Progestin-only pills (POPs) for contraception

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INTRODUCTION

Progestin-only pills (POPs) are one option for women who cannot or prefer not to use estrogen-containing contraception. In addition to oral pills, progestin-only contraception is available as an implant, intrauterine device (IUD), and injection. This topic will review patient selection, counseling, and administration of POPs.

Discussions of contraceptive selection and other types of progestin-only contraceptives include:

- (See "Contraception: Counseling and selection".)
- (See "Postpartum contraception: Counseling and methods".)
- (See "Etonogestrel contraceptive implant".)
- (See "Intrauterine contraception: Background and device types", section on 'Levonorgestrel IUD'.)
- (See "Depot medroxyprogesterone acetate (DMPA): Formulations, patient selection and drug administration".)

FORMULATIONS

While multiple types of progestins are used in combined estrogen-progestin contraceptive pills, norethindrone and drospirenone are the main progestins available as POPs (table 1). The progestin dose is substantially lower than the dose in any combination oral contraceptive (in combined oral contraceptives: norethindrone 0.35 to 1 mg and drospirenone 3 to 4 mg). The pills are dispensed in packs of 28 active pills. The norethindrone POP formulation is taken continuously (ie, no pill-free or nonhormonal pill week). The drospirenone formulation consists of 24 hormonally active tablets followed by 4 inert tablets.

- Norethindrone – Norethindrone is commonly available as 0.35 mg tablets (commercial names include Camila and Errin). The dose is substantially lower than the dose in any combination oral contraceptive pills, and norethindrone POPs do not consistently suppress ovulation (table 2) (see 'Mechanism and duration of action' below). It is dispensed in packs of 28 active pills, which are taken continuously (ie, no pill-free or nonhormonal pill week) [1]. **Unless otherwise noted, the information on POPs in this topic primarily applies to norethindrone POPs.**
- Drospirenone – Drospirenone, a third-generation progestin approved for use in the United States in 2019, is available in a package containing 24 tablets with 4 mg drospirenone and 4 inert tablets (commercial name Slynd) [2]. One tablet is taken daily until the pack is empty and then a new pack is started. The main mechanism of action is suppression of ovulation. Drospirenone has anti-mineralocorticoid activity comparable to a 25 mg dose of spironolactone. Patients at risk for hyperkalemia, either by medical condition or medication, should use drospirenone with caution. The manufacturer advises checking "serum potassium levels during the first treatment cycle in patients receiving daily, long-term treatment for chronic conditions of diseases with medications that may increase serum potassium concentrations." Negligible amounts of drospirenone are secreted in breast milk. An initial multicenter clinical trial reported pregnancy in 1.8 percent of users for a

Pearl Index of 4.0 (95% CI 2.3-6.4). A multicenter phase III trial reported a perfect-use Pearl Index of 0.7 (95% CI 0.3-1.4) [3]. While the initial drospirenone data suggest the efficacy (ie, perfect use) of this new POP may approach that of traditional estrogen-progestin combined contraceptives, larger data sets are needed. Data on real-use effectiveness are not yet available. (See 'Efficacy' below.)

- **Desogestrel** – In numerous countries (excluding the United States), desogestrel is available as a 75 mcg POP formulation [4]. This formulation has significant differences from norethindrone POPs discussed in this topic: The main mechanism of action is inhibition of ovulation, contraceptive efficacy is as high as that with estrogen-progestin contraceptive pills, and intake delay of up to 12 hours does not affect its contraceptive efficacy [5].

PATIENT SELECTION

Candidates — Most women can use POPs. We agree with the Centers for Disease Control and Prevention (CDC) guidelines regarding use of POPs in women with medical comorbidities. POPs appear to be appropriate contraceptive choices for many women with contraindications to estrogen-containing contraceptives or women who prefer to avoid estrogen exposure [6].

Contraindications — Women who should not use POPs include those with [6,7]:

- Known or suspected pregnancy. However, pregnancies conceived in women taking POPs have not been associated with adverse effects.
- Known or suspected breast cancer.
- Undiagnosed abnormal uterine bleeding.
- Benign or malignant liver tumors, severe cirrhosis, or acute liver disease.

Additionally, women who have undergone malabsorptive bariatric surgeries and those taking certain anticonvulsants are not advised to use POPs [6]. Full lists of medical eligibility criteria for contraception use are available online at United States Medical Eligibility Criteria for Contraceptive Use and World Health Organization Medical Eligibility Criteria for Contraceptive Use.

Pill versus other progestin-only methods — Women who desire a progestin-only contraceptive must decide among the etonogestrel implant; levonorgestrel-releasing intrauterine devices (IUDs); depot medroxyprogesterone acetate (DMPA) injection; and the POPs norethindrone, drospirenone, and desogestrel (where available). Factors for consideration include:

- **Efficacy** – For progestin-only methods, the long-acting contraceptives (etonogestrel implant and levonorgestrel-releasing IUDs) are the most efficacious (figure 1). The DMPA injection is also highly effective in women who return on time for repeat injections. By contrast, the efficacy of POPs in highly fertile women may be lower than that with other hormonal contraceptive methods. National survey data used to estimate contraceptive failure rates with typical use have not generally distinguished between users of estrogen-progestin contraceptive pills (9 percent failure rate in first year of use) and POPs. (See 'Efficacy' below.)
- **Dosing frequency and convenience** – POPs need to be taken daily and, ideally, at the same time of day. Daily dosing is less convenient than that of the injection (every 13 weeks), etonogestrel implant (three years), and levonorgestrel-releasing IUDs (three to six years). (See 'Need for back-up contraception' below.)
- **Resumption of fertility** – POPs, the etonogestrel implant, and IUDs are associated with a rapid return of fertility after method discontinuation (typically within one cycle). (See 'Discontinuation and resumption of fertility' below.)

  Conversely, the return of fertility with the DMPA injection is typically months and can be unpredictable. (See "Depot medroxyprogesterone acetate (DMPA): Formulations, patient selection and drug administration", section on 'Return to fertility after discontinuation'.)
- **Privacy** – The need to store and take a daily pill reduces privacy. Although not typically externally visible, strings of an IUD

and the etonogestrel implant can be palpated. The DMPA injection is completely private.

