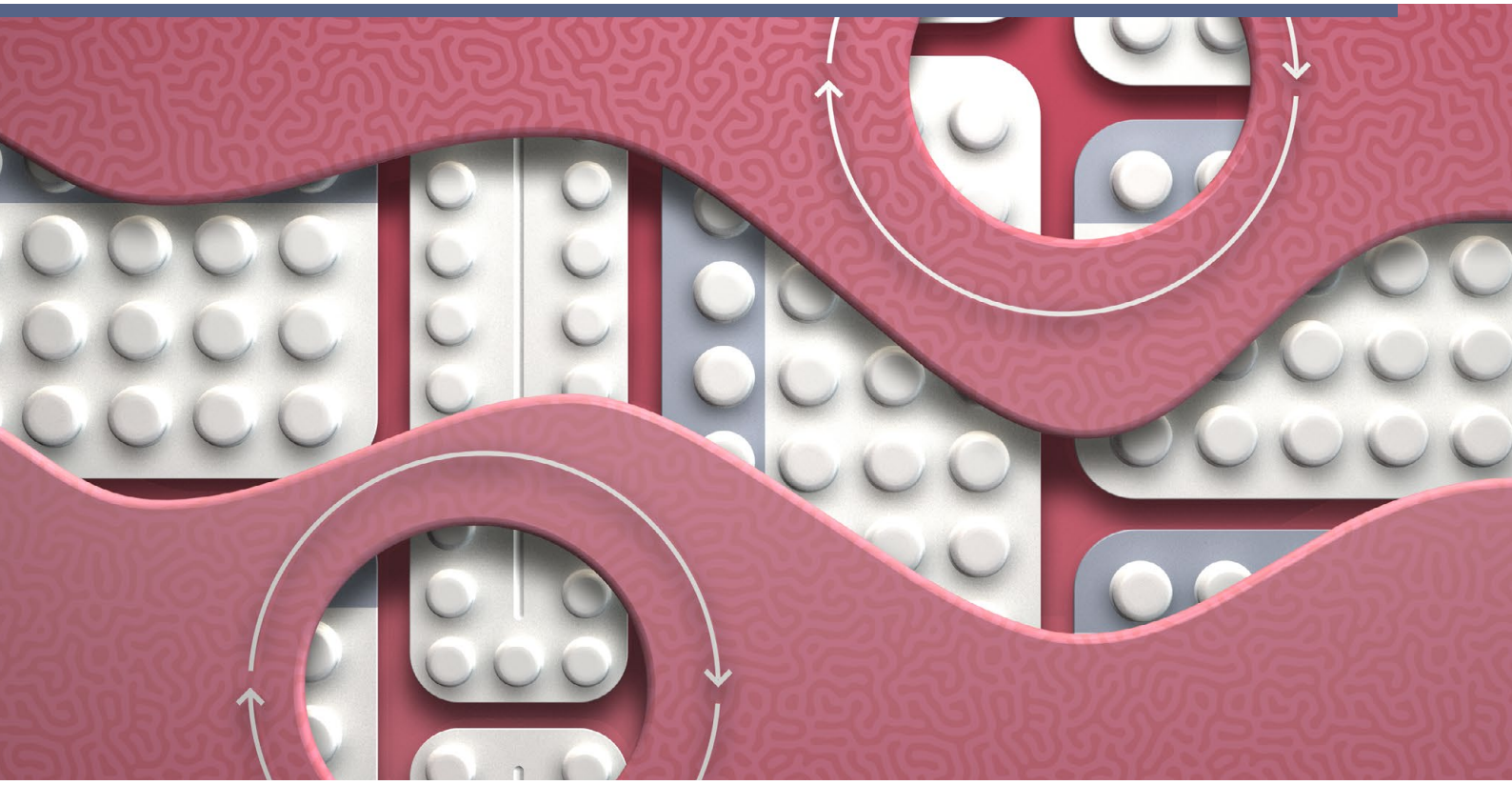

Oral contraceptives: selecting a pill

Oral contraceptive pills are a safe and effective contraceptive method widely used in New Zealand. For patients using a combined ethinylestradiol/progestogen pill, omitting the monthly withdrawal bleed may improve contraceptive efficacy and reduce associated symptoms such as pain, bloating or headache. Progestogen-only contraceptive pills are a suitable alternative for patients with contraindications to oestrogen use, such as those at high risk of venous thromboembolism.

