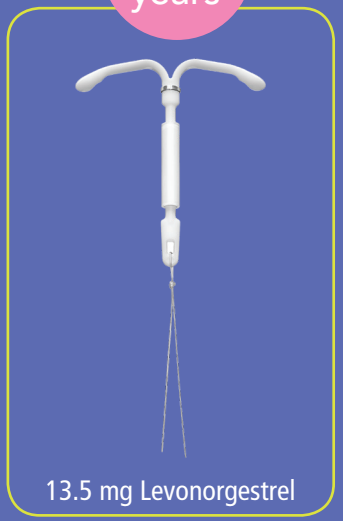
WHICH IUS TO PRESCRIBE?

Does patient require contraception only?

Yes

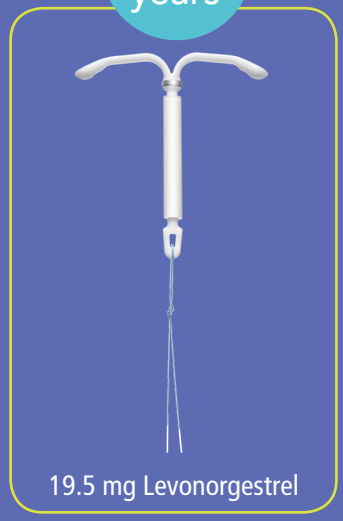
up to 3 years



8 µg/24 hr
Average in vivo LNG release rate over the first year of use

jaydess®
13.5 mg LEVONORGESTREL

up to 5 years



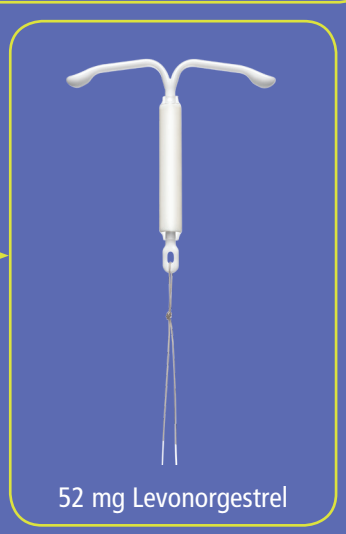
12 µg/24 hr
Average in vivo LNG release rate over the first year of use

Kyleena®
19.5 mg LEVONORGESTREL

No

Patient also requires:

- treatment of idiopathic menorrhagia
- protection from endometrial hyperplasia during oestrogen replacement therapy



20 µg/24 hr
Average in vivo LNG release rate over the first year of use

Mirena®
52 mg LEVONORGESTREL

Bayer Ltd.,
The Atrium, Blackthorn Road,
Sandyford, Dublin 18
Tel: (01) 2163300

Prescribing information and references can be found overleaf

CF Number: PP-JAY-IE-0002-4

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SPC for how to report adverse reactions.