- **Need for procedure** – Both the etonogestrel implant and levonorgestrel-releasing IUDs require insertion and removal by a trained clinician. DMPA requires injection, which can be done by a health care provider or, in some settings, by the patient. By contrast, POP use does not require any procedure and only minimal initial evaluation. (See 'Patient evaluation' below.)

- **Complications** – While the overall complication rates are low for all progestin-only methods, serious complications are less common with POPs [8]. (See 'Risks' below.)

COUNSELING POINTS

Mechanism and duration of action — Norethindrone POPs work by thickening cervical mucus to inhibit sperm migration, suppressing ovulation, lowering the midcycle peaks of follicle-stimulating hormone and luteinizing hormone, slowing movement of an egg through the fallopian tubes, and thinning the endometrium [7]. In contrast to estrogen-progestin oral contraceptive pills and desogestrel POPs, ovulation is not consistently suppressed with norethindrone POPs, and approximately half of users still ovulate [7,9]. Therefore, the effects of norethindrone POPs on cervical mucus and endometrium represent the critical factors in prevention of conception [10]. By contrast, drospirenone and desogestrel POPs do suppress ovulation [2,11].

Within hours of administration, all POPs reduce the volume of cervical mucus and increase its viscosity, which prevents sperm from passing through the cervical canal and endometrial cavity. These changes persist for 20 hours [12,13]. Upon discontinuation, fertility returns rapidly [7].

Efficacy — United States package insert information for norethindrone states the typical user failure rate is estimated to be approximately 5 percent, which places these POPs in the middle efficacy zone (figure 1) [14]. An initial clinical trial of drospirenone POPs reported an overall pregnancy rate of 1.8 percent [2]. While the efficacy (ie, perfect use) of this new POP may approach that of traditional estrogen-progestin combined contraceptives, larger data sets are needed.

- **Comparison of** norethindrone **and** drospirenone **POPs** – Studies directly comparing the efficacy of norethindrone and drospirenone POPs are not yet available. However, it is reasonable to believe that drospirenone POPs may be more effective. Norethindrone POPs contain one-third the hormone dose used in common estrogen-progestin contraceptive pills (0.3 versus 1 mg of norethindrone or norethindrone acetate) (table 2). By contrast, the drospirenone POP contains a higher dose of hormone compared with that found in drospirenone-containing oral contraceptive pills (4 versus 3 mg). However, this hypothesis is purely speculative and requires confirmation through randomly assigned trials.

- **Comparison of POPs and estrogen-progestin pills** – National survey data used to estimate contraceptive failure rates with typical use have not generally distinguished between users of estrogen-progestin contraceptive pills and users of POPs. Estrogen-progestin contraceptive failure rates for the first year of use have been estimated as 7 percent for typical-use failure and 0.3 percent for perfect use failure [15]. As the great majority of oral contraceptives used in the United States are estrogen-progestin contraceptive pills and the typical-use failure rate with POPs is likely to be higher than with estrogen-progestin contraceptive pills, the typical user failure rate with POPs is likely to be greater than 7 percent [16]. In addition, women choosing POPs are often subfertile as a result of breastfeeding or older reproductive age; the failure rate in these populations is thought to be lower than in more fertile populations, which may result in artificially low typical-use failure rates reported for POPs.

Side effects — Unscheduled bleeding and changes in menses are the most common side effects associated with POPs; an increased prevalence of follicular ovarian cysts [17] and acne flare [10] have also been reported. POPs do not cause significant weight gain [18] and are not likely to increase headache frequency [19].

- **Unscheduled bleeding and menstrual changes** – As with all continuous progestin-only contraceptives, menstrual irregularities are common in POP users and represent the most frequent cause for contraceptive discontinuation. Unscheduled bleeding and spotting are the most common bleeding patterns during POP use, and prospective as well as current users should be counseled accordingly [7].

- Norethindrone – Norethindrone users have more frequent, longer episodes and shorter, less predictable intervals than combined pill users [20], but up to one-half of users experience a mostly regular monthly bleeding pattern [21]. Amenorrhea and prolonged episodes of bleeding also occur, but less frequently than in depot-medroxyprogesterone acetate (DMPA) users [22].

- Drospirenone – In the subject diaries from the initial four trials of drospirenone, unscheduled bleeding was common but improved with time; unscheduled bleeding dropped from 64 percent in cycle 1 to 40 percent by cycle 13 [2]. In a single-arm safety trial of 102 adolescents (12 to 17 years) using drospirenone, the median number of overall bleeding days dropped from 14 to 11 days (cycles 2 to 4 versus cycles 11 to 13), but the number of unscheduled bleeding days increased from five to six days to eight days during the same time period [23]. Irregular bleeding led 5 percent of participants to withdraw from the study.

One consequence of unscheduled bleeding and spotting is that interpreting signs and symptoms of pregnancy, whether intrauterine or extrauterine, can be challenging in POP users. Pregnancy testing is appropriate for POP users experiencing nausea, breast tenderness, a change in bleeding pattern, or lower abdominal pain.

Unscheduled bleeding and its management in POP users are discussed in more detail separately. (See "Evaluation and management of unscheduled bleeding in women using contraception", section on 'Progestin-only pills'.)

- **Mood** – Available data on the impact of POPs on mood are limited and conflicting [24]. Challenges to interpreting the data include varied study designs, duration of follow-up, sources of information (trial versus pharmacy or hospital database), and types of progestins. A trial including 150 women followed for three months reported lower Beck Depression Scores for women receiving levonorgestrel oral pills compared with those receiving either placebo or combined estrogen-progestin oral contraceptive pills [25]. However, a nationwide cohort study of Danish women reported an increased risk of first use of antidepressants (relative risk [RR] 1.3, 95% CI 1.27-1.40) and first hospital discharge diagnosis of depression (RR 1.2, 95% CI 1.04-1.31) for women using norethindrone, levonorgestrel, or desogestrel progestin-only oral contraception; or levonorgestrel-releasing intrauterine devices (IUDs) [26]. The inability to control for potentially confounding factors and the modest elevations in relative risks make the clinical implications of this Danish database study uncertain [27,28].