KEY PRACTICE POINTS:

- Combined and progestogen-only oral contraceptives are equally effective for preventing pregnancy; the estimated rate of pregnancy is < 0.3% during the first year if used correctly and consistently, however, with typical use, the rate of pregnancy is 9%
- A reasonable choice for a first-time combined oral contraceptive (COC)-user is a formulation containing ≤ 35 micrograms ethinylestradiol with either levonorgestrel or norethisterone
- Avoid use of COCs in patients with risk factors for venous thromboembolism, myocardial infarction or ischaemic stroke, such as those aged over 35 years who smoke, have migraine with aura or are likely to be immobile for a prolonged period, e.g. undergoing major surgery
- Progestogen-only oral contraceptives, commonly referred to as progestogen-only pills (POPs), can be used if oestrogen is contraindicated
- COCs can be initiated from six weeks post-partum in patients who are breastfeeding; previous guidance recommended waiting until six months post-partum

This is a revision of a previously published article. What's new for this update:

- Includes recommendations from New Zealand Aotearoa's guidance on contraception, Ministry of Health (Dec, 2020), available from: **https://www.health.govt.nz/system/files/documents/publications/final_aotearoa_contraception_guidance.pdf**
- Table of available COCs updated
- New Zealand guidance recommends offering tailored regimens (where the hormone-free interval is omitted periodically or continuously) to all patients initiating or currently taking a COC to reduce the risk of unintended pregnancy and symptoms during the hormone-free interval

COCs: the first-line oral contraceptive choice

Oral contraceptives are available in two formulations, a combined ethinylestradiol/progestogen pill and a progestogen-only pill (POP). Combined oral contraceptives (COCs) are generally the first-line choice for those who wish to use an oral contraceptive, unless oestrogen use is contraindicated. This is because COCs require less strict adherence to regular dosing times than POPs and provide additional non-contraceptive benefits. When COCs and POPs are taken correctly, the estimated rate of pregnancy is < 0.3% during the first year of use.[1]

COCs prevent ovulation, thicken cervical mucus to inhibit sperm penetration of the upper reproductive tract and alter the endometrial lining to make implantation less likely. They are taken as one pill, daily, at approximately the same time of day.

All COCs in New Zealand contain the same oestrogen (ethinylestradiol) in varying doses along with differing progestogens (Table 1). The progestogens vary in their androgenic properties; norethisterone and levonorgestrel are more androgenic than desogestrel; drospirenone and cyproterone are anti-androgenic and therefore most effective for treating acne.[1]

Which COCs are available in New Zealand?

A range of fully or partly funded COCs are available in New Zealand. Other unfunded oral formulations are also available. For partly funded COCs, higher subsidy is available with Special Authority approval for patients with a low income if at least one fully funded option has been trialled and not tolerated, see: **schedule.pharmac.govt.nz/ScheduleOnline.php?code=A130802**

Table 1: COC formulations available in New Zealand, as of February, 2024.[4] Check the NZF (**www.nzf.org.nz**) or the PHARMAC website (**pharmac.govt.nz**) for funding and medicine supply information.

Oestrogen (ethinylestradiol) dose	Progestogen dose		Brand names
20 micrograms	Levonorgestrel 100 micrograms	●	Lo-Oralcon 20 ED Microgynon 20 ED
	Desogestrel 150 micrograms	●	Mercilon 28
	Drospirenone 3 mg		Yaz
30 micrograms	Levonorgestrel 150 micrograms	●	Oralcon 30 ED Levlen ED Lynley 150/30 ED Microgynon 30 ED Monofeme
	Drospirenone 3 mg		Yasmin
35 micrograms	Norethisterone 500 micrograms	●	Norimin 28 Day Brevinor 21 Day*
	Norethisterone 1 mg	●	Brevinor-1 28 Day Brevinor-1 21 Day*
	Cyproterone 2 mg	●	Ginet Diane-35 ED
50 micrograms	Levonorgestrel 125 micrograms		Microgynon 50 ED

● Fully funded

ED = every day formulation – this is a COC regimen that includes placebo pills to be taken during the hormone-free interval. N.B. Not all brand names include "ED" even though they are an ED regimen.

N.B. The following brands of COCs are also listed in the NZF (as they are either still registered or funded), but are currently unavailable: Erlidona, Norimin 1.

* COC formulations that do not contain placebo pills

Formulations with lower doses of ethinylestradiol are just as effective for preventing pregnancy as those with a higher dose.[2, 3]

Cautions and contraindications: when to avoid COCs

Venous thromboembolism (VTE) risk

COC use is associated with a three to 3.5-fold increase in the relative risk of VTE.[5] However, if there are no additional risk factors, the absolute risk of VTE associated with COC use is very small, particularly when compared to the risk during pregnancy and post-partum (Table 2).[1, 5] The risk of VTE is highest in the first few months after initiating a COC or following a break of at least one month and reduces over the first year of use.[5]

If the patient has existing risk factors for VTE, the absolute risk is higher and COCs should not be used.

