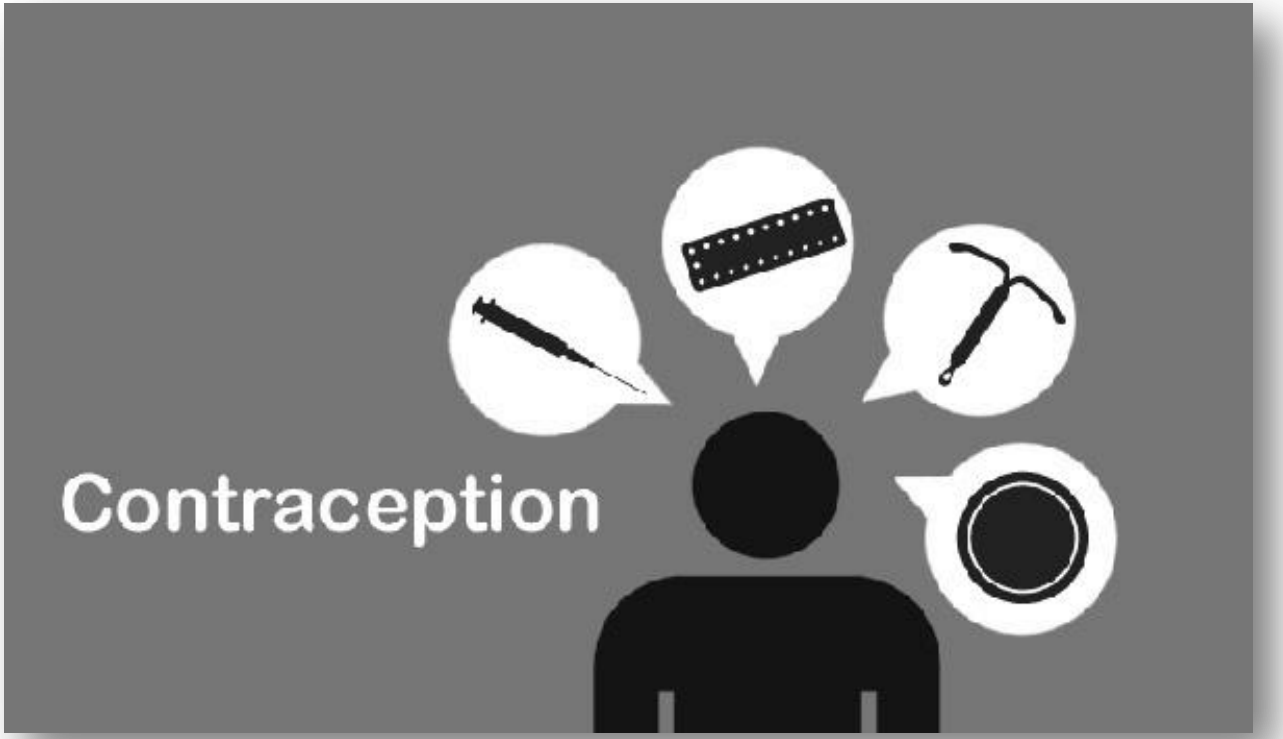
NHS Tayside Hormonal Contraception Guide:

NHS Tayside formulary, pharmacological content and other characteristics



Tayside Sexual & Reproductive Health Service (TSRHS)

(Latest update: 08/2022)

Combined hormonal contraception (CHC): pharmacological content

(NHS Tayside Formulary contraceptives are in green, "first choice" COC is in dark green with white font, current most cost-effective brands are in bold font, non-formulary brands are in red, COCs not licensed for contraception are in yellow)

