



MIRENA®

Intrauterine delivery system (IUS)

Important information, please read carefully!

Composition

Levonorgestrel 52 mg. The average *in vivo* release rate is approximately 20 micrograms /day during the first year.

For a full list of excipients, see section 'List of excipients'.

Pharmaceutical Form

Intrauterine delivery system (IUS).

The levonorgestrel (LNG) IUS consists of a white or almost white drug core covered with an opaque membrane, which is mounted on the vertical stem of a T-body. The white T-body has a loop at one end of the vertical stem and two horizontal arms at the other end. Brown removal threads are attached to the loop. The T-frame of Mirena contains barium sulphate, which makes it visible in X-ray examination. The vertical stem of the IUS is loaded in the insertion tube at the tip of the inserter. The IUS and inserter are essentially free of visible impurities.

Pharmacological Properties

Pharmacodynamic properties

Levonorgestrel is a progestin with anti-estrogenic activity used in gynecology in various ways: as the progestin component in hormone therapy and oral contraceptives and alone in the so-called 'minipills' and in subdermal implants. Mirena releases levonorgestrel directly into the uterus. This allows a very small daily dose, as the hormone is released directly into the target organ. The plasma concentrations of levonorgestrel are lower than with any other contraceptive method.

Mirena has mainly local progestogenic effects in the uterine cavity. The high levonorgestrel concentration in the endometrium down-regulates endometrial estrogen and progesterone receptors, making the endometrium insensitive to the circulating estradiol and a strong antiproliferative effect is seen. Morphological changes of the endometrium and a weak local foreign body reaction are observed during use of Mirena. Thickening of the cervical mucus prevents passage of the sperm through the cervical canal. The local milieu of the uterus and of the ovarian tubes inhibits sperm mobility and function, preventing fertilization. Ovulation is inhibited in some women.

The contraceptive efficacy of Mirena up to 5 years has been studied in 5 major clinical studies with 3330 women using Mirena. The contraceptive efficacy during extended use beyond 5 years has been studied in the Mirena Extension trial with 362 women using Mirena. The contraceptive efficacy of Mirena is summarized in the table below.

Table 1: Contraceptive efficacy

Contraceptive Efficacy within the first 5 years (N= 3330, Pooled data of contraceptive trials up to 5 Years)	
Year 1 Pearl Index	0.2
Years 1-5 cumulative failure rate (%)*	0.7
Contraceptive Efficacy beyond 5 years (N=362, Mirena Extension Trial)	
Year 6 Pearl Index	0.34
Year 7 Pearl Index	0.40
Year 8 Pearl Index	0.00
Years 6-8 cumulative failure rate (%)*	0.68

*Kaplan-Meier estimate

The failure rate also includes pregnancies due to undetected expulsions and perforations. Similar contraceptive efficacy has been observed in a large post-marketing study with more than 17000 women using Mirena. In a large prospective comparative non-interventional cohort study with an observation period of 1 year including more than 43.000 Mirena users, the Pearl Index of Mirena was 0.06 (95% CI: 0.04-0.09).

Because the use of Mirena does not require daily intake compliance by the users, the pregnancy rates in “typical use” are similar to those observed in controlled clinical trials (“perfect use”). The use of Mirena does not alter the course of the future fertility. About 80 % of the women wishing to become pregnant conceived within 12 months after removal of the system.

Mirena has been developed especially for women requiring long-term, effective contraception. Menorrhagia can also be effectively treated with Mirena. In menorrhagic women, the menstrual blood loss decreased by 62-94% at the end of three months and by 71- 95% at the end of six months of use. Compared to endometrial ablation or resection, Mirena demonstrated equal efficacy in reducing the menstrual blood loss up to two years. Reduced bleeding increases the hemoglobin level. Menorrhagia caused by submucosal myomas may not respond favourably to the treatment. Like oral contraceptive, Mirena also alleviates dysmenorrhea.

The effect of Mirena in the treatment of menorrhagia and in local progestin treatment in conjunction with estrogen replacement therapy is based on the action of levonorgestrel preventing proliferation of the endometrium. No cases of endometrial hyperplasia have been reported during a 12-month observation period. Prevention of proliferation has been equally good in patients administered estrogen orally, transdermally or subcutaneously. The amount of levonorgestrel released by Mirena is sufficient to prevent endometrial proliferation for five years. A sample should be taken from the uterus to check the endometrium before inserting a new Mirena in the uterine cavity, even if there has been no bleeding.

Pharmacokinetic properties

The active ingredient of Mirena is levonorgestrel. Levonorgestrel is directly released into the uterine cavity. Estimated *in vivo* release rates for different points in time are provided in table 2.

Table 2: Estimated *in vivo* release rates for Mirena:

Time	Estimated <i>in vivo</i> release rate [$\mu\text{g}/24$ hours]
24 days after insertion	21
60 days after insertion	21
1 year after insertion	19
3 years after insertion	14
5 years after insertion	11
8 years after insertion	7
Average over 1st year	20
Average over 3 years	18
Average over 5 years	15
Average over 8 years	13

Absorption

Following insertion, levonorgestrel is released into the uterine cavity without delay based on serum concentration measurements. More than 90% of the released levonorgestrel is systemically available.

After insertion of Mirena, levonorgestrel is detectable in serum/plasma after 1 hour. The maximum concentration is reached within 2 weeks after insertion and amounts to about 180 ng/L (CV 38.3%). In correspondence with the declining release rate, the geometric mean serum/plasma concentration of levonorgestrel declines continuously, as shown in table 3:

Table 3: Estimated Total LNG Geometric Mean Plasma Concentrations

Time after insertion	Estimated Total LNG Plasma Concentrations [ng/L] (geometric CV%)
24 days	175 (37.6)
2 months	169 (37.1)
1 year	159 (37.4)
3 years	139 (37.8)
5 years	123 (38.2)
8 years	100 (39.9)

The high local drug exposure in the uterine cavity, leads to a strong concentration gradient via the endometrium to the myometrium (gradient endometrium to myometrium >100-fold), and to low concentrations of levonorgestrel in serum (gradient endometrium to serum >1000-fold).

In postmenopausal women using Mirena together with non-oral estrogen treatment, the median serum concentration of levonorgestrel declines from 257 pg/ml (25th to 75th percentiles: 186 pg/ml to 326 pg/ml) at 12 months to 149 pg/ml (122 pg/ml to 180 pg/ml) at 60 months. When Mirena is used together with oral estrogen treatment, the serum levonorgestrel

concentration at 12 months is increased to approx. 478 pg/ml (25th to 75th percentiles: 341 pg/ml to 655 pg/ml) due to the induction of the Sex hormone-binding globulin (SHBG) by oral estrogen treatment.

Distribution

Levonorgestrel is bound non-specifically to serum albumin and specifically to the Sex hormone-binding globulin (SHBG). Less than 2% of the circulating levonorgestrel is present as free steroid. Levonorgestrel binds with high affinity to SHBG. Accordingly, changes in the concentration of SHBG in serum result in an increase (at higher SHBG concentrations) or in a decrease (at lower SHBG concentrations) of the total levonorgestrel concentration in serum. The concentration of SHBG declined on average by about 20% during the first two months after insertion of Mirena and remained stable thereafter increasing only slightly until the end of the 8 years of use. The mean apparent volume of distribution of levonorgestrel is about 106 L.

Body weight and serum SHBG concentration have been shown to affect systemic levonorgestrel concentration i.e. low body weight and/or a high SHBG level increase levonorgestrel concentration. In women of reproductive age with a low body weight (37 to 55 kg) the median serum concentration of levonorgestrel is about 1.5-fold higher.

