doctor, including your dentist, wants to prescribe you a new medicine, you should inform them that you are taking **Flame**. In certain cases, your doctor will advise you to use another contraceptive for a certain time while taking this medicine.

Certain medicines may decrease the effectiveness of the pill in pregnancy prevention; these include:

- certain medicines for treatment of epilepsy (primidone, phenytoin, barbiturates, topiramate, phenylbutazone, carbamazepine or felbamate)
- griseofulvin (a medicine for treatment of fungal infections)
- some medicines for treatment of HIV/AIDS (protease inhibitors) and other viral infections (ritonavir)
- rifampicin (for treatment of tuberculosis)
- preparations containing the Hypericum perforatum plant (St John’s wort)
- modafinil (a medicine for treatment of sleep disorders)
- dexamethasone (a medicine for treatment of certain inflammatory and autoimmune diseases)

Oral contraceptives can influence the results of certain laboratory tests. Inform your doctor that you are taking **Flame** if you are going to have a blood test.

Do not use **Flame** if you have hepatitis C (viral liver inflammation), and you are taking medicines containing ombitasvir/paritaprevir/ritonavir, dasabuvir, glecaprevir/pibrentasvir or sofosbuvir/velpatasvir/voxilaprevir as these medicines may cause an increase in liver function blood test results (increase in ALT liver enzyme). Your doctor will prescribe you other contraceptives before you start treatment with these medicines. **Flame** can be restarted about 2 weeks after completing treatment with these medicines. See section "Do not use the medicine if".

Use of the medicine and food

Flame can be taken with food or drinks.

Pregnancy, breastfeeding and fertility

Pregnancy
Do not use the medicine if you are pregnant or if pregnancy is suspected.
If you are planning to become pregnant, consult your doctor or pharmacist.
Breastfeeding
Do not use the medicine if you are breastfeeding.

Driving and using machines
The effect on the ability to drive or use machines while using **Flame** has not been studied.

Important information about some of the ingredients of the medicine
Flame contains lactose and sucrose. If you have been told by a doctor that you have an intolerance to some sugars, contact the doctor before taking this medicine.
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium-free".

3. How to use the medicine?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.
The dosage and manner of treatment will be determined by the doctor only.
Each blister pack of **Flame** contains 21 tablets. For each tablet, the day of the week when it should be taken is indicated on the pack.

The usual dosage is: one tablet each day, at the same time, in the order indicated by the arrows on the blister pack, for 21 days. Do not take any pills for 7 days following the 21 days on which you have taken **Flame**. Your period will start during the 7 days on which you don't take the pill (usually on the third day after taking the last tablet in the blister pack).
After the 7 day break, start a new pack on the eighth day, whether your period has ended or not. This way, you will always start a new blister pack on the same day of the week and your period will start around the same day every 4 weeks.
Taking the pill is not indicated for women who have not yet had their first period or for post-menopausal women.
Swallow the tablet whole with some water if necessary. Do not crush/halve/chew the pill as these actions may interfere with the absorption of the active ingredients of the tablet and thus impair its efficacy.

Starting the first pack
How to start your first pack if you have not used hormonal contraceptives in the last month?
Take the first tablet on the first day of your period in accordance with the day of the week marked on the blister pack. For example, if your period starts on a Friday, take a tablet marked "FRI/יום ו'" on the blister pack.

Switching to Flame from other combined contraceptive pills
Take **Flame** the day after taking the last active pill from the previous blister pack of the pills.

Switching to Flame from a pill containing progesterone only
If you are switching to **Flame** from a pill containing progesterone only, you can stop taking the pill containing progesterone only on any day and start taking **Flame** the next day. You must use an additional non-hormonal method of contraception (such as a condom or spermicide) during the first 7 days of taking the first blister pack.

Switching to Flame from injectable or implanted contraceptives or an IUD
If you are switching to **Flame** from an injectable contraceptive, an implant or an IUD, you can start using **Flame** on the day the implant or IUD is removed or on the day that was scheduled

for your next injection. You must use an additional non-hormonal method of contraception (such as a condom or spermicide) during the first 7 days of taking the first blister pack.

If you had an abortion or miscarriage in the first trimester of pregnancy
You can start taking **Flame** immediately.