- **Weight gain** – Although available data are limited, POPs do not appear to be associated with significant weight gain [29]. A 12-month observational study including 102 perimenopausal women reported nonsignificant increases in weight for women using a desogestrel pill or levonorgestrel-releasing IUD compared with control women [30]. However, women in both progestin groups did have a statistically significant small increase in fat mass.

- **Follicular cysts** – Sonographic studies have observed that follicular cysts are more common in POP users than women not using hormones [17]. The follicular changes tend to increase and regress over time [31,32]. No intervention other than reassurance is required in asymptomatic women. POP users who have persistent concerns about ovarian follicular changes or symptoms from follicular cysts (eg, pain) should be offered another method of contraception. For women with follicular cyst symptoms who do not want to change their contraceptive method, an alternate off-label option is to prescribe two or three progestin-only tablets daily. The higher progestin dose may more fully suppress follicle-stimulating hormone release and cyst formation, but supporting data are lacking [10]. (See "Management of an adnexal mass", section on 'Benign mass'.)

- **Effect on carbohydrate metabolism** – Most studies have reported that POPs have little impact on carbohydrate metabolism [33-36]. However, one study conducted in Latina women observed that lactating women with a history of gestational diabetes who used POPs postpartum had an elevated risk of being diagnosed with diabetes [37]. After adjustment for potential confounding factors, the use of POPs was associated with an almost threefold increase in the risk of type 2 diabetes mellitus compared with equivalent use of low-dose estrogen-progestin contraceptive pills (adjusted RR 2.87, 95% CI 1.57-5.27). Based on this one study, we suggest clinicians monitor glucose tolerance in high-risk lactating women using POPs. POPs are an appropriate contraceptive choice for women with diabetes, including those with vascular disease [6].

- **Effect on bone mineral density** – The only study assessing skeletal health in POP users was conducted in breastfeeding

women. Although breastfeeding resulted in a reversible reduction in spinal bone mineral density in women using barrier contraception, the small amounts of hormone in the POP protected against this loss [38].

Risks — POPs have not been associated with serious complications.

- **Cardiovascular risk** – We and others [6,39] believe POPs represent a reasonable contraceptive choice for patients with high risk of (or known) coronary artery disease, cerebrovascular disease, venous thromboembolic disease, hypertension, or other conditions in which use of contraceptive doses of estrogen are contraindicated. POPs have little effect on coagulation factors [33], blood pressure [34,40], inflammatory markers [41], or lipid levels [33-36]. A large cross-sectional analysis reported that use of norethindrone POPs is associated with lower high-density lipoprotein levels but has little effect on low-density lipoprotein or triglyceride levels [35]. POP benefits are believed to outweigh the risks in women with deep venous thrombosis or pulmonary embolism (active or history of), regardless of anticoagulation therapy [6]. Large epidemiologic studies and a systematic review have not identified a statistically increased risk of stroke, myocardial infarction, or venous thromboembolism with use of POPs [42-47]. In a case-control study of women with venous thromboembolism, use of POPs, the levonorgestrel-releasing IUD, or the progestin-only contraceptive implant was not a significant risk factor for venous thromboembolism [46]. Use of DMPA injection was identified as a significant risk factor, but the association was less robust than for estrogen-progestin contraceptives (odds ratio [OR] 2.2 versus 5.3).

- **Ectopic pregnancy risk** – POPs lower the overall risk of ectopic pregnancy, as well as intrauterine pregnancy, by preventing ovulation or conception. Since women taking POPs do not appear to have a higher absolute risk of ectopic pregnancy than women using no contraception, a history of ectopic pregnancy does not contraindicate POP use [1]. However, if pregnancy occurs, the likelihood that the pregnancy is ectopic is higher in POP users than in women not using contraception (5 versus 2 percent) [48]. Clinicians caring for women who conceive during use of POPs can perform an early sonogram to establish the location of the pregnancy.

- **Breast cancer** – The data for progestin-only contraceptives are inadequate to make a definitive conclusion regarding risk of breast cancer [7]. A United States population-based case-control study found no evidence that POP use was associated with an elevated risk of breast cancer [49]. Likewise, a large Nordic multi-country prospective cohort study reported that ever-use of POP was not associated with an elevated risk of breast cancer [50]. (See "Combined estrogen-progestin contraception: Side effects and health concerns", section on 'Breast cancer' and "Dysmenorrhea in adult women: Treatment".)

Noncontraceptive benefits — Daily use of a progestin protects against development of endometrial cancer [51]. Use of POPs for management of menorrhagia or pelvic pain has not been well studied. Norethindrone acetate has demonstrated efficacy in treating dysmenorrhea, abnormal uterine bleeding, and endometriosis-related pain, but at higher doses (2.5 to 15 mg per day) [52]. A single-arm trial of drospirenone in adolescent females reported reduced rates of dysmenorrhea, as well as reduced rates of pain medication used to treat dysmenorrhea, with continued drospirenone use over 13 cycles [23]. (See "Endometriosis: Treatment of pelvic pain", section on 'Progestins' and "Abnormal uterine bleeding: Management in premenopausal patients".)

Impact on sexually transmitted infection acquisition — POP use neither protects from nor increases the risk of acquiring STIs. However, progestin-induced thickening and increased viscosity of cervical mucus has been hypothesized to inhibit ascent of bacteria and thus potentially reduce the risk of development of pelvic inflammatory disease.

We counsel all women at risk for STI acquisition regarding concomitant condom use. (See "External (formerly male) condoms", section on 'Protection from STIs'.)

ADMINISTRATION

Patient evaluation — Physical examination and laboratory tests are not indicated before beginning POPs in women who are appropriate candidates for this method [53]. Clinicians are advised to measure baseline weight and body mass index (BMI), as having these baseline measurements may be helpful in monitoring POP users over time, but this is not required.