For information on non-oestrogen-containing contraceptive options appropriate for patients at high risk of VTE, see: "**Contraception: which option for which patient**".

Risk factors for VTE that are **contraindications** to COC use include:[1, 4–6]

- Current or past VTE
- Thrombogenic mutations, e.g. factor V Leiden*, prothrombin mutation, Protein S, Protein C, antithrombin deficiencies
- Major elective surgery, any surgery to the legs or surgery resulting in prolonged immobility, i.e. more than one week†
- Age ≥ 35 years and smoke ≥ 15 cigarettes per day**
- Fewer than three weeks post-partum with other risk factors for VTE

* If homozygous for factor V Leiden or heterozygous with a personal or family history of VTE, COCs should be avoided. If heterozygous but no personal or family history of VTE and no alternative contraceptive is suitable, COCs may be used but avoid formulations with a higher VTE risk (Table 5).[7]

† The COC should be stopped four weeks prior to surgery and can be restarted from two weeks after mobilisation.[8] These recommendations do not apply to minor surgical procedures, e.g. a tooth extraction, or those requiring a short duration of general anaesthesia (< 30 minutes).[8]

** Increasing age and smoking are independent risk factors for VTE, however, when these factors are in combination, the additive risks are considered to outweigh the benefits of COCs[5]

Risk factors for VTE where COC use is **strongly cautioned**, include:[4, 5]

- Family history of VTE in a first-degree relative aged < 45 years
- Obesity (body mass index [BMI] ≥ 35 kg/m^2)
- Immobile for a prolonged period due to illness or disability, i.e. without the added risk of VTE associated with surgery
- Travel > 3 hours, especially with other risk factors (see below)
- History of superficial thrombophlebitis
- Aged ≥ 35 years and smoke < 15 cigarettes per day or stopped smoking less than one year ago
- Fewer than three weeks postpartum without other risk factors

Table 2: Risk of VTE for different patient groups.[9, 10]

Group	Risk of VTE per 10,000 females per year
Childbearing age, non-COC users	2 – 4
COC users	7 – 10
Pregnant and post-partum	20 – 30*

* The risk of VTE two days before and after delivery is estimated to be 300 – 400 per 10,000 females per year and for the first 12 weeks post-partum is 40 – 65 per 10,000 females per year

Best practice tip: Remind patients who take COCs and are going to be travelling on long-haul flights (> 3 hours) to maintain mobility. Compression stockings are not essential unless other risk factors for VTE are present.[5] If the patient is going to spend more than one week at an altitude > 4500 metres they should consider switching to a non-oestrogen-containing contraceptive, particularly if they have other risk factors for VTE.[5]

Other cardiovascular disease (CVD) risk

COC use is associated with a 1.6-fold and 1.7-fold increase in the relative risk of myocardial infarction and ischaemic stroke, respectively.[11*] However, the absolute risk of each of these outcomes is small unless additional risk factors for arterial disease are present.[5] It is estimated that among 10,000 females the use of COCs for one year would result in:[5]

- Two additional cases of thrombotic stroke
- One additional case of myocardial infarction

* The duration of COC use was not reported in this meta-analysis

COCs should not be used if there are additional risk factors for myocardial infarction or stroke, including:[1, 4, 5]

- Current or past ischaemic heart disease, stroke, complicated valvular or congenital heart disease, e.g. pulmonary hypertension, and other vascular disease

- Impaired cardiac function or atrial fibrillation
- Hypertension (systolic ≥ 160 mmHg or diastolic ≥ 100 mmHg); COC use is strongly cautioned in those with systolic blood pressure > 140 mmHg or diastolic > 90 mmHg and those taking antihypertensive medicines, even if hypertension is well controlled
- Diabetes with vascular complications
- Multiple risk factors for CVD, e.g. increasing age, smoking, hypertension, obesity, dyslipidaemia, diabetes
- Migraine with aura or migraine without aura that is new onset during use of COC*

* Could consider initiating a COC with caution if history of migraine without aura, provided no other CVD risk factors

Current breast cancer

COCs should not be used in patients with current breast cancer and use is strongly cautioned against in those with a history of breast cancer or who are known carriers of gene mutations associated with breast cancer, e.g. BRCA1 or BRCA2.[5]

N.B. COCs may be protective against ovarian cancer associated with these mutations;[5] discussion with an oncologist is recommended.