Jaydess 13.5 mg intrauterine delivery system. See full Summary of Product Characteristics (SmPC) before prescribing. **Presentation:** The product consists of a whitish or pale yellow drug core (13.5mg levonorgestrel) covered with a semi-opaque membrane, which is mounted on the vertical stem of a T-body. In addition, the vertical stem contains a silver ring located close to the horizontal arms. **Indication:** Contraception for up to 3 years. **Dosage and administration:** Insertion into the uterine cavity using aseptic technique by physicians/healthcare providers who are experienced in IUS (intrauterine delivery system) insertions and/or have undergone training on the Jaydess insertion procedure. Follow full instructions for preparation for insertion, insertion and removal/replacement, particularly with regard to timing and positioning. Jaydess can be distinguished from other IUSs by the visibility of the silver ring on ultrasound. The T-frame of Jaydess contains barium sulphate which makes it visible in X-ray examination. The system should be removed no later than by the end of the third year. If the woman wishes to continue using the same method, a new system can be inserted immediately following removal of the original system. If pregnancy is not desired, the removal should be carried out within 7 days of the onset of menstruation, provided the woman is experiencing regular menses. If the system is removed at some other time during the cycle and the woman has had intercourse within a week, she is at risk of pregnancy unless a new system is inserted immediately following removal. After removal of Jaydess, the system should be examined to ensure that it is intact. Elderly patients: Jaydess has not been studied in women over the age of 65 years. There is no indication for the use of Jaydess in postmenopausal women. Paediatric population: Use of this product before menarche is not indicated. **Contraindications:** Pregnancy; acute or recurrent pelvic inflammatory disease (PID) or conditions associated with increased risk for pelvic infections; acute cervicitis or vaginitis; postpartum endometritis or infected abortion during the past three months; cervical intraepithelial neoplasia until resolved; uterine or cervical malignancy; progestogen-sensitive tumours, e.g. breast cancer; abnormal uterine bleeding of unknown aetiology; congenital or acquired uterine anomaly including fibroids which would interfere with insertion and/or retention of the IUS (i.e. if they distort the uterine cavity); acute liver disease or liver tumour; hypersensitivity to the active substance or to any of the excipients. **Warnings and Precautions:** Use with caution after specialist consultation, or consider removal of the system if any of the following conditions exist or arise for the first time: migraine, focal migraine with asymmetrical visual loss or other symptoms indicating transient cerebral ischemia; exceptionally severe headache; jaundice; marked increase in blood pressure; severe arterial disease such as stroke or myocardial infarction. May affect glucose tolerance, monitor the blood glucose concentration in diabetic users. However, there is generally no need to alter the therapeutic regimen in diabetics using LNG IUS. Medical examination/consultation: Before insertion, a woman must be informed of the benefits and risks of Jaydess, including the signs and symptoms of perforation and the risk of ectopic pregnancy, see below. 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. Genital infections should be successfully treated prior to insertion. The position of the uterus and the size of the uterine cavity should be determined. Fundal positioning of Jaydess is important in order to maximize the efficacy and reduce the risk of expulsion. Insertion and removal may be associated with some pain and bleeding. The procedure may precipitate a vasovagal reaction (e.g. syncope, or a seizure in an epileptic patient). A woman should be re examined 4 to 6 weeks after insertion to check the threads and ensure that the system is in the correct position. Follow-up visits are recommended once a year thereafter, or more frequently if clinically indicated. Jaydess is not for use as a post-coital contraceptive. The use of Jaydess for the treatment of heavy menstrual bleeding or protection from endometrial hyperplasia during oestrogen replacement therapy has not been established. Ectopic pregnancy: In clinical trials, the overall incidence of ectopic pregnancy with Jaydess was approximately 0.11 per 100 woman-years. Approximately half of the pregnancies that occur during Jaydess use are likely to be ectopic. For women who become pregnant while using Jaydess, the possibility of an ectopic pregnancy must be considered and evaluated. Women with a previous history of ectopic pregnancy, tubal surgery or pelvic infection carry an increased risk of ectopic pregnancy. Because an ectopic pregnancy may impact future fertility the benefits and risks of using Jaydess should be carefully evaluated, in particular for nulliparous women. Use in nulliparous women: Jaydess is not first choice for contraception in nulliparous women as clinical experience is limited. Effects on the menstrual bleeding pattern: Effects on the menstrual bleeding pattern are expected in most users of Jaydess. Those alterations are a result of the direct action of levonorgestrel on the endometrium and may not correlate with the ovarian activity. Irregular bleeding and spotting are common in the first months of use. Thereafter, the strong suppression of the endometrium results in the reduction of the duration and volume of menstrual bleeding. Scanty flow frequently develops into oligomenorrhea or amenorrhea. Pregnancy should be considered if menstruation does not occur within six weeks of the onset of previous menstruation. A repeated pregnancy test is not necessary in subjects who remain amenorrheic unless indicated by other signs of pregnancy. Pelvic infection: Pelvic infection has been reported during use of any IUS or IUD. In clinical trials, PID was observed more frequently at the beginning of Jaydess use. Before electing use of Jaydess, patients should be fully evaluated for risk factors associated with pelvic infection (e.g. multiple sexual partners, sexually transmitted infections, prior history of PID). As with other gynaecological or