Biotransformation

Levonorgestrel is extensively metabolized. The most important metabolic pathways are the reduction of the $\Delta 4$ -3-oxo group and hydroxylations at positions 2 α , 1 β and 16 β , followed by conjugation. CYP3A4 is the main enzyme involved in the oxidative metabolism of LNG. The available *in vitro* data suggest that CYP mediated biotransformation reactions may be of minor relevance for LNG compared to reduction and conjugation.

Elimination

The total clearance of levonorgestrel from plasma is approximately 1.0 ml/min/kg. Only trace amounts of levonorgestrel are excreted in unchanged form. The metabolites are excreted with the feces and urine at an excretion ratio of about 1. The excretion half-life which is mainly represented by metabolites, is about 1 day.

Linearity / non-linearity

The pharmacokinetics of levonorgestrel is dependent on the concentration of SHBG which itself is influenced by estrogens and androgens. A decrease of SHBG concentration leads to a decrease of total levonorgestrel concentration in serum indicating non-linear pharmacokinetics of levonorgestrel with regard to time. Based on the mainly local action of Mirena, no impact on the efficacy of Mirena is expected.

Preclinical safety data

The preclinical safety evaluation revealed no special hazard for humans based on studies of safety pharmacology, pharmacokinetics, toxicity, genotoxicity, and carcinogenic potential of levonorgestrel. Levonorgestrel is a widely-used progestin. The safety profile following systemic administration is well documented. Studies in monkeys with intrauterine delivery of levonorgestrel for 9 to 12 months confirmed local pharmacological activity with good tolerance and no signs of systemic toxicity. No embryotoxicity was seen in a study in rabbits.

Indications

- Contraception,
- Idiopathic menorrhagia,
- Protection from endometrial hyperplasia during estrogen replacement therapy.

Dosage and method of administration

Method of administration

Mirena is inserted into the uterine cavity. It is effective for 8 years for contraception and for 5 years in the indications Idiopathic menorrhagia and protection from endometrial hyperplasia during estrogen replacement therapy. For timing regarding removal/replacement, see section Removal/replacement.

The *in vivo* levonorgestrel release rate 24 days after insertion is approximately 21 μ g/day, decreasing continuously to approximately 19 μ g/day after 1 year, to 11 μ g/day after 5 years and to 7 μ g/day after 8 years of use. The average daily levonorgestrel release rates are approximately 20 μ g/day during the first year, 15 μ g/day during the first 5 years and 13 μ g/day over the complete 8 year period of use.

In women under hormonal replacement therapy, Mirena can be used in combination with oral or transdermal estrogen preparations without progestogens.

The contraceptive efficacy of Mirena up to 8 years, when inserted according to the insertion instructions, is presented in table 4 below.

Table 4: Contraceptive efficacy

Contraceptive Efficacy within the first 5 years (N= 3330, Pooled data of contraceptive trials up to 5 Years)	
Year 1 Pearl Index	0.2
Years 1-5 cumulative failure rate (%)*	0.7
Contraceptive Efficacy beyond 5 years (N=362, Mirena Extension Trial)	
Year 6 Pearl Index	0.34
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Year 8 Pearl Index	0.00
Years 6-8 cumulative failure rate (%)*	0.68

* Kaplan-Meier estimate

Insertion and removal/replacement

Insertion

Use of Mirena as a contraceptive: In women of fertile age, Mirena is to be inserted into the uterine cavity within seven days of the onset of menstruation. Mirena can be replaced by a new system at any time in the cycle. The system can also be inserted immediately after first trimester abortion.

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, the possibility of perforation should be considered and appropriate steps should be taken, such as physical examination and ultrasound.

Mirena is not recommended as the contraceptive method of first choice for young women who have never given birth.

Mirena in the treatment of idiopathic menorrhagia: In women of fertile age, Mirena is to be inserted into the uterine cavity within seven days of the onset of menstruation. Mirena can be replaced by a new system at any time in the cycle.

Mirena as a local progestin treatment in conjunction with estrogen replacement therapy: A sample should be taken from the uterine cavity to check the endometrium before insertion of Mirena because spotting is common during the first months of therapy. Mirena can be inserted at any time in an amenorrheic woman, or during the last days of menstruation or withdrawal bleeding. New specimens are not usually required during the 12 months following insertion. Vaginal ultrasonography is recommended 12 months after insertion. An endometrial sample should be taken if the endometrium is thicker than 5 mm or the patient has had extra bleedings. In the treatment of menorrhagia and in local progestin treatment in conjunction with estrogen replacement therapy Mirena releases a sufficient amount of levonorgestrel during a five-year period to prevent proliferation of the endometrium. A sample should be taken from the uterus to check the endometrium before insertion of a new Mirena, even if there has been no bleeding.

It is recommended that Mirena should only be inserted by physicians/health care professionals who are experienced in Mirena insertions and/or have undergone sufficient training for Mirena insertion.

Removal/replacement

Contraception

The system should be removed or replaced after 8 years.

If pregnancy is not desired, the removal should be carried out within 7 days of the onset of menstruation in women of fertile age, provided the woman is experiencing regular menses. If the system is removed at some other time during the cycle or the woman does not experience regular menses 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.

Idiopathic menorrhagia

The system should be removed or replaced in case symptoms of idiopathic menorrhagia return. The system should be removed or replaced after 5 years.

Protection from endometrial hyperplasia during estrogen replacement therapy

The system should be removed or replaced after 5 years.

Mirena is removed by gently pulling on the threads with forceps. The use of excessive force during removal may cause damage to the device. After removal of Mirena, the system should be examined to ensure that it is 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.

If the threads are not visible, determine the location of the system via ultrasound or other method. If the system is in the uterine cavity, it may be removed using narrow forceps. This may require dilatation of the cervical canal or other surgical intervention.

If the user wishes to continue using the same method, a new system can be inserted at the time of removal.

Instruction for use and handling and disposal:

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. Detailed instructions for insertion are in the package.

Additional information on special populations

Geriatric patients

Mirena has not been studied in women over the age of 65 years.

Patients with hepatic impairment

Mirena is contraindicated in women with acute liver disease or liver tumor (see Contraindications).

Patients with renal impairment

Mirena has not been studied in women with renal impairment.

Pediatric population

Use of this product before menarche is not indicated.

Contraindications

Known or suspected pregnancy;
Current or recurrent pelvic inflammatory disease;
Lower genital tract infection;
Postpartum endometritis;
Infected abortion during the past three months;
Cervicitis;
Cervical dysplasia;
Uterine or cervical malignancy;
Progestogen-dependent tumors;
Undiagnosed abnormal uterine bleeding;
Congenital or acquired uterine anomaly including fibroids if they distort the uterine cavity;
Conditions associated with increased susceptibility to infections;
Acute liver disease or liver tumor;
Thromboembolic process;
Hypersensitivity to the active substance or to any of the excipients

Special warnings and special precautions for use

Mirena may be used with caution after specialist consultation, or removal of the system should be considered if the patient experiences for the first time migraine, exceptionally severe headache, jaundice or marked increase in blood pressure, confirmed or suspected hormone dependent cancer, including breast cancer or if the patient is diagnosed with malignant hematological disease or leukemia, severe arterial disease such as stroke or myocardial infarction, or thrombophlebitis.

Glucose tolerance may be affected with Mirena in place and, therefore, the blood glucose concentration should be monitored in diabetics. However, there is generally no need to alter the therapeutic regimen in diabetics using Mirena. Irregular bleedings may mask symptoms of cervical or endometrial cancer. For this reason, the physician must ensure before insertion of Mirena that the patient has had a cervical smear, which should be normal, during the three months preceding the insertion. A uterine sample should be normal in conjunction with estrogen replacement therapy. Bleeding irregularities developing with Mirena in place should be investigated as described above at the discretion of the physician.

Mirena is not the method of first choice for postmenopausal women with advanced uterine atrophy.

Due to the limited exposure in Mirena trials in the indication protection from endometrial hyperplasia during estrogen replacement therapy, the available data are not sufficient to confirm or refute a risk for breast cancer when Mirena is used in this indication.