Post-partum

COCs can be started from six weeks post-partum if breastfeeding, provided breastfeeding is well established and there are no concerns with the infant's growth.[1]

COCs can be started from three weeks post-partum if not breastfeeding, provided there are no other risk factors for VTE*; those with additional risk factors should wait six weeks to begin the COC.[1]

* Other risk factors for VTE post-partum include immobility, transfusion at delivery, BMI ≥ 30 kg/m^2, caesarean section delivery, haemorrhage, pre-eclampsia, smoking

For further information on suitable contraceptive options post-partum, see: "**Contraception: which option for which patient**".

Age ≥ 50 years

The use of COCs is not recommended in those aged ≥ 50 years due to the risks outweighing the benefits.[12]

For further information on suitable contraceptive methods for older patients, see: "**Contraception: which option for which patient**".

For further information on medical conditions where COC use is contraindicated or cautioned, e.g. systemic lupus erythematosus, refer to the New Zealand Formulary: **http://www.nzf.org.nz/nzf_4178** and the United Kingdom Medical Eligibility Criteria: **https://www.fsrh.org/standards-and-guidance/uk-medical-eligibility-criteria-for-contraceptive-use-ukmec/**

Starting a COC: selecting a dose and formulation

A reasonable option for a first-time COC user is 30 – 35 micrograms ethinylestradiol with either 150 micrograms levonorgestrel or 500 micrograms norethisterone.[1] A lower dose of ethinylestradiol is recommended for older patients, e.g. > 40 years.[12]

The choice of oral contraceptive may also be influenced by whether the patient seeks non-contraceptive benefits from the medicine, e.g. a formulation containing cyproterone may be appropriate for a patient with acne or polycystic ovary syndrome, however, the benefits should be weighed against the higher VTE risk.

If a patient experiences adverse effects with one COC, another formulation may be trialled (see: "Adverse effects depend on dosing and formulation" and Table 3).

Initiation

The conventional method is to initiate a COC within the first five days of menses onset; no additional contraceptive precautions are required.[1] With the "quick start" method, the COC can be initiated on any day of the cycle, if it is reasonably certain the patient is not pregnant; additional protection (i.e. condoms) should be used for the first seven days (if not initiated during the first five days of menstruation).[1] Offer a pregnancy test 21 days after the last instance of unprotected sexual intercourse (before the COC was initiated).[1] N.B. Pregnancy tests are available on Practitioner's Supply Order (PSO) and can be provided to the patient to take home.

Tailored regimens can be offered to omit the pill-free week

COCs are typically taken in a regimen of 21 "active" hormone pills followed by a hormone-free interval of seven days, during which withdrawal bleeding occurs. However, there is no evidence to support any health benefits from having a monthly withdrawal bleed.[5] Lengthening the hormone-free interval by missing pills at the beginning or end of a cycle may increase the risk of pregnancy by allowing follicular development and ovulation in some patients.[1, 5]

Omitting the hormone-free interval may improve contraceptive effectiveness, reduce heavy bleeding and improve symptoms associated with the withdrawal bleed, such as bloating/fluid retention, headache and altered mood.[1, 5, 6] Data directly comparing the risk of cardiovascular events and cancer between standard and extended regimens

Table 3: Managing adverse effects associated with COCs.[1, 4, 5, 13]

Adverse effect	Suggested actions
Acne	Increase oestrogen; and/or Decrease progestogen or select a less androgenic or anti-androgenic progestogen, i.e. desogestrel, drospirenone* or cyproterone
Bloating/fluid retention	Decrease oestrogen; and/or Change to a progestogen with a mild diuretic effect, i.e. drospirenone*
Breakthrough bleeding	Increase oestrogen; and/or Change the type of progestogen, e.g. levonorgestrel or desogestrel
Breast tenderness	Decrease oestrogen and/or progestogen; and/or Change progestogen, e.g. levonorgestel
Headache	Decrease oestrogen; and/or Change progestogen, e.g. levonorgestrel If headaches occur in the hormone-free interval, consider an extended or continuous regimen
Abdominal cramping or heavy bleeding during the hormone-free interval	Extended or continuous regimen
Nausea	Decrease oestrogen and/or take the pill at night; and/or Change to a POP

* Drospirenone may increase potassium levels. If there are risk factors for hyperkalaemia such as renal insufficiency, liver dysfunction or adrenal gland insufficiency, a COC containing this progestogen should not be used. COC formulations containing drospirenone are currently not funded in New Zealand.

are not yet available, however, indirect evidence suggests no difference in cardiovascular risk.[5] There is also no evidence of endometrial thickening or histological abnormalities with extended or continuous regimens.[5] There is an increased risk of breakthrough bleeding when pills are taken continuously, but this declines with time.[5]

If breakthrough bleeding persists for three to four days when taking pills continuously, the pills should be stopped for four days and then resumed.[5]

If patients do not wish to omit the hormone-free interval completely, another option is to shorten this period from seven to four days. This reduces the chance of return to ovarian activity and therefore may decrease the risk of contraceptive failure, e.g. if pills are missed.[5]

A tailored regimen can be recommended to patients who are starting or already taking a COC (Table 4). There is an additional prescription co-payment cost associated with requiring more pill packs per year, i.e. if used continuously, a six-month prescription will last 18 weeks instead of 24 weeks. However, this cost may be offset by savings made from not having to purchase sanitary products.