surgical procedures, severe infection or sepsis (including group A streptococcal sepsis) can occur following IUD insertion, although this is extremely rare. If a woman experiences recurrent endometritis or PID or if an acute infection is severe or does not respond to treatment, Jaydess must be removed. Expulsion: In clinical trials with Jaydess, the incidence of expulsion was low and in the same range as that reported for other IUDs and IUSs. Symptoms of the partial or complete expulsion of Jaydess may include bleeding or pain. However, partial or complete expulsion can occur without the woman noticing it, leading to decrease or loss of contraceptive protection. As Jaydess typically decreases menstrual bleeding over time, an increase of menstrual bleeding may be indicative of an expulsion. A partially expelled Jaydess should be removed. A new system can be inserted at that time provided pregnancy has been excluded. A woman should be advised how to check the threads of Jaydess and to contact her healthcare provider if the threads cannot be felt. 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 sometime later, and may decrease the effectiveness of Jaydess. In case of a difficult insertion and/or exceptional pain or bleeding during or after insertion, appropriate steps should be taken immediately to exclude perforation, such as physical examination and ultrasound. Such a system must be removed; surgery may be required. Physical examination may not be sufficient to exclude partial perforation. In a large prospective comparative non-interventional cohort study in users of other IUDs (N=61,448 women) with a one-year observation 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 cohort of another LNG- IUS and 1.1 (95% CI: 0.7 - 1.6) per 1000 insertions in the copper IUD cohort. 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. Both risk factors were independent of the type of IUD inserted. The risk of perforations may be increased in women with fixed retroverted uterus. Re-examination after insertion should follow the guidance given under the heading "Medical examination/consultation" which may be adapted as clinically indicated in women with risk factors for perforation. Lost threads: If the removal threads are not visible at the cervix on follow-up examinations, unnoticed expulsion and pregnancy must be excluded. Ultrasound or, if appropriate, x-ray may be used to ascertain the correct position of Jaydess. Ovarian cysts/enlarged ovarian follicles: Sometimes atresia of the follicle is delayed and folliculogenesis may continue. These enlarged follicles cannot be distinguished clinically from ovarian cysts and have been reported in clinical trials as adverse drug events in approximately 13.2 % of women using Jaydess including ovarian cyst, hemorrhagic ovarian cyst and ruptured ovarian cyst. Should an enlarged follicle fail to resolve spontaneously, continued ultrasound monitoring and other diagnostic/therapeutic measures may be appropriate. Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use. Depression can be serious and is a well-known risk factor for suicidal behaviour and suicide. Advise women to contact their physician in case of mood changes and depressive symptoms, including shortly after initiating the treatment. **Interactions:** Interactions can occur with drugs that induce hepatic microsomal enzymes which can result in increased or decreased clearance of sex hormones. Substances that increase the clearance of levonorgestrel include phenytoin, carbamazepine and barbiturates as well as others. The influence of these drugs on the contraceptive efficacy of Jaydess is not known. Substances decreasing the clearance of levonorgestrel include azole antifungals (e.g. fluconazole, itraconazole, ketoconazole,), verapamil, macrolides (e.g. clarithromycin, erythromycin), diltiazem and grapefruit juice can increase plasma concentrations of the progestin. Magnetic resonance imaging (MRI): Non-clinical testing has demonstrated that a patient can be scanned safely after placement of Jaydess under the following conditions: Static magnetic field of 3-Tesla or less, maximum spatial gradient magnetic field of 720-Gauss/cm or less. **Fertility, pregnancy and lactation:** Fertility: The use of a levonorgestrel-releasing intrauterine system does not alter the course of future fertility. Upon removal of the intrauterine system, women return to their normal fertility. Pregnancy: The insertion of Jaydess in pregnant women is contraindicated. If a woman becomes pregnant while using Jaydess ectopic pregnancy should be excluded and timely removal of the system is recommended since any intrauterine contraceptive left in situ may increase the risk of abortion and preterm labour. Removal of Jaydess or probing of the uterus may also result in spontaneous abortion. Clinical experience of the outcomes of pregnancies under Jaydess treatment is limited due to the high contraceptive efficacy. Breast-feeding: A levonorgestrel-releasing IUS does not affect the quantity or quality of breast milk. Small amounts of progestogen (about 0.1 % of the levonorgestrel dose) pass into the breast milk in nursing mothers. **Effects on ability to drive and use machines:** Not known. **Undesirable Effects:** Very common: headache, abdominal/pelvic pain, acne/seborrhoea, bleeding changes including increased and decreased menstrual bleeding, spotting, infrequent bleeding and amenorrhoea, ovarian cyst, vulvovaginitis; Common: depressed mood/depression, decreased libido, migraine, nausea, alopecia, upper genital tract infection, dysmenorrhea, breast pain/discomfort, device expulsion (complete and partial), genital discharge, increased weight; Uncommon: dizziness, hirsutism, uterine perforation. **Marketing Authorisation Number: PA 1410/68/1. Marketing Authorisation Holder/ Further information available from:** Bayer Limited, The Atrium, Blackthorn Road, Dublin 18. Tel.: (01) 2163300. **Classification for sale or supply:** prescription only. **Date of preparation:** July 2020.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare Professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse events (refer to www.medicines.ie for the current SmPC). 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. Adverse events or quality complaints should also be reported to Bayer Limited Drug Safety on 01-2163300.