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, and examination of the breasts, should be conducted. Cervical smear should be performed as needed, according to Healthcare Professional's evaluation. 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. Because the insertion technique is different from other intrauterine devices, special emphasis should be given to training in the correct insertion technique. 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.

The women should be re examined 4 to 12 weeks after insertion and once a year thereafter, or more frequently if clinically indicated.

Mirena is not suitable for use as a post-coital contraceptive.

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.

Infrequent bleeding and amenorrhea

In women of fertile age, infrequent bleeding and amenorrhea develops gradually in 57% and 16% of women during the first year of use, respectively. By the end of Year 8 of Mirena use, infrequent bleeding and amenorrhea are experienced by 26% and 34% of Mirena users, respectively. The possibility of pregnancy should be considered if menstruation does not occur within six weeks of the onset of previous menstruation and a check should be made to ensure that the system is still in place.

Amenorrhea is an effect that can be positive for some and negative for others. In clinical studies, the discontinuation rate for amenorrhea during the first year of use was 1.7%. Due to the strong local effect of levonorgestrel on the endometrium, the endometrial lining does not react to estrogen and, therefore, proliferation does not occur. The duration and volume of menstrual bleeding is reduced. When women with different patterns were compared, no clear difference in follicle development, ovulation or estradiol or progesterone production was found. During the first three months, the volume of menstrual bleeding decreased by 88% in menorrhagic women. Reduced bleeding increased the hemoglobin level. Over a 12-month observation period, amenorrhea developed in more than 50% of users during local progestin treatment in conjunction with estrogen replacement therapy. Irregular bleeding and spotting were fairly common during the first three months of use.

Pelvic infections

The insertion tube helps to protect Mirena from contamination with micro-organisms during the insertion. On the basis of experience obtained from users of copper intrauterine devices, the risk of infection is greatest during the first month of use, after which the rate of infections decreases. The risk of infection is highest in young women or if the woman or her partner have multiple sexual partners. Pelvic infection may have serious consequences and it may impair fertility and increase the risk of ectopic pregnancy.

As with other gynecological or surgical procedures, severe infection or sepsis (including group A streptococcal sepsis) can occur following IUD insertion, although this is extremely rare.

If an acute infection does not respond to treatment within a few days, or if the woman experiences recurrent endometritis or other pelvic infection, Mirena must be removed. Some studies indicate that the rate of pelvic infections in users of Mirena is lower than in users of copper intrauterine devices.

Expulsion

Mirena may be expelled from the uterine cavity without the woman noticing it leading to loss of contraceptive protection. Symptoms of the partial or complete expulsion of the IUS may include bleeding and pain. However, the system can be expelled from the uterine cavity without the woman noticing it leading to loss of contraceptive protection. As Mirena normally decreases menstrual flow, increase of bleeding may be indicative of an expulsion.

Risk of expulsion is increased in

- Women with history of heavy menstrual bleeding
- Women with greater than normal BMI at the time of insertion; this risk increases gradually with increasing BMI

Counsel the woman on possible signs of expulsion and instruct her on how to check the threads of Mirena. Advise her to contact her doctor if the threads cannot be felt and avoid intercourse or use a barrier contraceptive (such as condoms) until the location of Mirena has been confirmed.

Partial expulsion may decrease the effectiveness of Mirena.

A partially expelled Mirena should be removed. A new system can be inserted at the time of removal, provided pregnancy has been excluded.

Perforation

Perforation or penetration of the uterine corpus or cervix by an intrauterine contraceptive may occur, most often during insertion, although it may not be detected until some time later and may decrease the effectiveness of Mirena. Such a system must be removed.

In a large prospective comparative non-interventional cohort study in IUD users (N = 61,448 women) with a 1-year observational period, the incidence of perforation was 1.3 (95% CI: 1.1 - 1.6) per 1000 insertions in the entire study cohort; 1.4 (95% CI: 1.1 - 1.8) per 1000 insertions in the Mirena cohort and 1.1 (95% CI: 0.7 - 1.6) per 1000 insertions in the copper IUD cohort. Extending the observational period to 5 years in a subgroup of this study (N = 39,009 women using Mirena or copper IUD), the incidence of perforation detected at any time during the entire 5-year period was 2.0 (95% CI: 1.6 - 2.5) per 1000 insertions.

The study showed that both breastfeeding at the time of insertion and insertion up to 36 weeks after giving birth were associated with an increased risk of perforation (see Table 5). These risk factors were confirmed in the subgroup followed up for 5 years. Both risk factors were independent of the type of IUD inserted.

Table 5: Incidence of perforation per 1000 insertions for the entire study cohort observed over 1 year, stratified by breastfeeding and time since delivery at insertion (parous women)

	Breastfeeding at time of insertion	Not breastfeeding at time of insertion
Insertion ≤ 36 weeks after delivery	5.6 (95% CI 3.9-7.9; n=6047 insertions)	1.7 (95% CI 0.8-3.1; n=5927 insertions)
Insertion > 36 weeks after delivery	1.6 (95% CI 0.0-9.1; n=608 insertions)	0.7 (95% CI 0.5-1.1; n=41910 insertions)

The risk of perforation may be increased in women with fixed retroverted uterus.

Ectopic pregnancy

Women with a previous history of ectopic pregnancy, tubal surgery or pelvic infection carry a higher risk of ectopic pregnancy. The possibility of ectopic pregnancy should be considered in the case of lower abdominal pain - especially in connection with missed periods or if an amenorrheic woman starts bleeding. In clinical trials the ectopic pregnancy rate with Mirena was approximately 0.1% per year. In a large prospective comparative non-interventional cohort study with an observation period of 1 year, the ectopic pregnancy rate with Mirena was 0.02%. This rate is lower than in women not using any contraception (0.3-0.5% per year). The absolute risk of ectopic pregnancy in Mirena users is low. However, when a woman becomes pregnant with Mirena in situ, the relative likelihood of ectopic pregnancy is increased.

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 possibility of expulsion or perforation should be considered. 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 follicles 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.

Fertility, pregnancy and lactation

Pregnancy

The use of Mirena during an existing or suspected pregnancy is contraindicated (see Contraindications).

If the woman becomes pregnant when using Mirena removal of the system is recommended, since any intrauterine contraceptive left in situ may increase the risk of abortion and preterm labor. Removal of Mirena or probing of the uterus may result in spontaneous abortion. Ectopic pregnancy should be excluded. 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 also be closely monitored. The woman should be instructed to report all symptoms that suggest complications of the pregnancy, like cramping abdominal pain with fever.

There have been isolated cases of masculinization of the external genitalia of the female fetus following local exposure to levonorgestrel during pregnancy with an LNG-IUS in place.

Lactation

About 0.1 % of the levonorgestrel dose is transferred to the infant during breast-feeding. However, it is not likely that there will be a risk for the infant with the dose released from Mirena, when it is inserted in the uterine cavity. There appears to be no deleterious effect on infant growth or development when using Mirena after six weeks postpartum. Progestogen-only methods do not appear to affect the quantity or quality of breast milk. Uterine bleeding has rarely been reported in women using Mirena during lactation.

Fertility

Upon removal of Mirena, women return to their normal fertility.

Effects on ability to drive and use machines

Not known.

Undesirable effects

Summary of the safety profile

The majority of women experience changes in menstrual bleeding pattern after insertion of Mirena. During the first 90 days, prolonged bleeding is experienced by 22% and irregular bleeding by 67% of women after postmenstrual insertion of Mirena, decreasing to 3% and 19% at the end of the first year of use, respectively. Concomitantly, amenorrhea is experienced by 0% and infrequent bleeding by 11% during the first 90 days, increasing to 16% and 57% at the end of the first year of use, respectively.

