MIRENA PATIENT INFORMATION

This provides medical and scientific information on Mirena in general. Please refer to the local Patient Information Leaflet for the information applicable in your country.

Mirena 20 micrograms/24 hours intrauterine delivery system
Levonorgestrel

Read all of this leaflet carefully before you start using this medicine.

• Keep this leaflet. You may need to read it again.
• If you have any further questions, ask your doctor or pharmacist.
• This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

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1. **WHAT MIRENA IS AND WHAT IT IS USED FOR**

Mirena is a T-shaped intrauterine delivery system (IUS) which after insertion releases the hormone levonorgestrel into the womb. The purpose of the T-body is to adjust the system to the shape of the womb. The vertical arm of the T-body carries a drug reservoir containing levonorgestrel. Two removal threads are tied to the loop at the lower end of the vertical arm.

Mirena is used for:

- Contraception (prevention of pregnancy)
- Idiopathic menorrhagia (excessive menstrual bleeding)
- Protection from endometrial hyperplasia (excessive growth of the lining of the womb) during estrogen replacement therapy.

2. **BEFORE YOU USE Mirena**

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<th>General notes</th>
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<td>Before you can begin using Mirena, your doctor will ask you some questions about your personal health history and that of your close relatives.</td>
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**About 2 in a 1000 women correctly using Mirena become pregnant in the first year.**

**About 7 in a 1000 women correctly using Mirena become pregnant in five years.**

In this leaflet, several situations are described where Mirena should be removed, or where the reliability of Mirena may be decreased. In such situations you should either not have sex or you should take extra non-hormonal contraceptive precautions, e.g. use a condom or another barrier method. Do not use rhythm or temperature methods. These methods can be unreliable because Mirena alters the monthly changes of body temperature and cervical mucus.

Mirena, like other hormonal contraceptives, does not protect against HIV infection (AIDS) or any other sexually transmitted disease.

**Do not use Mirena under any of the following conditions:**

- if you are pregnant or think you might be pregnant
- if you currently or recurrently have a pelvic inflammatory disease (infection of the female reproduction organs)
- if you have a lower genital tract infection
- if you have an infection of the womb after delivery
- if you have had an infection of the womb after abortion during the past 3 months
- if you have an infection of the cervix (neck of the womb)
- if you have cell abnormalities in the cervix
- if you have cancer or suspected cancer of the cervix or womb
- if you have tumors which depend on progestogen hormones to grow,
• if you have unexplained abnormal vaginal bleeding
• if you have an abnormality of the cervix or womb including fibroids if they distort the cavity of the womb
• if you have conditions associated with increased susceptibility to infections
• if you have an active liver disease or liver tumor
• if you are hypersensitive (allergic) to levonorgestrel or to any of the other ingredients of Mirena.

**Take special care with Mirena**

Consult a specialist who may decide to continue using Mirena or remove the system if any of the following conditions exists or appears for the first time while using Mirena:

• migraine, asymmetrical visual loss 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 of blood pressure
• severe disease of arteries such as stroke or heart attack.

Mirena may be used with caution in women who have congenital heart disease or valvular heart disease at risk of infective inflammation of the heart muscle. Antibiotic preventive medication should be administered to these patients when inserting or removing Mirena.

In diabetic users of Mirena, the blood glucose concentration should be monitored.

Irregular bleedings may mask some symptoms and signs of endometrial polyps or cancer, and in these cases diagnostic measures have to be considered.

Mirena is not the method of first choice for young women who have never been pregnant, nor for postmenopausal women with shrinking of the womb.

Due to the limited data from Mirena trials in the indication protection from endometrial hyperplasia (excessive growth of the lining of the womb) during estrogen replacement therapy, a breast cancer risk when Mirena is used in this indication cannot be confirmed or eliminated.

**Medical examination/consultation**

Examination before insertion may include a cervical smear test (Pap smear), examination of the breasts and other tests, e.g. for infections, including sexually transmitted diseases, as necessary. A gynecological examination should be performed to determine the position and size of the womb.

Mirena is not suitable for use as postcoital contraceptive (used after intercourse).

**Infections**

Pelvic infections in IUS (Intra Uterine System) users are often related to sexually transmitted diseases. The risk of infection is increased if the woman or her partner has several sexual partners. Pelvic infections must be treated promptly. Pelvic infection may impair fertility and increase the risk of a future extrauterine pregnancy (pregnancy outside the womb). Mirena
must be removed if there are recurrent pelvic infections or infections of the lining of the womb, or if an acute infection is severe or does not respond to treatment within a few days.

