bottom line
Three small studies show clomiphene induces pregnancy in women with PCOS. For every 6 women treated, 1 more will become pregnant. Recent larger studies comparing newer agents to clomiphene suggest complications are rare. Clomiphene might be more beneficial in those with body mass index (BMI) ≥30 kg/m².

Evidence
• Systematic review of RCTs of antiestrogens in PCOS: In 3 RCTs (N=133) that examined clomiphene (50 to 250 mg/d, 1 to 5 cycles) versus placebo, the pregnancy rate was higher with clomiphene (20% vs 3%); the number needed to treat (NNT) was 6. Live births and miscarriages were not reported.
• Systematic review of insulin-sensitizing drugs in PCOS: In a subgroup analysis of clomiphene versus metformin, for those with BMI ≥30 kg/m² (2 RCTs, N=500), clomiphene was superior to metformin for pregnancy (NNT=7) and live birth (NNT=5) rates; for those with BMI <30 kg/m² (3 RCTs, N=349), metformin was superior to clomiphene for pregnancy (NNT=8); the effect on live births was unclear.
• Metformin alone² improves pregnancy rates compared with placebo (NNT=9).

Implementation
Clomiphene is inexpensive, well-tolerated, safe, and effective. Contraindications include liver disease or dysfunction, endometrial carcinoma, ovarian cysts (not PCOS), undiagnosed uterine bleeding, and pregnancy.⁸¹⁰ Treatment should be initiated at 50 mg daily on cycle days 2 to 5 (follicular phase) and continued for 5 consecutive days with increases of 50 mg in subsequent cycles if anovulation persists. The Society of Obstetricians and Gynaecologists of Canada⁸ and the Food and Drug Administration¹⁰ advise 100 mg or less, but up to 250 mg is used in some specialty practices.¹¹ Ovarulation can be confirmed with a luteal serum progesterone level >25 nmol/L. In women who ovulate, 52% do so taking 50 mg, 22% taking 100 mg, and fewer with subsequent increases.¹¹ Anovulatory women should be treated for 6 cycles before considering alternate methods of ovulation induction.¹²

Tools for Practice articles are adapted from articles published on the Alberta College of Family Physicians (ACFP) website, summarizing medical evidence with a focus on topics and practice-modifying information. The ACFP summaries and the series in CFP are coordinated by Dr G. Michael Allan, and the summaries are co-authored by at least 1 practising family physician and are peer reviewed. Feedback is welcome and can be sent to toolsforpractice@cfpc.ca. Archived articles are available on the ACFP website: www.acfp.ca.