Oestrogen	Progestogen						
	First generation	Second generation	Third generation			Fourth generation	17 OH[4]
Ethinylestradiol (EE)	Norethisterone (NE)	Levonorgestrel (LNG)	Gestodene (GSD)	Norgestimate[1] (NGM)/ Norelgestromin[2] (NGMN)	Desogestrel (DSG)/ Etonorgestrel[3] (ENG)	Drospirenone (DRSP)/ Dienogest (DNG)/ Nomegestrol (NOM)	Cyproterone acetate (CPA)
15 mcg					NuvaRing® **~ SyreniRing®** (120 mcg ENG/24h)		
20 mcg	*(Loestrin 20®- taken off the market in 2019)* *(NE 1mg)*		Femodette® (GSD 75 mcg) ~ Millinette 20/75® ~ Sunya®		Mercilon® (DSG 150 mcg) ~ Gedarel 20/150® **~ Bimizza®**	Eloine® (3 mg) (DRSP 3 mg) ~ Daylette®	
30 mcg	*(Loestrin 30® - taken off the market in 2019)* *(NE 1.5 mg)*	Microgynon 30® Microgynon 30® ED[5] (LNG 150 mcg) **~ Levest®** ~ Rigevidon® ~ Ovranette®	Femodene® / Femodene® ED[5] (GSD 75 mcg) ~ Millinette 30/75® ~ Katya®		Marvelon® (DSG 150 mcg) **~ Gedarel 30/150®**	Yasmin® (DRSP 3 mg) ~ Lucette® ~ Yacella®	
35 mcg	Bevinor® (NE 0.5 mg) ~Ovysmen® Norimin® (NE 1 mg) Synphase® (triphasic) (NE 0.5/1/0.5 mcg) *BiNovum® (biphasic) (discontinued)* *(NE 0.5 mg/1 mg)* *TriNovum® (triphasic) (discontinued)* *(NE 0.5/0.75/1 mg)*	Logynon® ~ TriRegol® Logynon® ED[5] (EE 30/40 mcg) (LNG 50/75/125 mcg) (triphasic)	Triadene® (GSD 50/70/100 mcg, EE 30/40/30 mcg) (triphasic)	*(Cilest®- (taken off the market in 2019)* (250 mcg NGM) ~ Cilique® ~ Lizinna® Evra® (patch) (33.9 mcg EE/ 203 mcg NGMN/24h)			Dianette®[6] (CPA 2mg) **~ Co-cyprindiol**

Combined hormonal contraception (CHC): pharmacological content (cont.)

(NHS Tayside Formulary: non-formulary brands are in red)

Oestrogen	Progestogen						
	First generation	Second generation	Third generation			Fourth generation	17 OHP[4]
	Norethisterone (NE)	Levonorgestrel (LNG)	Gestodene (GSD)	Norgestimate[1] (NGM)/ Norelgestromin[2] (NGMN)	Desogestrel (DSG)/ Etonorgestrel[3] (ENG)	Drospirenone (DRSP)/ Dienogest (DNG)/ Nomegestrol (NOM)	Cyproterone acetate (CPA)
Mestranol							
50 mcg	Norinyl-1® (NE 1 mg)						
Estradiol Valerate (EV)							
1-3 mg						Qlaira® (DNG 0- 3 mg, EV 0-3 mg) (26d/2d) (quadriphasic *ED[5] tablet)*	
Estradiol Hemihydrate (EH)							
1.5 mg						Zoely® (NOM 2.5 mg/ EH 1.5 mg) (24d/4d) (monophasic *ED[5] tablet)*	

[1] Norgestimate: metabolized mostly to levonorgestrel and its metabolites

[2] Norelgestromin: metabolite of norgestimate

[3] Etonogestrel: active metabolite of the inactive prodrug desogestrel

[4] 17 OHP: 17 hydroxyprogesterone

[5] ED: every day (28-day) preparation that can be considered for women with compliance issues who do not want to use the COC continuously (unlicensed) and decline LARC

[6] Cyproterone acetate products are not licensed for oral contraception but for hormone treatment of acne

Check BNF and MIMS for other brands and the latest availability and price of non-proprietary tablets

Venous Thromboembolism risk (VTE) with combined hormonal contraception (CHC)

