

From The Medical Letter on Drugs and Therapeutics

Drospirenone (Slynd)—A New Progestin-Only Oral Contraceptive

The FDA has approved a progestin-only oral contraceptive (“minipill”) containing drospirenone (Slynd – Exeltis). All other progestin-only oral contraceptives available in the US contain norethindrone (Camila, and others).¹ Progestin-only oral contraceptives are similar in efficacy to combination oral contraceptives.² They are used predominantly by breastfeeding women and by those in whom estrogen is poorly tolerated or contraindicated. Combination oral contraceptives containing drospirenone and ethinyl estradiol have been available for years.

Pronunciation Key

Drospirenone: droe spye' re none Slynd: slind

Norethindrone

Progestin-only oral contraceptives containing norethindrone should be started on the first day of menses; backup nonhormonal contraception or abstinence is recommended for 48 hours if treatment is started >5 days after menses onset. Subsequent tablets are taken daily without a hormone-free interval. Taking the drug at the same time each day (within 3 hours) is crucial for prevention of pregnancy and breakthrough bleeding; if a dose is taken >3 hours late, backup nonhormonal contraception or abstinence is recommended for the next 48 hours (Table)

Mechanism of Action

Drospirenone prevents pregnancy primarily by suppressing ovulation. It appears to suppress ovulation more consistently than norethindrone. In one trial, ovulation inhibition was maintained with drospirenone alone despite multiple intentional delays in dosing.³

Table. Progestin-Only Oral Contraceptives

| | Norethindrone | Drospirenone |
|---------------------|--|---|
| Brand names | Camila, and others ^a | Slynd |
| Available strengths | 0.35 mg tabs (28 active tabs) | 4 mg tabs (24 active/4 inactive tabs) |
| Half-life | ~9 h | ~30 h |
| Dosage | 1 tab once/d × 28 d (no hormone-free days) ^b | 1 tab once/d × 28 d (4 hormone-free days) ^b |
| Missed doses | Backup contraception recommended for 48 h if dose is >3 h late | Backup contraception recommended for 7 d if ≥2 active tablet doses are missed |
| Cost ^c | \$25.00 | \$194.00 |

^a Other branded generics include Jencycla, Incassia, Heather, and Errin.

^b Taken at the same time each day.

^c Approximate WAC for 28 days' treatment. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price.

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Clinical Studies

In a pooled analysis of 2 single-arm trials that included a total of 1571 women 18-45 years old who took drospirenone over nine (trial 2) or thirteen (trial 1) 28-day cycles, the Pearl index (number of pregnancies per 100 woman-years) was 0.7258. Unscheduled bleeding or spotting occurred in 61.4% of women during the first cycle and in 40.3% during cycle 13. One woman developed hyperkalemia. No cases of venous thromboembolism (VTE) were reported in either trial.⁴

No head-to-head trials are available comparing drospirenone alone with norethindrone alone for prevention of pregnancy.

Adverse Effects

Nausea, irregular bleeding, headache, breast tenderness or pain, weight gain, dysmenorrhea, and decreased libido can occur with both drospirenone and norethindrone. Unlike norethindrone, drospirenone has antiminerlocorticoid activity and can cause hyperkalemia. Also unlike norethindrone, drospirenone is antiandrogenic; it should not exacerbate acne and might improve it. Hyperglycemia and amenorrhea have also occurred with use of drospirenone.

Combination oral contraceptives containing drospirenone and ethinyl estradiol have been associated with an increased risk of VTE⁵; whether drospirenone alone could increase the risk of VTE remains to be determined. Norethindrone-only oral contraceptives have not been associated with an increased risk of thromboembolism.

Contraindications

Drospirenone is contraindicated for use in women with hepatic or renal impairment or adrenal insufficiency. It is also contraindicated in women with cervical or other progestin-sensitive cancers, benign or malignant liver tumors, or undiagnosed abnormal uterine bleeding.

Drug Interactions

Drospirenone is partly metabolized by CYP3A4. Drugs that induce CYP3A4, such as rifampin, can increase the metabolism of drospirenone and decrease its effectiveness. Women who must take such drugs should use backup nonhormonal contraception while taking the enzyme inducer and for 28 days after stopping it. CYP3A4 inhibitors taken concurrently with drospirenone could increase the risk of hyperkalemia and other adverse effects.⁶ Concurrent use of drospirenone with other drugs that increase potassium levels, such as the antiandrogen aldosterone receptor antagonist spironolactone (Aldactone, and generics) that is often used off-label for treatment of acne, can increase the risk of hyperkalemia.

Dosage and Administration

Slynd is available in blister cards that contain 24 drospirenone 4-mg tablets and 4 inactive tablets. The first active tablet should be taken on the first day of menses; subsequent tablets (including inactive tablets) should be taken once daily at the same time each day. Women switching from another hormonal contraceptive method should start taking drospirenone on the day their next dose is due or on the day their implant or intrauterine device is removed.

If an active tablet dose is missed, it should be taken as soon as possible. If ≥ 2 active tablet doses are missed, the dose should be taken as soon as possible and backup nonhormonal contraception or abstinence is recommended for 7 days. If vomiting or diarrhea occurs within 3-4 hours after taking drospirenone, a new tablet should be taken as soon as possible.

Conclusion

The oral progestin drospirenone (Slynd) is an effective option for prevention of pregnancy (Box). How it compares in efficacy and tolerability to progestin-only oral contraceptives containing norethindrone remains to be determined. The management of late or missed doses appears to be more convenient with drospirenone. Drospirenone should have more favorable effects on acne, but it

Box. Summary: Drospirenone (Slynd)

- First progestin-only oral contraceptive that contains drospirenone; other progestin-only oral contraceptives contain norethindrone.
- Effective in reducing pregnancy rates in clinical trials.
- No trials are available comparing it directly with norethindrone alone.
- Taken daily with a 4-day hormone-free interval (24 active and 4 inactive tablets).
- Backup nonhormonal contraception is not required unless ≥ 2 active tablet doses are missed.

can cause hyperkalemia. Drospirenone is much more expensive than generic norethindrone.

ARTICLE INFORMATION

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