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Prescribing the oral contraceptive pill:

key considerations for primary care physicians

Despite the apparent simplicity in the two options available, the combined oral contraceptive pill (COCP) vs. the progestogen-only pill (POP), choosing the right oral contraceptive pill can be challenging. With an increasing number of preparations and their inherently varying pharmacological properties, several factors require consideration when prescribing in the primary care setting.[1] Assuming this is the most appropriate method of contraceptive cover, the aim of this article is to provide primary care physicians (PCPs) with a series of key considerations when counselling women on the oral contraceptive pill.

KEY CONSIDERATION 1: COCP OR POP?

One of the initial considerations for all PCPs is deciding between the COCP or POP.

With detailed guidance on the safety profile of the oral contraceptive pill available from the UK Medicine Eligibility Criteria (UK MEC),[2] a summary of the key patient characteristics and medical conditions favouring the use of the POP, over the COCP, has been listed in Table 1.

However, compared with the COCP, PCPs must be clear when counselling women of the higher risk of unscheduled bleeding along with the implication of a 'missed pill' with the POP.[3] While desogestrel-containing POPs have a longer window for retaining contraceptive efficacy compared with more traditional POPs (12 hours vs. 3 hours), alternative forms of contraception should be sought if adherence is considered problematic. It is important to note that the two POPs now available over the counter in the UK, Hana and Lovima, contain desogestrel.

KEY CONSIDERATION 2: TYPE AND DOSE OF OESTROGEN IN COCP

The majority of COCPs contain varying doses, between 20–35 µg, of the synthetic oestrogen, ethinylestradiol.

Analysing comparative studies of the different COCP preparations available is difficult because of the wide variations in the oestrogen dose, as well as the type and dose of progesterone present.[4] However, PCPs are generally encouraged to start with the lowest possible oestrogen dose when prescribing the COCP.[5] The aim is to avoid the side effects associated with higher doses, of which headaches, bloating, and weight gain are the most common, and which subsequently may lead to discontinuation. However, lower doses have

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Table 1. Summary of patient characteristics and medical conditions more suitable for POP compared with COCP

Patient characteristics	Age	>45 years old
	BMI	>30
	Smoking	Age >35 years old and >15 cigarettes a day
	Breastfeeding	<6 weeks post-delivery
Medical conditions	Cardiac	Impaired cardiac function
		Cardiac arrhythmias
	Neurological	Migraine with aura
	Haematological	Personal or strong family history of VTE
	Vascular disease	
	Organ transplant	

BMI = body mass index. COCP = combined oral contraceptive pill. POP = progestogen-only pill. VTE = venous thromboembolism.

Table 2. Summary of characteristics of synthetic progestogens and indications for use[a]

Generation	Progestogen	COCP preparation		Available as POP	Physiological activity	Best formulation for use
		Monophasic	Multiphasic			
1st	Medroxyprogesterone	✓	X	✓	Moderate androgenic Minor glucocorticoid	Irregular or missed periods
	Norethisterone	✓	✓	✓	Moderate progestogenic Mild androgenic	Menorrhagia, adenomyosis
2nd	Levonorgestrel	✓	✓	✓	Strongly progestogenic Strongly androgenic	Menorrhagia, adenomyosis
3rd	Desogestrel	✓	X	✓	Strongly progestogenic	Dysmenorrhoea, endometriosis
	Norgestimate	✓	X	X	Medium progestogenic Weakly androgenic	Moderate acne
	Gestodene	✓	X	X	Strongly progestogenic Mildly androgenic	Dysmenorrhoea
4th	Drospirenone	✓	X	X	Anti-androgenic Anti-mineralocorticoid	Acne, PCOS, PMS
	Dienogest	X	✓	✓ POP not licensed for contraceptive purposes in UK	Anti-androgenic	Endometriosis
	Nomegestrol	✓	X	X	Targeted anti-oestrogenic at endometrium Partial anti-androgenic	Menorrhagia, PCOS, PMS

[a]The indications for use apply regardless of whether the progestogen is prescribed in combination with oestrogen or if available, as the POP. COCP = combined oral contraceptive pill. PCOS = polycystic ovarian syndrome. PMS = pre-menstrual syndrome. POP = progestogen-only pill.

