PACKAGE LEAFLET

Package leaflet: Information for the user

Levosert 52 mg Intrauterine Delivery System
levonorgestrel

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Levosert is and what it is used for

Levosert is an intrauterine delivery system (IUS) for insertion in the womb (uterus), where it slowly releases the hormone levonorgestrel.

It is used for:
Contraception
Levosert is an effective, long-term and non-permanent (reversible) method of contraception. Levosert prevents pregnancy by thinning the lining of your womb (uterus), by making the normal mucus in the opening of the womb (cervical canal) thicker, so that the sperm cannot get through to fertilise the egg and by preventing the release of eggs (ovulation) in some women. Furthermore, the presence of the T-shaped frame causes local effects on the lining of the womb.
Levosert should be removed after 8 years of use when used for contraception.

Treating heavy menstrual bleeding
Levosert is also useful for reducing menstrual blood flow, so it can be used if you suffer from heavy menstrual bleeding (periods). This is called menorrhagia. The hormone in Levosert acts by thinning the lining of your uterus, so that there is less bleeding every month.
Levosert should be removed or exchanged after 8 years of use, or earlier if heavy or bothersome menstrual bleeding returns.

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

2. What you need to know before you use Levosert

Do not use Levosert if you
- are pregnant or suspect that you may be pregnant;
- have or have had pelvic inflammatory disease;
- have an unusual or unpleasant vaginal discharge, or vaginal itching, as this may indicate an infection;
- have or have had inflammation of the lining of your womb following delivery of your baby;
- have or have had an infection of the womb after delivery or after abortion during the past 3 months;

- have or have had inflammation of the cervix (neck of your womb);
- have or have had an abnormal smear test (changes in the cervix);
- have or have had liver problems;
- have liver tumour;
- have an abnormal womb, including uterine fibroids, especially those that distort the uterine cavity;
- have an abnormal vaginal bleeding pattern;
- have any condition which makes you susceptible to infections. A doctor will have told you if you have this.
- have or have had hormone dependent cancer, such as breast cancer;
- have or have had any type of cancer or suspected cancer including blood (leukaemia), uterine and cervical cancer, unless in remission;
- have or have had trophoblastic disease. A doctor will have told you if you have this.
- are allergic (hypersensitive) to levonorgestrel or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Before you have Levosert fitted, your doctor or nurse will carry out some tests to make sure that Levosert is suitable for you to use. This will include a pelvic examination and may also include other examinations such as a breast examination, if your doctor or nurse feels this is appropriate.

Genital infections will need to be successfully treated before you can have Levosert fitted.

If you have epilepsy, tell the doctor or nurse fitting Levosert because, although rare, a fit can occur during insertion. Some women might feel faint after the procedure. This is normal and your doctor or nurse will tell you to rest for a while.

Levosert may not be suitable for all women.

Levosert, like other hormonal contraceptives, does not protect against HIV infection (AIDS) or any other sexually transmitted disease (e.g. chlamydia, genital herpes, genital warts, gonorrhoea, hepatitis B and syphilis). You will need condoms to protect yourself from these diseases.

Talk to your doctor before using Levosert if you:
- have or develop migraine, dizziness, blurred vision, unusually bad headaches or if you have headaches more often than before;
- have yellowing of the skin or whites of the eyes (jaundice);
- are diabetic (too high blood glucose level), have high blood pressure or abnormal blood lipid levels;
- have had cancer affecting your blood (including leukaemia) which is now in remission;
- are on long-term steroid therapy;
- have ever had an ectopic pregnancy (development of the foetus outside the womb) or a history of ovarian cysts;
- have had or have severe arterial disease, such as heart attack, or stroke, or if you have any heart problems;
- have a history of blood clots (thrombosis);
- are taking any other medicines as some medicines may stop Levosert from working properly;
- have irregular bleedings;
- have fits (epilepsy).

Your doctor will decide if you can use Levosert if you have or have had some of the above conditions.

