

# Estradiol cypionate + medroxyprogesterone acetate



Essential medicine status ✓

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

ATC codes: G03AA08

Indication	Contact with health services for reasons associated with reproduction ICD11 code: <a href="#">QA4Z</a>
INN	Estradiol + medroxyprogesterone
Medicine type	Chemical agent
List type	Core
Formulations	Parenteral > General injections > IM: 5 mg + 25 mg
EML status history	First added in 2007 ( <a href="#">TRS 946</a> )
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 <a href="#">about patents</a> .

Wikipedia [Estradiol cypionate + medroxyprogesterone acetate](#)

DrugBank [Estradiol cypionate \(Estradiol\)](#)  
[Medroxyprogesterone acetate](#)

## Summary of evidence and Expert Committee recommendations

In 2005, the Expert Committee rejected the application for two combination injectable contraceptives (medroxyprogesterone acetate plus estradiol cypionate and norethisterone enanthate plus estradiol valerate), questioning the public health need for these preparations in view of the lack of compelling evidence of better efficacy, convenience and safety. A revised application for inclusion of medroxyprogesterone acetate 25 mg plus estradiol cypionate 5 mg was submitted in 2007 by the Geneva Foundation for Medical Education and Research. The new application presented the same evidence for comparative effectiveness and safety from a Cochrane systematic review (1) and additional results for comparative safety based on three observational studies. The systematic review included two multicentre studies that directly compared the proposed combination with medroxyprogesterone-only injection. Comparative contraceptive efficacy was not reported in the review although other evidence from the same systematic review shows that the proposed product is an effective contraceptive. In terms of potential advantages of the proposed combination, the results of the review suggest less menstrual disturbance, better control of bleeding and greater intention to continue contraception with the combination injectable contraceptive (medroxyprogesterone acetate plus estradiol cypionate) than with medroxyprogesterone-only injections. To address the concerns raised at the previous meeting, the application presented new information from three observational studies (2-4) all of 1 year's duration. The studies were designed to measure changes in surrogate biochemical markers, but not in cardiovascular events or fracture outcomes. The results generally showed that the injectable combined contraceptive did not have deleterious effects on lipid metabolism, coagulation or bone mineral density. The studies were of insufficient duration to identify any effects on clinical outcomes such as cardiovascular events or fractures. Importantly, although the application acknowledged the need for a sterile injection technique for administration of this product, it did not provide an assessment of the possible risks associated with a monthly injection regimen. The application did not provide information on the cost-effectiveness of the combination injectable contraceptive. Based on the information provided, the acquisition cost of the product would appear to be substantially more than that of the alternatives. The Committee noted that

combination injectable medroxyprogesterone acetate/estradiol cypionate is recommended in WHO guidelines (the WHO Medical eligibility criteria for contraceptive use (5); and the Selected practice recommendations for contraceptive use (6)), although there are currently no such products on the Model List. Notwithstanding the previous inclusion of progestogen-only injectable contraceptives (POIC), and the similarity in contraceptive effectiveness between them and the combined injectable contraceptive (CIC), the differences in safety profile and convenience may serve to increase tolerance and continuation rates in women with different organic conditions and preferences. The Committee therefore decided to add medroxyprogesterone acetate plus estradiol cypionate 25 mg + 5 mg combination injectable contraceptive to the Model List of Essential Medicines. The Committee also recommended that the Uppsala Collaborating Centre for Drug Monitoring be requested to monitor reports of adverse events in relation to use of this product.

1. Gallo MF et al. Combination injectables for contraception. In: The Cochrane Library. Chichester, John Wiley & Sons, Ltd., 2006.
2. United Nations Development Programme/United Nations Population Fund/World Health Organization/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, Task Force on Long-acting Systemic Agents for Fertility Regulation. Comparative study of the effects of two once-a-month injectable contraceptives (Cyclofem and Mesigyna) and one oral contraceptive (Ortho-Novum 1/35) on coagulation and fibrinolysis. *Contraception*, 2003, 68:159–176.
3. United Nations Development Programme/United Nations Population Fund/World Health Organization/World Bank, Special Programme of Research, Development and Research Training in Human Reproduction. Comparative study of the effects of two once-a-month injectable steroidal contraceptives (Mesigyna and Cyclofem) on lipid and lipoprotein metabolism. *Contraception*, 1997, 56:193–207.
4. United Nations Development Programme/United Population Fund/World Health Organization/World Bank, Special Programme of Research, Development and Research Training in Human Reproduction, Task Force on Long-acting Systemic Agents for Fertility Regulation. Comparative study of the effects of two once-a-month injectable steroidal contraceptives (Mesigyna and Cyclofem) on glucose metabolism and liver function. *Contraception*, 1998, 57:71–81.
5. WHO medical eligibility criteria for contraceptive use. Geneva, World Health Organization, 2004 ([http://www.who.int/reproductive-health/publications/MEC\\_3/mec.pdf](http://www.who.int/reproductive-health/publications/MEC_3/mec.pdf)).
6. Selected practice recommendations for contraceptive use. Geneva, World Health Organization, 2004 (<http://www.who.int/reproductive-health/publications/spr/spr.pdf>).