By the end of Year 8 of Mirena use, prolonged bleeding and irregular bleeding are experienced by 3% and 10% of Mirena users, respectively; amenorrhea occurs in 34 %, and infrequent bleeding in 26% of Mirena users.

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

Tabulated list of adverse reactions

The frequencies of adverse drug reactions (ADRs) reported with Mirena are summarized in the table below. Frequencies are defined as very common ($\geq 1/10$), common ($\geq 1/100$ to $<1/10$), uncommon ($\geq 1/1000$ to $<1/100$), rare ($\geq 1/10000$ to $<1/1000$) and unknown. The table below reports adverse reactions by MedDRA system organ classes (MedDRA SOCs). The frequencies are crude incidences of the events observed in clinical trials in the indications contraception and idiopathic menorrhagia/ heavy menstrual bleeding, including 5091 women and 12,101 woman-years.

Adverse reactions in clinical trials in the indication protection from endometrial hyperplasia during estrogen replacement therapy (including 514 women and 1218.9 woman-years) were observed at a similar frequency unless specified by footnotes.

Table 6: adverse drug reactions

System Organ Class	Very Common	Common	Uncommon	Rare	Unknown
Immune system disorders					Hypersensitivity including rash, urticaria and angioedema

System Organ Class	Very Common	Common	Uncommon	Rare	Unknown
Psychiatric disorders		Depressed mood/ Depression			
Nervous system disorders	Headache	Migraine			
Gastrointestinal disorders	Abdominal/pelvic pain	Nausea			
Skin and subcutaneous tissue disorders		Acne Hirsutism	Alopecia		
Musculoskeletal, connective tissue and bone disorders		Back pain**			
Reproductive system and breast disorders	Bleeding changes including increased and decreased menstrual bleeding, spotting, infrequent bleeding and amenorrhoea Vulvovaginitis* Genital discharge*	Upper genital tract infection Ovarian cyst Dysmenorrhea Breast pain** Intra-uterine contraceptive device expelled (complete and partial)	Uterine perforation** *		
Investigations					Blood pressure increased

The most appropriate MedDRA term is used to describe a certain reaction and its synonyms and related conditions.

*Endometrial protection trials: "common"

** Endometrial protection trials: "very common"

*** This frequency is based on a large prospective comparative non-interventional cohort study in IUD users which showed that breastfeeding at the time of insertion and insertion up to 36 weeks after giving birth are independent risk factors for perforation, (see section 'Special warnings and precautions for use'). In clinical trials with Mirena that excluded breastfeeding women the frequency of perforation was "rare".

A separate study with 362 women who have used Mirena for more than 5 years showed a consistent adverse reaction profile in Years 6 through 8.

Pregnancy, puerperium and perinatal conditions:

When a woman becomes pregnant with Mirena in situ, the relative risk of ectopic pregnancy is increased.

Reproductive system disorders:

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

Breast disorders:

The risk of breast cancer is unknown when Mirena is used in the indication protection from endometrial hyperplasia during estrogen replacement therapy. Cases of breast cancer have been reported (frequency unknown, see Section Special warnings and special precautions of use).

Injury, poisoning and procedural complications:

The following ADRs have been reported in connection with the insertion or removal procedure of Mirena:

Procedural pain, procedural bleeding, insertion-related vasovagal reaction with dizziness or syncope. The procedure may precipitate a seizure in an epileptic patient.

Infections and Infestations:

Cases of sepsis (including group A streptococcal sepsis) have been reported following IUD insertion (see section special warnings and precautions for use).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: <https://e-meso.pom.go.id/ADR>

Interaction with other medicaments and other forms of interaction

Note: The prescribing information of concomitant medications should be consulted to identify potential interactions.

Effects of other medicinal products on Mirena

Interactions can occur with drugs that induce or inhibit microsomal enzymes, which can result in increased or decreased clearance of sex hormones.

Substances increasing the clearance of levonorgestrel, e.g.:

Phenytoin, barbiturates, primidone, carbamazepine, rifampicin, and possibly also oxcarbazepine, topiramate, felbamate, griseofulvin, and products containing St. John's wort.

The influence of these drugs on the contraceptive efficacy of Mirena is not known, but it is not believed to be of major importance due to the local mechanism of action.

Substances with variable effects on the clearance of levonorgestrel:

When co-administered with sex hormones, many HIV/HCV protease inhibitors and non-nucleoside reverse transcriptase inhibitors can increase or decrease plasma concentrations of the progestin.

Substances decreasing the clearance of levonorgestrel (enzyme inhibitors), e.g.:

Strong and moderate CYP3A4 inhibitors such as azole antifungals (e.g. fluconazole, itraconazole, ketoconazole, voriconazole), verapamil, macrolides (e.g. clarithromycin, erythromycin), diltiazem and grapefruit juice can increase plasma concentrations of the progestin.

List of excipients

Polydimethylsiloxane elastomer
Silica, colloidal anhydrous
Polyethylene
Barium sulphate
Iron oxide

Storage

Store below 30°C

Presentation

Box @ 1 IUS
Reg. No.: XXXXX

Harus dengan resep dokter

Manufactured by:
Bayer Oy,
Turku-Finland

Imported by:
PT. Bayer Indonesia,
Depok-Indonesia

LEMBAR INFORMASI UNTUK PASIEN

Mirena Levonorgestrel 52 mg Sistem pengantaran intrauterin

Bacalah seluruh isi brosur ini dengan saksama sebelum mulai menggunakan obat ini.

- Simpan brosur ini. Anda mungkin memerlukannya nanti.
- Jika ada pertanyaan lebih lanjut, tanyakan kepada dokter atau apoteker Anda.
- Obat ini telah diresepkan untuk Anda. Jangan berikan kepada orang lain. Obat ini dapat membahayakan mereka, bahkan jika mereka memiliki gejala yang sama dengan Anda.
- Jika efek samping menjadi parah, atau jika Anda mengamati efek samping yang tidak dicantumkan dalam brosur ini, beri tahu dokter atau apoteker.

1. APA ITU MIRENA DAN APA KEGUNAANNYA

Mirena adalah sistem penghantaran obat dalam rahim (intrauterine delivery system/IUS) berbentuk T yang setelah dipasang akan melepaskan hormon levonorgestrel ke dalam rahim. Badan berbentuk T dimaksudkan untuk menyesuaikan sistem dengan bentuk rahim. Lengan vertikal di badan berbentuk T putih membawa reservoir obat yang berisi levonorgestrel. Dua benang pelepas berwarna coklat diikatkan ke lubang di ujung bawah lengan vertikal tersebut.

Mirena digunakan untuk:

- Kontrasepsi (pencegahan kehamilan)
- Menoragia idiopatik (perdarahan menstruasi yang berlebihan)
- Perlindungan terhadap hiperplasia endometrium (pertumbuhan lapisan rahim yang berlebihan) selama terapi hormon estrogen.

2. HAL YANG PERLU ANDA KETAHUI SEBELUM MENGGUNAKAN MIRENA

Catatan umum

Sebelum Anda dapat mulai menggunakan Mirena, dokter akan mengajukan beberapa pertanyaan tentang riwayat kesehatan pribadi Anda dan kerabat dekat Anda.

Sekitar 2 di antara 1.000 perempuan yang menggunakan Mirena dengan benar menjadi hamil dalam tahun pertama.

Sekitar 7 di antara 1.000 perempuan yang menggunakan Mirena dengan benar menjadi hamil dalam lima tahun.

Sekitar 7 di antara 1.000 perempuan yang menggunakan Mirena dengan benar menjadi hamil selama periode penggunaan 3 tahun setelah 5 tahun (Tahun ke-6 - 8).

