PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

Kyleena®
Intrauterine delivery system

The intrauterine delivery system contains: 19.5 mg levonorgestrel.

Inactive ingredients and allergens in this medicine - see section 6 "Further Information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed to treat you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

Kyleena is not indicated for use before the first menstrual bleeding (menarche) and is not indicated for use in postmenopausal women.

1. WHAT IS THE MEDICINE INTENDED FOR?

What is Kyleena?
Kyleena is used for the prevention of pregnancy (contraception) for up to five years.
Kyleena is a T-shaped intrauterine delivery system (IUS) which after placement inside the womb slowly releases a small amount of the hormone levonorgestrel.

Kyleena works by reducing the monthly growth of the lining of the womb and thickening the cervical mucus. These actions prevent the sperm and egg from coming into contact and so prevent fertilization of an egg by sperm.

Therapeutic group: Kyleena belongs to a group of medicines containing the female hormone progestogen.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient levonorgestrel or to any of the other ingredients contained in the medicine. For the list of inactive ingredients, see section 6 "Further Information".
- you are pregnant (see in section 2 "Pregnancy, breast-feeding and fertility").
- you currently have a pelvic inflammatory disease (PID; infection of the female reproduction organs) or have had this condition multiple times in the past.
- you have conditions associated with increased susceptibility to pelvic infections.

- you have an infection in the lower genital tract (an infection in the vagina or the cervix [neck of the womb]).
- you have had an infection of the womb after delivery of a child, after an abortion or after miscarriage during the past 3 months.
- you currently have cell abnormalities in the cervix.
- you have cancer or suspected cancer of the cervix or womb.
- you have tumors whose growth are sensitive to progestogen hormones, e.g., breast cancer.
- you have unexplained uterine bleeding.
- you have an abnormality of the cervix or womb including fibroids that distort the cavity of the womb.
- you have an active liver disease or liver tumor.

Special warnings regarding use of the medicine
- Before you can begin using Kyleena, your doctor will ask you some questions about your personal health history.
- In this leaflet, several situations are described where Kyleena should be removed, or where the reliability of Kyleena may be decreased. In such situations you should either not have sex or you should use a condom or another barrier method.
- Kyleena, like other hormonal contraceptives, does not protect you against HIV infection (AIDS) or any other sexually transmitted disease.
- Kyleena is not suitable for use as an emergency contraceptive (postcoital contraceptive).

Before using Kyleena, tell the doctor if:
- you have diabetes. There is generally no need to alter your diabetic medication while using Kyleena, but this may need to be checked by your doctor.
- you have epilepsy. A fit (seizure) can occur during placement or removal.
- you have had an ectopic or extrauterine pregnancy (pregnancy outside the womb) in the past.

In addition, also talk to your doctor if any of the following conditions exist before you use Kyleena or appear for the first time while using Kyleena:
- migraine, with visual disturbances or other symptoms which may be signs of a transient cerebral ischemia (temporary blockage of the blood supply to the brain).
- exceptionally severe headache.
- jaundice (a yellowing of the skin, whites of the eyes and/or nails).
- marked increase in blood pressure.
- severe disease of the arteries such as stroke or heart attack.

The following signs and symptoms could mean that you may have an extrauterine pregnancy and you should see

your doctor immediately (see also in section 2 “Pregnancy, breast-feeding and fertility”):
- your menstrual periods have stopped and then you start having persistent bleeding or pain.
- you have pain in your lower abdomen that is severe or persistent.
- you have normal signs of pregnancy, but you also have bleeding and feel dizzy.
- you have a positive pregnancy test.

