West of Scotland Sexual Health Managed Clinical Network

NHS Ayrshire & Arran | NHS Dumfries & Galloway | NHS Forth Valley | NHS Greater Glasgow and Clyde | NHS Lanarkshire

West of Scotland Guideline ***Approved May 2022***

COMBINED HORMONAL CONTRACEPTION

What's New

Remote prescribing can be facilitated with the use of self-reported BP and BMI recordings

FSRH CEU guidance on Emergency Contraception (EC)[1] has been updated to include more detailed advice on delaying versus immediate starting combined oral contraception (COC) after ulipristal acetate (UPA) EC use[3].

If UPA-EC is chosen, hormonal contraception should not generally be started for 5 days after the UPA-EC has been taken.
There is one exception to this. In the specific situation in which combined oral contraceptive pills are restarted after a scheduled hormone-free interval and then pills are missed later in the first week of pill taking, use of LNG-EC should be considered but if UPA-EC is chosen, pill-taking can be resumed immediately

Combined Oral Contraception (COC)

- Described as any oral hormonal preparation containing an oestrogen in conjunction with a progestogen.
- In current practice, low dose COCs contain 20 – 35 micrograms (mcg) of ethinylestradiol (EE) in combination with a progestogen.
- Progestogens include norethisterone, levonorgestrel, desogestrel, gestodene, norgestimate and drospirenone.
- The primary mode of action of this type of preparation is to prevent ovulation. These pills are packed in 21 day packs but are also available as every-day packs with placebo tablets to aid concordance with the method.
- Extended and tailored regimens can be offered (with the client made aware of off license use)
- There are 2 products containing oestradiol (Zoely® with oestradiol hemihydrate combined with nomegestrol in a 28 day pack, and Qlaira® with oestradiol valerate combined with dienogest in a 28 day pack), but neither are approved by SMC for contraceptive use within Scotland

Combined Transdermal Patch (CTP)

- Currently in the UK there is one transdermal contraceptive patch which releases 33.9 micrograms ethinylestradiol and 203 micrograms norelgestromin per 24 hours (Evra®).
- One patch to be applied once weekly for three weeks, followed by a 7 day patch free interval
- Extended and tailored regimens can also be discussed

Combined Vaginal Ring (CVR)

- The combined vaginal ring (Nuvaring®) consists of ethylene vinylacetate (latex-free) and releases 15 micrograms ethinylestradiol and 120 micrograms etonogestrel daily. One ring should be inserted vaginally for 3 weeks of use per cycle.
- This should then be removed and a new ring inserted after a 7-day ring-free break.
- Rings must be kept refrigerated prior to dispensing to the client. Thereafter, they can be stored at room temperature and used within 4 months. Women should therefore only be supplied with up to 3 rings at a time.
- Extended and tailored regimens can also be discussed

Indications for CHC Use

- Women wishing to control their fertility or menstrual cycle and who have no contraindications to its use (see UK Medical Eligibility Criteria below).

Women wishing to use CHC for menstrual control should be informed that this is outside the product licence (with the exception of Qlaira).

Efficacy

- A Cochrane review comparing the combined patch, ring and pill has concluded that these methods have similar efficacy.
    - Perfect use: (following directions for use) the failure rate is 0.3%
    - Typical use: (actual use including inconsistent or incorrect use) is 9%.
    - **Women should be informed of the typical use failure rate**

The Faculty have recommended caution in women greater than 90kg using the CTP due to concerns over efficacy. This is independent of BMI. These women should consider alternative methods of contraception other than the CTP.

Side Effects

Common side effects

- Nausea
- Headache
- Mastalgia
- Skin reactions including photosensitivity
- Chloasma
- Reduced menstrual loss
- Unscheduled bleeding
- Amenorrhoea
- Contact lenses may irritate

Less common side effects

- Changes in libido
- Mood changes (no evidence causes depression)
- Chorea
- Hypertension
- Impairment of LFTs
- Hepatic tumours

Further information is available in the Faculty guidance comparing the side effects of the combined hormonal methods.