Practice point: Advise patients that while tailored regimens are unapproved, they are recommended by the Royal Australia and New Zealand College of Obstetricians and Gynaecologists and the United Kingdom's Royal College of Obstetricians & Gynaecologists Faculty of Sexual and Reproductive Health.[1, 5]

Table 4: Examples of different regimens for COC use.[5]

Regimen	Duration of hormone pills (days)	Hormone-free interval (days)
Standard	21	7
Shortened hormone-free interval	21	4
Extended	63 or 84, i.e. 3 or 4 packets of pills	4 – 7 (every 3 – 4 packets of pills)
Continuous use	Continuous use of active pills	None

Ensure that patients understand how to follow the tailored regimen correctly

Tailoring a COC regimen requires deviation from the instructions on the COC packaging which may lead to medicine errors. Discuss the regimen options with the patient and ensure that they understand how to omit the hormone-free interval, i.e. by discarding the unused placebo pills and starting on the next pack of active pills.

For further information on initiating an oral contraceptive, including changing from another method of contraception, refer to the New Zealand Formulary: **www.nzf.org.nz/nzf_4163**

Patient information on how to take a pill continuously can be found here: **www.familyplanning.org.nz/advice/contraception/combined-oral-contraceptive-pill**

Long-term outcomes associated with COC use

Cancer

COCs are associated with a reduced risk of several cancers including endometrial, ovarian and colorectal cancers, but an increased risk of breast and cervical cancers (see: "Revisiting the link between hormonal contraception and breast cancer risk").[5]

A longitudinal study conducted in the United Kingdom which followed females* for up to 44 years estimated that COC use resulted in the prevention of:[15]

- 19% of colorectal cancers
- 34% of endometrial cancers
- 34% of ovarian cancers

COC use was associated with an estimated:

- 25% of cervical cancers†
- 3% of breast cancers

The increased risk of breast and cervical cancer was only present in current and recent users; the risk was no longer present in this study five years after stopping the COC.[15]

* Average age at recruitment was approximately 28 years; 82% had at least one child at the time of recruitment

† Human papillomavirus (HPV) infection is necessary for the development of cervical cancer. It is not certain whether the COC itself increases the risk of cervical cancer, or whether its use is associated with an increase in HPV infection rates due to sexual activity without a condom. COC use for more than five years is associated with a small increase in the risk of cervical cancer, but the risk reduces over time.[1,5]

Adverse effects and risks associated with COC use depend on dosing and formulation

Lower doses of oestrogen are associated with lower risks. Research has shown that doses of 20 micrograms of ethinylestradiol, daily, are associated with lower risks of VTE, stroke, and myocardial infarction than doses of 30 micrograms and above, daily, but more risk of breakthrough bleeding.[5]

The choice of progestogen may influence risks. Evidence regarding the safety of different progestogens is conflicting but suggests that COCs containing levonorgestrel or norethisterone may be associated with lower rates of VTE (Table 5), stroke, and myocardial infarction than COCs containing the newer generation progestogens.[5] In addition, discontinuation rates due to adverse effects such as headache, breast tenderness and nausea are lower for levonorgestrel-containing than norethisterone-containing COCs.[14]

Table 5. VTE risk according to COC formulation.[9, 10]

Group	Risk of VTE per 10,000 females per year
Non-COC users	2 – 4
Low-dose* COC with levonorgestrel or norethisterone	5 – 7
Low-dose* COC with drospirenone, desogestrel, cyproterone	9 – 12
High-dose† COC with levonorgestrel	9 – 12

* Low dose = 20 – 35 micrograms ethinylestradiol

† High dose = 50 micrograms ethinylestradiol

Mood changes

Evidence of an association between COC use and changes in mood is variable.[5] Some women may experience negative mood changes when taking a COC, however, causation has not been established.[5] Most observational studies suggest no increase in the incidence of depression with COC treatment.[5] However, COCs should be used with caution if there is a history of depression and all patients should be monitored for abnormal changes in mood.[4, 5]

Weight gain due to use of COCs is unlikely

Most evidence suggests no association between COC use and weight gain.[5] A 2014 Cochrane review covering 49 studies concluded there was no convincing evidence that use of COCs affects body weight or composition, and if any effect exists it is likely to be small.[16]

POPs: the oral contraceptive option when oestrogen use is contraindicated

Progestogen-only formulations are a suitable alternative for those who wish to use an oral contraceptive but have contraindications to oestrogen use or prefer not to use a COC.