Dalam brosur ini, dijelaskan beberapa situasi saat Mirena sebaiknya dilepas, atau saat keefektifan Mirena mungkin berkurang. Dalam situasi tersebut, Anda tidak boleh berhubungan seksual atau Anda sebaiknya melakukan tindakan pencegahan ekstra dengan alat kontrasepsi nonhormonal, misalnya menggunakan kondom atau metode penghalang lainnya. Jangan gunakan metode kalender atau suhu. Metode-metode tersebut dapat menjadi tidak andal karena Mirena mengubah perubahan suhu tubuh dan mukus serviks setiap bulannya.

Mirena, seperti alat kontrasepsi hormonal lainnya, tidak melindungi dari infeksi HIV (AIDS) atau penyakit menular seksual lainnya.

Jangan gunakan Mirena dalam kondisi-kondisi berikut:

- jika Anda hamil atau mengira bahwa Anda mungkin hamil
- jika Anda sedang atau kembali mengalami penyakit peradangan panggul (infeksi organ reproduksi wanita)
- jika Anda mengalami infeksi saluran kelamin bawah
- jika Anda mengalami infeksi rahim setelah melahirkan
- jika Anda pernah mengalami infeksi rahim setelah aborsi selama 3 bulan terakhir
- jika Anda mengalami infeksi serviks (leher rahim)
- jika Anda memiliki sel yang abnormal di serviks
- jika Anda memiliki kanker atau diduga memiliki kanker serviks atau rahim
- jika Anda memiliki tumor yang pertumbuhannya tergantung pada hormon progestogen
- jika Anda mengalami perdarahan rahim abnormal yang tidak dapat dijelaskan
- jika Anda memiliki kondisi serviks atau rahim yang abnormal termasuk fibroid, jika kondisi tersebut mengubah bentuk rongga rahim
- jika Anda memiliki kondisi yang berkaitan dengan peningkatan kerentanan terhadap infeksi
- jika Anda memiliki penyakit hati atau tumor hati yang aktif
- jika Anda hipersensitif (alergi) terhadap levonorgestrel atau terhadap kandungan bahan lainnya dari Mirena.

Beri perhatian khusus ketika menggunakan Mirena

Berkonsultasilah dengan dokter spesialis yang dapat memutuskan untuk melanjutkan penggunaan Mirena atau melepas sistem tersebut jika salah satu kondisi berikut terjadi atau muncul untuk pertama kalinya saat menggunakan Mirena:

- migrain, kehilangan penglihatan asimetris, atau gejala lainnya yang mungkin merupakan tanda-tanda iskemia serebral transien (penyumbatan sementara pasokan darah ke otak)
- sakit kepala yang luar biasa parah
- penyakit kuning (kulit, bagian putih mata, dan/atau kuku yang menguning)
- peningkatan tekanan darah yang mencolok
- penyakit arteri yang parah seperti stroke atau serangan jantung.

Mirena dapat digunakan dengan perhatian pada perempuan yang memiliki penyakit jantung bawaan atau penyakit katup jantung yang berisiko mengalami peradangan otot jantung akibat infeksi.

Pada pengguna Mirena yang memiliki diabetes, kadar gula darah sebaiknya dipantau. Namun, umumnya Anda tidak perlu mengubah pengobatan diabetes saat menggunakan Mirena.

Perdarahan tidak teratur dapat menutupi beberapa gejala dan tanda polip atau kanker endometrium, dan dalam kasus ini, tindakan diagnostik harus dipertimbangkan.

Mirena bukanlah metode pilihan pertama untuk perempuan pascamenopause yang mengalami penyusutan rahim.

Data yang tersedia menunjukkan bahwa Mirena tidak meningkatkan risiko kanker payudara pada perempuan pramenopause yang berusia kurang dari 50 tahun. Karena keterbatasan data penelitian Mirena dalam hal indikasi perlindungan terhadap hiperplasia endometrium (pertumbuhan lapisan rahim yang berlebihan) selama terapi hormon estrogen, risiko kanker payudara ketika Mirena digunakan untuk indikasi ini tidak dapat dikonfirmasi atau dihilangkan.

Pemeriksaan/konsultasi medis

Pemeriksaan sebelum pemasangan dapat meliputi tes usap serviks (Pap smear), pemeriksaan payudara, dan tes lainnya, misalnya untuk infeksi, termasuk penyakit menular seksual, bila diperlukan. Pemeriksaan ginekologi sebaiknya dilakukan untuk menentukan posisi dan ukuran rahim.

Mirena tidak cocok untuk digunakan sebagai alat kontrasepsi pascakoitus (digunakan setelah berhubungan seksual).

Infeksi

Selang insersi membantu mencegah Mirena terkontaminasi mikroorganisme selama pemasangan, dan alat insersi Mirena telah dirancang untuk meminimalkan risiko infeksi. Meskipun begitu, terdapat peningkatan risiko infeksi panggul segera dan selama bulan pertama setelah pemasangan sistem ini pada pengguna Alat Kontrasepsi Dalam Rahim (intrauterine device/IUD) Berlapis Tembaga. Infeksi panggul pada pengguna IUS (Sistem Dalam Rahim/Intra Uterine System) sering kali berkaitan dengan penyakit menular seksual. Risiko infeksi meningkat jika perempuan atau pasangannya memiliki beberapa pasangan seksual. Infeksi panggul harus segera diobati. Infeksi panggul dapat mengganggu kesuburan dan meningkatkan risiko kehamilan di luar kandungan (kehamilan di luar rahim) pada masa mendatang. Pada kasus yang sangat jarang terjadi, infeksi berat atau sepsis (infeksi yang sangat berat, yang dapat berakibat fatal) dapat terjadi sesaat setelah pemasangan IUD.

Mirena harus dilepas jika terdapat infeksi panggul berulang atau infeksi lapisan rahim, atau jika infeksi akut yang terjadi parah atau tidak merespons terhadap pengobatan dalam beberapa hari.

Berkonsultasilah dengan dokter tanpa menunda-nunda jika Anda mengalami nyeri perut bagian bawah, demam, nyeri yang berkaitan dengan hubungan seksual, atau perdarahan yang tidak normal secara terus-menerus. Nyeri hebat atau demam yang timbul sesaat setelah pemasangan mungkin berarti bahwa Anda memiliki infeksi berat yang harus segera diobati.

Pelepasan keluar

Kontraksi otot rahim selama menstruasi kadang dapat mendorong IUS sehingga bergeser atau terlepas keluar. Hal ini lebih mungkin terjadi jika Anda kelebihan berat badan atau mengeluarkan banyak darah saat haid. Jika IUS bergeser, sistem mungkin tidak berfungsi seperti yang dimaksudkan. Jika IUS terlepas keluar, Anda tidak lagi terlindungi dari kehamilan.

Kemungkinan gejala saat sistem terlepas keluar adalah nyeri dan perdarahan yang tidak normal, tetapi Mirena mungkin juga terlepas dan keluar tanpa Anda sadari. Karena Mirena menurunkan aliran darah menstruasi, peningkatan aliran darah menstruasi mungkin merupakan indikasi bahwa sistem terlepas keluar. Lihat “Bagaimana cara memastikan bahwa Mirena terpasang di tempatnya” untuk mengetahui cara memeriksa apakah Mirena terpasang di tempatnya dan apa yang harus dilakukan jika Anda menduga bahwa Mirena tidak lagi terpasang di tempatnya.

Perforasi

Perforasi atau penetrasi dinding rahim dapat terjadi, sering kali selama penempatan, meskipun mungkin tidak dideteksi hingga beberapa waktu kemudian.

Mirena yang telah berada di luar rongga rahim tidak efektif dalam mencegah kehamilan. Anda mungkin memerlukan operasi bedah untuk melepas Mirena. Risiko perforasi meningkat pada perempuan yang menyusui dan pada perempuan yang melahirkan hingga 36 minggu sebelum pemasangan dan mungkin meningkat pada perempuan dengan rahim yang tetap berada dalam posisi miring ke belakang (rahim tetap berada dalam posisi terbalik).