Consult a doctor without delay if you have persistent lower abdominal pain, fever, pain in conjunction with sexual intercourse or abnormal bleeding.

**Expulsion**

The muscular contractions of the womb during menstruation may sometimes push the IUS out of place or expel it. Possible symptoms are pain and abnormal bleeding. If the IUS is displaced, the effectiveness may be reduced. If the IUS is expelled, you are not protected against pregnancy anymore. It is recommended that you check for the threads with your finger, for example while having a shower. If you have signs indicative of an expulsion or you cannot feel the threads, you should avoid intercourse or use another contraceptive, and consult your doctor. As Mirena decreases menstrual flow, increase of menstrual flow may be indicative of an expulsion.

**Perforation**

Rarely, most often during insertion, Mirena may penetrate or perforate the wall of the womb which may decrease the protection against pregnancy. An IUS which has become lodged outside the cavity of the womb is not effective and must be removed as soon as possible. The risk of perforation may be increased if Mirena is inserted shortly after delivery (see section 3. “When should Mirena be inserted?”), in lactating women, or in women with the uterus fixed and leaning backwards (towards the bowel).

**Extrauterine pregnancy**

It is very rare to become pregnant while using Mirena. However, if you become pregnant while using Mirena, the risk that you could carry the fetus outside of your womb (have an extrauterine pregnancy) is relatively increased. About 1 in a 1000 women correctly using Mirena have an extrauterine pregnancy per year. Woman who already had an extrauterine pregnancy, surgery of the tubes from the ovaries to the womb or a pelvic infection carry a higher risk. An extrauterine pregnancy is a serious condition which calls for immediate medical attention. The following symptoms could mean that you may have an extrauterine pregnancy and you should see your doctor immediately:

- Your menstrual periods have ceased and then you start having persistent bleeding or pain
- You have vague or very bad pain in your lower abdomen
- You have normal signs of pregnancy, but you also have bleeding and feel dizzy

**Faintness**

Some women feel dizzy after Mirena is inserted. This is a normal physical response. Your doctor will tell you to rest for a while after you have had Mirena inserted.

**Enlarged ovarian follicles (cells that surround a maturing egg in the ovary)**

Since the contraceptive effect of Mirena is mainly due to its local effect, ovulatory cycles with follicular rupture usually occur in women of fertile age. Sometimes degeneration of the follicle is delayed and the development of the follicle may continue. Most of these follicles give no symptoms, although some may be accompanied by pelvic pain or pain during intercourse. These enlarged follicles may require medical attention, but they usually disappear on their own.
Taking other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

The metabolism of levonorgestrel may be increased by concomitant use of other medicines, such as epilepsy medication (e.g. phenobarbital, phenytoin, carbamazepin) and antibiotics (e.g. rifampicin, rifabutin, nevirapine, efavirenz). Since the mechanism of action of Mirena is mainly local, this is not believed to have major importance for the efficacy of Mirena.

Pregnancy

Mirena must not be used during an existing or suspected pregnancy.

It is very rare for a woman to become pregnant with Mirena in place. But if Mirena comes out, you are no longer protected and must use another form of contraception until you see your doctor.

Some women may not have their periods while using Mirena. Not having a period is not necessarily a sign of pregnancy. If you do not have your period and have other symptoms of pregnancy (for example nausea, tiredness, breast tenderness) you should see your doctor for an examination and have a pregnancy test.

If you become pregnant with Mirena in place, you should have Mirena removed as soon as possible. If you leave Mirena in place during pregnancy, the risk of having a miscarriage, infection or preterm labor will be increased. The hormone in Mirena is released into the womb. This means that the fetus is exposed to a relatively high concentration of hormone locally, although the amount of the hormone received through the blood and placenta is little. The effect of such an amount of hormone on the fetus should be taken into consideration.

Breast-feeding

Mirena can be used during breast-feeding. Levonorgestrel has been identified in small quantities in the breast milk of nursing women (0.1 % of the dose being transferred to the infant). There appears to be no negative effects on infant growth or development when using Mirena six weeks after delivery. Progestogen-only methods do not appear to affect the amount or the quality of breast milk.

Ask your doctor or pharmacist for advice before taking any medicine when you are pregnant or breast-feeding.

Driving and using machines

No known effects.

Important information about some of the ingredients of Mirena

The T-frame of Mirena contains barium sulphate, which makes it visible in X-ray examination.
3. HOW TO USE Mirena

How effective is Mirena?