Risks

At first prescription of CHC all women should be informed that:

- CHC use is safe for the majority but can be associated with rare but serious harms
- Venous thrombo-embolism (VTE):
  - There is a small increase in the risk of VTE with CHC use.
  - This risk is highest in the first 4 months of CHC use.
  - It reduces but remains stable thereafter.
  - The risk returns to that of non-users within weeks of discontinuation. (see table below).
  - When counselling women it is important to emphasise that while some progestogens within CHCs may be associated with a higher risk of VTE than others, the risk of a venous thrombosis in women who use the CHC is very small – smaller than that associated with pregnancy and the puerperium.

CHC use and Risk of VTE

	Risk of VTE per 10,000 women years
Non contraceptive users and not pregnant	2
CHC containing ethinylestradiol plus levonorgestel, norgestimate or norethisterone	5-7
CHC containing etonogestrel (ring) or norelgestromin (patch)	6-12
CHC containing ethinylestradiol plus gestodene, desogestrel or drospirenone	9-12
Pregnancy	29
Immediate Postpartum period	300-400

- There may be a small increase in the risk of heart attack with CHC use. (Please see UKMEC tables)
- There may be an increased stroke risk, particularly in migraine sufferers with associated aura (see UKMEC)
- Any increased risk of breast cancer is likely to be small (RR 1.24) and returns to no increased risk 10 years after stopping COC. Users of COCs have not been found to be associated with increased mortality from breast cancer.
- There may be a very small increase in the risk of cervical cancer that increases with increasing duration of use. This returns to that of never-users 10 years after stopping CHC
- Use of COC is associated with a reduced risk of ovarian and endometrial cancer that continues for several decades after stopping.

Key symptoms that should prompt women to seek urgent medical review
► Calf pain, swelling and/or redness
► Chest pain and/or breathlessness and/or coughing up blood
► Loss of motor or sensory function

Key symptoms that should prompt women to seek medical review
► Breast lump, unilateral nipple discharge, new nipple inversion, change in breast skin
► New onset migraine
► New onset sensory or motor symptoms in the hour preceding onset of migraine
► Persistent unscheduled vaginal bleeding

New medical diagnoses that should prompt women to seek advice from their contraceptive provider (and review of the suitability of CHC)
► High blood pressure
► High body mass index (>35 kg/m2)
► Migraine or migraine with aura
►Deep vein thrombosis or pulmonary embolism
► Blood clotting abnormality
► Antiphospholipid antibodies
► Angina, heart attack, stroke or peripheral vascular disease
► Atrial fibrillation
► Cardiomyopathy
► Breast cancer or breast cancer gene mutation
► Liver tumour
► Symptomatic gallstones

Possible Drug Interactions

It is recommended that you check the current status of drug interactions with Medscape drug interaction checker (http://reference.medscape.com/drug-interactionchecker), current CEU Guidance, BNF (www.medicinescomplete.com) and, if necessary, any interaction with HIV drugs (www.hiv-druginteractions.org)

Ulipristal acetate e.g. ellaOne®

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There is one exception to this. In the specific situation in which combined oral contraceptive pills are restarted after a scheduled hormone-free interval and then pills are missed later in the first week of pill taking, use of LNG-EC should be considered but if UPA-EC is chosen, pill-taking can be resumed immediately.

