What

CLINICAL SERVICES Recommendation 27: Medical management of induced abortion at gestational ages < 12 weeks

For medical abortion at < 12 weeks:

a. **Recommend** the use of 200 mg mifepristone administered orally, followed 1–2 days later by 800 µg misoprostol administered vaginally, sublingually or buccally. The minimum recommended interval between use of mifepristone and misoprostol is 24 hours.*

b. When using misoprostol alone: **Recommend** the use of 800 µg misoprostol administered buccally, sublingually or vaginally.*

c. **(NEW) Suggest** the use of a combination regimen of letrozole plus misoprostol (letrozole 10 mg orally each day for 3 days followed by misoprostol 800 µg sublingually on the fourth day) as a safe and effective option.*‡

Remarks:

- Evidence from clinical studies demonstrates that the combination regimen (Recommendation 27a) is more effective than misoprostol alone.
- All routes are included as options for misoprostol administration, in consideration of patient and provider preference.
- The suggested combination regimen of letrozole plus misoprostol may be safe and effective up to 14 weeks of gestation.

* Repeat doses of misoprostol can be considered when needed to achieve success of the abortion process. In this guideline we do not provide a maximum number of doses of misoprostol.

‡ Further evidence is needed to determine the safety, effectiveness and acceptability of the letrozole plus misoprostol combination regimen at later gestational ages, especially in comparison with that of the mifepristone plus misoprostol combination regimen (the available evidence focused on comparison with the use of misoprostol alone).

Source: Recommendations 27a and 27b carried forward from WHO (2018) where they were Recommendation 3a *(120)*. Recommendation 27c is new.

Rationale for Recommendation 27c (combination regimen of letrozole plus misoprostol)

A systematic review assessed the efficacy, safety and acceptability of alternative methods of medical abortion to the standard regimens using mifepristone and/or misoprostol. The literature search identified seven studies, all of which reported on the combination of letrozole plus misoprostol (intervention) versus misoprostol alone (comparison) for medical abortion. No studies were identified that compared letrozole plus misoprostol versus mifepristone plus misoprostol. The study settings included China, Egypt and the Islamic Republic of Iran. A summary of the evidence is presented in Supplementary material 2, EtD framework for New medical methods for abortion.

Overall, the evidence favoured the intervention. The use of letrozole in combination with misoprostol showed lower rates of ongoing pregnancy and higher rates of successful abortion, based on low- to very low-certainty evidence. In addition, fewer women experienced side-effects, based on moderate-certainty evidence.

Discussion on the cost-effectiveness, equity, feasibility and acceptability favoured the intervention. Letrozole's typical use for infertility and cancer treatment makes it more readily accessible than mifepristone in certain parts of the world. In addition, the low cost of letrozole is another contributing factor to making this an alternative method for medical abortion.