Contact your doctor promptly if any of the following occur (see also section 4 “Side Effects”):
- severe pain (like menstrual cramps) or heavy bleeding after placement or if you have pain/bleeding which continues for more than a few weeks. This may be, for example, a sign of infection, perforation or that Kyleena is not in the correct position.
- you no longer feel the threads in your vagina. This may be a sign of expulsion or perforation. You can check by gently putting a finger into your vagina and feeling for the threads at the end of your vagina near the opening of your womb (cervix). Do not pull the threads because you may accidentally pull out Kyleena. Use a barrier contraceptive (such as condoms) until your doctor has checked that the IUS is still in position.
- you or your partner can feel the lower end of Kyleena. Avoid intercourse until your doctor has checked that the IUS is still in position.
- your partner feels the removal threads during intercourse.
- you think you may be pregnant.
- you have persistent abdominal pain, fever, or unusual discharge from the vagina, which may be a sign of infection. Infections must be treated immediately.
- you feel pain or discomfort during sexual intercourse, which may be for example a sign of infection, ovarian cyst or that Kyleena is not in the correct position.
- there are sudden changes in your menstrual periods (for example, if you have little or no menstrual bleeding, and then you start having persistent bleeding or pain, or you start bleeding heavily), which may be a sign of Kyleena not being in the correct position or expelled.

Use of sanitary pads is recommended. If tampons or menstrual cups are used, you should change them with care so as not to pull the threads of Kyleena. If you think you may have pulled Kyleena out of place (see list above for possible signs), avoid intercourse or use a barrier contraceptive (such as condoms), and contact your doctor.

Psychiatric disorders
Some women using hormonal contraceptives including Kyleena have reported depression or depressed mood. Depression may be serious and may sometimes lead to suicidal thoughts. If you experience mood changes and

depressive symptoms, contact your doctor for further medical advice as soon as possible.

Children and adolescents
Kyleena is not indicated for use before the first menstrual bleeding (menarche).

Drug interactions
If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. You should also tell the doctor or pharmacist if you might start taking any other medicines.

Pregnancy, breast-feeding and fertility

Pregnancy
Kyleena must not be used during pregnancy.
Some women may not have their periods while using Kyleena. Not having a period is not necessarily a sign of pregnancy. If you do not have your period and have other symptoms of pregnancy you should see your doctor for an examination and have a pregnancy test.

If you have not had a period for 6 weeks and are concerned, then consider having a pregnancy test. If this is negative, there is no need to carry out another test unless you have other signs of pregnancy.

If you become pregnant with Kyleena in place, you should see your doctor immediately to have Kyleena removed. The removal may cause a miscarriage. However, if Kyleena is left in place during pregnancy, not only is the risk of having a miscarriage higher, but also the risk of having preterm labor. If Kyleena cannot be removed, talk with your doctor about the benefits and risks of continuing the pregnancy.

If the pregnancy is continued, you will be closely monitored during your pregnancy and you should contact your doctor right away if you experience stomach cramps, pain in your stomach or fever.

Kyleena contains a hormone, called levonorgestrel, and there have been isolated reports of effects on the genitalia of female babies if exposed to levonorgestrel intra-uterine devices while in the womb.

If you want to become pregnant you should contact your doctor to have Kyleena removed.

Extrauterine pregnancy (pregnancy outside the womb)
It is uncommon to become pregnant while using Kyleena. However, if you become pregnant while using Kyleena, the risk that the pregnancy could develop outside the womb (have an extrauterine or ectopic pregnancy) is increased. Women who have already had an extrauterine pregnancy, surgery of the fallopian tubes or a pelvic infection carry a higher risk for this type of pregnancy. An extrauterine

pregnancy is a serious condition which calls for immediate medical attention (see section 2, "Special warnings regarding use of the medicine") and may impact future fertility.

Breast-feeding
You can use Kyleena during breast-feeding. Levonorgestrel (the active ingredient in Kyleena) has been identified in small quantities in the breast milk of breast-feeding women. However, no negative effects have been seen on infant growth and development or the amount or the quality of the breast milk.

Fertility
Your usual level of fertility will return after Kyleena is removed.

Driving and using machines
Kyleena has no known influence on the ability to drive or use machines.