Kehamilan di luar kandungan

Kehamilan sangat jarang terjadi ketika menggunakan Mirena. Namun, jika Anda menjadi hamil ketika menggunakan Mirena, risiko bahwa Anda dapat mengandung janin di luar rahim (mengalami kehamilan di luar kandungan) relatif meningkat. Sekitar 1 di antara 1.000 perempuan yang menggunakan Mirena dengan benar mengalami kehamilan di luar kandungan per tahun. Tingkat kehamilan ini lebih rendah daripada perempuan yang tidak menggunakan kontrasepsi apa pun (sekitar 3 hingga 5 di antara 1.000 perempuan per tahun). Perempuan yang sudah mengalami kehamilan di luar kandungan, pembedahan tuba falopi dari ovarium ke rahim, atau infeksi panggul memiliki risiko yang lebih tinggi. Kehamilan di luar kandungan merupakan kondisi serius yang memerlukan perhatian medis segera. Gejala berikut dapat berarti bahwa Anda mungkin mengalami kehamilan di luar kandungan dan Anda sebaiknya segera berkonsultasi dengan dokter:

- Periode menstruasi Anda telah berhenti lalu Anda mulai mengalami perdarahan atau nyeri secara terus-menerus
- Anda mengalami nyeri yang tidak jelas atau sangat parah di perut bagian bawah
- Anda memiliki tanda-tanda kehamilan normal, tetapi Anda juga mengalami perdarahan dan merasa pusing

Pingsan

Beberapa perempuan merasa pusing setelah Mirena dipasang. Hal ini adalah respons fisik yang normal. Dokter akan memberi tahu Anda untuk beristirahat sebentar setelah dipasang Mirena.

Pembesaran folikel ovarium (sel yang mengelilingi sel telur yang matang di ovarium)

Karena efek kontrasepsi Mirena terutama terjadi karena efek lokal, siklus ovulasi dengan folikel yang pecah biasanya terjadi pada wanita usia subur. Kadang-kadang degenerasi folikel tertunda dan perkembangan folikel dapat berlanjut. Sebagian besar folikel ini tidak memberikan gejala, meskipun beberapa mungkin disertai dengan nyeri panggul atau nyeri selama berhubungan seksual. Pembesaran folikel ini mungkin memerlukan perhatian medis, tetapi biasanya menghilang dengan sendirinya.

Informasi tambahan untuk populasi khusus

Anak dan remaja

Mirena ditujukan bagi wanita usia subur. Tidak ada indikasi yang relevan untuk penggunaan Mirena sebelum perdarahan menstruasi pertama (menarke).

Pasien lansia (65 tahun ke atas)

Mirena belum diteliti pada perempuan yang berusia lebih dari 65 tahun.

Pasien dengan gangguan fungsi hati

Mirena tidak boleh digunakan pada perempuan dengan gangguan hati ([lihat bagian 'Jangan gunakan Mirena'](#)).

Pasien dengan gangguan fungsi ginjal

Mirena belum diteliti pada perempuan dengan gangguan ginjal.

Mengonsumsi obat lainnya

Mekanisme aksi Mirena terutama terjadi secara lokal, konsumsi obat lainnya diyakini tidak meningkatkan risiko kehamilan saat menggunakan Mirena. Namun, sebaiknya Anda memberi tahu tenaga kesehatan profesional jika Anda sedang mengonsumsi atau baru-baru ini mulai mengonsumsi obat lain, termasuk obat yang dijual bebas.

Kehamilan

Mirena tidak boleh digunakan saat hamil atau diduga hamil.

Perempuan dengan Mirena yang terpasang sangat jarang menjadi hamil. Namun, jika Mirena terlepas dan keluar, Anda tidak lagi terlindungi dan harus menggunakan metode kontrasepsi lain hingga Anda berkonsultasi dengan dokter.

Beberapa perempuan mungkin tidak haid ketika menggunakan Mirena. Tidak haid bukan berarti tanda kehamilan. Jika Anda tidak haid dan memiliki gejala kehamilan lainnya (misalnya mual, lelah, payudara nyeri ketika disentuh), Anda sebaiknya berkonsultasi dengan dokter untuk diperiksa dan menjalani tes kehamilan.

Jika Anda hamil saat Mirena terpasang di tempatnya, Mirena harus dilepas sesegera mungkin. Jika Mirena berada di tempatnya selama kehamilan, risiko keguguran, infeksi, atau persalinan prematur akan meningkat. Jika Mirena tidak dapat dilepas, berkonsultasilah dengan penyedia layanan kesehatan Anda mengenai manfaat dan risiko melanjutkan kehamilan tersebut, dan kemungkinan efek hormon pada bayi yang sedang berkembang.

Menyusui

Mirena dapat digunakan selama menyusui. Sejumlah kecil levonorgestrel telah diidentifikasi dalam ASI perempuan yang menyusui (0,1% dosis tersebut sampai kepada bayi). Tidak terlihat efek negatif terhadap pertumbuhan atau perkembangan bayi ketika menggunakan Mirena enam minggu setelah melahirkan. Metode progestogen saja tidak terlihat memengaruhi jumlah atau kualitas ASI.

Minta saran dari dokter atau apoteker sebelum mengonsumsi obat apa pun ketika Anda hamil atau menyusui.

Mengemudi dan mengoperasikan mesin

Tidak ada efek yang diketahui.

Informasi penting tentang beberapa kandungan bahan Mirena

Struktur berbentuk T dari Mirena mengandung barium sulfat, yang membuatnya terlihat dalam pemeriksaan sinar X.

3. CARA MENGGUNAKAN MIRENA

Seberapa efektif Mirena?

Dalam hal kontrasepsi, Mirena sama efektifnya dengan alat kontrasepsi dalam rahim berlapis tembaga yang paling efektif saat ini. Mirena memiliki tingkat kegagalan sebesar 0,2% dalam tahun pertama. Tingkat kegagalan dapat meningkat jika sistem terlepas keluar atau terjadi perforasi (lihat bagian 'Pemeriksaan/konsultasi medis').

Dalam pengobatan perdarahan menstruasi berlebihan idiopatik, Mirena menyebabkan penurunan perdarahan menstruasi yang signifikan setelah tiga bulan. Beberapa pengguna sama sekali tidak haid.

Kapan sebaiknya Mirena dipasang?

Anda dapat memasang Mirena dalam waktu tujuh hari sejak onset atau dimulainya perdarahan menstruasi.

Anda sebaiknya memasang Mirena dalam waktu tujuh hari sejak onset atau dimulainya perdarahan menstruasi. Dalam kasus ini, metode kontrasepsi penghalang tambahan tidak diperlukan. Mirena juga memungkinkan untuk dipasang pada waktu lain selama siklus menstruasi jika sudah pasti bahwa Anda tidak hamil. Beri tahu dokter, jika Anda melakukan hubungan seksual tanpa pengaman sejak perdarahan menstruasi terakhir. Jika Mirena dipasang lebih dari tujuh hari sejak perdarahan menstruasi dimulai, gunakan metode penghalang seperti kondom atau diafragma selama tujuh hari berikutnya atau jangan berhubungan seksual selama tujuh hari berikutnya. Mirena tidak dapat digunakan sebagai kontrasepsi darurat.

IUS juga dapat dipasang segera setelah aborsi trimester pertama dengan syarat bahwa tidak ada infeksi kelamin. IUS sebaiknya hanya dipasang setelah rahim kembali ke ukuran normal setelah melahirkan, dan tidak lebih awal daripada 6 minggu setelah melahirkan (lihat bagian 'Sebelum Anda menggunakan Mirena – Perforasi'). Mirena dapat diganti dengan sistem baru kapan saja selama siklus.