Liver enzyme inducing drugs

- Increase the metabolism of estradiol and progestogens and the efficacy of CHC may be reduced.
- Risks of CHC use and taking liver enzyme inducing drugs outweigh potential benefits (UKMEC 3) and an alternative method unaffected by enzyme inducing drugs is recommended. Further information regarding the effects of CHC on other medications can be found in FSRH drug interactions guidance. http://www.fsrh.org/standards-and-guidance/documents/ceu-clinical-guidance-drug-interactions-with-hormonal/
- Short term (< 2months) liver enzyme inducing drug use:
  Can continue using CHC but they should be advised to use additional contraceptive precautions (e.g. condoms) while taking the enzyme-inducing drug and for 28 days after stopping treatment. To minimise the risk of contraceptive failure the CEU recommends an extended regimen (taking CHC continuously or tricycling with a shortened pill-/patch- or ring-free interval of 4 days.
- Long term liver enzyme inducing drug use:
  If still chooses to use COC as a long-term method, she should use a regime containing at least 50 micrograms of Ethinylestradiol.
  A 50 micrograms EE dose may be made up from an appropriate 30 micrograms plus 20 micrograms preparation.
  An extended or tricycling regime with a pill-free interval of 4 days should be followed
  Additional contraception is not required.
  If women are on Rifampicin or Rifabutin, an alternative method of contraception should be advised as the regimen above may not be effective.
- Breakthrough bleeding:
  This may indicate low serum EE concentrations. If other causes (e.g. chlamydia) have been excluded, the dose of EE can be increased up to a maximum of 70 micrograms EE.
- For women using the combined contraceptive patch or ring, information should be given on the use of alternative contraceptive methods if liver enzyme-inducers are to be used long term. The use of two patches or two rings is not recommended.

Lamotrigine:
Please note that Lamotrigine is not a liver enzyme inducing drug and that use of CHC inwomen taking antiepileptic drugs is UKMEC1.

However the estrogen in CHC can reduce Lamotrigine levels which may result in change in seizure frequency. Therefore women on lamotrigine should not start CHC without informing their neurologist.

Withdrawal of CHC in a client already on lamotrigine can result in Lamotrigine toxicity, and patients should be made aware of this.

Further information is available in the Lamotrigine SPC which is available on line.

Antibiotics

- Non-enzyme inducing antibiotics:
  The CEU no longer advises that additional precautions are required to maintain contraceptive efficacy when using antibiotics with combined hormonal methods.
  However if the **antibiotics** (and/or the illness) caused **vomiting or diarrhoea**, then the usual **additional precautions** relating to these conditions should be observed.

- Rifampicin:
  Women who are given Rifampicin short term (.e.g. for meningococcal meningitis prophylaxis) should be advised to use the barrier method in addition to COC during treatment and for 28 days after stopping Rifampicin.

Anti-obesity medication

- Orlistat (Xenical/Alli) – these may cause diarrhoea and reduce absorption. Additional precautions are advised in these situations.

Further information regarding the effects of combined hormonal contraception on other medications can be found in FSRH Drug interactions guidance - https://www.fsrh.org/standards-and-guidance/documents/ceu-clinical-guidance-drug-interactionswith-hormonal/

Assessment of Client Suitability

History

Clinical history taking and examination allow an assessment of medical eligibility for CHC use and possible contraceptive options for the woman. In this context the history should include relevant social, sexual (to assess risk of sexually transmitted infections – STI), medical, family and drug history as well as details of reproductive health and previous contraceptive use.
This history should be updated annually.

Examination

- Blood pressure and BMI should be recorded and noted
- Self-reported recordings are acceptable for remote prescribing
- Breast examination, pelvic and genital examinations, cervical cytology screening and routine lab tests do not contribute substantially to CHC safety and are not recommended routinely but should be performed if clinically indicated for other reasons

Choice of Preparation

Aim to choose the lowest dosage of oestrogen and progestogen that

- Maintains efficacy
- Has fewest side effects
- Gives good cycle control
- Takes into account differential risk of VTE
- Is cost effective

A monophasic COC containing 20 - 35 micrograms of ethinylestradiol with a low dose of either norethisterone or levonorgestrel is a suitable first line option. Examples are Rigevidon, Ovranette, Microgynon 30, Ovysmen, Brevinor,. Tailored regimes may improve bleeding patterns and hence improve compliance. Please see FSRH guidance for alternative COC regimes.

Transdermal or Intravaginal preparations may be advantageous in situations where GI absorption is compromised eg Inflammatory bowel disease, or in situations where this method will improve compliance.

