levonorgestrel had a similar effect on hirsutism scores compared with all other OCs. OCs containing antiandrogenic progestins (one trial using CPA and one trial using DSP) were associated with slightly lower Ferriman–Gallwey scores than other OCs, with a weighted mean difference of −2.86 [95% CI (−4.96 to −0.76)], a difference that is probably not clinically important (71).

Which OCs should be used for hirsutism?

For most women, we do not suggest one particular OC formulation over another for treating hirsutism. This recommendation is consistent with the Endocrine Society clinical guideline on the diagnosis and treatment of PCOS (40). There were no clinically important advantages of OCs containing the antiandrogen progestins CPA or DSP in our meta-analysis. Although we were concerned that OCs containing levonorgestrel (the most androgenic progestin) would be less effective for hirsutism, this was not observed in our meta-analysis. Whereas a potential benefit of OCs containing levonorgestrel is their lower VTE risk, an important concern is the adverse effects of levonorgestrel on metabolic biomarkers (72). Although there are no data to suggest that the metabolic effects are associated with adverse clinical outcomes, we tend to avoid this progestin in women with PCOS, a population with metabolic concerns at baseline. As noted previously, for women with hirsutism at higher risk for VTE (*e.g.*, those who are obese or over age 39 years), we suggest initial therapy with an OC containing the lowest effective dose of EE (usually 20 mcg) and a low-risk progestin (Table 2). Our approach is similar to that of the consensus statement from the Androgen Excess and PCOS Society, which also suggests using a low-dose OC product to minimize VTE risk (6).

Ovarian androgen suppression may be similar with OCs containing different doses of EE. In a meta-analysis of 42 studies, the suppression of serum total and free testosterone concentrations was similar with OCs containing 20 vs 30/35 mcg EE (74). Limited data suggest that OCs containing DSP with 20 or 30 mcg EE have a similar effect on Ferriman–Gallwey scores (75). Transdermal contraceptive patch and OCs suppressed serum androgens to a similar degree in one study, but the outcome of hirsutism was not addressed (76).

Antiandrogens

Our systematic review identified seven trials of antiandrogens, as follows: three of finasteride, two of flutamide, and two of spironolactone. In analyses of individual antiandrogens compared with placebo, spironolactone 100 mg/d, finasteride 2.5 to 5 mg/d, and flutamide 500 mg/d, each showed a significant reduction in hirsutism scores. When all antiandrogens were pooled together as a class, and results were expressed in Ferriman–Gallwey units, antiandrogens were significantly more effective than placebo, with a pooled weighted mean difference of −7.02 [95% CI (−11.51 to −2.52)]. There was no statistically significant difference among the three antiandrogens.

Available antiandrogens and their dosing regimens are shown in Table 3. Spironolactone, an aldosterone antagonist, exhibits dose-dependent competitive inhibition of the androgen receptor as well as inhibition of 5α-reductase activity (77). Although there are no rigorous dose-response trials to date, spironolactone's effects are known to be dose dependent (77). The drug is generally well tolerated, but should not be used if there is renal impairment. Spironolactone may have a dose-dependent association with menstrual irregularity unless the patient uses an OC concomitantly. Spironolactone use may rarely result in hyperkalemia, and it may cause increased diuresis and occasionally postural hypotension and dizziness early in treatment. OCs containing DSP have a mild mineralocorticoid effect and should not be used with a potassium-sparing diuretic. As with all antiandrogens, if a patient inadvertently uses spironolactone during early pregnancy, there is a danger that a male fetus could be feminized (78) because of the exquisite sensitivity of the fetal genitalia to exposure to maternal synthetic sex hormone ingestion (79), although the absolute risk of this is not known.

Clinicians worldwide use CPA to treat hirsutism and acne, but it is not available in the United States. CPA is a progestogenic compound with antiandrogen activity by virtue of its effects in inhibiting the androgen receptor and to a lesser degree in inhibiting 5α-reductase activity (80). It also suppresses serum gonadotropin and androgen levels. In one systematic review, the OC CPA (2 mg) with 35 mcg EE was similar to antiandrogen therapy and more effective than placebo (81).

Finasteride inhibits type 2 5α-reductase activity. Because enhanced 5α-reductase activity in hirsutism

Table 3. Antiandrogens Used for the Treatment of Hirsutism

Antiandrogens	Dosing
CPA[a]	50–100 mg/d on menstrual cycle days 5–15, with EE 20–35 mg on days 5–25
Spironolactone	100–200 mg/d [given in divided doses (twice daily)]
Finasteride	2.5–5 mg/d
Flutamide[b]	250–500 mg/d (high dose) 62.5 to ≤250 mg/d (low dose)

[a] Not available in the United States; also prescribed as an OC (2 mg CPA + 35 mcg EE).

[b] Flutamide not recommended because of hepatotoxicity.