Situation	VTE risk per 10,000 healthy women per year
Non contraceptive user, not pregnant	2
Pregnant women	29
Postpartum period	300- 400
CHC containing norethisterone, levonorgestrel or norgestimate (mainly first and second generation progestogens)	5-7
CHC containing etonorgestrel (ring) or norelgestromin (patch)	6-12
CHC containing gestodene, desogestrel, drospirenone or cyproterone acetate (mainly third generation progestogens)	9-12

Newer synthetic estrogens and progestogens ("forth generation progestogens") such as estradiol valerate/dienogest (Qlaira®) and estradiol hemihydrate/nomegestrol acetate (Zoely®) are being incorporated into combined oral contraception (COC) products. Long-term safety data for these new formulations are not yet available. Therefore, the risks and benefits of use must be assumed to be as for other combine hormonal contraception (CHC).

Reference: FSRH- Venous Thromboembolism (VTE) and Hormonal Contraception 2014

Progestogen-only contraception: pharmacological content (excluding emergency contraception)

(NHS Tayside Formulary contraceptives are in green, "first choice" IUS and contraceptive injections are in in dark green with white font, the current most cost-effective POP is in bold font)

Via	Progestogen			
	First generation	Second generation	Third generation	17 OHP-17 hydroxyprogesterone
	Norethisterone (NE)	Levonorgestrel (LNG)	Desogestrel (DSG)/ Etonorgestrel[1] (ENG)	Medroxyprogesterone acetate (MDPA)
Oral	Micronor® (NE 350 mcg) ~ Noriday®	Norgeston® (LNG 30 mcg)	**DSG 75 mcg (generic brand)** ~ Cerazette® ~ Cerelle®	
Intrauterine		Mirena® IUS (52 mg) 5 year licence **Levosert® IUS** (52 mg) (not as part of HRT) (currently) 6 year licence Benilexa® IUS (52 mg) (not as part of HRT) 6 year licence Kyleena® IUS (19.5 mg) (not as part of HRT) 5 year licence Jaydess® IUS (13.5 mg) (not as part of HRT) 3 year licence		
Subdermal			Nexplanon® (68 mg Etonogestrel[2])	
Intramuscular				DepoProvera® (DMPA 150 mg) (every 13 weeks)
Subcutaneous				SayanaPress® (DMPA 104 mg) (every 13 weeks)

[1]Etonogestrel: active metabolite of the inactive prodrug desogestrel

Non-contraceptive benefits of hormonal contraceptive methods

Method	Ovulation suppression*	Risk of irregular vaginal bleeding	Likelihood of amenorrhea (at longterm)	Estrogenic benefits** & risks
CHC- cyclical use	+	+/- (tends to settle with time)	na	+
CHC- continuous use (off license)	++	+/- (tends to settle with time)	++	++
DepoProvera® or SayanaPress®	++	+ (tends to settle with time)	++	- -
IUS (Mirena®, Levosert®, Benilexa®) (52 mg LNG)	- or +/-	+ (tends to settle with time)	++	-
IUS (Kyleena®) and (Jaydess®) (19.5 mg or 13.5 mg LNG)	-	+ (tends to settle with time)	+/-	-
POP (second generation: NE, LNG)	+/-	++	+/-	-
POP (third generation: DSG)	++	+ (tends to settle with time)	+	-
SDI (Nexplanon®)	++	++	+/-	-

CHC: combined hormonal contraception (combined pill, patch or vaginal ring)
DSG: desogestrel
IUS: intrauterine system (hormone "coil")
NE: norethisterone
LNG: levonorgestrel
POP: progestogen-only pill
SDI: subdermal contraceptive implant

Scale:	
na:	not applicable
– – :	negative effect
– :	no effect
+/- :	variable effect
+ :	good effect
++ :	very good effect

* Ovulation suppression: benefits for women with PMS, endometriosis, recurrent ovarian cysts, menstrual migraine, epilepsy influenced by hormones, ovulation pain
** Estrogen: benefits women with hirsutism, acne, hormone- related (reproductive) depression, PMS and premature ovarian insufficiency