In contraception, Mirena is as effective as today's most effective copper IUDs. Mirena has a failure rate of approximately 0.1% per year. The failure rate may increase in case of expulsion or perforation (see under section 2, "Medical examination/consultation").

In the treatment of idiopathic excessive menstrual bleeding Mirena causes a strong reduction of menstrual bleeding already after three months. Some users have no periods at all.

When should Mirena be inserted?

You can have Mirena inserted within seven days from the onset of the menstrual bleeding. The IUS can also be inserted immediately after a first trimester abortion provided that there are no genital infections. The IUS should be inserted only after the womb has returned to its normal size after delivery, and not earlier than 6 weeks after delivery. Mirena can be replaced by a new system at any time of the cycle.

When Mirena is used to protect the lining of the womb during estrogen replacement therapy, it can be inserted at any time in an amenorrheic woman (woman who has no monthly bleeding), or during the last days of menstruation or withdrawal bleeding.

Mirena should be inserted by a physician/health care professional who is experienced in Mirena insertion.

How is Mirena inserted?

After a gynecological examination, an instrument called a speculum is inserted into the vagina, and the cervix is cleansed with an antiseptic solution. The IUS is then inserted into the womb via a thin, flexible plastic tube (the inserter). Local anesthesia may be applied to the cervix prior to insertion, if appropriate.

Some women may experience pain and dizziness after insertion. If these do not pass within half an hour in the resting position, the IUS may not be correctly positioned. An examination should be carried out and the IUS removed if necessary.

When should I see my doctor?

You should have your IUS checked 4 - 12 weeks after insertion, and thereafter regularly, at least once a year. In addition, you should contact your doctor if any of the following occurs:

- You no longer feel the threads in your vagina
- You can feel the lower end of the system
- You think you may be pregnant
- You have persistent abdominal pain, fever, or unusual discharge from the vagina
- You or your partner feel pain or discomfort during sexual intercourse.
- 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
- You have other medical problems, such as migraine headaches or intense headaches that recur, sudden problems with vision, jaundice, or high blood pressure.
- You experience any of the conditions mentioned in Section 2 “Before you use Mirena”.
For how long can Mirena be used?

Mirena is effective for five years, after which the IUS has to be removed. If you like, you may have a new Mirena inserted when the old one is removed.

What if I want to become pregnant or have Mirena removed for another reason?

The IUS can be easily removed at any time by your doctor, after which pregnancy is possible. Removal usually is a painless procedure. Fertility returns to normal after removal of Mirena.

If pregnancy is not desired, Mirena should not be removed after the seventh day of the menstrual cycle unless contraception is covered with other methods (e.g. condoms) for at least seven days before the removal. When the woman has no menses, she should use barrier methods of contraception for seven days before removal until her menstruation reappears. A new Mirena can also be inserted immediately after removal, in which case no additional protection is needed.

Can I become pregnant after stopping use of Mirena?

Yes. After Mirena is removed, it does not interfere with your normal fertility. You may become pregnant during the first menstrual cycle after Mirena is removed.

Can Mirena affect my menstrual periods?

Mirena does affect your menstrual cycle. It can change your menstrual periods so that you have spotting (a small amount of blood loss), shorter or longer periods, lighter or heavier bleeding, or no bleeding at all.

Many women have frequent spotting or light bleeding in addition to their periods for the first 3-6 months after they have Mirena inserted. Some women may have heavy or prolonged bleeding during this time. Please inform your doctor, especially if this persists.

Overall, you are likely to have a gradual reduction in the number of bleeding days and in the amount of blood lost each month. Some women eventually find that periods stop altogether. As the amount of menstrual bleeding is usually reduced with the use of Mirena, most women experience an increase in their blood hemoglobin value.

When the system is removed, periods return to normal.

Is it abnormal to have no periods?

Not when you are using Mirena. If you find that you do not have periods with Mirena it is because of the effect of the hormone on the lining of the womb. The monthly thickening of the lining does not happen. Therefore there is nothing to come away as a period. It does not necessarily mean that you have reached menopause or are pregnant. Your own hormone levels remain normal.

In fact not having periods can be a great advantage for a woman’s health.

How will I know if I’m pregnant?

Pregnancy is unlikely in women using Mirena, even if they do not have periods.

If you have not had a period for six 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, e.g. sickness, tiredness or breast tenderness.
Can Mirena cause pain or discomfort?