You must also tell your doctor if any of these conditions occur for the first time whilst you have Levosert in place.

You must see a doctor or nurse as soon as possible if you develop painful swelling in your leg, sudden chest pain or difficulty in breathing as these may be a sign of a blood clot. It is important that any blood clots are treated promptly.

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 are pain and abnormal bleeding but Levosert may also come out without you noticing. As Levosert decreases menstrual flow, increase of menstrual flow may be indicative of an expulsion.
It is recommended that you check for the threads with your finger, for example while having a shower. See also section 3 "How to use Levosert – How can I tell whether the system 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 healthcare professional.

Psychiatric disorders
Some women using hormonal contraceptives including Levosert have reported depression or depressed mood. Depression can 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.

Levosert and smoking
Women are advised to give up smoking. Smoking increases the risk of developing a heart attack, stroke, or blood clot.

Use of tampons and menstrual cups
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 Levosert.

Other medicines and Levosert
The effect of hormonal contraceptives such as Levosert may be reduced by medicines that increase the amounts of enzymes made by the liver. Please tell your doctor if you are taking:
- phenobarbital, phenytoin or carbamazepine (to treat epilepsy);
- griseofulvin (an antifungal);
- rifampicin or rifabutin (antibiotics);
- nevirapine or efavirenz (for HIV).

Tell your doctor if you are taking, have recently taken or might take any other medicines. Levosert should not be taken simultaneously with another hormonal contraceptive method.

Pregnancy, breast-feeding and fertility
Levosert must not be used during pregnancy or if you may suspect that you are pregnant.

Can I become pregnant whilst using Levosert?
It is very rare for women to become pregnant with Levosert in place.
Missing a period may not mean that you are pregnant. Some women may not have periods whilst using the system.
If you have not had a period for 6 weeks 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.
If you become pregnant with Levosert in place, you should see your healthcare professional immediately to have Levosert removed. The removal may cause a miscarriage. However, if Levosert is left in place during pregnancy, not only is the risk of having a miscarriage higher, but also the risk of preterm labor. If Levosert cannot be removed, talk with your healthcare professional 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.
Levosert 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.

What if I want a baby?
If you want a baby, ask your doctor to remove Levosert. Your usual level of fertility will return very quickly after the system is removed.

Can I breast feed while using Levosert?
Very small amounts of the hormone in Levosert are found in breast milk. A risk to the newborns/infants is not expected. Breast-feeding can be continued during use of Levosert.

Driving and using machines
There are no known effects on the ability to drive or use machines.

Levosert contains barium sulphate.
The T-frame of Levosert contains barium sulphate so that it can be seen on X-rays.

3. How to use Levosert

Only a doctor or specially trained nurse can fit the system (see special instructions for insertion in the package).
They will explain the fitting procedure and any risks associated with its usage. You will then be examined by your doctor or nurse before Levosert is fitted. If you have any concerns over its usage you should discuss it with them.

The device should be inserted either during your period or within seven days from the beginning of your period. If you already have the device and it is time to replace it with a new one, you do not need to wait until your period.
If you have just had a baby, you should wait at least 6 weeks before having Levosert fitted. Levosert can sometimes be fitted immediately after you have had an abortion, provided that you have no genital infections.

How quickly should Levosert work?
Contraception
You are protected from pregnancy as soon as the system is fitted.

Heavy menstrual bleeding
Levosert usually results in lighter periods after 3 to 6 months of treatment.

How will Levosert affect my periods?
Many women have spotting (a small amount of blood loss) for the first 3-6 months after the system is fitted. Others will have prolonged or heavy bleeding. You may have an increase in bleeding however, usually in the first 2 to 3 months, before a reduction in blood loss is achieved. Overall, you are likely to have fewer days of bleeding in each month and you might eventually have no periods at all. This is due to the effect of the hormone (levonorgestrel) on the lining of the womb. If a remarkable reduction in blood loss is not achieved after 3 to 6 months, other treatments should be considered.

