

## FACULTY



**Dr Ginni Mansberg**

B.MED  
General Practitioner  
Sans Souci, NSW

### Why extend the cycle?

#### Benefits of extended-regimen COCPs

A Cochrane review evaluated the use of 21/7 day regimens with extended-regimen COCPs. The review included six randomised controlled trials with results and conclusions as follows:<sup>3</sup>

- Contraceptive efficacy and compliance were similar in both the extended and cyclic arms of the trials
- Five out of six studies found that bleeding patterns were similar or improved with extended dosing regimens
- Extended dosing reduced associated symptoms such as menstrual headaches, genital irritation, tiredness, bloating and menstrual pain



## Seasonique – Extending Oral Contraceptive Regimens Extends the Choices for Women

### THE MONTHLY MENSES MYTH

Combined oral contraceptive pills (COCPs) were traditionally prescribed as a 28-day regimen, consisting of a 21-day course of hormones followed by a hormone-free interval (HFI) of seven days. The attempt to mimic the “natural” 28-day menstrual cycle is both unnecessary from a health perspective<sup>1-3</sup> and often unwanted from a patient perspective<sup>4,5</sup>, and a growing awareness of this has led to the development of extended OCP options.

A 2016 study of contraceptive use in Australia reported that the oral contraceptive pill remains the most popular contraceptive choice amongst women aged 16 to 49 years.<sup>1</sup> Women’s attitudes to monthly menstrual cycles have, however, shifted. Women with regular menstrual cycles are interested in decreasing the frequency of their periods, and over 80% of women of reproductive age report that they would prefer shorter, lighter menses and/or amenorrhea to their current cycle.<sup>2</sup>

### When to consider extending the COCP regimen

The reduction in hormone fluctuations may contribute to reducing the incidence of associated symptoms, including:<sup>2</sup>

- Dysmenorrhea
- Menstrual migraine (without aura)
- Premenstrual syndrome
- Menorrhagia
- Ovarian cysts
- Endometriosis
- Pelvic pain

Extended regimens should also be considered for women who forget to take their COCP, or who are taking medications that reduce the efficacy of their oral contraceptive as the chance of ovulation is reduced. Moreover, many women prefer extended regimens because of the inconvenience of menstrual bleeds when traveling, playing sport or in a social context.<sup>4</sup>

The RANZCOG Combined Hormonal Contraceptives 2019 guidelines, states that potential disadvantages of extended regimens could be increased cost (depending on the reference script, although some private scripts are more costly) and, for some women, unpredictable bleeding<sup>5</sup>. However, there may be costs savings resulting from reduced need for sanitary products.

## The role of low-dose estrogen

A 2008 study compared the same hormone combination of levonorgestrel (LNG) 150 mcg and (ethinylloestradiol) EE 30 mcg in three different cycle regimens:<sup>6</sup>

- 1) Three 21/7 day cycles (21 days of active tablets followed by seven days of placebo, for three consecutive cycles)
- 2) One 84/7 day cycle (84 days of active tablets followed by seven days of placebo)
- 3) One 84/7EE cycle (84 days of active tablets followed by seven days of low-dose oestrogen 10 mcg)

The study concluded that replacing the HFI with EE after an extended regimen of 84 days of active tablets was the most effective method of decreasing FSH and inhibin B levels and the number of developing follicles.<sup>6</sup> The 84-day extended regimen showed consistently lower estradiol levels, and replacing the seven-day HFI with low-dose EE provides greater pituitary-ovarian suppression, and decreased risk of escape ovulation.<sup>6, 7</sup>

## Seasonique – extending the OCP regimen with low dose EE

Seasonique is the only extended-regimen COCP with low-dose EE in place of the HFI available in Australia. This combination includes 91 tablets: 84 active tablets containing LNG 150 mcg / EE 30 mcg active tablets and seven low-dose EE 10 mcg tablets. This formulation incorporates a new dosing schedule of levonorgestrel and ethinylloestradiol, which are both considered first-line COCP options.<sup>8</sup> For more information please refer to the Seasonique product information.

## Addressing common patient concerns and misconceptions

There are many misconceptions surrounding the use of extended-regimen COCPs and it is important for GPs and other primary health practitioners to recognise common patient concerns and be able to educate women regarding the safe and effective use of their COCPs.

Here are some helpful questions and answers regarding extended-regimen COCPs.

### 1. Is a hormone free interval essential?

Some women are wary of extended COCP regimens, as they believe it is 'natural' to menstruate monthly. While there are some women who desire a cycle that more closely resembles a natural cycle, others enjoy having a decreased bleed or no monthly bleed.<sup>9</sup> It is important to reassure women that bleeding that occurs when taking the contraceptive pill is not a menstrual bleed but rather a withdrawal bleed that occurs as a result of changes in exogenous hormone levels. Withdrawal bleeding on COCP is usually shorter and lighter than menstruation and there is no physiological requirement to schedule a regular withdrawal bleed every month.<sup>10</sup> Many women go without any withdrawal bleed for extended amount of time when using a LARC or IUD.