Initiation and dosing — We suggest that POPs be initiated on the first day of menses; back-up contraceptive is not necessary if POPs are started within the first five days of start of menses (including for women switching from non-intrauterine device [IUD] contraception) [53]. Some clinicians initiate POPs at any time in the cycle, as long as they are reasonably certain that the patient is not pregnant (table 3). Back-up contraception is needed for two additional days if the patient is >5 days from onset of menses. Although the US Selected Practice Recommendations for Contraceptive Use recommends two rather than seven days of back-up contraception with POP initiation, presumably because of the rapid effect of the POP on cervical mucus; clinically, it is simpler to advise all women initiating contraception more than five days from onset of menses to use back-up contraception (or abstinence) for seven days [53]. Providing or prescribing a one-year supply of POPs enhances continuation rates [53,54].

Because of the short duration of action and the short half-life of POPs, it is **essential that the pill be taken at the same time each day** to maximize contraceptive efficacy [55-57]. Women initiating norethindrone POPs are counseled that POPs are taken continuously with no hormone-free days. Women who miss taking a norethindrone POP dose by more than three hours are advised to use additional contraception (eg, condoms) for 48 hours after the late dose [7]. (See 'Need for back-up contraception' below.)

Some clinicians have theorized that taking a daily dose of two POP tablets (two tablets as a single dose) might increase the contraceptive efficacy of POPs in young, nonlactating women who are presumably highly fecund [1,58]. For women with normal fertility (ie, not postpartum, lactating, or perimenopausal) who desire to use POPs, the author prescribes the two-pill regimen (ie, 0.35 mg norethindrone, two tablets taken daily). The additional cost is a disadvantage of this approach. The author and other experts counsel patients that there are no published data regarding this off-label contraceptive strategy [59].

Need for back-up contraception — Back-up contraception (eg, condoms) should be used or the woman should abstain from sex for at least two days if the norethindrone POP is taken **more than three hours late or missed** on any given day, or if the patient starts POPs more than five days from the onset of menses [7]. Women with delayed or missed pill intake should also resume taking daily POPs as soon as possible, even if this means that two pills are taken on one day (the missed pill and the usual time pill) [53]. Emergency contraception (EC), not including ulipristal acetate, can be offered to women who have unprotected intercourse during the 48-hour window that back-up contraception or abstinence is advised. Back-up contraception/abstinence can be discontinued after POPs have been taken correctly, on time, for two consecutive days.

Vomiting or severe diarrhea within three hours of taking a POP may decrease contraceptive effectiveness. These clinical scenarios are managed in a similar way to a late or missed pill. The woman should continue taking POPs daily at the same time each day and use back-up contraception (eg, condoms) or avoid sex until two days after vomiting or diarrhea has resolved [53].

If the woman has been using an IUD and is switching to POPs, she may have residual sperm in her reproductive tract, which could result in fertilization and implantation if the IUD is removed. Options discussed with the patient include [53]:

- Advise the woman to retain the IUD for at least two days after POPs are started and then return for IUD removal.
- Advise the woman to abstain from sexual intercourse or use barrier contraception for seven days before removing the IUD and starting POPs.
- If the woman cannot return for interval IUD removal and has had unprotected vaginal intercourse within seven days, advise the woman to use EC at the time of IUD removal. For EC methods other than ulipristal acetate, POPs can be started immediately after EC use. Women using ulipristal acetate initiate POPs no sooner than five days after ulipristal use. (See "Emergency contraception".)

Follow-up — Routine follow-up is unnecessary [53]. The woman should return if she has concerns about the method, side effects, change in health status that might affect use of hormonal contraception, or if she wants to switch methods.

Discontinuation and resumption of fertility — POPs can be discontinued at any time the patient desires. Upon discontinuation, fertility returns rapidly and women who desire pregnancy can attempt conception any time they are ready [7]. Women who are changing their contraceptive method from POPs to a levonorgestrel-releasing IUD, the etonogestrel implant, or depot medroxyprogesterone acetate (DMPA) injections may need back-up contraception or abstinence for seven days if the

switch occurs more than five to seven days from the onset of menses (timing varies with contraceptive method) [53]. Women changing to all other contraceptive methods do not require a period of abstinence or back-up contraception.

- (See "Intrauterine contraception: Insertion and removal", section on 'Women who are switching from another method'.)
- (See "Etonogestrel contraceptive implant", section on 'Back-up contraception'.)
- (See "Depot medroxyprogesterone acetate (DMPA): Formulations, patient selection and drug administration", section on 'Switching from DMPA to another method'.)

DRUG INTERACTIONS

Hepatic enzyme-inducing anti-epileptic medications, including phenytoin, carbamazepine, topiramate, and barbiturates; and the antimicrobial drugs rifampicin and rifabutin appear to reduce the efficacy of POPs [6,7]. We advise women requiring treatment with these medications to select a different contraceptive method or consistently use a back-up method of contraception (eg, condoms) with every act of vaginal intercourse. The anticonvulsant lamotrigine is compatible with POP use [6]. The advantages of POPs for women who are also taking the antiretroviral fosamprenavir appear to be greater than the risks (established or theoretical); all other antiretroviral medications are compatible with POP use [6,60].