If you have given birth or if you had an abortion or miscarriage in the second trimester of pregnancy
Your doctor may advise you to start taking **Flame** from the 28th day after childbirth or after a second-trimester abortion or miscarriage. You must use an additional non-hormonal, method of contraception (such as a condom or spermicide) during the first 7 days of taking the first blister pack. If you have already had sexual intercourse during this time, you must make sure that you are not pregnant before you start taking **Flame** or wait until your period begins.

If unexpected bleeding occurs
Unexpected bleeding (spotting) may occur between periods, especially during the first months of use. In general, this irregular bleeding stops once your body has become used to the pill (after about 3 blister packs). Nevertheless, if the unexpected bleeding persists or appears for the first time after prolonged use of **Flame**, contact your doctor immediately.

If no bleeding occurs after completing the blister pack
If menstrual bleeding has not started after 7 days of discontinuing the pill and you have taken all the pills properly, you are unlikely to be pregnant. Start the next blister pack on the eighth day. However, if the menstrual bleeding has not started after taking two complete blister packs, contact your doctor immediately and do not start the next blister pack before you have his approval.

If you have accidentally taken a higher dosage of Flame
There are no known cases of serious harm after taking too many **Flame** tablets.
Taking too many **Flame** tablets may cause nausea, vomiting, abdominal pain, dizziness, drowsiness/tiredness, breast tenderness, or slight vaginal bleeding. Special treatment is probably unnecessary.

If a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.
In case of an overdose or any abnormal use, contact your doctor or pharmacist.

If you forgot to take Flame
The contraceptive efficacy of the pill is maintained only if **less than 12 hours have passed since the time at which you should have taken the tablet**. Take the tablet as soon as you remember and continue taking the next tablets at the usual time.
If **more than 12 hours have passed since the time at which you should have taken the tablet**, or if you have missed more than one tablet, the contraceptive efficacy of the pill may be reduced. In such case:

- Take the last forgotten tablet immediately when you remember and continue taking the rest of the tablets as usual, even if that means taking 2 tablets on the same day. Continue taking **Flame** until the end of the blister pack.
- In addition, use an additional non-hormonal method of contraception (such as a condom or a spermicide) for 7 days.
  If the 7-day period requiring the use of an additional method of contraception extends beyond the day on which you take the last tablet in the current blister pack, start the next blister pack on the day after taking the last tablet of the current blister pack (i.e. with no break).

In any case, consult your doctor.

If you are suffering from diarrhea or vomiting
If diarrhea or vomiting happens **within 3 to 4 hours** after taking the tablet, the active ingredients in **Flame** may have not been absorbed adequately by your body. This situation is similar to forgetting to take a tablet. Therefore, after vomiting or diarrhea, take an additional tablet from a spare blister pack. If the diarrhea or vomiting persists, consult your doctor.

If you want to stop taking Flame
When you stop taking **Flame**, your period may not return spontaneously (post-treatment amenorrhea). You must consult your doctor in such case.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take a medicine. Wear glasses if you need them.
If you have any further questions on the use of this medicine, consult the doctor or pharmacist.

4. <u>Side effects</u>
Like any medicine, the use of **Flame** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

If you suffer from a side effect, especially if it is severe or prolonged, or if there is a change in your health and you are concerned that it may be due to **Flame**, contact your doctor.

<u>Serious side effects</u>
There is an increased risk of formation of blood clots in the veins (venous thromboembolism) or in the arteries (arterial thromboembolism) for all women using combined hormonal contraceptives. For more detailed information, see section 2 "Before using the medicine". The serious side effects associated with the use of the pill are described in the sections "**Flame** and thrombosis (blood clots)" and "Contraceptive pills and cancer". Read these sections for more information.

<u>Angioedema</u>
Contact a doctor immediately if you experience any of the following symptoms of angioedema: swollen face, tongue and/or throat and/or difficulty swallowing or rash (hives) potentially with difficulty breathing (see also "Special warnings regarding the use of the medicine").