Kyleena 19.5 mg intrauterine delivery system. See full Summary of Product Characteristics (SmPC) before prescribing. **Presentation:** The product consists of a whitish or pale yellow drug core (19.5mg levonorgestrel) covered with a semi-opaque membrane, which is mounted on the vertical stem of a T-body. In addition, the vertical stem contains a silver ring located close to the horizontal arms. **Indication:** Contraception for up to 5 years. **Dosage and administration:** Insertion into the uterine cavity using aseptic technique by physicians/healthcare providers who are experienced in IUS (intrauterine delivery system) insertions and/or have undergone training on the Kyleena insertion procedure. Follow full instructions for preparation for insertion, insertion and removal/replacement, particularly with regard to timing and positioning. Kyleena can be distinguished from other IUSs by the combination of the visibility of the silver ring on ultrasound and the blue colour of the removal threads. The T-frame of Kyleena contains barium sulphate which makes it visible in X-ray examination. The system should be removed no later than by the end of the fifth year. If the woman wishes to continue using the same method, a new system can be inserted immediately following removal of the original system. If pregnancy is not desired, the removal should be carried out within 7 days of the onset of menstruation, provided the woman is experiencing regular menses. After removal of Kyleena, the system should be examined to ensure that it is intact. Elderly patients: Kyleena has not been studied in women over the age of 65 years. There is no indication for the use of Kyleena in postmenopausal women. Paediatric population: Use of this product before menarche is not indicated. **Contraindications:** Pregnancy; acute or recurrent pelvic inflammatory disease (PID) or conditions associated with increased risk for pelvic infections; acute cervicitis or vaginitis; postpartum endometritis or infected abortion during the past three months; cervical intraepithelial neoplasia until resolved; uterine or cervical malignancy; progestogen-sensitive tumours, e.g. breast cancer; abnormal vaginal bleeding of unknown aetiology; congenital or acquired uterine anomaly including fibroids which would interfere with insertion and/or retention of the IUS (i.e. if they distort the uterine cavity); acute liver disease or liver tumour; hypersensitivity to the active substance or to any of the excipients. **Warnings and Precautions:** Use with caution after specialist consultation, or consider removal of the system if any of the following conditions exist or arise for the first time: migraine, focal migraine with asymmetrical visual loss or other symptoms indicating transient cerebral ischemia; exceptionally severe headache; jaundice; marked increase in blood pressure; severe arterial disease such as stroke or myocardial infarction. May affect glucose tolerance, monitor the blood glucose concentration in diabetic users. However, there is generally no need to alter the therapeutic regimen in diabetics using levonorgestrel - IUS. Medical examination/consultation: Before insertion, a woman must be informed of the benefits and risks of Kyleena, including the signs and symptoms of perforation and the risk of ectopic pregnancy, see below. A physical examination including pelvic examination, examination of the breasts, and a cervical smear should be performed. Pregnancy and sexually transmitted diseases should be excluded. Genital infections should be successfully treated prior to insertion. The position of the uterus and the size of the uterine cavity should be determined. Fundal positioning of Kyleena is important in order to maximize the efficacy and reduce the risk of expulsion. Insertion and removal may be associated with some pain and bleeding. The procedure may precipitate a vasovagal reaction (e.g. syncope, or a seizure in an epileptic patient). A woman should be re examined 4 to 6 weeks after insertion to check the threads and ensure that the system is in the correct position. Follow-up visits are recommended once a year thereafter, or more frequently if clinically indicated. Kyleena is not for use as a post-coital contraceptive. The use of Kyleena for the treatment