**Estradiol cypionate + medroxyprogesterone acetate**

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

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**Indication**
Contact with health services for reasons associated with reproduction  
**ICD11 code:** QA4Z

**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 (TRS 946)

**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**
[Estradiol cypionate + medroxyprogesterone acetate](https://en.wikipedia.org/wiki/Estradiol_cypionate_%2B_medroxyprogesterone_acetate)

**DrugBank**
[Estradiol cypionate (Estradiol)](https://www.drugbank.ca/drugs/DB00105)  
[Medroxyprogesterone acetate](https://www.drugbank.ca/drugs/DB00610)

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**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