Table: CHC Preparations

Monophasic preparations Grouped by progestogen type and generation	Oestrogen dose	Brand names
Norethisterone (1st)	35 micrograms EE	Brevinor® Norimin®
Levonorgestrel (2nd)	30mcg EE	Microgynon 30® Ovranette® Rigevidon® Levest Maexeni Ambelina
Desogestrel (3rd)	30 mcg EE 20 mcg EE	Marvelon® Gedarel 30/150® Cimizt Mercilon® Gedarel 20/150® Bimizza
Gestodene (3rd)	30 mcg EE 20 mcg EE	Femodene® Katya® Akizza Millinette 30/75® Femodette® Sunya® Millinette 20/75®
Cyproterone (equivalent to 3rd)	35 mcg EE	Co-cyprindiol Dianette® Clairette® Teragezza
Norgestimate (3rd)	35 mcg EE	 Cilique Lizinna
Drospirenone (4th)	20 mcg EE 30 mcg EE	Eloine Yasmin® Lucette Yacella Dretine Yiznell Dretine
Triphasic pills with varied progestogens	30 – 40 mcg EE	 TriRegol® Triadene
Phasic with Dienogest (4th)	1 – 3 mg Estradiol valerate	Qlaira®
Nomegestrel acetate (4th)	1.5mg Estradiol hemihydrate	Zoely
Low Dose Patch with norelgestromin	20 mcg EE	Evra®
Intravaginal ring with etonogestrel	15 mcg EE	Nuvaring® SyreniRing

Prices vary between health boards and between Primary and Secondary Care. First choice preparation will be guided by the stock arrangements/availability within each service.

Documentation

- The full visit history should be completed / updated on NaSH.
- Written method information including information about actions after missed pills, ring or patch and a contact number is given to client.
- Record prescription on NaSH
- Nurse supplying where appropriate under patient group direction.
- Consider notifying GP of prescription, if permission is given for correspondence

First Prescription

At first prescription of CHC all women should be informed that CHC use is safe for the majority but can be associated with rare but serious harms. The risks, benefits and side effects mentioned above should be discussed.

Follow Up Arrangements

Return Visit

- The women should be encouraged to attend their GP for follow up and ongoing supply of CHC
- 12 months supply (except for NuvaRing) may be issued to clients at the initial visit and
- thereafter provided no problems have been identified.
- .

Nuvaring must be used within 4 months after dispensing. Clients should therefore only be issued with a 3-month supply at any visit. Even with extended use, no more than one box of 3 rings can be issued at one time

Start Times

Circumstances for CHC start	When to start	Additional contraceptive precautions required
Women having menstrual cycles	Start CHC up to and including Day 5 (day 1 for Qlaira®)	None
	At any other time if it is reasonably certain that she is not pregnant (see Quick start guideline)	For 7 days 9 days for Qlaira®
Women with secondary amenorrhoea	At any time, if it is reasonably certain that she is not pregnant	For 7 days 9 days for Qlaira®
Postpartum		
Not breastfeeding	With no additional risk factors for VTE (UKMEC 2)from 3 weeks With additional VTE risk factors (UKMEC 3)- from 6 weeks	7 days 9 days for Qlaira
	If >21 days postpartum and cycles have not returned as for other amenorrhoeic women	For 7 days 9 days for Qlaira®
Breastfeeding	From 6 weeks postpartum	7 days (9 for Qlaira)
Post Abortion	Up to and including day 5 post medical or surgical abortion <24 weeks gestation (day 1 for Qlaira)	None

Switching from other contraceptive methods:		
All Hormonal methods except IUS: *	CHC can be started immediately if hormonal method used consistently and correctly, or if it is reasonably certain she is not pregnant. If previous method injectable or implant can start CHC at any time up to when repeat injection due or implant removed (not expired)	None if previous method reliably suppresses ovulation If POP(other than Desogestrel) for 7 days (9 days if Qlaira)
Switching from IUS	CHC can be started immediately Removal of IUS is not recommended if unprotected intercourse has occurred in the last 7 days due to risk of pregnancy	For 7 days (9 days for Qlaira) Or defer removal of IUS until new method effective
Switching from IUD	CHC can be started at any time of the cycle	None if up to and including day 5 (IUD can be removed at that time) If starting CHC after day 5, required for 7 days (9 days for Qlaira) and defer removal of IUD if unprotected intercourse in the previous 7 days
Switching from barrier method	CHC can be started at any time. At any other time if it is reasonably certain she is not pregnant.	Non if up to and including day 5. If starting CHC after day 5, required For 7 days 9 days for Qlaira

***Please note if changing from one CHC to an alternative CHC and have had a 7 day hormone free interval, additional precautions and need for EC maybe required.**

Current Prescribing Guidelines

Yasmin®/Lucette®

Please note: Yasmin®/Lucette® are non formulary in most Health Boards and non formulary systems may apply. They do not have SMC approval.