3. HOW SHOULD YOU USE THE MEDICINE?
Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain.

Placement of Kyleena
Placement of Kyleena will be done by a physician who has undergone training on the insertion procedure and after a gynecological examination.

Kyleena can either be placed:
- within 7 days from the start of your menstrual bleed (your monthly period).
- immediately after a first trimester abortion provided that there are no genital infections.
- after giving birth only after the womb has returned to its normal size, and not earlier than 6 weeks after delivery (see in section 4 "Perforation").

Examination by your doctor before placement may include:
- a cervical smear test (Pap smear).
- examination of the breasts.
- other tests, e.g., for infections, including sexually transmitted diseases, as necessary. Your doctor will also do a gynecological examination to determine the position and size of the womb.

After a gynecological examination:
- an instrument called a speculum is placed into the vagina, and the cervix may be cleansed with an antiseptic solution. Kyleena is then placed into the womb using a thin, flexible plastic tube (the placement tube). Local anesthesia may be applied to the cervix prior to placement.
- some women feel dizzy or faint during placement or after Kyleena is placed or removed.
- you may experience some pain and bleeding during or just after placement.

After placement of Kyleena you should receive a patient reminder card from your doctor for follow-up examinations. Bring this with you to every scheduled appointment.

Follow-up examination
You should have your Kyleena checked 4-6 weeks after placement, and thereafter regularly, at least once a year. Your doctor may determine how often and what kinds of check-ups are required in your particular case. Bring the patient reminder card you have received from your doctor to every scheduled appointment.

Removal of Kyleena
Kyleena should be removed no later than the end of the fifth year of use.
Kyleena can be easily removed at any time by your doctor, after which pregnancy is possible. Some women feel dizzy or faint during or after Kyleena is removed. You may experience some pain and bleeding during removal of Kyleena.
If pregnancy is not desired, Kyleena should not be removed after the seventh day of the menstrual cycle (monthly period) unless you use other methods of contraception (e.g., condoms) for at least 7 days before the IUS removal. If you have irregular periods (menses) or no periods, you should use a barrier method of contraception for 7 days before removal.
A new Kyleena can also be placed immediately after removal, in which case no additional protection is needed.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Kyleena 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.

Contact your doctor immediately if you notice any of the following symptoms:
- allergic reactions including rash, hives (urticaria) and angioedema (characterised by sudden swelling of e.g. the eyes, mouth, throat)

See also section 2 "Special warnings regarding use of the medicine", for when to contact your doctor promptly.

The following is a list of possible side effects by how common they are:

Very common side effects: may affect more than 1 in 10 people
- headache
- abdominal/pelvic pain
- acne/greasy skin
- bleeding changes including increased and decreased menstrual bleeding, spotting, infrequent periods and

absence of bleeding (see also in section 4 “irregular and infrequent bleeding”)
- ovarian cyst (see also in section 4 “ovarian cyst”)
- inflammation of the external genital organs and vagina (vulvovaginitis)

Common side effects: may affect up to 1 in 10 people
- depressed mood/depression
- decreased libido
- migraine
- dizziness
- feeling sick (nausea)
- hair loss
- upper genital tract infection
- painful menstruation
- breast pain/discomfort
- device expulsion (complete and partial) – (see in section 4 “expulsion”)
- genital discharge
- increased weight

Uncommon side effects: may affect up to 1 in 100 people
- excessive body hair
- perforation of the womb (see in section 4 “perforation”)

Description of selected possible side effects:

Irregular or infrequent bleeding
Kyleena is likely to affect your menstrual cycle. It can change your menstrual periods so that you have spotting (a small amount of bleeding), irregular, shorter or longer periods, lighter or heavier bleeding, or no bleeding at all. You may have bleeding and spotting between menstrual periods, especially during the first 3-6 months. Sometimes the bleeding is heavier than usual at first.
Overall, you are likely to have a gradual reduction in the amount and number of days of bleeding each month. Some women eventually find that periods stop altogether.
The monthly thickening of the lining of the womb may not happen due to the effect of the hormone and therefore there is nothing to come or shed away as a menstrual period. It does not necessarily mean that you have reached menopause or are pregnant. Your own hormone levels usually remain normal.
When the system is removed, your period should soon return to normal.