If you have had Levosert fitted for quite a long time and then start to have bleeding problems, contact your doctor or healthcare provider for advice.

How often should I have the system checked?
You should have the system checked usually 6 weeks after it is fitted, again at 12 months and then once a year until it is removed.

How can I tell whether the system is in place?
After each menstrual period, you can feel for the two thin threads attached to the lower end of the system. Your doctor will show you how to do this.
Do not pull the threads because you may accidentally pull it out. If you cannot feel the threads, contact your doctor or nurse as soon as possible and in the meantime avoid intercourse or use a barrier contraceptive (such as condoms). The threads may have simply drawn up into the womb or cervical canal. If the threads still cannot be found by your doctor or nurse, they may have broken off, or Levosert may have come out by itself, or in rare cases it may have perforated the wall of your womb (uterine perforation, see section 4).
You should also go to your doctor if you can feel the lower end of the device itself or you or your partner feel pain or discomfort during sexual intercourse.

What happens if the system comes out by itself?
If the system comes out either completely or partially, you may not be protected against pregnancy. It is rare but possible for this to happen without you noticing during your menstrual period. An unusual increase in the amount of bleeding during your period might be a sign that this has happened. Tell your doctor or healthcare provider if there are any unexpected changes in your bleeding pattern.

If you stop using Levosert
Your doctor can remove the system at any time. The removal is very easy. Unless you plan to have a new system or an intra-uterine device fitted immediately, it is important to use another form of contraception in the week leading up to the removal. Intercourse during this week could lead to pregnancy after Levosert is removed.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

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

With Levosert, side effects are most common during the first months after the system is fitted and decrease as time goes on.

If you experience any of the following serious side effects please contact your doctor or nurse immediately:
- **Severe pain or fever developing shortly after insertion** may mean that you have a severe infection which must be treated immediately. In rare cases very severe infection (sepsis) can occur.

- **Severe pain and continued bleeding** as this might be a sign of damage or tear in the wall of the womb (perforation). Perforation is uncommon, but occurs most often during the fitting of the Levosert, although the perforation may not be detected until sometime later. A Levosert which has become lodged outside the cavity of the womb is not effective in preventing pregnancy and must be removed as soon as possible; very rarely this may require surgery. The risk of perforation is low, but is increased in breast-feeding women and in women who have had a baby up to 36 weeks before insertion and may be increased in women with the uterus fixed and leaning backwards (fixed retroverted uterus). If you suspect you may have experienced a perforation, seek prompt advice from a healthcare provider and remind them that you have Levosert inserted, especially if they were not the person who inserted it.
  Possible signs and symptoms of perforation may include:
  - severe pain (like menstrual cramps) or more pain than expected
  - heavy bleeding (after insertion)
  - pain or bleeding which continues for more than a few weeks
  - sudden changes in your periods
  - pain during sex

- you can no longer feel the Levosert threads (see “How can I tell whether the system is in place?" in section 3).

- **Lower abdominal pain especially if you also have a fever or have missed a period or have unexpected bleeding**, as this might be a sign of ectopic pregnancy (development of the foetus outside the womb). The absolute risk of ectopic pregnancy in Levosert users is low. However, when a woman becomes pregnant with Levosert in place, the relative likelihood of ectopic pregnancy is increased.

- **Lower abdominal pain or experience painful or difficult sex** as this might be a sign of ovarian cysts or pelvic inflammatory disease. This is important as pelvic infections can reduce your chances of having a baby and can increase the risk of ectopic pregnancy.

Other side effects
Very common (may affect more than 1 in 10 women) side effects can include:
- absent, light or infrequent menstrual periods (see “How will Levosert affect my periods?” in section 3),
- vaginal bleeding including spotting;
- bacterial or fungal infections of the vagina and the outer genitalia (vulva);
- spots (acne).