of heavy menstrual bleeding or protection from endometrial hyperplasia during oestrogen replacement therapy has not been established. Ectopic pregnancy: In clinical trials, the overall incidence of ectopic pregnancy with Kyleena was approximately 0.20 per 100 woman-years. Approximately half of the pregnancies that occur during Kyleena use are likely to be ectopic. For women who become pregnant while using Kyleena, the possibility of an ectopic pregnancy must be considered and evaluated. Women with a previous history of ectopic pregnancy, tubal surgery or pelvic infection carry an increased risk of ectopic pregnancy. Because an ectopic pregnancy may impact future fertility the benefits and risks of using Kyleena should be carefully evaluated on an individual basis. Effects on the menstrual bleeding pattern: Effects on the menstrual bleeding pattern are expected in most users of Kyleena. Those alterations are a result of the direct action of levonorgestrel on the endometrium and may not correlate with the ovarian activity. Irregular bleeding and spotting are common in the first months of use. Thereafter, the strong suppression of the endometrium results in the reduction of the duration and volume of menstrual bleeding. Scanty flow frequently develops into oligomenorrhea or amenorrhea. Pregnancy should be considered if menstruation does not occur within six weeks of the onset of previous menstruation. A repeated pregnancy test is not necessary in amenorrhoeic subjects unless indicated by other signs of pregnancy. Pelvic infection: Pelvic infection has been reported during use of any IUS or IUD. In clinical trials, PID was observed more frequently at the beginning of Kyleena use. Before electing use of Kyleena, patients should be fully evaluated for risk factors associated with pelvic infection (e.g. multiple sexual partners, sexually transmitted infections, prior history of PID). As with other gynaecological or surgical procedures, severe infection or sepsis (including group A streptococcal sepsis) can occur following IUD insertion, although this is extremely rare. If a woman experiences recurrent endometritis or PID or if an acute infection is severe or does not respond to treatment, Kyleena must be removed. Expulsion: In clinical trials with Kyleena, the incidence of expulsion was low and in the same range as that reported for other IUDs and IUSs. Symptoms of the partial or complete expulsion of Kyleena may include bleeding or pain. However, partial or complete expulsion can occur without the woman noticing it, leading to decrease or loss of contraceptive protection. As Kyleena typically decreases menstrual bleeding over time, an increase of menstrual bleeding may be indicative of an expulsion. A partially expelled Kyleena should be removed. A new system can be inserted at that time provided pregnancy has been excluded. A woman should be advised how to check the threads of Kyleena and to contact her healthcare provider if the threads cannot be felt. 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 sometime later, and may decrease the effectiveness of Kyleena. 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. Such a system must be removed; surgery may be required. Physical examination may not be sufficient to exclude partial perforation. A large prospective comparative non-interventional cohort study in users of other IUDs (N=61,448 women) with a 1-year observational period, 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. Both risk factors were independent of the type of IUD inserted. Extending the observational period to 5 years in a subgroup of this study (N=39009 women inserted with another levonorgestrel-IUS or copper IUD, 73% of these women had information available over the complete 5 years of follow-up), 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. Breastfeeding at the time of insertion and insertion up to 36 weeks after giving birth were confirmed as risk factors also in the subgroup that were followed up for 5 years. The risk of perforations may be increased in women with fixed retroverted uterus. Re-examination after insertion should follow the guidance given under the heading "Medical examination/consultation" which may be adapted as clinically indicated in women with risk factors for