### 2. Does a withdrawal bleed confirm absence of pregnancy?

Some women worry that each missed monthly period represents a possible pregnancy and may use the monthly withdrawal bleeds to reassure themselves that they are not pregnant.<sup>11, 12</sup> However, with reassurance regarding the safety of this approach, most women would prefer to delay or minimise the frequency of bleeds.<sup>12</sup>

It's important to note that 20-40% of pregnant women will experience bleeding during the first trimester,<sup>13</sup> and the best way to avoid pregnancy is to adhere to a regular schedule of daily pill taking- perfect use of COCP results in 99.7% efficacy, while typical use results in 91% efficacy.<sup>13</sup>

## Take home messages<sup>12,2,16,22</sup>

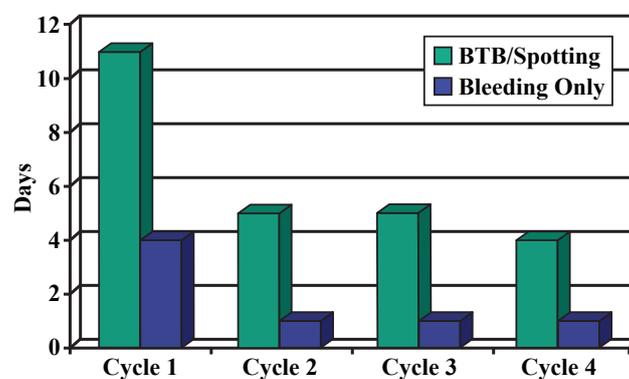
- Seasonique is an extended-regimen COCP containing LNG/EE which eliminates the HFI, decreases the frequency of menses from every month to every three months, and reduces the intensity and duration of the withdrawal bleed.
- Extended-regimen COCPs may be preferred by women seeking effective contraception who want to avoid monthly menses and the impact on their daily life and in addition would like to reduce the hormonal fluctuations.
- For women who simply don't wish to have a monthly period.
- Extended-regimen COCPs may be useful for women with medical conditions who would benefit from less frequent withdrawal bleeds.
- Fertility is quickly resumed on discontinuation of extended-regimen COCPs with 99% of women reported spontaneous menstruation or pregnancy within three months of discontinuation.

### 3. How do extended-regimen COCPs compare to traditional 21/7 regimens in regards to pregnancy and fertility?

Studies investigating the return to fertility following the discontinuation of extended-regimen COCPs have shown that fertility promptly resumes. Among women who discontinued extended-regimen COCPs without commencing another form of hormonal contraception, the median time to withdrawal bleeding was 32 days, with 77% of women returning to ovulatory capacity within this time. Moreover, 99% of women reported spontaneous menstruation or pregnancy within three months of discontinuation.<sup>12</sup>

### 4. Does extending the COCP cycle increase the risk of side effects?

After a year of use, around 10% of women taking any low dose COCP still report unscheduled bleeding.<sup>14</sup> The most common causes are non-adherence to the strict daily medication-taking, gut malabsorption (i.e. significant vomiting, severe diarrhoea, chronic malabsorption), certain medications and smoking.<sup>14</sup> Undiagnosed chlamydial infection also increases the risk of break-through bleeding.<sup>15</sup> Extended-regimen LNG/EE with low dose EE supplementation (84/7 regimen) has a higher rate of breakthrough bleeding than standard dosing of the COCP.<sup>8</sup> However, the rate of breakthrough bleeding and spotting was found to decrease with subsequent cycles.<sup>16,17</sup>



**Figure 1:** Median unscheduled break-through bleeding (BTB)/spotting and bleeding days for extended-regimen LNG/EE with low-dose EE supplementation.<sup>17</sup> The graph indicates BTB/spotting at a rate of less than 1.5 days per month in cycles two to four.<sup>17</sup>

Adapted from Anderson FD, et al. *Contraception*. 2006;73(3):229-34.

Some patients may express concern that cumulative oestrogen exposure may increase certain safety risks. However, current data suggests that extended regimens have the same rates of adverse events as 21/7 day cycles. Moreover there is no evidence that the risk of stroke, myocardial infarction or thrombosis is increased with extended regimens<sup>3</sup> over standard COCP regimens<sup>12</sup>

### 5. Is it safe to delay withdrawal bleeds for up to three months? Doesn't the endometrium 'build up'?

Women may be concerned about the theoretical effects on the endometrium with extended-regimen COCPs,<sup>18</sup> especially those that contain oestrogen tablets in place of the HFI. Analysis of endometrial effects of extended-regimen LNG/EE with low dose EE supplementation found no evidence of endometrial hyperplasia and confirmed that this regimen has an acceptable safety profile. Studies have also shown a rapid return to normal cycling endometrial histology following discontinuation of the regimen.<sup>12,19</sup> Advise patients that when they take any COCP (whether an extended regimen or a monthly regimen) the bleed they experience is a withdrawal bleed, as the uterine lining does not thicken or 'build up' as it does in the absence of a COCP.<sup>20</sup>

### 6. Is there an increased risk of VTE with extended regimens?

The risk for VTE complications with COCP use increases substantially in the presence of other risk factors.<sup>8</sup> Extended-regimen COCPs may theoretically expose women to an increased cumulative amount of oestrogen compared with traditional 21/7 day cycles. While the risk of VTE in extended regimens is a concern, current data does not demonstrate an increased risk of VTE with these extended-regimens.<sup>16,21</sup>

Seasonique, like many other COCPs, is contraindicated with presence or risk of VTE.<sup>8</sup>

## Seasonique - a familiar contraceptive with a unique dosing regimen

Extended-regimen COCPs may be preferred by women in the following circumstances:<sup>4, 8, 16</sup>

- (Young) women who are missing several days each month of school, university and workdays because of hormonal fluctuations, menstrual pain and other menstruation-related problems (who may also request a medical sick-leave certificate)
- Women who want to avoid monthly menses and minimise hormone fluctuations
- Those who simply don't wish to have a monthly period
- Those who want to avoid the inconvenience of menstrual bleeds when traveling, playing sport or in a social context
- Women with medical comorbidities who would benefit from less frequent menstrual bleeds

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