Common (may affect up to 1 in 10 women) side effects can include:
- depression, nervousness or other mood changes;
- reduced sex drive;
- headache;
- migraine;
- feeling faint (presyncope);
- dizziness;
- back pain;
- abdominal discomfort;
- feeling sick (nausea);
- bloated abdomen;
- vomiting;
- painful periods;
- increased vaginal discharge;
- tender, painful breasts;
- spasm of the womb;
- Levosert coming out by itself;
- weight gain.

Uncommon (may affect up to 1 in 100 women) side effects can include:
- fainting;
- eczema;
- inflammation of the neck of the womb (cervicitis);
- bloating or swelling of your legs or ankles;
- increased growth of hair on the face and body;
- hair loss;
- itchy skin (pruritus);
- skin discolouration or increased skin pigment, especially on the face (chloasma).

Rare (may affect up to 1 in 1,000 women) side effects can include:
- rashes, itching.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

HPRA Pharmacovigilance
Website: www.hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Levosert

Store in the original package. Keep the pouch in the outer carton in order to protect from light. Do not open the Levosert pack. Only your doctor or healthcare provider should do this.

Keep this medicine out of the sight and reach of children.

Do not use the system after the expiry date which is stated on the label and the outer pack after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Levosert contains

- Levosert contains 52 mg of levonorgestrel, the active substance. The hormone is contained within a substance called polydimethylsiloxane. This is surrounded by a membrane (skin) also made of polydimethylsiloxane.

What Levosert looks like and contents of the pack

- Levosert consists of a small T-shaped frame made from a plastic called polyethylene. This structure provides a device for releasing the hormone gradually into the uterus (womb).
- There are two fine threads, made of polypropylene and copper phtalocyanine blue, attached to the bottom of the frame. These allow easy removal and allow you or your doctor to check that the device is in place.

Pack sizes:
One Intrauterine System with the inserter device.
Multipack five packs of one Intrauterine System with one inserter device.

Not all pack sizes may be marketed.

Each pack contains one Levosert.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Gedeon Richter Plc.
Gyömrői út 19-21.
1103 Budapest
Hungary

Manufacturer
Odyssea Pharma SA
Rue du Travail 16
4460 Grâce Hollogne
Belgium

Gedeon Richter Plc.
Gyömrői út 19-21.
1103 Budapest
Hungary

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Austria	Levosert
Cyprus	Levosert
Germany	Levosert
Denmark	Levosert Two
Spain	Levosert
Ireland	Levosert
Iceland	Levosert
Italy	Benilexa
Malta	Levosert
Norway	Levosert
Sweden	Levosert
Slovenia	Levosert
United Kingdom	Benilexa Two Handed

This leaflet was last revised in

The following information is intended for healthcare professionals only
See special instruction leaflet enclosed in the pack.

Instructions for use and handling

Levosert 52 mg Intrauterine Delivery System
Levonorgestrel

Prescriber Check List
Ask yourself the following questions before prescribing/inserting Levosert:

Have I checked that the patient's needs meet the **indications of contraception or heavy menstrual bleeding and for duration of use of up to eight years**?

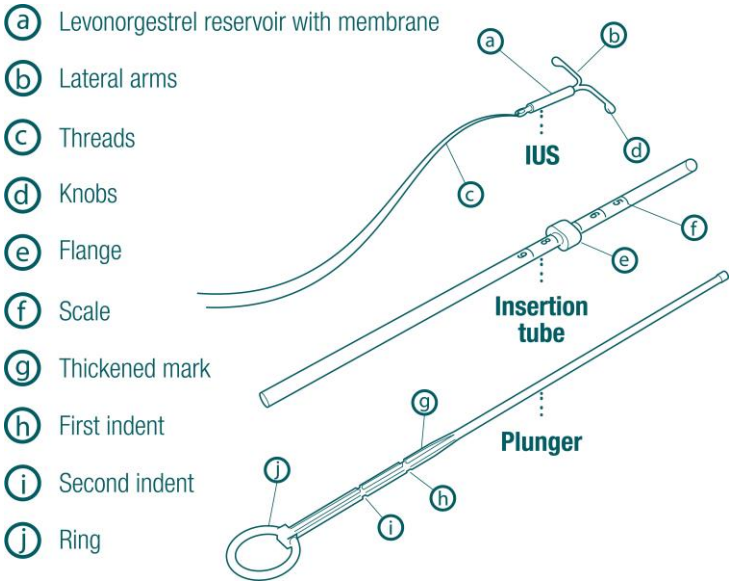
Have I completed the patient card included in the pack and given this to the patient as a reminder? (any insertions of more than eight years in duration should be reported as **off label use**)