perforation. Lost threads: If the removal threads are not visible at the cervix on follow-up examinations, unnoticed expulsion and pregnancy must be excluded. Ultrasound or, if appropriate, x-ray may be used to ascertain the correct position of Kyleena. Ovarian cysts/enlarged ovarian follicles: Sometimes atresia of the follicle is delayed and folliculogenesis may continue. These enlarged follicles cannot be distinguished clinically from ovarian cysts and have been reported in clinical trials as adverse drug events in approximately 22.2 % of women using Kyleena including ovarian cyst, hemorrhagic ovarian cyst and ruptured ovarian cyst. Should an enlarged follicle fail to resolve spontaneously, continued ultrasound monitoring and other diagnostic/therapeutic measures may be appropriate. Psychiatric disorders: Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use. Depression can be serious and is a well-known risk factor for suicidal behaviour and suicide. Women should be advised to contact their physician in case of mood changes and depressive symptoms, including shortly after initiating the treatment. **Interactions:** Interactions can occur with medicinal products that induce microsomal enzymes, which can result in increased clearance of sex hormones. Substances known to increase the clearance of levonorgestrel are Phenytoin, barbiturates, primidone, carbamazepine, rifampicin, and possibly also oxcarbazepine, topiramate, felbamate, griseofulvin, and products containing St. John's wort. The influence of these medicinal products on the efficacy of Kyleena is not known. Many HIV/HCV protease inhibitors and non-nucleoside reverse transcriptase inhibitors when co-administered with sex hormones can have variable effects on the clearance of levonorgestrel (i.e. increase or decrease plasma concentrations of the progestin). Magnetic resonance imaging (MRI): Non-clinical testing has demonstrated that a patient can be scanned safely after placement of Kyleena under the following conditions: Static magnetic field of 3-Tesla or less, maximum spatial gradient magnetic field of 36000-Gauss/cm or less and maximum whole body averaged specific absorption rate (SAR) of 4 W/kg in the First Level Controlled mode for 15 minutes of continuous scanning. **Fertility, pregnancy and lactation:** Fertility: The use of a levonorgestrel-releasing intrauterine system does not alter the course of future fertility. Upon removal of the intrauterine system, women return to their normal fertility. Pregnancy: The insertion of Kyleena in pregnant women is contraindicated. If a woman becomes pregnant while using Kyleena ectopic pregnancy should be excluded and timely removal of the system is recommended since any intrauterine contraceptive left in situ may increase the risk of abortion and preterm labour. Removal of Kyleena or probing of the uterus may also result in spontaneous abortion. Clinical experience of the outcomes of pregnancies under Kyleena treatment is limited due to the high contraceptive efficacy. Breast-feeding: A levonorgestrel-releasing IUS does not affect the quantity or quality of breast milk. Small amounts of progestogen (about 0.1 % of the levonorgestrel dose) pass into the breast milk in nursing mothers. **Effects on ability to drive and use machines:** Kyleena has no known influence on the ability to drive or use machines. **Undesirable Effects:** Very common: headache, abdominal/pelvic pain, acne/seborrhoea, bleeding changes including increased and decreased menstrual bleeding, spotting, infrequent bleeding and amenorrhoea, ovarian cyst, vulvovaginitis; Common: depressed mood/depression, decreased libido, migraine, dizziness, nausea, alopecia, upper genital tract infection, dysmenorrhea, breast pain/discomfort, device expulsion (complete and partial), genital discharge, increased weight; Uncommon: hirsutism, uterine perforation. With the use of levonorgestrel-IUS, cases of hypersensitivity including rash, urticaria and angioedema have been reported. **Marketing Authorisation Number: PA 1410/081/001. Marketing Authorisation Holder/ Further information available from:** Bayer Limited, The Atrium, Blackthorn Road, Dublin 18. Tel.: (01) 2163300. **Classification for sale or supply:** prescription only. **Date of preparation:** July 2020