Combined Hormonal Contraception: tailored regimes (unlicensed)

Regimen	Details	Purpose
Shortened hormone-free interval (HFI)	HFI of only 4 days	More forgiving of late restart, increased efficacy.
Extended use	E.g. tricycling- 3 cycles back to back (3 packets, 3 rings or 9 patches)	See below
Flexible extended use or continuous use	Method used continuously (≥ 21 days; HFI omitted) until breakthrough bleeding occurs for 3–4 days, then, if used at least for 2 weeks, HFI of 4 days before restarting again	Reduced or no vaginal bleeding and pain, reduced headaches/migraines, fewer perimenopausal symptoms, fewer mood swings, improved compliance- increased efficacy, choice, convenience, saving money (pain killers, sanitary products, washing).

FSRH/CEU guidance:
Women should be given information about both standard and tailored CHC regimens to broaden contraceptive choice.

Please consider giving your patient the Patient Information Leaflet "Different Ways to take the Combined Pill" (LN0238) (on Staffnet).

Please check out the FSRH Guideline "Combined Hormonal Contraception" (2019) for more info:

https://www.fsrh.org/standards-and-guidance/documents/combined-hormonal-contraception/

Possible side effects of hormonal contraceptive methods: classification according to hormone class

Side effect	Estrogenic	Progestogenic
Acne +/- seborrhoea	-	+ (especially first and second generation progestogens)
Anxiety	-	+
Bloating	+	+
Breast swelling	+	+/-
Breast tenderness	+	+/-
Decreased sex drive	+ (via increase of SHBG)	+/- (assoc. with depression)
Depression	-	+
Growth of uterine fibroids	+	-
Headaches	+	+
Hirsutism	-	+
Irregular bleeding	+/-	+
Mood swings	+/-	+
Nausea/vomiting	+	-
Raised BP	+	-
Weight gain	+/- (water retention: cyclical gain)	+/- (increased appetite: sustained gain- mainly DMPA)

Possible side effects on combined hormonal contraception (CHC): advice and treatment options