Some women feel pain (like menstrual cramps) in the first few weeks after insertion. You should return to your doctor or clinic if you have severe pain or if the pain continues for more than three weeks after you have had Mirena inserted.

Will Mirena interfere with sexual intercourse?

Neither you nor your partner should feel the IUS during intercourse. If you do, intercourse should be avoided until your doctor has checked that the IUS is still in the correct position.

How long should I wait to have sexual intercourse after the insertion?

To give your body a rest, it is best to wait about 24 hours after having Mirena inserted before having sexual intercourse. However, as soon as it is inserted, Mirena will prevent pregnancy.

Can tampons be used?

Use of sanitary pads is recommended. If tampons are used, you should change them with care so as not to pull the threads of Mirena.

What happens if Mirena comes out by itself?

It is rare but possible for Mirena to come out during your menstrual period without you noticing. An unusual increase in the amount of bleeding during your period could mean that your Mirena has come out through your vagina. It is also possible for part of Mirena to come out of your womb (you and your partner may notice this during sexual intercourse). If Mirena comes out completely or partially, you will not be protected from pregnancy.

How can I tell whether Mirena is in place?

You can check yourself if the threads are in place after your period. Gently put a finger into your vagina after your period and feel 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 Mirena. If you cannot feel the threads, contact your doctor.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Mirena can cause side effects, although not everybody gets them.

Below, we list possible side effects when Mirena is used for contraception (prevention of pregnancy) and idiopathic menorrhagia (excessive menstrual bleeding).

Possible side effects when Mirena is used for protection of endometrial hyperplasia (excessive growth of the lining of the womb) during estrogen replacement therapy were observed at a similar frequency unless specified by footnotes:

**Very common:** 10 or more in every 100 patients are likely to get these:

- Headache
- Abdominal/pelvic pain
• Bleeding changes including increased and decreased menstrual bleeding, spotting, oligomenorrhea (infrequent periods) and amenorrhea (absence of bleeding)
• Vulvovaginitis* (inflammation of the external genital organs or vagina)
• Genital discharge*

**Common:** between 1 and 10 in every 100 patients are likely to get these:

• Depressed mood / depression
• Migraine
• Nausea (feeling sick)
• Acne
• Hirsutism (excessive body hair)
• Back pain'
• Upper genital tract infection
• Ovarian cyst
• Dysmenorrhea (painful menstruation)
• Breast pain'
• Intrauterine contraceptive device expelled (complete and partial)

**Uncommon:** between 1 and 10 in every 1,000 patients are likely to get these:

• Alopecia (hair loss)

**Rare:** between 1 and 10 in every 10,000 patients are likely to get these:

• Uterine perforation

**Unknown frequency:**

• Hypersensitivity (allergic reaction) including rash, urticaria (hives) and angioedema (characterized by sudden swelling of e.g. the eyes, mouth, throat)
• Blood pressure increase

**Description of selected possible side effects:**

The removal threads may be felt by the partner during intercourse.

If you become pregnant while using Mirena, there is a possibility that the pregnancy is outside the womb (see section 2 "Extrauterine pregnancy").

**The following possible side effects have been reported in connection with Mirena insertion or removal procedures:**

Procedural pain, procedural bleeding, insertion-related vasovagal reactions with dizziness or syncope (fainting). The procedure may result in a seizure (fit) in an epileptic patient.

* Endometrial protection trials: “common”
† Endometrial protection trials: “very common”
The risk of breast cancer is unknown when Mirena is used in the indication protection from endometrial hyperplasia (excessive growth of the lining of the womb) during estrogen replacement therapy. Cases of breast cancer have been reported (frequency unknown).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE Mirena

Keep out of the reach and sight of children.

No special precautions for storage.

Do not use Mirena after the expiry date which is stated on the package. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Mirena contains

The active substance is levonorgestrel 52 mg.

The other ingredients are:

- polydimethylsiloxane elastomer
- silica, colloidal anhydrous
- polyethylene
- barium sulfate
- iron oxide

What Mirena looks like and contents of the pack

Pack size: One sterile intrauterine delivery system for intrauterine use

Marketing Authorisation Holder and Manufacturer

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

7. INFORMATION FOR HEALTHCARE PROFESSIONALS ONLY

The following information is intended for medical or healthcare professionals only

- Medical examination/consultation
Before insertion, the woman must be informed of the efficacy, risks and side effects of Mirena. A physical examination including pelvic examination, examination of the breasts, and a cervical smear should be performed. Pregnancy and sexually transmitted diseases should be excluded, and genital infections have to be successfully treated. The position of the uterus and the size of the uterine cavity should be determined. Fundal positioning of Mirena is particularly important in order to ensure uniform exposure of the endometrium to the progestogen, prevent expulsion and maximize efficacy. Therefore, the instructions for the insertion should be followed carefully. Insertion and removal may be associated with some pain and bleeding. The procedure may precipitate fainting as a vasovagal reaction, or a seizure in an epileptic patient.