Yasmin® contains 30 micrograms ethinylestradiol plus 3 micrograms drospirenone (an anti-mineralocorticoid gestogen).

Indications:
This should be offered only as second line oral contraceptive where there have been side effects related to fluid retention, mood change, acne or true weight gain related to oral contraception and other methods of contraception have been discussed. Careful documentation of the side effects should be made. **Clients should have tried at least two COCs with different gestogens**.

Cocyprindiol

Dianette® Clairette®, Acnocin® and Cicafem® contains 35mcg EE plus 2mcg cyproterone acetate and are not licensed as a COC.
Recent data confirms that **co-cyprindiol has a VTE risk which is greater than second generation CHCs, but is equivalent to that of third generation CHC.**

Indications:

- In the UK the CSM advises: Co-cyprindiol **is not indicated solely as a contraceptive**; it is a treatment option for women with severe acne, which has not responded to oral antibiotics, or for moderately severe hirsutism.
- It should be withdrawn 3 – 4 months after the treated conditions has resolved or if there is no improvement in symptoms.
- If a women wishes to continue with a combined oral contraceptive pill an alternative preparation should be offered with a progestogen with low androgenic side effects eg: gestodene, desogestrel, drospirenone
- There are however a number of women whose skin control deteriorates significantly on withdrawal of Co-cyprindiol and they should be counselled on an individual basis with regard to the risks and benefits of this preparation for them as it may be that it is on balance appropriate for them to continue with Dianette®.

Evra® / Nuvaring®

- If availability of hormone is likely to be improved by the transdermal / transmucosal route of absorption as opposed to the use of an oral preparation (inability to take tablets, bowel disease)
- Where a woman chooses and is suitable for combined hormonal contraception, and continuation of the method would be improved by the transdermal / transmucosal system of a once weekly patch change or four weekly ring change (including one week ring free).
- Please discuss with a senior colleague
- Cost effectiveness should also be considered with the recent reduction in price per cycle

Advice for Missed Pills

If one pill has been missed (between 24 hours and 48 hours late)

Continuing Contraceptive Cover

- The missed pill should be taken as soon as it is remembered
- The remaining pills should be continued at the usual time

Minimising the risk of pregnancy
Emergency contraception (EC) is not usually required but may need to be considered if pills have been missed earlier in the packet or in the last week of the previous packet

If two or more pills have been missed (more than 48 hours late)

Continuing Contraceptive Cover

- The most recent missed pill should be taken as soon as possible
- The remaining pills should be continued at the usual time
- Condoms should be used or sex avoided until seven consecutive active pills have been taken. This advice may be overcautious in the second and third weeks, but the advice is a backup in the event that further pills are missed

Minimising the risk of pregnancy

If pills are missed in the first week (Pills 1-7)	If pills are missed in the second week (Pills 8-14)	If pills are missed in the third week (Pills 15-21)
EC should be considered if unprotected sex occurred in the pill-free interval or in the first week of pill-taking	No indication for EC if the pills in the preceding 7 days have been taken consistently and correctly (assuming the pills thereafter are taken correctly and additional contraceptive precautions are used).	OMIT THE PILL-FREE INTERVAL by finishing the pills in the current pack (or discarding any placebo tablets) and starting a new pack the next day

Everyday Pill Regimens

If a woman misses any inactive pills, she should discard the missed inactive pills and then continue taking pills daily, one each day.
If an active pill is missed, follow the guidance as for missed pills above.