Please read the following instructions for use carefully as there may be some difference in the type of inserter device compared with other IUDs you have used previously:

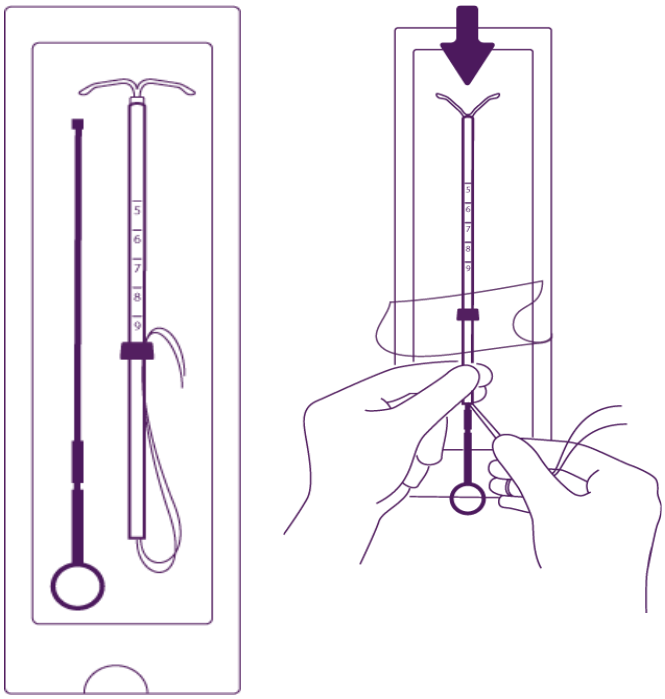
Conditions for use

1. In women of fertile age, Levosert is inserted within seven days of the onset of menstruation. It can be replaced by a new system at any time of the cycle.
2. It is strongly recommended that Levosert should only be inserted by physicians/health care professionals who have undergone sufficient training and have read carefully these instructions before Levosert insertion.
3. Levosert is supplied in a sterile pack which should not be opened until required for insertion. The exposed product should be handled with aseptic precautions. Do not use if the inner package is damaged or open.
4. Determine the position (anteversion, retroversion) and size of the uterus by a gynaecological examination. Exclude pregnancy and contraindications.
5. Place a speculum, use appropriate antiseptic solution to clean the vagina and cervix.
6. Use cervical dilators if cervical stenosis is diagnosed. Do not force to overcome resistance. If cervical dilatation is required, consider using analgesics and/or a paracervical block.
7. Grasp the cervix with a Tenaculum forceps and apply a gentle traction in order to straighten alignment of the cervical canal and uterine cavity.
8. Determine the uterine depth by hysterometry. If uterine depth is < 5.5 cm discontinue the procedure.