SPECIAL POPULATIONS

- **Adolescent and young women** – POPs can be used any time after menarche. However, the need for consistent timing of ingestion and possibly lower efficacy may make this option less ideal for adolescent and young women. Contraceptive needs and counseling of adolescents are discussed in detail separately. (See "Contraception: Issues specific to adolescents".)
- **HIV** – Although the body of evidence is limited, POP use does not appear to increase the risk of HIV acquisition or disease progression [61]. POP use is compatible with nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors. A discussion on the issues surrounding contraceptive selection in women with HIV infection is presented elsewhere. (See "HIV and women", section on 'Choice of contraception'.)
- **Obese** – POPs are not contraindicated for obese women [6]. However, data on efficacy of POPs specific to obese women are lacking. Given the availability of alternate contraceptive options (eg, intrauterine devices [IUDs], etonogestrel implant, depot medroxyprogesterone acetate [DMPA] injections, and combined estrogen-progestin methods), we prefer to avoid POPs in obese women. For obese women who have additional comorbidities with estrogen use or who want to avoid estrogen use but who do not wish to use the etonogestrel implant, IUDs, or DMPA, an alternate option is to take two POPs daily, although supporting data for this approach are lacking. (See "Contraception: Counseling for females with obesity", section on 'Contraceptive implant'.)
- **Perimenopause** – There are no age limits to POP use in medically eligible women [6]. The reduced fecundity of women over age 35 to 40 years means they can expect higher contraceptive efficacy with use of POPs [62].
- **Postabortion, postpartum, and lactating women** – POPs may be initiated immediately postabortion or postdelivery, and should be initiated by three weeks after delivery to assure effectiveness [6,39,60]. Breastfeeding is not a contraindication to use of POPs.
  - (See "Contraception: Postabortion", section on 'Progestin-only pills'.)
  - (See "Postpartum contraception: Counseling and methods".)
- **Medical comorbidities** – Most women with medical comorbidities are candidates for POP contraception. Full lists of medical eligibility criteria for contraception use are available online at United States Medical Eligibility Criteria for Contraceptive Use and World Health Organization Medical Eligibility Criteria for Contraceptive Use.

- **Physical or intellectual disability** – There are no contraindications to POP use specific to women with intellectual or physical disabilities. However, women who desire menstrual suppression to aid with menstrual hygiene are advised to avoid POPs, as unscheduled bleeding and spotting are the most common bleeding patterns. The 52 mg levonorgestrel-releasing IUDs, injectable DMPA, and combined hormonal contraceptives are preferred for this indication. (See "Hormonal contraception for suppression of menstruation".)

RESOURCES FOR PATIENTS AND CLINICIANS

- Bedsider.org – A free website developed by the National Campaign to Prevent Teen and Unplanned Pregnancy, a private nonprofit group
- CHOICE Project – A free website sponsored by the Washington University School of Medicine in St. Louis that provides resources on contraceptive options and training resources for clinicians
- Center for Young Women's Health – A free website run by Boston Children's Hospital that addresses reproductive health needs of teens and young adults
- Beyond the Pill – A free website run by the University of California San Francisco
- SexualityandU.ca – An educational site run by the Society of Obstetricians and Gynecologists of Canada that includes descriptions of various methods and a tool to help with selection of birth control
- Planned Parenthood – A nonprofit organization dedicated to reproductive health with resources for patients and clinicians
- ACOG Contraceptive FAQs – American College of Obstetricians and Gynecologists addresses frequently asked questions (FAQs) about contraception
- ACOG LARC Program – American College of Obstetricians and Gynecologists Long-Acting Reversible Contraception Program
- United States Medical Eligibility Criteria for Contraceptive Use
- United States Selected Practice Recommendations for Contraceptive Use
- World Health Organization Medical Eligibility Criteria for Contraceptive Use

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Contraception".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or email these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topic (see "Patient education: Hormonal methods of birth control (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

Patient populations

- Progestin-only contraception represents an option for women in whom an estrogen-containing contraceptive is either contraindicated or causes additional health concerns. The Centers for Disease Control and Prevention (CDC) provides guidelines regarding use of progestin-only pills (POPs) in women with medical comorbidities. (See 'Patient selection' above.)
- Most women with medical comorbidities are candidates for POP contraception. Full lists of medical eligibility criteria for contraception use are available online at United States Medical Eligibility Criteria for Contraceptive Use and World Health Organization Medical Eligibility Criteria for Contraceptive Use. (See 'Special populations' above.)
- Patients using hepatic enzyme-inducing anti-epileptic medications are educated that these medications may reduce the efficacy of POPs. Such medications include the anticonvulsants phenytoin, carbamazepine, topiramate, and barbiturates and the antituberculosis drug rifampin. (See 'Drug interactions' above.)

Formulations and mechanism of action

- Norethindrone (0.35 mg tablet), drospirenone (4 mg tablet), and desogestrel (75 mcg tablet) are available as POPs (table 1). For norethindrone POPs, the progestin dose is substantially lower than the dose in any combination oral contraceptive. The norethindrone and desogestrel pills are dispensed in packs of 28 active pills while drospirenone packs contain 24 active pills and 4 inert tablets. (See 'Formulations' above.)
- The effects of norethindrone POPs on cervical mucus and endometrium are the critical factors in prevention of conception; ovulation is not consistently suppressed. By contrast, suppression of ovulation is the main mechanism of drospirenone and desogestrel POPs. (See 'Mechanism and duration of action' above.)

Efficacy and use

- The typical user failure rate with POPs is estimated to be over 7 percent (figure 1). Women choosing POPs are often subfertile as a result of breastfeeding or older reproductive age so the failure rate is thought to be higher in more fertile populations. (See 'Efficacy' above.)
- Menstrual irregularities and unscheduled bleeding are common in POP users and represent the most frequent causes for contraceptive discontinuation. (See 'Side effects' above.)
- Physical examination and laboratory tests are not indicated before beginning POPs in women who are appropriate candidates for this method. **It is essential that the** norethindrone **POPs be taken at the same time each day** to maximize contraceptive efficacy. A back-up contraceptive (eg, condoms) should be used for at least two days if the POP is taken more than three hours late or forgotten on any given day. (See 'Administration' above.)