Ketika Mirena digunakan untuk melindungi lapisan rahim selama terapi hormon estrogen, Mirena dapat dipasang kapan saja pada perempuan dengan amenorea (perempuan yang tidak mengalami haid bulanan), atau selama hari terakhir menstruasi atau berhentinya perdarahan.

Mirena sebaiknya dipasang oleh dokter/tenaga kesehatan profesional yang berpengalaman dalam pemasangan Mirena.

Bagaimana cara memasang Mirena?

Setelah pemeriksaan ginekologi, instrumen yang disebut spekulum dimasukkan ke dalam vagina, lalu serviks dibersihkan dengan larutan antiseptik. IUS kemudian dipasang ke dalam rahim melalui selang plastik yang tipis dan fleksibel (alat pemasang). Anestetik lokal mungkin diberikan ke serviks sebelum pemasangan, jika diperlukan.

Beberapa perempuan mungkin mengalami nyeri dan pusing setelah pemasangan. Jika gejala ini tidak hilang dalam waktu setengah jam pada posisi beristirahat, IUS mungkin tidak diposisikan dengan benar. Pemeriksaan sebaiknya dilakukan dan IUS dilepas jika perlu.

Setelah pemasangan Mirena, Anda mungkin menerima kartu pengingat pasien dari dokter untuk pemeriksaan tindak lanjut. Bawa kartu ini bersama Anda ke setiap pertemuan yang dijadwalkan.

Kapan sebaiknya saya berkonsultasi dengan dokter?

Anda harus memeriksakan IUS 4–12 minggu setelah pemasangan, dan selanjutnya secara teratur, minimal setahun sekali. Jika Anda menerima kartu pengingat pasien dari dokter, bawa kartu ini bersama Anda ke setiap pertemuan yang dijadwalkan.

Di samping itu, Anda sebaiknya menghubungi dokter jika terjadi salah satu hal berikut:

- Anda tidak lagi merasakan adanya benang di vagina Anda
- Anda dapat meraba ujung bawah bagian alat
- Anda mengira bahwa Anda mungkin hamil
- Anda mengalami nyeri perut, demam, atau keluarnya lendir yang tidak biasa dari vagina secara terus-menerus
- Anda atau pasangan Anda merasakan nyeri atau tidak nyaman selama berhubungan seksual.
- Terdapat perubahan mendadak pada periode menstruasi Anda (misalnya, jika Anda mengeluarkan sedikit darah saat menstruasi atau tidak mengalami perdarahan menstruasi, lalu Anda mulai mengalami perdarahan atau nyeri secara terus-menerus, atau Anda mulai mengeluarkan banyak darah)
- Anda memiliki masalah medis lain, seperti sakit kepala migrain atau sakit kepala intens yang kambuhan, masalah penglihatan yang terjadi tiba-tiba, penyakit kuning, atau tekanan darah tinggi.
- Anda mengalami salah satu kondisi yang disebutkan dalam Bagian ‘Sebelum Anda menggunakan Mirena’.

Berapa lama Mirena dapat digunakan?

Mirena efektif selama 8 tahun untuk pencegahan kehamilan (kontrasepsi). Apakah Anda menggunakan Mirena untuk alasan ini? Jika ya, Mirena Anda harus dilepas atau diganti paling lambat setelah 8 tahun.

Mirena efektif selama 5 tahun untuk perdarahan menstruasi yang berlebihan (menoragia idiopatik). Apakah Anda menggunakan Mirena untuk alasan ini? Jika ya, Mirena Anda harus dilepas atau diganti ketika perdarahan menstruasi yang berlebihan muncul kembali, atau paling lambat setelah 5 tahun.

Mirena efektif untuk perlindungan dari pertumbuhan lapisan rahim yang berlebihan (hiperplasia endometrium) selama terapi hormon estrogen selama 5 tahun. Apakah Anda menggunakan Mirena untuk alasan ini? Jika ya, maka Mirena Anda harus dilepas atau diganti setelah 5 tahun.

Jika Anda mau, Anda dapat memasang Mirena yang baru saat Mirena yang lama dilepas.

Bagaimana jika saya ingin hamil atau melepas Mirena karena alasan lain?

IUS dapat dilepas dengan mudah kapan pun oleh dokter. Setelah dilepas, kehamilan mungkin terjadi. Prosedur pelepasan biasanya tidak menimbulkan rasa sakit. Kesuburan kembali normal setelah Mirena dilepas.

Jika tidak ingin hamil, Mirena tidak boleh dilepas setelah hari ketujuh siklus menstruasi (haid bulanan) kecuali kontrasepsi dilakukan dengan metode lain (misalnya kondom) selama minimal tujuh hari sebelum pelepasan. Jika Anda memiliki periode haid (mens) yang tidak teratur atau tidak haid, Anda sebaiknya menggunakan metode kontrasepsi penghalang selama tujuh hari sebelum pelepasan hingga Anda menstruasi kembali. Mirena baru juga dapat segera dipasang setelah pelepasan. Dalam hal ini, tidak diperlukan perlindungan tambahan.

Apakah saya bisa hamil setelah berhenti menggunakan Mirena?

Ya. Setelah Mirena dilepas, kesuburan normal Anda tidak akan terganggu. Anda dapat hamil selama siklus menstruasi pertama setelah Mirena dilepas.

Apakah Mirena dapat memengaruhi periode menstruasi saya?

Mirena memengaruhi siklus menstruasi Anda. Mirena dapat mengubah periode menstruasi Anda sehingga Anda mengalami bercak (darah yang keluar dalam jumlah kecil), haid yang lebih sebentar atau lebih lama, perdarahan yang lebih sedikit atau lebih banyak, atau tidak mengalami perdarahan sama sekali.

Banyak perempuan sering mengalami bercak atau perdarahan sedikit di luar waktu haid selama 3–6 bulan pertama setelah Mirena dipasang. Beberapa perempuan mungkin mengalami perdarahan yang banyak atau lama selama waktu ini. Beri tahu dokter, khususnya jika hal ini terjadi terus-menerus.

Secara keseluruhan, Anda kemungkinan mengalami penurunan bertahap dalam jumlah hari haid dan dalam jumlah darah yang keluar setiap bulan. Haid pada beberapa perempuan akhirnya berhenti sama sekali. Karena jumlah perdarahan menstruasi biasanya berkurang dengan penggunaan Mirena, sebagian besar perempuan mengalami peningkatan nilai hemoglobin darah.

Ketika alat dilepas, haid kembali normal.

Apakah tidak normal jika tidak haid?

Tidak ketika Anda menggunakan Mirena. Jika Anda mendapati bahwa Anda tidak haid ketika dipasang Mirena, hal tersebut karena efek hormon pada lapisan rahim. Penebalan lapisan rahim setiap bulan tidak terjadi. Oleh karena itu, tidak ada lapisan yang meluruh keluar sebagai haid. Hal ini bukan berarti bahwa Anda telah mencapai menopause atau hamil. Kadar hormon Anda sendiri tetap normal.

Bahkan, tidak haid dapat bermanfaat besar untuk kesehatan perempuan.

Bagaimana cara untuk mengetahui bahwa saya hamil?

Kehamilan kemungkinan besar tidak terjadi pada perempuan yang menggunakan Mirena, bahkan jika mereka tidak haid.

Jika Anda tidak haid selama enam minggu dan khawatir, pertimbangkan untuk melakukan tes kehamilan. Jika negatif, tidak perlu melakukan tes lagi kecuali Anda memiliki tanda-tanda kehamilan lain, misalnya pusing, lelah, atau payudara nyeri ketika disentuh.

Apakah Mirena dapat menyebabkan nyeri atau ketidaknyamanan?

Beberapa perempuan merasakan nyeri (seperti kram perut saat menstruasi) pada beberapa minggu pertama setelah pemasangan. Anda sebaiknya mendatangi kembali dokter atau klinik jika mengalami nyeri hebat atau jika nyeri berlanjut selama lebih dari tiga minggu setelah Anda dipasang Mirena.

