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 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 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 angiooedema 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**