Etonogestrel-releasing implant

Essential medicine status ✓

ATC codes: G03AC08

Indication	Contact with health services for insertion of contraceptive device ICD11 code: QA21.2
INN	Etonogestrel
Medicine type	Chemical agent
List type	Core
Formulations	**Implant > Subdermal:** 68 mg single rod
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	Main patents have expired but secondary patents might remain active in some jurisdictions. For more information on specific patents and license status for developing countries visit www.MedsPal.org Read more about patents.
Wikipedia	Etonogestrel-releasing implant
DrugBank	Etonogestrel

Summary of evidence and Expert Committee recommendations

An application was submitted by Merck Sharp & Dohme, Kenilworth, NJ, USA, for the inclusion of a long-acting etonogestrel-releasing subdermal implant on the Model List of Essential Medicines. It was proposed that the listing would complement the current listing of the levonorgestrel-releasing implant and allow countries to choose the implant best suited to local needs. Etonogestrel implants are widely available, including through government and international donor purchasing programmes. Both Implanon® and Implanon NXT® are WHO prequalified products. Implanon NXT® is bioequivalent to Implanon®; it includes an applicator to facilitate insertion and radiopaque barium sulfate to facilitate detection of the implant at the time of insertion and removal (1). The preloaded, sterile, single-use applicator is suited to mobile clinics and environments with limited health infrastructure and avoids the need for incision required for manually-loaded two rod systems. The UN Commission on Life-Saving Commodities for Women and Children has prioritized implants as one of the 13 life-saving commodities for long-term contraception (2). Etonogestrel-releasing implants are included in WHO's Medical eligibility criteria for contraceptive use and are rated 1 (no restriction) or 2 (advantages outweigh theoretical or proven risks) for most of the conditions listed (3, 4). The etonogestrel-releasing implants, containing 68 mg of etonogestrel, provide up to three years' reversible contraception, with rapid return to fertility on implant removal (5). Three contacts with health service providers are required – for insertion, for a 3-month check and for removal. The application calculated event rates for efficacy end-points from pooled data from available studies (5–17), which showed a pregnancy rate of 0.15% (3 of 1995 subjects) and continuation rates of 86.5% at year 1, 77.4% at year 2 and 65.6% at year 3. The application presented results of a meta-analysis of direct comparisons between etonogestrel-releasing implants and other long-acting reversible contraceptives (LARCs): levonorgestrel-releasing implants, depot medroxyprogesterone acetate (DMPA), levonorgestrel intrauterine devices (IUDs) and copper-containing IUDs. No significant differences were observed in rates of pregnancy between etonogestrel-releasing implants and other LARCs or in rates of continuation between etonogestrel- and levonorgestrelreleasing implants. Continuation rates for etonogestrel-releasing implants were significantly higher compared with DMPA within the first year of use, but no significant differences in continuation rates were observed between etonogestrelreleasing implants and copper-containing IUDs overall. Tolerability end-points of amenorrhoea and bleeding patterns were examined from pooled data from the available studies. In patients using etonogestrel-releasing implants, rates of amenorrhoea were 32% at the end of year 1 and 35% at the end of year 2. Rates of

bleeding at the end of years 1 and 2 respectively were: infrequent bleeding 27% and 24%; frequent bleeding 3% and 2%; and prolonged bleeding 8% and 5%. The percentages of patients using etonogestrel-releasing implants who discontinued as a result of bleeding issues over the duration of the studies were 0.07% (amenorrhoea) and 5.5% (any bleeding issue). Meta-analysis results demonstrated that levonorgestrel-releasing implants were associated with less amenorrhoea at years 1 and 2 than etonogestrel-releasing implants. Etonogestrel-releasing implants were associated with less discontinuation due to heavy bleeding than copper-containing IUDs. Levonorgestrel IUD was associated with fewer discontinuations for frequent and prolonged bleeding than etonogestrel-releasing implant. The Expert Committee noted the pricing agreement described in the application under which etonogestrel-releasing implants are available at reduced cost in targeted countries and with a differential pricing structure elsewhere. The Committee also noted the “Co-operation Agreement for the Receipt and Use of Implanon” (CARUI) described in the application for family planning programmes in the developing world. The Committee also noted that etonogestrel-releasing implants have been reported to be cost–effective in a variety of settings (18-21). 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 etonogestrel-releasing implants could lead to improved contraceptive use and resultant beneficial outcomes. The Committee considered that etonogestrel implant was well-suited for use in low-resource settings, being highly effective and long-acting and offering the convenience of a preloaded applicator dosage form, making it particularly useful where infrastructure is limited. Based on the evidence presented, the Expert Committee recommended that etonogestrel contraceptive implant (single rod, 68 mg) be added to the core list of the Model List of Essential Medicines for women of reproductive age. The Committee considered that contraceptive efficacy and safety of etonogestrel implant have been satisfactorily demonstrated in women aged 18–40 years. References: 1. Schnabel P, Merki-Feld GS, Malvy A, Duijkers I, Mommers E, van den Heuvel MW. Bioequivalence and x-ray visibility of a radiopaque etonogestrel implant versus a non-radiopaque implant: a 3-year, randomized, double-blind study. Clin Drug Investig. 2012;32(6):413-22. 2. 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