Levonorgestrel

Section: 22. Medicines for reproductive health and perinatal care > 22.1. Contraceptives > 22.1.3. Intrauterine devices

ATC codes: G02BA03

Indication	Contact with health services for insertion of contraceptive device ICD11 code: QA21.2
INN	Levonorgestrel
Medicine type	Chemical agent
List type	Core
Formulations	Intrauterine system with reservoir containing 52 mg of levonorgestrel.
EML status history	First added in 2015 (TRS 994)
Sex	Female
Age	Adolescents and adults
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Levonorgestrel
DrugBank	Levonorgestrel

Summary of evidence and Expert Committee recommendations

An application was submitted by the WHO Department of Reproductive Health and Research, Geneva, requesting the inclusion of a levonorgestrel-releasing intrauterine system (LNG-IUS) on the Model List to provide long-acting contraception in women of reproductive age. Compared to other contraceptives, LNG-IUS offers relevant advantages in women who are breastfeeding at least four times a day (from four weeks postpartum to one year) or have heavy menstrual bleeding. It is also suitable for use as endometrial protection during estrogen therapy for menopausal symptoms. A 2010 review classified the hierarchy of contraceptive effectiveness in descending order as: (i) female sterilization, long-acting hormonal contraceptives (LNG-IUS and implants); (ii) copper-containing intrauterine devices (Cu-IUDs) of ≥ 300 mm2 surface area; (iii) Cu-IUDs of < 300 mm2 surface area and short-acting hormonal contraceptives (injectables, oral contraceptives, the patch and vaginal ring); and (iv) barrier methods and natural methods (1). The LNG-IUS contraceptive method is included in WHO's Medical eligibility criteria for contraceptive use (2, 3), Selected practice recommendations for contraceptive use (4), and Family planning: a global handbook for providers (5). The contraceptive action of levonorgestrel released from the intrauterine system is associated with a thickening of cervical mucus, impedance of endocervical sperm transport, and alteration of the endometrium, preventing implantation. The LNG-IUS has high contraceptive efficacy, with reported first-year pregnancy rates of 0.1%. While it is approved for 5 years of contraceptive use, there is evidence of effectiveness for up to 7 years of continuous use. After removal, there is rapid return to fertility. A 2004 Cochrane systematic review compared the effectiveness, acceptability and tolerability of progestogen-releasing intrauterine systems with other reversible contraceptive methods (6). No significant difference in the risk of unwanted pregnancy was observed between LNG-IUS and non-hormonal IUDs of > 250 mm2 or levonorgestrel

implant; however, the included studies may not have been sufficiently powered to detect a difference. The LNG-IUS was associated with a lower risk of pregnancy than non-hormonal IUDs of ≤ 250 mm2. Women using the LNG-IUS were also more likely to experience an absence of menstrual bleeding. Users report reduction in menstrual bleeding and 15–20% become amenorrhoeic one year after insertion. The LNG-IUS has been shown to be superior to oral treatments with either cyclic medroxyprogesterone acetate or combined oral contraceptives in reducing menstrual bleeding and in improving blood haemoglobin levels among women suffering from documented menorrhagia (7). A recent review of safety outcomes for LNG-IUS users concluded that there were no differences between LNG-IUS and Cu-IUDs in measures of bone mineral density, no clinically significant metabolic effects or effects on cardiovascular disease risk markers, no association with increased risks of venous or arterial thrombotic effects, and no evidence of increased incidence of bacterial vaginosis or cytological abnormalities (7). The authors concluded that current data support the view that there is no increased risk of primary diagnosis of breast cancer among premenopausal women who use the LNG-IUS, although the risk remains unknown in women using the LNG-IUS together with estrogens for hormone replacement therapy. The Committee noted the higher cost of LNG-IUS compared with other contraceptive methods and devices. The Committee considered that it was important for people to have a choice of contraceptive methods available to them, and that the addition of new, effective and safe contraceptive alternatives such as the LNG-IUS could lead to improved contraceptive use and resultant beneficial outcomes. Based on the available evidence for effectiveness and safety, the Committee recommended the addition of the levonorgestrel-releasing intrauterine system to the core list of the EML for long-acting contraception in women of reproductive age. The Committee considered that this contraceptive option would be particularly useful in women with menorrhagia, given the observed reduction in menstrual bleeding. It is also a suitable contraceptive for women who are breastfeeding at least four times a day. 1. Mansour D, Inki P, Gemzell-Danielsson K. Efficacy of contraceptive methods: A review of the literature. Eur J Contracept Reprod Health Care. 2010;15(1):4-16. 2. Medical eligibility criteria for contraceptive use, fourth edition. Geneva: World Health Organization; 2010. 3. Medical eligibility criteria for contraceptive use, fifth edition: Executive Summary. Geneva: World Health Organization; 2015. Available from: http://www.who.int/reproductivehealth/publications/family_planning/Ex-Summ-MEC-5/en/. 4. Selected practice recommendations for contraceptive use, second edition. Geneva: World Health Organization; 2004. 5. Family planning: a global handbook for providers. 2011 update. Geneva: World Health Organization; 2011. 6. French R, Sorhaindo A, Van Vliet H, Mansour D, Robinson A, Logan S, et al. Progestogen-releasing intrauterine systems versus other forms of reversible contraceptives for contraception. Cochrane Database Syst Rev. 2004;3:CD001776. 7. Gemzell-Danielsson K, Inki P, Heikinheimo O. Safety and Efficacy of the levonorgestrel-releasing intrauterine system. Expert Rev of Obstet Gynecol. 2013;8(3):235-47.