Description

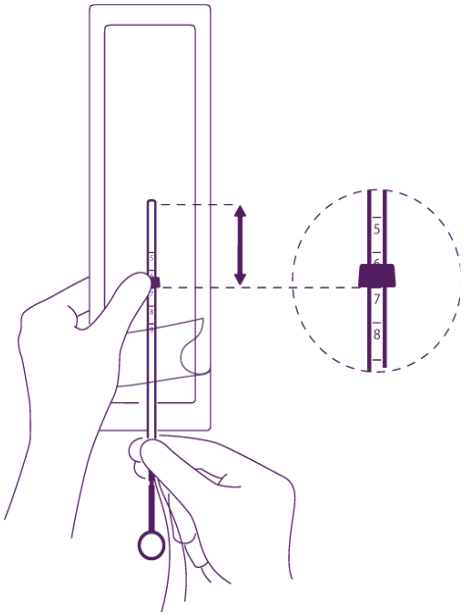


Preparation for insertion



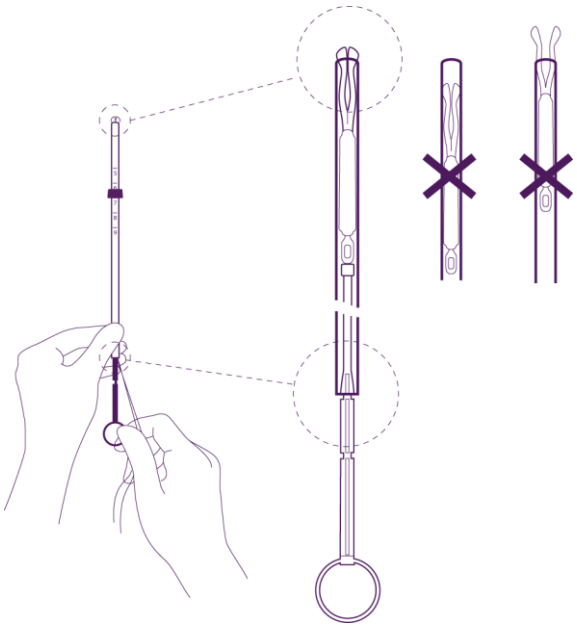
Introduce the plunger and the IUS in the insertion tube

Partly open the blister (about 1/3 from the bottom) and introduce the plunger in the insertion tube. Extricate the threads from the flange. Pull the thread to introduce the IUS into the tube. The arms of the IUS must stay in a horizontal plane, parallel to the flat side of the flange.



Position the lower edge of the flange at the sounded value

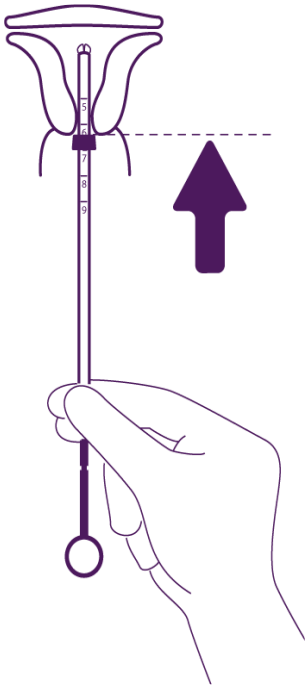
Position the blue flange so as the lower edge of the flange indicates the value found by hysterometry. The flat sides of the flange must always remain parallel to the arms. This will allow the arms to open correctly in the uterine cavity.



