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Drospirenone: a new cardiovascular-active progestin with antialdosterone and antiandrogenic properties.

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Drospirenone (DRSP) is a novel progestogen derived from 170alpha-spirolactone. Its pharmacodynamic profile is closer to progesterone than any other currently available progestogen. DRSP has progestational, antialdosterone and antiandrogenic properties, but is devoid of any estrogenic, androgenic, glucocorticoid, antiglucocorticoid or mineralocorticoid activities. The affinity of DRSP for the mineralocorticoid receptor makes it an antagonist of aldosterone, which is not only important in the renin-angiotensin-aldosterone system (RAAS), but also acts directly on the cardiovascular system. DRSP (1, 2 or 3 mg) in combination with 1 mg 17beta-estradiol (E2) is being developed by Schering AG as a continuous combined product for hormone replacement therapy (HRT). Phase II/III trials of E2/DRSP combinations have demonstrated clinical efficacy for the treatment of hot flushes, as well as improvement of bone density in the hip. Within 1 year of treatment with E2/DRSP, more than 80% of recipients regained amenorrhea. E2/DRSP at all three doses of DRSP is associated with a highly favorable safety profile, with excellent endometrial protection after 1 and 2 years (no cases of hyperplasia or cancer), favorable lipid profiles, with no evidence of attenuation of the beneficial effects on lipids of E2, probably due to DRSP's lack of androgenicity. Recipients of E2/DRSP combinations showed a small decrease in body weight, probably due to DRSP's antialdosterone properties. Adverse events with E2/DRSP did not differ significantly from those observed with standard HRT preparations. Phase III studies with E2/DRSP show that DRSP does not antagonize the well-documented reductions of blood pressure associated with E2; rather, small DRSP dose-related reductions in systolic and diastolic blood pressures were observed, which should be beneficial for recipients, especially those who are mildly hypertensive. These effects on blood pressure are probably due to DRSP displaying aldosterone receptor antagonism, a property which, in other settings, has been shown to convey benefits in terms of cardiovascular disease. Further studies of the cardiovascular effects of E2/DRSP combinations are anticipated.