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Topic 5461 Version 39.0

GRAPHICS

Classification of progestins used in combined oral contraceptive pills

First generation
▪ Norethindrone acetate ▪ Ethynodiol diacetate ▪ Lynestrenol ▪ Norethynodrel
Second generation
▪ dl-Norgestrel ▪ Levonorgestrel
Third generation
▪ Desogestrel ▪ Gestodene ▪ Norgestimate
Unclassified
▪ Drospirenone ▪ Cyproterone acetate

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Graphic 87416 Version 1.0

Selected hormonal contraceptives: Oral contraceptives (birth control pills) and other delivery methods

United States brand name	Progestin (mg)*	Estrogen (micrograms)	Notes
Monophasic combinations			
Beyaz 28 ¶	Drospirenone (3)	Ethinyl estradiol (20)	Also approved for acne and premenstrual dysphoric disorder. In patients with conditions requiring chronic therapy with medications that may increase potassium, monitor serum potassium during the first treatment cycle and periodically thereafter if patient begins medication or develops a condition that increases risk for hyperkalemia.
Gianvi 28 Δ			
Loryna 28 Δ			
Nikki 28 Δ			
Yaz Δ			
Amethyst 28	Levonorgestrel (0.09)	Ethinyl estradiol (20)	
Aviane 28	Levonorgestrel (0.1)	Ethinyl estradiol (20)	Packaged as active tablets for 21 days and placebo for 7 days.
Balcoltra 28			
Falmina 28			
Larissia 28			
Lessina 28			
Lutera 28			
Orsythia 28			
Sronyx 28			
Blisovi Fe 1/20 ◊	Norethindrone acetate (1)	Ethinyl estradiol (20)	Available in a 28-day regimen with active pills for 24 days and ferrous fumarate for 4 days.
Gemmily			
Junel Fe 1/20 28 ◊ §			
Larin Fe 1/20 ◊ §			
Loestrin Fe 1/20 28 ◊			
Melodetta 24 Fe chewable §			
Microgestin Fe 1/20 28 ◊			
Minastrin Fe 1/20 chewable			
Taytulla capsules			
Apri 28	Desogestrel (0.15)	Ethinyl estradiol (30)	Packaged as active tablets for 21 days and placebo for 7 days.
Cyred Eq 28			
Emoquette 28			
Enskyce 28			
Juleber 28			
Reclipsen 28			
Ocella 28 ¥	Drospirenone (3)	Ethinyl estradiol (30)	In patients with conditions requiring chronic therapy with medications that may increase potassium, monitor serum potassium during the first treatment cycle and periodically thereafter if patient begins medication or develops a condition that increases risk for hyperkalemia.
Safyral 28 ¶			
Tydemy 28 ¶			
Yasmin 28 ¥			
Zarah 28 ¥			
Chateal 28	Levonorgestrel (0.15)	Ethinyl estradiol (30)	Packaged as active tablets for 21 days and placebo for 7 days.
Kurvelo 28			
Levora 0.15/30			
Marlissa 28			
Portia 28			
Blisovi Fe 1.5/30	Norethindrone acetate (1.5)	Ethinyl estradiol (30)	Packaged as active tablets for 21 days and ferrous fumarate tablets for 7 days.
Larin FE 1.5/30 ‡			
Loestrin Fe 1.5/30 28 ‡			
Microgestin Fe 1.5/30 28			
Junel Fe 1.5/30 28			
Cryselle 28	Norgestrel (0.3) †	Ethinyl estradiol (30)	Packaged as active tablets for 21 days and placebo for 7 days.
Elinest 28			
Low-Ogestrel 28			
Kelnor 28	Ethynodiol diacetate (1)	Ethinyl estradiol (35)	Packaged as active tablets for 21 days

Pirmella 1/35			and placebo for 7 days.
Zovia 1/35E 28			
Balziva 28	Norethindrone (0.4)	Ethinyl estradiol (35)	Packaged as active tablets for 21 days and placebo for 7 days.
Briellyn 28			
Philith 28			
Vyfemla			
Brevicon 28	Norethindrone (0.5)	Ethinyl estradiol (35)	Packaged as active tablets for 21 days and placebo for 7 days.
Necon 0.5/35 28			
Nortrel 0.5/35 28			
Wera			
Alyacen 1/35 28	Norethindrone (1)	Ethinyl estradiol (35)	Packaged as active tablets for 21 days and placebo for 7 days.
Cyclafem 1/35			
Dasetta 1/35 28			
Nortrel 1/35 28 ‡			
Ortho-Novum 1/35 28			
Femynor	Norgestimate (0.25)	Ethinyl estradiol (35)	Packaged as active tablets for 21 days and placebo for 7 days.
Mili			
MonoNessa 28			
Ortho-Cyclen 28			
Previfem 28			
Sprintec 28			
VyLibra			
Cleo-35, Cyestra-35, Diane 35 Not available in the United States; Canadian product shown	Cyproterone (2)	Ethinyl estradiol (35)	Labeled approval in Canada is for treatment of acne.
Kelnor 1/50 28	Ethynodiol diacetate (1)	Ethinyl estradiol (50)	Packaged as active tablets for 21 days and placebo for 7 days. **NOTE: Pills containing 50 mcg of ethinyl estradiol are not indicated for routine contraceptive use because of increased risk of cardiovascular events compared with lower-dose oral contraceptive pills.**
Ogestrel 0.5/50 28	Norgestrel (0.5) †	Ethinyl estradiol (50)	Packaged as active tablets for 21 days and placebo for 7 days. **NOTE: Pills containing 50 mcg of ethinyl estradiol are not indicated for routine contraceptive use because of increased risk of cardiovascular events compared with lower-dose oral contraceptive pills.**
Zoely Δ	Nomegestrol acetate (2.5)	Estradiol (as hemihydrate) (1.5 **milligrams**)	Not available in the United States; United Kingdom and European Union product shown.
Multiphasic combinations			
Natazia 28	Dienogest (0,2,3,0)	Estradiol valerate (3,2,2,1) NOTE: Estradiol strength listed in milligrams (mg)	Packaged as active tablets for 26 days and placebo for 2 days.
Lo Loestrin Fe	Norethindrone acetate (1,0)	Ethinyl estradiol (10,10)	Packaged as active tablets for 26 days and ferrous fumarate for 2 days.
Azurette 28	Desogestrel (0.15,0,0)	Ethinyl estradiol (20,0,10)	Packaged as active tablets for 26 days and placebo for 2 days or ferrous fumarate for Lo Loestrin Fe.
Bekyree 28			
Kariva 28			
Mircette 28			
Pimtrea 28			
Viorele 28			
Volnea 28			
Estrostep Fe 28	Norethindrone acetate (1,1,1)	Ethinyl estradiol (20,30,35)	Also approved for acne. Packaged as active tablets for 21 days and ferrous fumarate tablets for 7 days.
Tilia Fe 28			
Tri-Legest Fe 28 §			
	Norgestimate (0.18,0.215,0.25)	Ethinyl estradiol (25,25,25)	Packaged as active tablets for 21 days

