Medroxyprogesterone acetate

Statut de médicament essentiel

Section: 22. Medicines for reproductive health and perinatal care > 22.1. Contraceptives > 22.1.2. Injectable hormonal contraceptives

Codes ATC: G03AC06

Indication	Contact with health services for reasons associated with reproduction Code ICD11: QA4Z
INN	Medroxyprogesterone
Type de médicament	Chemical agent
Type de liste	Liste de base
Formulations	Parenteral > General injections > IM: 150 mg per mL in 1 mL vial Parenteral > General injections > SC: 104 mg per 0.65 mL in pre-filled syringe ; 104 mg per 0.65 mL in single dose injection delivery system
Historique des statuts LME	Ajouté pour la première fois en 1984 (TRS 722) Modifié en 1987 (TRS 770) Modifié en 1995 (TRS 867) Modifié en 2005 (TRS 933) Modifié en 2017 (TRS 1006)
Sexe	Féminin
Âge	Adolescents et adultes
Équivalence thérapeutique	La recommandation concerne ce médicament spécifique
Renseignements sur le brevet	Patents have expired in most jurisdictions Lire la suite sur les brevets.
Wikipédia	Medroxyprogesterone acetate
DrugBank	Medroxyprogesterone acetate

Recommandation du comité d'experts

The Expert Committee recommended the addition of the subcutaneous injection formulation of depot medroxyprogesterone acetate to the core list of the EML. The Committee considered that the subcutaneous formulation, with appropriate training for administration, would provide an effective, safe and convenient contraceptive treatment choice. The possibility of self-administration may be an advantage in settings where availability of health-care providers is limited. The Committee also recommended the current listing of the intramuscular formulation be amended as proposed in the application, to clarify its route of administration.

Contexte

Depot medroxyprogesterone acetate (DPMA) for IM injection (150 mg/mL) has been included on the EML since 1985, initially on the Complementary List and then moved to the core list in 2005.

Pertinence pour la santé publique

Estimates have indicated that contraceptive use contributes to reduced maternal mortality and morbidity. In an analysis of 172 countries, contraceptive use was estimated to have reduced maternal mortality by 44%, thereby averting 272 040 maternal deaths (1). A significant unmet need for contraception exists, with an estimated 222 million women in low-income countries lacking access (2). Addressing this unmet need may avert a further 30% of maternal deaths (3).

Bénéfices

Evidence for the clinical effectiveness of medroxyprogesterone acetate was evaluated at the time of listing. The application presented the results of two phase 3, open-label, non-comparative, multinational 1-year studies which assessed the efficacy and safety of subcutaneous DMPA (DMPA-SC) (4). In each study, participants received contraceptive injection every 3 months for up to 1 year. The combined total was 16 023 woman-cycles of exposure. No unintended pregnancies were reported in either study. Both the Pearl Index (number of pregnancies per 100 woman-years of use) and the cumulative pregnancy rate at 1 year (the primary end-point) were 0 (95% confidence intervals not calculated as no pregnancies were reported). A small comparative study in 58 women assessed efficacy, ovulation suppression and return to ovulation at 12 months after a single dose of DMPA-SC or DMPA-IM (5). Pharmacokinetic parameters of the SC formulation were also assessed. Results indicated that suppression of ovulation was immediate following single-dose SC administration. DMPA-SC consistently suppressed ovulation for the 13-week dosing interval, with the earliest return to ovulation occurring at 15 weeks. Median time to return to ovulation was 30 weeks. The cumulative rate of ovulation at 12 months post-injection (the primary efficacy end-point) was 97.4% and 94.7% in the SC and IM groups, respectively. Suppression of ovulation did not appear to be affected by body mass index or race.

Torts

Evidence for the safety of medroxyprogesterone acetate was evaluated at the time of its original listing. The overall safety profile of DMPA-SC is consistent in most respects with that of DMPA-IM and reflects the known physiological effects of medroxyprogesterone acetate. With the exception of injection site reactions, the types of adverse events seen with DMPA-SC are similar to those with DMPA-IM and include bleeding irregularities, amenorrhoea, weight gain, headache and mild, reversible loss of bone mineral density. A higher rate of injection site reactions was observed in patients receiving DMPA-SC (4).

Preuves supplémentaires

A systematic review of 14 studies investigated the safety of DMPA-SC in women with various characteristics or medical conditions (6). The review found evidence to support DMPA-SC as a safe contraceptive treatment for use by women with conditions and characteristics that included age, obesity, endometriosis and HIV infection. The review also found that the two formulations appear to be therapeutically equivalent when used by healthy women.

Rapport coût/efficacité

The unit price for DMPA-SC is US$ 1 to qualified purchasers in 69 of the world's poorest countries with a partnership consortium. For populations and countries not included in the agreement, prices are based on a differential pricing structure and take into consideration the local economic conditions and family planning climates. In comparison, the median supplier price of DMPA-IM, according to the International Medical Products Price Guide, is US$ 0.75 per unit (8).

Directives de l'OMS

The WHO Medical eligibility criteria for contraceptive use (7) states that DMPA-IM and DMPA-SC appear therapeutically equivalent, demonstrating similar pharmacokinetics, effects on serum estradiol levels and high contraceptive efficacy. It recommends that all guidance for DMPA-SC should follow the current recommendations for DMPA-IM (very low-quality evidence).

Disponibilité

Pfizer Ltd.

Autres considérations

Comments on the application received from Médecins Sans Frontières (MSF) indicated that the organization did not support addition of this SC formulation to the EML, based on an anticipated low probability of programmes involving self-administration and the additional cost in resource-limited settings compared with the IM formulation.

Considérations relatives à la mise en œuvre

N/A

1. Ahmed S, Li Q, Liu L, Tsui AO. Maternal deaths averted by contraceptive use: an analysis of 172 countries. Lancet. 2012;380(9837):111–25.
2. Singh S, Darroch JE. Adding it up: costs and benefits of contraceptive services—estimates for 2012. New York: Guttmacher Institute; 2012 (http://www.guttmacher.org/pubs/AIU-2012-estimates.pdf., accessed 13 March 2017).
3. Cleland J, Conde-Agudelo A, Peterson H, Ross J, Tsui A. Contraception and health. Lancet. 2012;380(9837):149–56.
4. Jain J, Jakimiuk AJ, Bode FR, Ross D, Kaunitz AM. Contraceptive efficacy and safety of DMPA-SC. Contraception. 2004;70(4):269–75.
5. Jain J, Dutton C, Nicosia A, Wajszczuk C, Bode FR, Mishell DR Jr. Pharmacokinetics, ovulation suppression and return to ovulation following a lower dose subcutaneous formulation of Depo-Provera. Contraception. 2004;70(1):11–8.
6. Dragoman MV, Gaffield ME. The safety of subcutaneously administered depot medroxyprogesterone acetate (104mg/0.65mL): a systematic review. Contraception. 2016;94(3):202–15.
7. Medical eligibility criteria for contraceptive use, fifth edition. Geneva: World Health Organization; 2015.
8. International Medical Products Price Guide. Arlington, VA: Management Sciences for Health; 2015 http://mshpriceguide.org/en/search-results-by-name-2/?searchYear=2015&searchString=Medroxyprogesterone+Acetate&searchType=Name, accessed 13 March 2017).