Table 3. Indications for use according to COCP regimen

Regimen type	Pattern of COCP use	Indications
Traditional	21 days on pill 7 days off pill	For women keen to maintain a regular bleed and are symptom free during their periods
Tailored use	24 days on pill 4 days off pill	Shorter bleeding time and suitable for women keen to reduce symptoms from their periods but who wish to maintain a regular withdrawal bleed
Extended	3 months on pill 7 days off pill	Ideal for those with severe pain or mood swings in the lead up to or during their periods, for example, endometriosis, PMS
Continuous	Continuous use with no pill-free days	Ideal for those with severe pain or mood swings in the lead up to or during their periods, for example, endometriosis, PMS May be associated with unscheduled bleeding

COCP = combined oral contraceptive pill. PMS = pre-menstrual syndrome.

been associated with unscheduled bleeding, with one meta-analysis suggesting that the risk was nearly doubled for women on a 20 µg COCP versus a 30 µg preparation.[4] Therefore, PCPs are advised to steadily increase the oestrogen dose until adequate cycle control is achieved.

For women keen to explore natural oestrogen preparations and potentially avoid the side effects associated with synthetic preparations, estradiol valerate (Qlaira) and estradiol hemihydrate (Zoely) are now available in the UK. However, women should be counselled that data regarding their tolerability are limited. One large multicentre study in Asia has suggested a high tolerability for estradiol valerate preparations (92% of women reported being either satisfied or somewhat satisfied).[6] However, this has not been replicated for estradiol hemihydrate preparations, with a higher incidence of acne, weight gain, and discontinuation rates compared with more established COCPs.[7] It is important to stress though that research focusing on targeted and natural oestrogen preparations remains ongoing.

KEY CONSIDERATION 3: COCP PREPARATION AND REGIMEN

COCPs can be further subdivided into monophasic or multiphasic preparations depending on whether the hormone dose varies throughout the pill pack.[5] While multiphasic preparations aim to mimic the body's natural hormone response and therefore reduce the likelihood of side effects, this would not be recommended for women who are susceptible to hormonal fluctuations such as in pre-menstrual syndrome (PMS).[8] It is important to note here that the majority of preparations widely available in the UK are monophasic (Table 2).[1,5]

With the COCP forming a key management option for several gynaecological problems, deciding whether the COCP is to be given as a cyclical, extended, or continuous regimen is also important. While recent guidance has recommended moving away from a traditional cyclical regimen, towards an extended or continuous regimen for

Table 4. Side effects of progestogens in relation to physiological activity

Physiological activity	Side effects
Progestogenic	Breast tenderness, change in bowel activity, bloating, increased appetite, tiredness, mood changes, skin changes
Androgenic	Oily skin, acne, hirsutism, weight gain, mood changes
Glucocorticoid	Mood swings, increased appetite, water retention
Mineralocorticoid	Water retention, bloating

women who suffer from pain or mood swings during their periods, this has been associated with unscheduled bleeding.[8] PCPs should also consider each woman's own preference regarding the regularity of menstruation when choosing the regimen.

A summary of the different regimens and indications for use is provided in Table 3.

KEY CONSIDERATION 4: TYPE OF PROGESTERONE

The options for progesterone cover have increased dramatically over the last few years. Traditionally, synthetic progesterones or progestogens are classified by the decade of their introduction or 'generation'. While newer generations are generally associated with fewer progestogenic side effects, even within each generation there can be significant variations in their mechanism of action.[9-10] With progestogens known to exert a wide range of androgenic, glucocorticoid, and mineralocorticoid effects, these must be carefully considered by PCPs when prescribing progesterone either as the POP (if available) or in combination with oestrogen.

A summary of the key progestogens available in the UK, physiological activity, and indications for prescribing are presented in Table 2. Preparations containing cyproterone have not been included in this list because of their main mechanism of action being as an anti-androgen. In addition, the common side effects of progestogens in relation to their physiological activity have been provided in Table 4.

At present, natural or micronised progesterones are unlicensed for the contraceptive pill.

CONCLUSION

With up to 50% of women discontinuing the oral contraceptive within the first year of its use,[5] being aware of the different preparations, as well as their availability, is important for PCPs. While the purpose of this article was not to 'name' every single type of contraceptive pill that is currently available — which would be difficult considering the amount of research and change that is ongoing in this area — the aim instead was to provide PCPs with a set of key considerations. By doing so, it will not only enable a more individualised approach to be delivered but also, more importantly, provide reassurance for women.

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