Ortho Tri-Cyclen Lo 28			and placebo for 7 days.
Tri-Lo-Marzia			
Tri-Lo-Sprintec			
TriNessa Lo			
Caziant 28	Desogestrel (0.1,0.125,0.15)	Ethinyl estradiol (25,25,25)	Packaged as active tablets for 21 days and placebo for 7 days.
Cyclessa 28			
Velivet			
Enpresse 28	Levonorgestrel (0.05,0.075,0.125)	Ethinyl estradiol (30,40,30)	
Levonest 28¥			
Myzilra 28¥			
Trivora 28¥			
Ortho Tri-Cyclen 28	Norgestimate (0.18,0.215,0.25)	Ethinyl estradiol (35,35,35)	Also approved for acne. Packaged as active tablets for 21 days and placebo for 7 days.
Tri-Femynor 28			
Tri-Linyah 28			
Tri-Previfem 28			
Tri-Sprintec 28			
TriNessa 28			
Alyacen 7/7/7 28	Norethindrone (0.5,0.75,1)	Ethinyl estradiol (35,35,35)	Packaged as active tablets for 21 days and placebo for 7 days.
Cyclafem 7/7/7 28			
Dasetta 7/7/7 28			
Nortrel 7/7/7 28			
Ortho-Novum 7/7/7 28			
Pirmella 7/7/7			
Aranelle 7/9/5 28	Norethindrone (0.5,1,0.5)	Ethinyl estradiol (35,35,35)	Packaged as active tablets for 21 days and placebo for 7 days.
Leena 7/9/5 28			
Extended combinations			
Amethia Lo 91	Levonorgestrel (0.1)	Ethinyl estradiol (20,10)	Packaged as a 91-day regimen: 84 days of the combination and 7 days of ethinyl estradiol only.
Camrese Lo 91			
LoJaimiess 91			
LoSeasonique 91			
Fayosim 91	Levonorgestrel (0.15)	Ethinyl estradiol (20,25,30,10)	Packaged as a 91-day regimen: 84 days of the combination and 7 days of ethinyl estradiol only.
Rivelsa 91			
QuarteSe 91			
Amethia 91	Levonorgestrel (0.15)	Ethinyl estradiol (30,10)	Packaged as a 91-day regimen: 84 days of the combination and 7 days of ethinyl estradiol only.
Ashlyna			
Camrese 91			
Jaimiess 91			
Seasonique 91			
Introvale 91	Levonorgestrel (0.15)	Ethinyl estradiol (30)	Packaged as a 91-day regimen: active tablets for 84 days and placebo for 7 days.
Jolessa 91			
Quasense 91			
Continuous combinations			
May use any monophasic 21/7 combination by taking active hormone pills for 28 or more days continuously. Refer to example (Amethyst) at right; any progestin may be used, and higher doses of ethinyl estradiol may be used in some women. Refer to the topic in UpToDate.	Levonorgestrel (0.09)	Ethinyl estradiol (20)	
Progestin-only			
Camila 28	Norethindrone (0.35)	None	Packaged as active tablets for 28 days.
Deblitane			
Errin 28			
Heather			
Incassia			
Jencycla			

Jolivette 28 Lyleq Nora-BE 28 Norlyda Ortho Micronor Sharobel			
Slynd	Drospirenone (4)	None	Packaged as active tablets for 24 days and placebo for 4 days. In patients with conditions requiring chronic therapy with medications that may increase potassium, monitor serum potassium during the first treatment cycle and periodically thereafter if patient begins medication or develops a condition that increases risk for hyperkalemia.
Transdermal patch, weekly			
Xulane Zafemy	Norelgestromin (releases 0.15 mg/day)	Ethinyl estradiol (releases 35 mcg/day)	May have diminished efficacy in women ≥90 kg. A new patch is applied every 7 days for 3 weeks followed by a patch-free week. This is therapeutically equivalent to Ortho Evra, which is no longer available in the United States.
Twirla	Levonorgestrel (releases 0.12 mg/day)	Ethinyl estradiol (releases 30 mcg/day)	Contraindicated in women with BMI ≥30 kg/m^2 due to decreased efficacy and increased risk of VTE. Diminished efficacy was observed in women with BMI ≥25 kg/m^2. A new patch is applied every 7 days for 3 weeks followed by a patch-free week.
Vaginal ring, monthly			
NuvaRing EluRyng	Etonogestrel (releases 0.12 mg/day)	Ethinyl estradiol (releases 15 mcg/day)	Ring is inserted for 3 weeks followed by 1 week without ring in place. A new ring is inserted 7 days after the last was removed.
Annovera	Segesterone (releases 0.15 mg/day)	Ethinyl estradiol (releases 13 mcg/day)	Ring is inserted for 3 weeks followed by 1 week without ring in place. The ring is then reinserted for the first 21 days of subsequent 28-day cycles. One system provides contraception for 13 28-day cycles (1 year). Not yet adequately evaluated in women with BMI >29 kg/m^2.

- Oral and IUD emergency contraceptive options are listed in a table that is available separately in UpToDate.
- Generic (non-branded) products are also available for most combination oral contraceptives in the United States.
- Descriptions are for US-available products unless noted otherwise. Consult local product information before use.

Fe: contains iron; BMI: body mass index; VTE: venous thromboembolism; IUD: intrauterine device.
* Different progestins are not equivalent on a milligram basis. Refer to the UpToDate overview of combined hormonal contraceptives for guidance on selection.
¶ Also contains 451 mcg of levomefolate calcium per tablet. Beyaz is taken for 24 days followed by 4 days of levomefolate calcium alone. Safyral and Tydemy are taken for 21 days followed by 7 days of levomefolate calcium alone.
Δ Taken as active pills for 24 days and placebo for 4 days.
◊ Packaged as active tablets for 21 days and ferrous fumarate tablets for 7 days.
§ Also available as a 21-day regimen that does not contain iron.
¥ Packaged as active tablets for 21 days and placebo for 7 days.
‡ Also available in a 21-day regimen.
† The progestin norgestrel contains two isomers; only levonorgestrel is bioactive. The amount of norgestrel in each tablet is twice the amount of levonorgestrel.