Clinical problem	Suggestions
Acne/ hirsutism	Take history and exclude pathology. Consider checking FAI levels. Give lifestyle, skin care and diet advice. Treat condition(s). Encourage perseverance for 3/12. Change progestogen to less androgenic third generation progestogen. Omit pill-free interval (unlicensed). Increase estrogen content* unless higher VTE risk. Change to an EE/cyproterone acetate COC (Dianette®/ Co-Cyprindiol®) (licensed only for acne treatment). Change to non-hormonal method.
Bloating	Take history, give lifestyle and diet advice. Exclude GI and ovarian pathology. Encourage perseverance for 3/12. Change progestogen. Change to progestogen-only or non-hormonal method. Reduce estrogen content** if due to water retention.
Breast tenderness (bilateral)	Exclude pathology. Improve bra support. Encourage perseverance for 3/12. Add evening primrose oil. Reduce estrogen content**. Change to progestogen-only or non-hormonal method.
Headache	General advice: take a history and exclude other pathology. Check BP. Give lifestyle advice and suggest more suitable analgesia. Complicated migraine: stop CHC immediately and start progestogen-only or non-hormonal method. Classical migraine: encourage perseverance for 3/12. Omit pill-free interval (unlicensed). Reduce estrogen content**. Start progestogen-only or non-hormonal method. Other headaches: encourage perseverance for 3/12. Omit pill-free interval (unlicensed). Reduce estrogen content*. Change to progestogen-only or non-hormonal method.
Heavy withdrawal bleeding in pill-free interval	Take history, screen for STIs. Exclude pregnancy. Do pelvic exam +/- arrange pelvic USS. Consider FBC, TFT and haemophilia screen. Add mefenamic +/- tranexamic acid. Encourage perseverance for 3/12. Omit pill-free interval (unlicensed). Change progestogen. Change to estradiol/dienogest COC (Qlaira®) (not recommended by the SMC). Change to a progestogen-only (especially recommended: Mirena® IUS) or non-hormonal method.
Loss of sex drive	Encourage perseverance for 3/12. Take medical and psychosexual history, explore relationship issues including GBV. Consider referral to Sexual Problems Clinic. Change progestogen to a more androgenic second generation progestogen (norethisterone/ levonorgestrel). Reduce estrogen content** or change to combined transdermal contraception (which has less effect on SHBG). Change to a progestogen-only or non-hormonal method.
Mood changes (depression, anxiety +/- irritability)	Take a history (previous sensitivity to progestogens?, history of PMS or postnatal depression?). Exclude suicidal ideation. Explore and treat other causes or signpost to other agencies. Encourage perseverance for 3/12. Omit hormone-free interval when on CHC (unlicensed). Change progestogen (consider use of drospirenone). Do not use biphasic or triphasic COCs. Might try progestogen-only method (but avoid DepoProvera®/SayanaPress® as irreversible for > 3/12) with close monitoring of mood or non-hormonal method. Consider PMS treatment according to RCOG guideline (if applicable). Discuss referral to computerized CBT programme, counselor or mental health services.
Nausea	Take a history and exclude other causes. Do a pregnancy test. Encourage perseverance for 3/12. Take tablet at night. Take tablet with food. Reduce estrogen content**. Change to a progestogen-only or non-hormonal method.
Unscheduled bleeding	Check history (before and after starting CHC), compliance and drug interactions (including OTC drugs like St John's Wort). Exclude pregnancy. Screen for STIs. Check compliance with cervical screening program. Inspect cervix. Add Mefenamic acid. Encourage perseverance for 3/12. Change progestogen. Increase estrogen content* or change to vaginal ring (more expensive option). Change to Mirena® IUS, DepoProvera®/SayanaPress® or non-hormonal method. See FSRH CEU Guideline "Unscheduled bleeding on hormonal contraception" for more info.
Water retention	Take history, exclude other pathology, give lifestyle and diet advice. Encourage perseverance for 3/12. If evidence of water retention: reduce estrogen content** or change to EE/drospirenone COC (Yasmin®/ Lucette®/ Daylette®) with anti-mineralcorticoid activity (not recommended by the SMC). Change to a progestogen-only or non-hormonal method.
Weight gain	Take history, give lifestyle and diet advice. Conisder checking TFT. Encourage perseverance for 3/12. If proven weight gain: change to an IUS or non-hormonal method. Might try different progestogen or progestogen-only method. Avoid DepoProvera® and SayanaPress®.

*Increase estrogen content: change to 35 mcg EE combined oral contraceptive pill like Cilique® or to the combined transdermal patch (Evra®) which leads to approximately 34 mcg/24 hours systemic EE levels.

**Reduce estrogen content: change to a 20 mcg EE combined oral contraceptive pill or to the combined vaginal ring (NuvaRing®) which leads to approximately 15 mcg/24 hours systemic EE levels (but has a much higher cost).

Suggestions modified from: FSRH guidance and Mansour D, Searle S, Smith D at al: Rational Prescribing of Oral Contraceptives. CH-OCS-0005-01/2016.

Perimenopausal Contraception – Basics I

Perimenopausal Contraception BASICS

Age < 40: premature insufficiency of ovaries (POI) might be transitional- continue with contraception unless ovaries removed

Age 40 -49: contraception can be stopped:

- 2 years after last "natural" menstrual period (and not on hormonal contraception, no IUS in situ, no hx of endometrial ablation etc) or
- 2 years after 2nd result of FSH* of > 30 IU/l, taken at least 4-6 weeks apart

Age ≥ 50: contraception can be stopped:

- 1 year after last "natural" menstrual (and not on hormonal contraception, no IUS in situ, no hx of endometrial ablation etc) or
- 1 year after result of a single FSH* > 30 IU/l

Age ≥ 55:

- contraception could be stopped even if still having periods- pregnancy very unlikely due to poor oocyte quality
- Might consider continuing contraception for another year or two if periods troublesome (non-contraceptive indication)

** If FSH normal- consider repeating in a year if wanting to stop contraception before the age of 55*

Perimenopausal Contraception BASICS

- Amenorrhoea in patients on any hormonal contraception or who had an endometrial ablation is not an indicator of (peri)menopause/POI
- Amenorrhoea after radio- or chemotherapy might be transitional and not an indicator of an iatrogenic (peri)menopause/POI
- FSH might be indicated in women ≥ 51 on hormonal contraception who wish to stop contraception
- FSH measurements are unreliable when being taken while on combined hormonal contraception or HRT, for up to 6 weeks after stopping
- Stopping and restarting CHC or HRT increases the VTE risk
- FSH might be suppressed by DMPA (DepoProvera/SayanaPress) injections (false-negative)- best to be taken shortly before the next injection is due
- FSH measurements are not affected by the POP, SDI (implant) or any IUS type

Contraception and the (peri)menopause: When to stop contraception

Method used	40- 49 years	≥ 50 years
Combined hormonal contraception, Depo-Provera® or SayanaPress®	Continue if satisfied with method & no CI	Stop & switch method
Condoms, diaphragms and Cu-IUD*	Stop /remove two years after LMP	Stop/remove)one year after LMP or at the age of 55
POP, Nexplanon® or IUS**	Continue if happy with method or stop two years after two FSH levels >30 IU/L (least 6 weeks apart)	Stop one year after one FSH level >30 IU/L or at the age of 55; if FSH premenopausal could repeat after a year

• Any IUD with ≥ 380mm² of copper inserted at the age of ≥40 can be used extendedly (Nova-T, T-Safe etc) (unlicensed)

*** Currently only a Mirena® IUS inserted at the age of ≥45 could be used extendedly until age 55 for contraception but not as part of HRT (unlicensed); the FSRH might extend this recommendation for other 52 mg LNG IUS in the future- see website for update*

Intrauterine Systems: devices available on the UK market

Method	Mirena® IUS	Benilexa® IUS	Levosert® IUS	Kyleena® IUS	Jaydess® IUS
Total LNG content	52 mg	52 mg	52 mg	19.5 mg	13.5 mg
License	5 years	6 years	6 years	5 years	3 years
Licensed Indication(s)	Contraception, HMB, part of HRT	Contraception, HMB, not as part of HRT	Contraception, HMB, not as part of HRT	Contraception	Contraception
Menstrual reduction	++	++	++	+	+
Amenorrhoea (at 3 years)	23.6%	"like Mirena® IUS"	"like Mirena® IUS"	18.9%	12.7%
Ovulation suppression (first year only)	+/- < 25%	?	?	None or minimal	None or minimal
Inserter diameter & type	4.4 mm EvoInserter® (one handed)	4.8 mm One handed device	4.8 mm Two handed device	3.8 mm EvoInserter® (one handed)	3.8 mm EvoInserter® (one handed)
Extended use for <u>contraception only</u> recommended when inserted aged ≥ 45	Yes (FSRH)	No (might change in the future)	No (might change in the future)	No	No
Size	Width 32 mm Length 32 mm	Width 32 mm Length 32 mm	Width 32 mm Length 32 mm	Width 28 mm Length 30 mm	Width 28 mm Length 30 mm
Price per unit & licensed year (BNF 08.22)	£88 (£18/year)	£71 (£12/year)	£66 (£11/year)	£76 (£15/year)	£69 (£23/year)
Comments	Gold standard	Inserter larger than Mirena inserter. Not ideal in women aged ≥ 45 as <u>not licensed a part of HRT</u> and extended use currently not recommended by the FSRH.	Challenging inserter. Ongoing clinical trials- license likely extended in the future > 6 years. Not ideal in women aged ≥ 45 as <u>not licensed a part of HRT</u> and extended use currently not recommended by the FSRH.	Easier and less painful insertion	Easier and less painful insertion

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