Contact the doctor immediately if you experience any of the following symptoms:
- swelling of one leg or along a vein in the leg or foot
- sudden unexplained shortness of breath or rapid breathing
- sudden cough without apparent cause, which may contain blood
- sharp chest pain, which may be increase with deep breathing
- sensation of light-headedness or dizziness
- rapid or irregular heartbeat
- intense pain in the abdomen, acute pain in the abdomen (acute abdomen)
- immediate loss of vision or painless blurring of vision that can progress to loss of vision, that usually appear in one eye
- pain, discomfort, pressure, heaviness in the chest
- sensation of squeezing or fullness in the chest, arm or under the breastbone
- fullness, indigestion or choking feeling
- upper body discomfort radiating to the back, jaw, throat, arm and stomach
- sweating, nausea or vomiting
- extreme weakness, anxiety or shortness of breath
- sudden weakness or numbness in the face, arm or leg, especially on one side of the body
- sudden confusion, difficulty speaking or understanding

- sudden difficulty seeing in one or both eyes
- sudden difficulty walking, loss of balance or coordination
- sudden severe or prolonged headache with no known cause
- loss of consciousness or fainting, with or without seizure
- swelling and slight cyanosis of the extremities
- if you feel a lump in or near your breast

Additional side effects:
Very common side effects (effects that occur in more than 1 in 10 users):
- Headache, migraine
- Bleeding between periods (spotting)

Common side effects (effects that occur in 1-10 in 100 users):
- Vaginal infection including vaginal fungal infection
- Changes in mood (e.g. depression) or changes in sexual drive
- Nervousness or dizziness
- Nausea, vomiting or abdominal pain
- Acne
- Pain, tension, enlargement and secretion from the breasts
- Painful menstrual bleeding or changes in the menstrual blood flow, absence of periods
- Changes in cervical secretions
- Fluid retention or edema
- Weight gain or loss

Uncommon side effects (effects that occur in 1-10 in 1,000 users):
- Changes in appetite
- Abdominal cramps, bloating
- Rash, appearance of dark spots on the face which may persist, excessive hair growth, hair loss
- Increased blood pressure, changes in lipid levels in the blood

Rare side effects (effects that occur in 1-10 in 10,000 users):
- Allergic reactions, including very rare cases of urticaria, allergic edema of the face (angioedema), severe respiratory and circulatory disorders
- Glucose intolerance
- Intolerance to contact lenses
- A blood clot in a vein or an artery, for example:
  - in a leg or foot (deep vein thrombosis)
  - in a lung (pulmonary embolism)
  - heart attack, stroke, mini-stroke or temporary stroke-like symptoms, known as a transient ischemic attack
  - in very rare cases, blood clots in the liver, stomach/intestine, kidneys or one eye

  The risk of a blood clot may be higher if you have other conditions that increase the risk (see section 2 for more information on factors that increase the risk of blood clots and the symptoms of blood clots).
- Jaundice due to obstruction of bile ducts
- Nodular erythema (Erythema nodosum)
- A decrease in folic acid levels in the blood (this is very important if you become pregnant immediately after discontinuing **Flame**)

Very rare side effects (effects that occur in less than 1 in 10,000 users):
- Increased risk of benign liver tumor, malignant liver tumor
- Aggravation of lupus erythematosus

- Aggravation of porphyria (accumulation of porphyrin in the tissues)
- Aggravation of chorea (a movement disorder)
- Inflammation of the optic nerve (may lead to partial or complete blindness)
- Aggravation of varicose veins
- Inflammation of the pancreas, inflammation of the colon due to hypoxia
- Gallstones, decreased bile secretion (**Flame** may aggravate existing gallbladder disorders or lead to the onset of such disorders)
- Rash with blisters (erythema multiforme)
- Hemolytic uremic syndrome (a condition of renal failure caused by blood clots)

Side effects with unknown frequency (effects for which a frequency has not yet been determined):
- Inflammatory bowel disease (Crohn's disease, ulcerative colitis)
- Liver damage (for example liver inflammation, abnormal liver function)

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect which is not mentioned in this leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health by clicking the link "דיווח על תופעות לוואי עקב טיפול תרופתי" found on the homepage of the Ministry of Health website (www.health.gov.il) directing to the online form for reporting side effects or via the link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (תאריך תפוגה) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** store in the original package, below 25°C.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredients, the medicine also contains:
Lactose monohydrate, sucrose, maize starch, calcium carbonate, talc, macrogol 6000, povidone, titanium dioxide (E171), silica colloidal anhydrous, magnesium stearate, sodium calcium edetate, quinoline yellow (E104).

What the medicine looks like and what the package contains:
Yellow, round, biconvex tablets.
The tablets come in trays (blisters) of 21 tablets. Each package contains 1, 3 or 4 blisters. Not all package sizes may be marketed.
Revised in July 2024 according to MOH guidelines.
Drug registration number at the national drug registry of the Ministry of Health: 140-58-31529-00
Manufacturer and registration holder: Dexcel Ltd., 1 Dexcel St., Or Akiva 3060000, Israel