Pelvic Infection
The Kyleena inserter and Kyleena itself are sterile. Despite this, there is an increased risk of pelvic infection (infections in the lining of the womb or the fallopian tubes) at the time of placement and during the first 3 weeks after the placement. Pelvic infections in IUS users are often related to the presence of sexually transmitted diseases. The risk of infection is increased if you or your partner have multiple

sexual partners or if you have had pelvic inflammatory disease (PID) before.
Pelvic infections must be treated promptly.
Pelvic infections such as PID may have serious consequences and it may impair fertility and increase the risk of a future extrauterine pregnancy (pregnancy outside the womb). In extremely rare cases severe infection or sepsis (very severe infection, which may be fatal) can occur shortly after insertion.

Kyleena must be removed if you experience recurring PID or if an infection is severe or does not respond to treatment.

Expulsion
The muscular contractions of the womb during menstruation may sometimes push the IUS out of place or expel it. This is more likely to occur if you are overweight at the time of IUS insertion or have a history of heavy periods. If the IUS is out of place, it may not work as intended and therefore, the risk of pregnancy is increased. If the IUS is expelled, you are not protected against pregnancy anymore. Possible symptoms of an expulsion of the IUS are pain and abnormal bleeding, but Kyleena may also be expelled without you noticing. As Kyleena decreases menstrual flow, increase of menstrual flow may be indicative of expulsion.

It is recommended that you check for the threads with your finger, for example while having a shower. See also section 2 "Special warnings regarding use of the medicine" for how to check if Kyleena is in place. If you have signs indicative of an expulsion or you cannot feel the threads, you should use another contraceptive (such as condoms), and consult your doctor.

Perforation
Penetration or perforation of the wall of the womb may occur during placement of Kyleena, although the perforation may not be detected until some time later. If Kyleena becomes lodged outside the cavity of the womb, it is not effective at preventing pregnancy and it must be removed as soon as possible. You may need surgery to have Kyleena removed. The risk of perforation is increased in breast-feeding women and in women who have insertion up to 36 weeks after birth, and may be increased in women whose uterus leans backwards (fixed retroverted uterus). If you suspect you may have experienced a perforation, seek prompt advice from a doctor and remind him that you have Kyleena inserted, especially if he was not the person who inserted it.

Ovarian cyst
Since the contraceptive effect of Kyleena is mainly due to its local effect in the womb, ovulation (release of the egg) usually continues while using Kyleena. Sometimes an ovarian cyst may develop. In most cases there are no symptoms.

An ovarian cyst may require medical attention, or more rarely surgery, but it usually disappears on its own.

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

Reporting of side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants in order 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 (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- This medicinal product does not require any special storage conditions. It is recommended to store at room temperature.
- Do not open the blister. Only your doctor should do this.

6. FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains:
  Poly(dimethylsiloxane) elastomer; silica, colloidal anhydrous; polyethylene; barium sulfate; polypropylene; copper phthalocyanine; silver.
- What does the medicine look like and what are the contents of the package:
  Kyleena is a T-shaped intrauterine delivery system (IUS). The vertical arm of the white T-body carries a drug reservoir containing levonorgestrel. Two blue removal threads are tied to the loop at the lower end of the vertical arm. In addition, the vertical stem contains a silver ring located close to the horizontal arms, which is visible under ultrasound examination.
- This deliver system is available in a single-unit pack.
- **Registration holder and address:** Bayer Israel Ltd., 36 Hacharash St., Hod Hasharon 4527702.
- **Manufacturer and address:** Bayer OY, Turku, Finland.
- Revised in November 2022 according to MOH guidelines.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
  161-26-35400-00, 161-26-35400-01

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