POPs thicken cervical mucus to inhibit sperm penetration and may also prevent ovulation (50% of cycles).[17] The desogestrel-only formulation consistently inhibits ovulation (97% of cycles), but is not funded in New Zealand (Table 6).[1]

Initiation

The conventional method is to initiate a POP within the first five days of the menstrual cycle; additional contraceptive precautions are not required. With the "quick start" method, the POP can be initiated on any day of the cycle if the patient is reasonably certain they are not pregnant.[1] Patients who are sexually active should be advised to use condoms or avoid sexual intercourse for the first two days after initiating hormone pills (48 hours). A pregnancy test 21 days after the last occurrence of unprotected sexual intercourse before starting the POP is also recommended.[1]

Which POPs are available in New Zealand?

There are two fully funded POPs available in New Zealand (Table 6). Although robust head-to-head studies are not available, evidence suggests that when used correctly the different formulations of POPs available in New Zealand are equally effective in preventing pregnancy.[17]

Managing breakthrough bleeding associated with COC use

Some patients may experience breakthrough spotting or bleeding while taking COCs. This is more common within the first three months of initiation and typically settles over time.[1]

When prescribing a COC, inform patients about the possibility of breakthrough bleeding and provide reassurance that this does not reduce the contraceptive effectiveness of the COC. Patients should also be reminded that missing a pill increases the risk of breakthrough bleeding and, depending on when in the pack it is missed, may reduce the contraceptive effectiveness.

If bleeding does not settle after three months and other causes have been excluded, consider the following strategies to improve breakthrough bleeding:[1, 5, 13]

- **Increasing oestrogen dose:** changing to a formulation with a higher dose of ethinylestradiol (to a maximum of 35 micrograms)
- **Changing progestogen type:** limited evidence suggests that a levonorgestrel-containing COCs may be preferable over a formulation containing norethisterone, and that desogestrel may be preferable to levonorgestrel
- **Smoking cessation:** breakthrough bleeding is more common in COC users who smoke although the mechanism for this is not well defined

If the first instance of breakthrough bleeding is more than three months following the initiation of the COC or bleeding is persistent, consider whether there might be another clinical explanation, e.g. missed pills, medicine interactions, sexually transmitted infection, pregnancy, cervical or uterine pathology.[1]

For further information on investigating and managing abnormal vaginal bleeding, see: **https://bpac.org.nz/2019/bleeding.aspx**

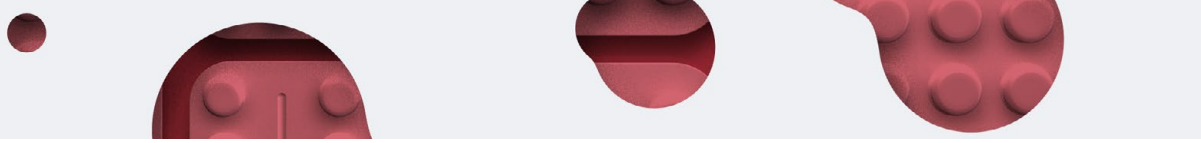

Table 6: POP formulations available in New Zealand, as of February, 2024.[4]

Progestogen type and dose		Brand name
Levonorgestrel 30 micrograms	●	Microlut
Norethisterone 350 micrograms	●	Noriday 28 Day
Desogestrel 75 micrograms		Cerazette

● Fully funded

Contraindications and cautions to POP use

POPs should not be used in patients with unexplained vaginal bleeding, severe liver disease (e.g. decompensated cirrhosis) or current breast cancer.[1, 4] Use of hormonal contraceptives in people with a history of breast cancer is generally not recommended unless other methods are not available or acceptable, as the theoretical or proven risks usually outweigh the benefits (see: "Revisiting the link between hormonal contraception and breast cancer risk").[8] Any consideration should ideally be discussed with an oncologist.[8] POPs should be used with caution in patients with current or a history of ischaemic heart disease or stroke.[1]

For further information on medical conditions where POP use is contraindicated or cautioned, refer to the New Zealand Formulary: **www.nzf.org.nz/nzf_70966** and the United Kingdom Medical Eligibility Criteria: **www.fsrh.org/standards-and-guidance/uk-medical-eligibility-criteria-for-contraceptive-use-ukmec/**