Missed / Detached Patch or Ring

Situation	Timeframe	Additional contraceptive protection required?
Extension of patch/ring-free interval	≤ 48 hours > 48 hours	No Yes (7 days) consider EC if unprotected intercourse in patch/ring-free interval
Patch/ring detachment/removal	≤ 48 hours > 48 hours	No (providing there has been consistent and correct use for 7 days prior to removal/detachment Yes (7 days). Consider EC if patch/ring was detached/removed in week 1 and unprotected intercourse occurred in patch/ring-free interval or week 1
Extended use of patch	≤ 9 days > 9 days	No Yes for 7 days
Extended use of ring	≤ 4 weeks > 4 weeks	No (ring-free interval can be taken) Yes. However, if the woman has worn the ring for > 4 but ≤ 5 weeks, efficacy could be maintained by starting a new ring immediately without a ring-free interval

UKMEC	DEFINITION OF CATEGORY
CATEGORY 1	A condition for which there is no restriction for the use of the contraceptive method.
CATEGORY 2	A condition where the advantages of using the method generally outweigh the theoretical or proven risks.
CATEGORY 3	A condition where the theoretical or proven risks usually outweigh the advantages of using the method.
CATEGORY 4	A condition which represents an unacceptable health risk if the contraceptive method is used.

New UK Medical Eligibility Criteria https://www.fsrh.org/documents/ukmec-2016/

Combined Hormonal Contraception Regimens

Type of regimen	Period of CHC use	HFI
Standard use	21 days (21 active pills or 1 ring, or 3 patches)	7 days
Tailored use		
Shortened hormone-free interval (HFI)	21 days (21 active pills or 1 ring, or 3 patches)	4 days
Extended use (tricycling)	9 weeks (3 x 21 active pills or 3 rings, or 9 patches used consecutively)	4 or 7 days
Flexible extended use	Continuous use (≥21 days) of active pills, patches or rings until breakthrough bleeding occurs for 3–4 days	4 days
Continuous use	Continuous use of active pills, patches or rings	None

Key messages for women considering use of tailored CHC regimens

- The evidence from studies is that combined hormonal contraception (CHC) is as safe and at least as effective for contraception if it is taken as an extended or continuous regimen as it is when it is taken in a traditional 21/7 cycle.
- A woman who is using CHC does not need to have a monthly withdrawal bleed to be healthy.
- There is no build-up of menstrual blood inside a woman who uses CHC for an extended time without a break; extended CHC use keeps the lining of the womb thin.
- Withdrawal bleeds during cyclical use of CHC have been reported by women who are pregnant; women should not consider monthly bleeds on CHC to be reassurance that they are not pregnant.
- By using extended or continuous CHC the frequency of withdrawal bleeds and associated symptoms (e.g. headache, mood change) is reduced; this could be useful for women who have heavy or painful bleeding or problematic symptoms associated with the hormone-free interval (HFI).
- The ovaries start to become active during the traditional 7-day HFI. Fewer and/or shorter breaks in CHC use could mean that the risk of pregnancy could ***theoretically*** be lower with extended or continuous regimens than if a 7-day break is taken every month.
- There can be irregular bleeding or spotting in the first few months of CHC use, particularly with extended or continuous regimens; this does not usually mean that there is any medical problem and it generally improves with time.
- The evidence from studies is that using extended or continuous regimens of CHC does not affect the return of a woman's fertility when she stops CHC.

References:

- *FSRH* UK Medical Eligibility Criteria for contraceptive use (UKMEC2016)
- FSRH Drug Interactions with Hormonal Contraception. January 2019 (accessed Jan 2022)
- FSRH Combined hormonal contraception January 2019, amended November 2020https://www.fsrh.org/standards-and-guidance/documents/combined-hormonalcontraception/ [accessed January 2022]
- FSRH Guideline Emergency Contraception March 2017, amended Dec 2020 (accessed Jan 2022)
- Medscape.com/drug-interactionchecker

Sexwise Patient Information Leaflets:

www.sexwise.org.uk/contraception/combined-pill-coc

https://sexwise.org.uk/contraception/contraceptive-patch
https:/sexwise.org.uk/contraception/contraceptive-vaginal-ring