Akankah Mirena mengganggu hubungan seksual?

Anda atau pasangan Anda seharusnya tidak merasakan adanya IUS selama berhubungan seksual. Jika Anda merasakannya, hubungan seksual sebaiknya dihindari hingga dokter memeriksa bahwa IUS masih berada di posisi yang benar.

Berapa lama saya sebaiknya menunggu untuk berhubungan seksual setelah pemasangan?

Untuk mengistirahatkan tubuh Anda, paling baik untuk menunggu sekitar 24 jam setelah Mirena dipasang sebelum melakukan hubungan seksual. Namun, begitu dipasang, Mirena akan mencegah kehamilan.

Apakah tampon atau mangkuk menstruasi dapat digunakan?

Sebaiknya gunakan pembalut menstruasi. Jika tampon atau mangkuk menstruasi digunakan, Anda sebaiknya menggantinya dengan hati-hati agar tidak menarik benang Mirena. Jika Anda merasa bahwa Anda mungkin telah menarik Mirena sehingga tidak terpasang di tempatnya (lihat "Kapan sebaiknya saya berkonsultasi dengan dokter" untuk kemungkinan tanda-tandanya), hindari hubungan seksual atau gunakan kontrasepsi penghalang (seperti kondom), lalu hubungi dokter.

Apa yang terjadi jika Mirena terlepas dan keluar sendiri?

Sangat jarang terjadi, tetapi mungkin saja Mirena terlepas dan keluar selama periode menstruasi tanpa Anda sadari. Peningkatan jumlah perdarahan yang tidak biasa selama haid dapat berarti bahwa Mirena telah terlepas dan keluar dari vagina Anda. Mirena juga mungkin terlepas dan keluar sebagian dari rahim Anda (Anda dan pasangan Anda dapat merasakan hal ini selama berhubungan seksual). Jika Mirena terlepas dan keluar seluruhnya atau sebagian, Anda tidak akan terlindungi dari kehamilan.

Bagaimana cara memastikan bahwa Mirena terpasang di tempatnya?

Anda dapat memeriksa sendiri apakah benang berada di tempatnya setelah haid Anda selesai. Cukup letakkan jari tangan dengan perlahan ke dalam vagina Anda setelah haid selesai dan rasakan benang di ujung vagina dekat leher rahim (serviks) Anda.

Jangan tarik benang tersebut karena Anda dapat tanpa sengaja menarik Mirena keluar. Jika Anda tidak dapat merasakan benang tersebut, hal ini mungkin menunjukkan bahwa sistem telah terlepas keluar atau perforasi telah terjadi. Dalam kasus ini, Anda harus menghindari hubungan seksual atau menggunakan kontrasepsi penghalang (seperti kondom), lalu hubungi dokter.

4. KEMUNGKINAN EFEK SAMPING

Seperti obat pada umumnya, Mirena dapat menimbulkan efek samping pada beberapa orang. Di bawah ini, kami mencantumkan kemungkinan efek samping ketika Mirena digunakan untuk kontrasepsi (pencegahan kehamilan) dan menoragia idiopatik (perdarahan menstruasi yang berlebihan). Kemungkinan efek samping ketika Mirena digunakan untuk perlindungan terhadap hiperplasia endometrium (pertumbuhan lapisan rahim yang berlebihan) selama terapi hormon estrogen diamati pada frekuensi yang serupa kecuali disebutkan dalam catatan kaki:

Sangat umum: 10 pasien atau lebih dari setiap 100 pasien mungkin mengalami hal ini:

- Sakit kepala
- Nyeri perut/panggul
- Perubahan perdarahan termasuk peningkatan dan penurunan perdarahan menstruasi, bercak, haid yang tidak teratur, dan amenorea (tidak adanya perdarahan menstruasi)
- Vulvovaginitis* (peradangan organ kelamin bagian luar atau vagina)
- Keputihan*

Umum: antara 1 dan 10 pasien dari setiap 100 pasien mungkin mengalami hal ini:

- Penurunan suasana hati/depresi
- Migrain
- Mual (ingin muntah)
- Jerawat
- Hirsutisme (rambut tubuh yang berlebihan)
- Nyeri punggung⁺
- Infeksi saluran kelamin atas
- Kista ovarium
- Dismenorea (menstruasi yang menyakitkan)
- Nyeri payudara⁺
- Perangkat kontrasepsi dalam rahim terlepas keluar (seluruhnya dan sebagian)

Tidak umum: antara 1 dan 10 pasien dari setiap 1.000 pasien mungkin mengalami hal ini:

- Alopesia (rambut rontok)
- Perforasi rahim

Frekuensi tidak diketahui:

- Hipersensitivitas (reaksi alergi) termasuk ruam, urtikaria (kaligata), dan angioedema (ditandai dengan pembengkakan tiba-tiba misalnya pada mata, mulut, tenggorokan)
- Peningkatan tekanan darah

* Uji coba perlindungan endometrium: “umum”

+ Uji coba perlindungan endometrium: “sangat umum”

Deskripsi kemungkinan efek samping yang dipilih:

Benang pelepas dapat dirasakan oleh pasangan selama berhubungan seksual.

Jika Anda hamil saat menggunakan Mirena, terdapat kemungkinan bahwa kehamilan tersebut berada di luar rahim (lihat bagian ‘Kehamilan di luar kandungan’).

Kasus sepsis (infeksi sistemik sangat berat, yang mungkin berakibat fatal) telah dilaporkan setelah pemasangan IUD

Risiko kanker payudara tidak diketahui ketika Mirena digunakan untuk indikasi perlindungan terhadap hiperplasia endometrium (pertumbuhan lapisan rahim yang berlebihan) selama terapi hormon estrogen.

Kasus kanker payudara telah dilaporkan (frekuensi tidak diketahui).

Kemungkinan efek samping berikut telah dilaporkan sehubungan dengan prosedur pemasangan atau pelepasan Mirena:

Nyeri akibat menjalani prosedur, perdarahan akibat menjalani prosedur, reaksi vasovagal terkait pemasangan yang disertai pusing atau sinkop (pingsan). Prosedur tersebut dapat menyebabkan kejang (sawan) pada pasien epilepsi.

Jika efek samping menjadi parah, atau jika Anda mengamati efek samping yang tidak dicantumkan dalam brosur ini, beri tahu dokter atau apoteker.

5. CARA MENYIMPAN MIRENA

Simpan pada suhu di bawah 30°C.

Jauhkan dari jangkauan dan pandangan anak-anak.

Tidak ada perhatian khusus untuk penyimpanan.

Jangan gunakan Mirena setelah tanggal kedaluwarsa yang dicantumkan di kemasan. Tanggal kedaluwarsa mengacu pada hari terakhir dari bulan tersebut.

Jangan membuang obat ke dalam saluran pembuangan air limbah atau sampah rumah tangga. Tanyakan kepada apoteker bagaimana cara membuang obat yang tidak lagi diperlukan. Tindakan-tindakan ini akan membantu melindungi lingkungan.

6. KEMASAN DAN INFORMASI LAIN

Apa saja kandungan Mirena

Bahan aktif Mirena adalah levonorgestrel 52 mg.

Zat tambahan lainnya:

- elastomer polidimetilsiloksan
- silika koloid anhidrat
- polietilena
- barium sulfat
- besi oksida

Seperti apa bentuk Mirena dan isi kemasannya

Besar kemasan: Satu sistem pengantaran intrauterin steril untuk penggunaan intrauterine

No. Reg. : XXXXX

Harus dengan resep dokter

Dibuat oleh:

Bayer Oy,
Turku-Finlandia

Diimpor oleh:

PT. Bayer Indonesia,
Depok-Indonesia