Revisiting the link between hormonal contraception and breast cancer risk

A **United Kingdom-based study published in 2023** suggests that the risk of developing breast cancer in people who take progestogen-only contraceptives is comparable to those taking combined hormonal contraceptives. In the initial analysis of records from a large primary care database, it was found that people who received any form of hormonal contraception had an increased risk of invasive breast cancer (odds ratio [OR] 1.33) compared to people who had never taken hormonal contraception. This increase was similar across all forms of hormonal contraception: oral combined (OR 1.23, 95% confidence interval [CI] 1.14 – 1.32, $p < 0.001$), oral progestogen-only (OR 1.26, CI 1.16 – 1.37, $p < 0.001$), injected progestogen (OR 1.25, CI 1.07 – 1.45, $p = 0.004$), progestogen-releasing IUD (OR 1.32, CI 1.17 – 1.49, $p < 0.001$).

The authors of the study then performed a meta-analysis, combining these results with available data from previous studies on progestogen-only contraceptives, and found similar, comparable risks between all forms of progestogen-only contraceptives. The relative risk of breast cancer with oral combined or progestogen-only contraceptive use is increased approximately 20 – 30%, however, the absolute risk after five years of hormonal contraceptive use is small:

- For people aged 16 – 20 years, the estimated 15-year absolute risk of breast cancer increased from 0.084% to 0.093%; an additional eight cases per 100,000 users
- For people aged 25 – 29 years, the estimated 15-year absolute risk of breast cancer increased from 0.50% to 0.57%; an additional 61 cases per 100,000 users
- For people aged 35 – 39 years, the estimated 15-year absolute risk of breast cancer increased from 2.0% to 2.2%; an additional 265 cases per 100,000 users

The full article is available from: **journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1004188**

Should we be concerned about these findings? While it is recommended that the new information is included when discussing the risks and benefits of contraceptive options with patients, the UK Faculty of Sexual and Reproductive Healthcare **has not currently recommended** any major changes to clinical practice in response to the study.

Best Practice Tip: The absolute risk of breast cancer with progestogen-only contraceptive use is still very small, especially in younger patients with no familial breast cancer risk. The decision to prescribe any type of hormonal contraception should consider this low risk in the context of the possible benefits of use, e.g. reduced risk of an unplanned pregnancy and other non-contraceptive benefits such as reducing the risk of endometrial and ovarian cancers.

Correct and consistent use is essential for POPs to provide effective contraception

POPs are taken continuously, i.e. an active pill each day. Advise patients considering a POP that regular adherence is essential for these medicines to be maximally effective. Norethisterone and levonorgestrel-only pills must be taken within three hours of the regular dosing time each day. Desogestrel-only pills have a wider window for error and must be taken within 12 hours of the regular dosing time.

Benefits of POPs

POPs offer the same level of contraceptive effectiveness as COCs and can be used in clinical situations where COCs are not recommended.[17]

POPs may be used when breastfeeding and can be initiated at any time post-partum, unlike COCs which should not be used in the first six weeks if breastfeeding (see: "Cautions and contraindications: when to avoid COCs").[1]

Adverse effects associated with POPs

Bleeding patterns may be unpredictable, due to the variable inhibition of ovulation; it is estimated that 50% of patients taking a POP will continue to have a normal menstrual cycle, 40% an irregular menstrual cycle and 10% no menstrual cycle.[18] Up to 70% of patients taking POPs report breakthrough bleeding and 10% report frequent bleeding, i.e. more than five episodes in 90 days.[17, 19]

Problematic bleeding may settle over time without treatment,[1] but does not always. Changing to a different POP, e.g. a desogestrel-only pill, may improve bleeding regularity in some patients.[1] An alternative method of contraception may be required in some cases. For example, the levonorgestrel IUD Mirena may be suitable for woman who experience persistent heavy menstrual bleeding.

N.B. There is no convincing evidence that POPs cause weight gain.[1]

Interactions between COCs or POPs and other medicines

The effectiveness of COCs and POPs can be reduced by interactions with medicines that induce hepatic metabolism by the CYP3A4 enzyme, e.g. rifampicin, rifabutin, carbamazepine, oxcarbazepine, nevirapine, phenytoin, phenobarbital, primidone, ritonavir, St John's wort and topiramate.[1, 20] COC or POP absorption may be reduced by concurrent use of laxatives if they cause diarrhoea or are used excessively or inappropriately. The effectiveness of other medicines may be affected by COCs or POPs, e.g. there is a moderate theoretical risk that oestrogens increase levothyroxine requirements.