Because irregular bleeding/spotting is common during the first months of therapy, it is recommended to exclude endometrial pathology before insertion of Mirena.

If the woman continues the use of Mirena inserted earlier for contraception, endometrial pathology has to be excluded in case bleeding disturbances appear after commencing estrogen replacement therapy.

If bleeding irregularities develop during a prolonged treatment, appropriate diagnostic measures should also be taken.

- **Oligo/amenorrhea**

In women of fertile age, oligomenorrhea and amenorrhea develop gradually in 57% and 16% of women, respectively. The possibility of pregnancy should be considered if menstruation does not occur within six weeks of the onset of previous menstruation.

When Mirena is used in combination with continuous estrogen replacement therapy, a non-bleeding pattern gradually develops in most women during the first year.

- **Expulsion**

Partial expulsion may decrease the effectiveness of Mirena. A displaced Mirena should be removed. A new system can be inserted at that time.

- **Lost threads**

If the retrieval threads are not visible at the cervix on follow-up examinations, pregnancy must be excluded. The threads may have been drawn up into the uterus or cervical canal and may reappear during the next menstrual period. If pregnancy has been excluded, the threads may usually be located by gently probing with a suitable instrument. If they cannot be found, the system may have been expelled. Ultrasound diagnosis may be used to ascertain the correct position of the system. If ultrasound is not available or successful, X-ray may be used to locate Mirena.

- **Ovarian cysts**

Since the contraceptive effect of Mirena is mainly due to its local effect, ovulatory cycles with follicular rupture usually occur in women of fertile age. Sometimes atresia of the follicle is delayed and folliculogenesis may continue. Ovarian cysts have been reported as adverse drug reactions in approximately 7% of women using Mirena. Most of these cysts are asymptomatic, although some may be accompanied by pelvic pain or dyspareunia.
In most cases, the ovarian cysts disappear spontaneously during two to three months’ observation. Should this not happen, continued ultrasound monitoring and other diagnostic/therapeutic measures are recommended. Rarely, surgical intervention may be required.

- Insertion and removal/replacement

Postpartum insertions should be postponed until the uterus is fully involuted, however not earlier than six weeks after delivery. If involution is substantially delayed, consider waiting until 12 weeks postpartum. In case of a difficult insertion and/or exceptional pain or bleeding during or after insertion, physical examination and ultrasound should be performed immediately to exclude perforation.

Mirena is removed by gently pulling on the threads with a forceps. If the threads are not visible and the system is in the uterine cavity, it may be removed using a narrow tenaculum. This may require dilatation of the cervical canal or other surgical intervention.

If pregnancy is not desired, the removal should be carried out during the menstruation in women of fertile age, provided that there appears to be a menstrual cycle. If the system is removed in the mid-cycle and the woman has had intercourse within a week, she is at a risk of pregnancy unless a new system is inserted immediately following removal.

After removal of Mirena, the system should be checked to be intact. During difficult removals, single cases have been reported of the hormone cylinder sliding over the horizontal arms and hiding them together inside the cylinder. This situation does not require further intervention once completeness of the IUS has been ascertained. The knobs of the horizontal arms usually prevent complete detachment of the cylinder from the T-body.

- Instructions for use and handling

Mirena is supplied in a sterile pack which should not be opened until required for insertion. The exposed product should be handled with aseptic precautions. If the seam of the sterile package is broken, the product should be discarded.

- Pregnancy

Removal of Mirena or probing of the uterus may result in spontaneous abortion. If the woman wishes to continue the pregnancy and the system cannot be withdrawn, she should be informed about the risks and the possible consequences of premature birth to the infant. The course of such a pregnancy should be closely monitored. Ectopic pregnancy should be excluded. The woman should be instructed to report all symptoms that suggest complications of the pregnancy, like cramping abdominal pain with fever.

Because of the intrauterine administration and the local exposure to the hormone, the possible occurrence of virilizing effects in the fetus should be taken into consideration.

Company Core Patient Information version 14 dated 22nd March 2011