Mirena 52mg Intrauterine Delivery System. (Levonorgestrel). See full Summary of Product Characteristics (SmPC) before prescribing. **Presentation:** The levonorgestrel intrauterine delivery system (IUD) consists of a white or almost white drug core (52mg Levonorgestrel) covered with an opaque membrane, which is mounted on the vertical stem of a T-body. The T-frame of Mirena contains barium sulphate, which makes it visible in X-ray examination. **Indication:** Contraception, idiopathic menorrhagia, protection from endometrial hyperplasia during oestrogen replacement therapy. **Dosage and administration:** Insertion into the uterine cavity using aseptic technique by practitioner with experience in Mirena insertion and/or sufficient training. Effective for six years in the indication contracepton and five years in the indication idiopathic menorrhagia and protection from endometrial hyperplasia during oestrogen replacement therapy. In women on hormone replacement therapy (HRT), Mirena can be used with oral/transdermal oestrogen preparations without progestogens. Follow full instructions for insertion/removal/replacement, particularly with regard to timing and positioning. Exclude pregnancy, sexually transmitted diseases and endometrial pathology. Treat genital infections. Investigate bleeding irregularities. Re-examine 4 to 12 weeks after insertion and at least once a year. Remove after 6 years in the indication contraception and after 5 years in the indication idiopathic menorrhagia and protection from endometrial hyperplasia during oestrogen replacement therapy. Mid-cycle removal involves a risk of pregnancy unless a new system is inserted immediately. Insertion and removal may be associated with pain, bleeding or a vasovagal reaction. Seizure may be precipitated in an epileptic patient. After removal the device should be checked to be intact. Elderly patients: Mirena has not been studied in women over the age of 65 years. Paediatric population: Safety and efficacy have not been studied in women aged below 18. There is no relevant indication for the use of Mirena before menarche. Hepatic impairment: Mirena is contraindicated in women with acute liver disease or liver tumor. Renal Impairment: Mirena has not been studied in women with renal impairment. **Contraindications:** Known or suspected pregnancy, progestogen-dependent tumours (e.g. breast cancer), current or recurrent pelvic inflammatory disease (PID), cervicitis, lower genital tract infection, postpartum endometritis, infected abortion during the past three months, conditions associated with increased susceptibility to infections, cervical dysplasia, uterine or cervical malignancy, undiagnosed abnormal uterine bleeding, congenital or acquired uterine anomaly including fibroids if they distort the uterine cavity, acute liver disease or liver tumour, hypersensitivity to levonorgestrel or to any of the excipients. **Warnings and Precautions:** Use of Mirena in conjunction with an oestrogen for HRT. If used in conjunction with HRT, the safety information of the oestrogen applies in addition. Use with caution after specialist consultation, consider removal of the system if any of the following conditions exist or arise for the first time: migraine, focal migraine with asymmetrical visual loss or other symptoms indicating transient cerebral ischemia; exceptionally severe headache; jaundice; marked increase in blood pressure; severe arterial disease such as stroke or myocardial infarction; acute venous thromboembolism. Mirena may be used with caution in women who have congenital heart disease or valvular heart disease at risk of infective endocarditis. The need for antibiotic prophylaxis during insertion and removal of Mirena should be considered in patients with congenital or valvular heart disease. It is recommended that physicians consult local guidelines. Use with caution in postmenopausal women with advanced uterine atrophy. May affect glucose tolerance, monitor blood glucose concentration in diabetic users. Chloasma may occasionally occur, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun or UV radiation whilst using Mirena. Irregular bleedings may mask some symptoms and signs of endometrial polyps or cancer; consider diagnostic measures. Mirena does not protect against HIV infection (AIDS) and other sexually transmitted diseases. Appropriate diagnostic/therapeutic measures and individual benefit-risk assessment should be undertaken in women with liver cancer. A biological effect on the risk of liver cancer cannot be excluded. Medical examination/consultation: Before insertion, the woman must be informed of the efficacy, risks including signs and symptoms of these risks as described in the Package Booklet and side effects of Mirena. A physical examination including pelvis and 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 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. Follow instructions for insertion carefully. Mirena is not suitable for post-coital contraception. Oligo/amenorrhoea: In women of fertile age, oligomenorrhoea and/or amenorrhoea develops gradually in 57% and 16% of women during the first year of use, respectively. By the end of Year 6 of Mirena use, oligomenorrhea and amenorrhea are experienced by 31% and 24% 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. A repeated pregnancy test is not necessary in amenorrhoeic subjects unless indicated by other signs of pregnancy. When Mirena is used in combination with continuous oestrogen replacement therapy, a non-bleeding pattern gradually develops in most women during the first year. 