Interactions between oral contraceptives and other medicines can be checked here: **www.nzf.org.nz/nzf_1**

Reminder: accredited pharmacists can supply selected oral contraceptives without a prescription

The reclassification of selected oral contraceptives in 2017 allows accredited pharmacists to supply the following formulations without a prescription to medically eligible patients:[21]

- COCs with ≤ 35 micrograms of ethinylestradiol combined with levonorgestrel or norethisterone (can be supplied to patients aged 16 – 39 years)
- POPs with levonorgestrel, norethisterone or desogrestrel alone (can be supplied to patients aged 16 – 52 years)

Registered pharmacists must complete an approved training programme to be able to supply these oral contraceptives.

A comprehensive assessment is required to determine whether the patient meets the requirements for the pharmacist-supply of the COC or POP. The selected oral contraceptive **must** have been prescribed by a medical practitioner in the last three years, the patient must have had at least one further appointment with a medical practitioner since initiating the oral contraceptive and the patient must see a medical practitioner at least once every three years (to assess continued suitability of the oral contraceptive and for a sexual health check). The pharmacist must supply the same formulation of oral contraceptive that the patient was originally prescribed (refer to the Practice Guidelines for some exceptions to this). With consent from the patient, the pharmacist should notify the patient's medical practitioner that they are supplying their COC or POP.

The practice guidelines for the pharmacist-supply of selected oral contraceptives is available here: **https://www.psnz.org.nz/Folder?Action=View%20File&Folder_id=167&File=Pharmacist%20SOC%20Guidelines%20(May%202018).pdf**

Managing patients taking enzyme-inducing medicines

Patients who are taking an oral contraceptive and an enzyme-inducing medicine short-term, i.e. fewer than two months, should be advised to use condoms for the duration of treatment with the enzyme-inducing medicine and for a further four weeks after stopping.

If the enzyme-inducing medicine is required long-term, recommend an alternative contraceptive, e.g. medroxyprogesterone injection or an intrauterine contraceptive.

 For further information on the use of antiepileptic medicines in females, see: **www.bpac.org.nz/2018/antiepileptic.aspx**

Most broad-spectrum antibiotics do not interact with oral contraceptives

Most antibiotics, aside from rifampicin and rifabutin, do not have a clinically relevant interaction with oral contraceptives and patients do not need to take extra precautions as long as they are taking their contraceptive consistently and correctly.[20] However, if the antibiotic or the illness it is treating causes vomiting or diarrhoea, additional contraceptive precautions might be required (see: "Recommendations for missed COCs or POPs").

Recommendations for missed COCs or POPs [4, 5]

A missed COC pill is when ≥ 24 hours have passed since the regular dosing time. The missed pill should be taken as soon as it is remembered, and the next pill taken at the usual time, even if that means taking two pills at once. No extra contraceptive precautions are necessary.

If two or more COC pills are missed, one active pill should be taken as soon as it is remembered, and the normal regimen then resumed. Condoms should be used, or sex avoided, until seven consecutive hormone pills have been taken. For patients using a standard COC regimen, additional precautions depend on when in the regimen the pills are missed:

- Week 1 (after hormone-free interval) – if unprotected sex has occurred during the hormone-free interval or week 1, offer use of emergency contraception
- Week 3 (prior to hormone-free interval) – omit the hormone-free interval

Theoretically, up to eight consecutive pills could be missed during week 2 or 3 of a standard regimen or at any time during a continuous regimen, before additional contraceptive precautions would be required (provided the hormone-free interval is omitted if the missed pills are in week 3 of a standard regimen, and seven hormone pills were taken consecutively before the missed pills). However, evidence is lacking on the outcomes of this practice, therefore, there is currently a lack of consensus on this recommendation.

For POPs, a missed pill is if more than three hours have passed since the regular dosing time for norethisterone or levonorgestrel-only pills or more than 12 hours for desogestrel-only pills. The missed pill should be taken as soon as it is remembered. If more than one pill has been missed, only one should be taken. The next pill should be taken at the regular dosing time and condoms should be used, or sex avoided, for the next 48 hours. If unprotected sexual intercourse has occurred after the missed pill and within 48 hours of restarting the POP, emergency contraception should be offered.

Vomiting and diarrhoea may interfere with the absorption of COCs and POPs. If vomiting occurs and less than two hours have passed since taking a COC or POP, another pill should be taken as soon as possible. If the replacement POP is taken more than three hours after the regular dosing time (12 hours for a desogestrel-only pill), additional contraceptive precautions will need to be taken during the illness and until two consecutive hormone pills have been taken. If the replacement COC is taken within 24 hours of the regular dosing time, additional contraceptive precautions are not required.

If vomiting or diarrhoea is persistent, i.e. lasting more than 24 hours, an additional contraceptive method should be used during the illness and until:

- Seven consecutive hormone pills have been taken if using COCs
- Two consecutive hormone pills have been taken if using POPs

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