Adjust the position of the IUS in the insertion tube

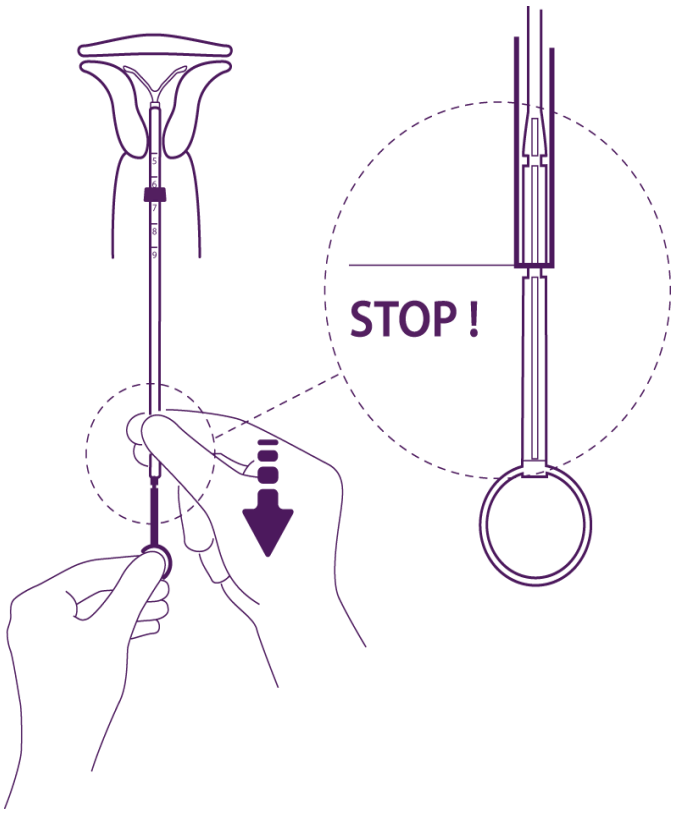
Hold the plunger firmly while pulling the thread and moving the tube to adjust the position of the IUS.
The knobs of the lateral arms must be closely opposed to each other, slightly above the upper extremity of the insertion tube (see zoom 1) and the distal edge of the tube must be aligned with the first indent of the plunger (see zoom 2). If the tube is not aligned with the first indent of the plunger you must pull the thread more firmly.

Insertion



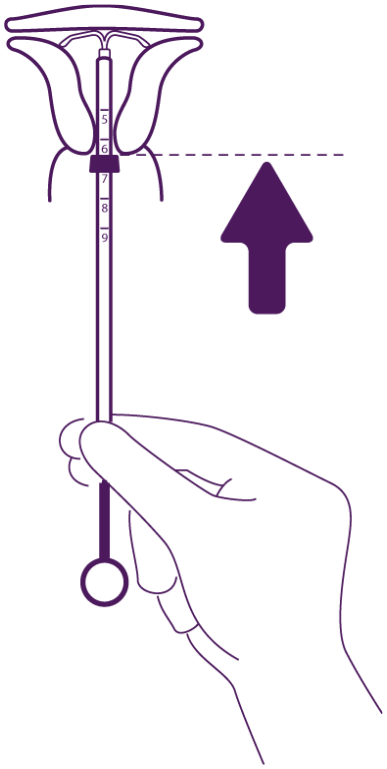
Introduce the device in the cervical canal until the blue flange is in contact with the cervix

Take the whole device out of the blister, by holding firmly the plunger and tube together in the correctly adjusted position. Introduce the assembly into the cervical canal until the blue flange is in contact with the cervix.



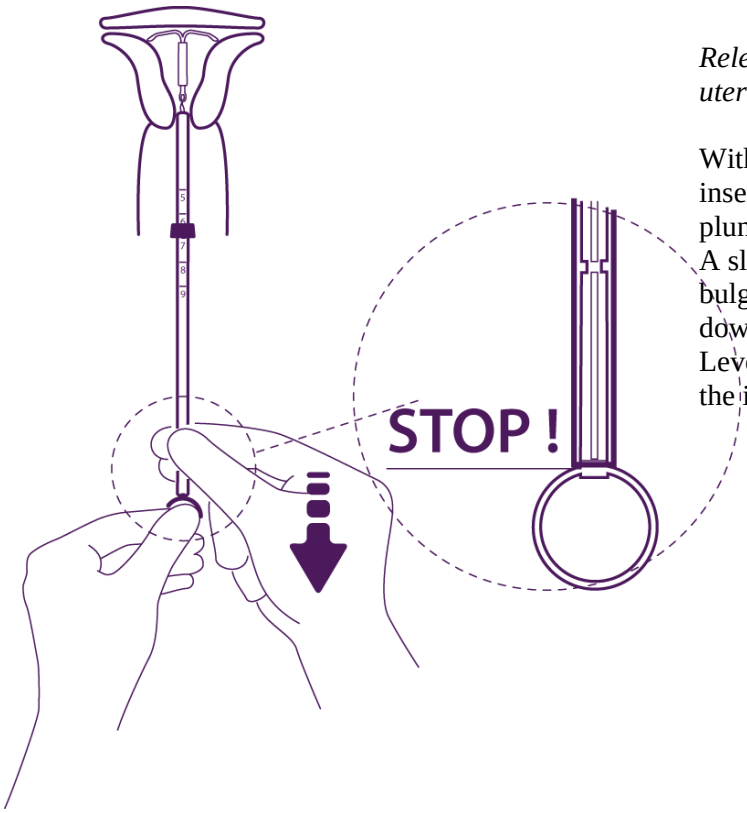
Release the arms of the intrauterine device