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 oestrogen replacement therapy. If bleeding irregularities develop during prolonged treatment, appropriate diagnostic measures should also be taken. Pelvic infection: A decision to use Mirena must include consideration of the risks of PID. In users of copper IUD, the highest rate of pelvic infections occurs during the first month after insertion and decreases later. Known risk factors for PID are multiple sexual partners. PID may have serious consequences and it may impair fertility and increase the risk of ectopic pregnancy. As with other gynae or surgical procedures, sepsis (including with group A streptococcus) can occur rarely following IUD insertion. If the woman experiences recurrent endometritis or pelvic infections or if an acute infection is severe or does not respond to treatment within a few days, Mirena must be removed. Bacteriological examinations are indicated and monitoring is recommended, even with discrete symptoms indicative of infections. Signs and symptoms of PID should be investigated appropriately and treated promptly. Expulsion: Symptoms of the partial or complete expulsion of any IUD may include bleeding or pain; the system can be expelled from the uterine cavity without the woman noticing it leading to loss of contraceptive protection. Partial expulsion may decrease the effectiveness of Mirena. As Mirena decreases menstrual flow, increase of menstrual flow may indicate an expulsion. After expulsion, Mirena may be replaced within 7 days from the onset of the next menstruation. A displaced Mirena should be removed. A new system can be inserted at that time. The woman should be advised how to check the threads of Mirena. 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 sometime later, and may decrease the effectiveness of Mirena. Such a system must be removed; surgery may be required. In a large prospective comparative non-interventional cohort study in users of other IUDs (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. 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. Both risk factors were independent of the type of IUD inserted. 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. Breastfeeding at the time of insertion and insertion up to 36 weeks were confirmed as risk factors also in this subgroup. The risk of perforation may be increased in women with fixed retroverted uterus. Re-examination after insertion should follow the guidance given under the heading "Medical examination/consultation" which may be adapted as clinically indicated in women with risk factors for perforation. Lost threads: If threads are not visible, exclude pregnancy. If they cannot be found, the possibility of expulsion or perforation should be considered. Ultrasound or, if appropriate, x-ray may be used to ascertain the correct position of Mirena. Breast Cancer: Oral contraceptives, including progestogen-only preparations, are associated with a slightly increased risk of breast cancer. The risk of breast cancer is increased in post-menopausal women using systemic HRT. The risk is higher with combined oestrogen-progestogen HRT than oestrogen-only HRT. Ectopic pregnancy: Women with a previous history of ectopic pregnancy/ tubal surgery / pelvic infection carry a higher risk. The possibility of ectopic pregnancy should be considered in the case of lower abdominal pain - especially in connection with missed periods or if an amenorrhoeic woman starts bleeding. 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%. In clinical trials, the absolute rate of ectopic pregnancies with Mirena was approximately 0.1% per year, compared to 0.3-0.5% per year in women not using any contraception. The relative likelihood of ectopic pregnancy is increased if pregnancy occurs with Mirena in situ. Ovarian Cysts: Delayed follicular atresia may occur and folliculogenesis may continue. Ovarian cysts may be accompanied by pelvic pain/dyspareunia. Should they not disappear spontaneously, continue ultrasound monitoring and other diagnostic/therapeutic measures. Rarely, surgical intervention may be required. Psychiatric Disorders: Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use. Depression can be serious and is a well-known risk factor for suicidal behaviour and suicide. Women should be advised to contact their physician in case of mood changes and depressive symptoms, including shortly after initiating the treatment. **Interactions:** The prescribing information of concomitant medications should be consulted to identify potential interactions. 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 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. **Fertility, pregnancy and lactation:** Pregnancy: If pregnancy occurs, removal of the system is recommended. IUS left in situ, removal of Mirena or probing of the uterus may increase the risk of spontaneous abortion or preterm labour. Exclude ectopic pregnancy. If Mirena cannot be gently removed, inform the woman about the risks and possible consequences and monitor pregnancy closely. Teratogenicity cannot be completely excluded. Clinical experience of pregnancy under Mirena is limited. Lactation: Levonorgestrel blood concentrations are lower with Mirena than any other hormonal contraceptive. Levonorgestrel has been identified in breast milk (about 0.1%) but it is not likely that there will be a risk for the child with the dose released from Mirena. Uterine bleeding is rarely reported during use in lactation. Fertility: Upon removal of Mirena, women return to their normal fertility. **Effects on ability to drive and use machines:** No studies on the ability to drive and use machines have been performed. **Undesirable Effects:** Very common: headache, abdominal/pelvic pain, bleeding changes including increased and decreased menstrual bleeding, spotting, oligomenorrhoea and amenorrhoea, vulvovaginitis, genital discharge. Common: depressed mood/depression, libido decreased, migraine, dizziness, nausea, acne, hirsutism, back pain, upper genital tract infection, ovarian cyst, dysmenorrhoea, breast pain, intra-uterine contraceptive device expelled (complete and partial), weight increase. Uncommon: alopecia, chloasma/skin hyperpigmentation, uterine perforation. Unknown frequency: hypersensitivity including rash, urticaria and angioedema, blood pressure increased. **Marketing Authorisation Number:** PA 1410/8/1. **Marketing Authorisation Holder/ Further information available from**: Bayer Limited, The Atrium, Blackthorn Road, Dublin 18. Tel.: (01) 2163300. **Classification for sale or supply:** prescription only. **Date of preparation:** February 2021.

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