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Graphic 69223 Version 42.0

Title X birth control methods options chart [1,2]

Birth control method options		Risk of pregnancy*	How the method is used	How often the method is used	Menstrual side effects	Other possible side effects to discuss	Other considerations	
Most effective	Female sterilization 	0.5 out of 100	Surgical procedure	Permanent	None	Pain, bleeding, infection	Provides permanent protection against an unintended pregnancy	Counsel all clients about the use of condoms to reduce the risk of STIs, including HIV infection
	Male sterilization 	0.15 out of 100						
	IUD 	**LNG:** 0.2 out of 100 **CopperT:** 0.8 out of 100	Placement inside uterus	Lasts up to 3 to 12 years	**LNG:** Spotting, lighter or no periods **CopperT:** Heavier periods	Some pain with placement	**LNG:** No estrogen; may reduce menstrual cramps **CopperT:** No hormones; may cause more menstrual cramps	
	Implant 	0.05 out of 100	Placement into upper arm	Lasts up to 3 years	Spotting, lighter or no periods		No estrogen	
Moderately effective	Injectables 	4 out of 100	Shot in arm, hip or under the skin	Every 3 months	Spotting, lighter or no periods	May cause appetite increase/ weight gain	No estrogen May reduce menstrual cramps	Counsel all clients about the use of condoms to reduce the risk of STIs, including HIV infection
	Pill 	8 out of 100	Take a pill	Every day at the same time	Can cause spotting for the first few months Periods may become lighter	May have nausea and breast tenderness for the first few months	Some clients may report improvement in acne May reduce menstrual cramps and anemia Lowers risk of ovarian and uterine cancer	
	Patch 	9 out of 100	Put a patch on skin	Each week				
	Ring 		Put a ring in vagina	Each month				
	Diaphragm 	12 out of 100	Use with spermicide and put in vagina	Every time you have sex	None	Allergic reaction, irritation	No hormones	
Least effective	Male condom 	13 out of 100	Put over penis	Every time you have sex	None	Allergic reaction, irritation	No hormones No prescription necessary	Counsel all clients about the use of condoms to reduce the risk of STIs, including HIV infection
	Female condom 	21 out of 100	Put inside vagina					
	Withdrawal 	20 out of 100	Pull penis out of the vagina before ejaculation			None	No hormones Nothing to buy	
	Sponge 	12 to 24 out of 100	Put inside vagina			Allergic reaction, irritation	No hormones No prescription necessary	
	Fertility awareness based methods 	24 out of 100	Monitor fertility signs Abstain or use condoms on fertile days	Daily		None	No hormones Can increase awareness and understanding of a woman's fertility signs	
	Spermicides 	28 out of 100	Put inside vagina	Every time you have sex		Allergic reaction, irritation	No hormones No prescription necessary	

IUD: intrauterine device; LNG: levonorgestrel; STI: sexually transmitted infection.
* The number of women out of every 100 who have an unintended pregnancy within the first year of typical use of each method. Other methods of birth control: (1) lactational amenorrhea method (LAM) is a highly effective, temporary method of contraception; and (2) emergency contraception: emergency contraceptive pills or a copper IUD after unprotected intercourse substantially reduces risk of pregnancy.

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1. *Trussell J. Contraceptive failure in the United States. Contraception 2011; 83:397.*
2. *Sundaram A, Vaughan B, Kost K, et al. Contraceptive failure in the United States. Perspect Sex Reprod Health 2017; 49:7.*

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Graphic 119765 Version 3.0

Checklist used to assess the possibility of pregnancy

The provider can be reasonably certain that the patient is not pregnant if the patient has no symptoms or signs of pregnancy and meets ANY of the following criteria:
☐ The patient has not had intercourse since last normal menses.
☐ The patient has been correctly and consistently using a reliable method of contraception.
☐ The patient is within 7 days from the first day of menstrual bleeding.
☐ The patient is within 4 weeks postpartum (for nonlactating patients).
☐ The patient is within the first 7 days postabortion or miscarriage.
☐ The patient is fully or nearly fully breastfeeding, amenorrheic, and less than 6 months postpartum.

A systematic review of studies evaluating the performance of a pregnancy checklist compared with urine pregnancy test to rule out pregnancy concluded the negative predictive value of a checklist similar to the one above was 99 to 100%.

Data from:

1. *Tepper NK, Marchbanks PA, Curtis KM. Use of a checklist to rule out pregnancy: A systematic review. Contraception 2013; 87:661.*
2. *Curtis KM, Tepper NK, Jatlaoui TC, et al. United States Medical Eligibility Criteria for Contraceptive Use, 2016. MMWR Recomm Rep 2016; 65:1.*

Graphic 67567 Version 19.0

Contributor Disclosures

Andrew M Kaunitz, MD Grant/Research/Clinical Trial Support: Endoceutics [Menopausal symptoms]; Evafem [Contraception]; AbbVie [Polycystic ovary syndrome]; Myovant Sciences [Symptomatic fibroids]; Medicines360 [Heavy menstrual bleeding]; Merck [Contraceptive implant]. Consultant/Advisory Boards: Merck [Contraception]; Mithra Pharmaceuticals [Contraception]; Pfizer [Contraception, menopause]. **Courtney A Schreiber, MD, MPH** Patent holder: Penn, Saul [Medical management of nonviable pregnancy]. Grant/Research/Clinical Trial Support: Bayer [Contraception]; Medicines360 [Contraception]; VeraCept [Contraception]. Consultant/Advisory Boards: Danco Pharmaceuticals [Early pregnancy loss]; Medicines360 [Consultant]. Other Financial Interest: American Board of Obstetrics and Gynecology. **Kristen Eckler, MD, FACOG** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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