Hold the plunger, release the thread and pull the insertion tube down until its lower extremity reaches the second indent of the plunger.



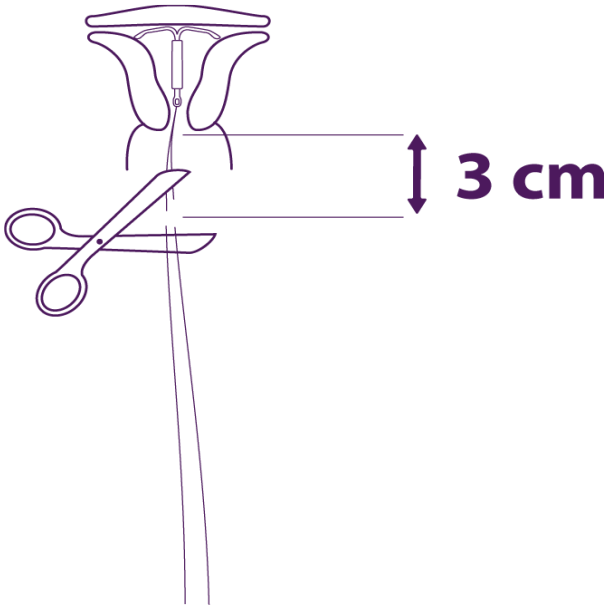
Push the IUS against the fundus

To position the IUS in the uterine cavity, push the insertion tube simultaneously with the plunger, until the blue flange is again in contact with the cervix.
Levosert is then correctly placed in the uterine cavity.



Release the IUS from the tube into the uterine cavity

Without moving the plunger, pull the insertion tube down to the ring of the plunger.
A slight resistance marks the passage of the bulge of the plunger. Nevertheless pull down the tube to the ring of the plunger.
Levosert is then released completely from the insertion tube.



Remove sequentially the inserter components and cut the threads

Remove sequentially, first the plunger, then the insertion tube.
Cut the threads at around 3 cm from the cervix.

Insertion of Levosert is now complete.

Important information to consider during or after insertion:

- If you suspect the IUS is not in the correct position:
  - Check insertion with an ultrasound or other appropriate radiologic test.
  - If incorrect insertion is suspected, remove Levosert. Do not reinsert the same Levosert IUS after removal.

IMPORTANT!

In case of difficult insertion and/or exceptional pain or bleeding during or after insertion, physical examination and ultrasound should be performed immediately to exclude perforation of the uterine body or cervix. Physical examination alone (including checking of threads) may not be sufficient to exclude partial perforation. If necessary remove the system and insert a new, sterile system.
Please report any case of uterine perforation or insertion difficulties via
HPRA Pharmacovigilance
Website: www.hpra.ie

How to remove Levosert

Levosert is removed by gently pulling on the threads with forceps. The use of excessive force/sharp instruments during removal may cause breakage of the device. If the threads are not visible and the device is in the uterine cavity, it may be removed using a narrow tenaculum or intrauterine thread retriever. This may require dilatation of the cervical canal.

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. To ensure continuous contraception a new system should be immediately inserted, or an alternative contraceptive method should have been initiated.

After removal of Levosert, the system should be examined to ensure that it is intact and has been completely removed. 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.