SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
PRIMARY HEALTH CARE: FAMILY PLANNING
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020)

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the complete chapter for family planning.
Note: The PHC chapter has been updated to align to previous NEMLC recommendations as well as the recent NEMLC-approved Adult Hospital Level STGs and EML, 2019 edition.

SECTION	MEDICINE / MANAGEMENT	ADDED/DELETED/AMENDED/NOT ADDED
	Low dose LNG-IUS	Not recommended for inclusion to EML
	Vaginal contraceptive ring	Not recommended for inclusion to EML
	Low dose DMPA	Not recommended for inclusion to EML
	Transdermal contraceptive patch	Not recommended for inclusion to EML
Therapeutic Interchange Database (for PHC STGs and EML)	Monophasic-progestin only pills	Only agents of low VTE risk included in therapeutic group
	Monophasic preparations: combination of estrogen and progestin in each pill	Available agents categorised according to VTE risk
	Triphasic preparation: combination of estrogen and progestin	Only agents of low to moderate VTE risk included in therapeutic group

7.2 CONTRACEPTION, HORMONAL

Low dose LNG-IUS: *not recommended for inclusion to EML*
Vaginal contraceptive ring: *not recommended for inclusion to EML*
Low dose DMPA: *not recommended for inclusion to EML*
Transdermal contraceptive patch: *not recommended for inclusion to EML*

An important factor for family planning is dependent on choice, where the party/parties concerned has/have a right to choose whether to use contraceptives and also which method to use. However, uptake of contraceptives in the public sector has to date, not increased since 2014.

Contraception method uptake in South Africa, 2016: The South African Demographic Health Survey, 2016[1] was a nationally representative sample of persons aged 15-49. Below is the contraceptive use method uptake.

Current contraceptive method	Frequency	Percent
Not using any method	4,489	52.7
Injection - 3 month	1,395	16.4
Male condom	946	11.1
Injections - 2 month	619	7.3
Pill	369	4.3
Female sterilization	302	3.6
Implants	277	3.3
IUD	58	0.7
Withdrawal method	17	0.2
Male sterilization	15	0.2
Female condom	15	0.2
Emergency contraception	5	0.1
Periodic abstinence	4	0.1
Other modern method	3	0.0
Total	**8,514**	**100.0**

[1] National Department of Health and ICF. 2019. South Africa Demographic and Health Survey 2016. Pretoria: National Department of Health - NDoH - ICF. Available at http://dhsprogram.com/pubs/pdf/FR337/FR337.pdf

Currently, there are five pharmacological contraceptive options recommended in the STGs and EML[2]. Increasing the contraception options would provide a broader base to choose from (with the intention of increasing uptake - it is suggested that introducing a new contraceptive method may increase contraceptive prevalence by 8%[3]. Though increasing contraceptive uptake is multifactorial and includes factors such as adequate knowledge translation and adequate counselling of women to make informed choices, feasibility, acceptability, affordability as well as integration of health services.

The contraceptive modalities reviewed by the Adult Hospital Level Committee (includes:

- Low dose DMPA
- Transdermal contraceptive patch
- Low dose levonorgestrel IUD
- Contraceptive vaginal ring

CONTRACEPTIVE REVIEWS

Low dose LNG-IUS: *not recommended for inclusion to EML*

Refer to medicine review below:

Low dose LNG-IUS-Contracept

http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/404-phc-medicines-reviews

Recommendation: Based on the evidence reviewed, the Adult Hospital Level Committee reccomends that this agent may be considered as an alternative to the Copper IUCD, if the latter is unavailable. The Committee acknowledges that low dose LNG-IUS is smaller and may be more acceptable by adolescents.

Rationale: Low dose LNG-IUS is comparable in efficacy and safety to copper IUD; However, this agent is cost prohibitive for inclusion in the Adult Hospital Level EML.

Level of Evidence: II Moderate RCTs, Systematic Review (for safety), Observational studies

Review indicator: Price reduction

NEMLC MEETING OF 5 DECEMBER 2019:

NEMLC accepted the proposal as recommended by the Adult Hospital Level Committee, noting that low dose LNG-IUS is currently unaffordable.

Vaginal contraceptive ring: *not recommended for inclusion to EML*

Refer to medicine review below:

Vaginal contraceptive ring_A

http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/404-phc-medicines-reviews

Recommendation: Based on the evidence reviewed, the Adult Hospital Level Committee reccomends that the vaginal contraceptive ring be considered as an additional contraceptive option for women.

Rationale: The vaginal ring has been shown to be as efficacious as the combined oral coontraceptives, with less side effects. It is an ideal alternative option for birth spacing. However, acceptability amongst South African women is unknown, and the modality is more expensive than standard-dose LNG-IUS (see table 1, below).

Level of Evidence: I Systematic review, RCT of moderate quality

Review indicator: Price reduction

NEMLC MEETING OF 5 DECEMBER 2019:

NEMLC accepted the proposal as recommended by the Adult Hospital Level Committee, noting that the etonorgestrel 11.70mg/ethinyl estradiol 2.7mg vaginal contraceptive ring is currently unaffordable.

[2] PHC STGs and EML, 2018

[3] Ross, J. and J. Stover. 2013. "Use of modern contraception increases when more methods become available: analysis of evidence from 1982-2009," Global Health Science and Practice, Vol. 1(2): 203-212

Low dose DMPA: *not recommended for inclusion to EML*
Refer to medicine review below:

Low Dose DMPA-Contraceptive

http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/404-phc-medicines-reviews

Recommendation: Based on the evidence reviewed, the Adult Hospital Level Committee recomends that subcutaneous DMPA should be considered as a therapeutic alternative of the progestogen injectable therapeutic group. There is no preference for either formulation as they seem to have similar therapeutic efficacy and safety profile. The option of self-administration has been shown to be feasible and acceptable in Sub-Saharan Africa (Malawi, Uganda and Senegal); where training and support is available to women.

Rationale: Available evidence among healthy women suggests that DMPA-SC and DMPA-IM appears to be therapeutically equivalent interms of safety and efficacy. Satisfication rate for DMPA-SC is similar to that of the IM formulation. Data from other countries in sub-Saharan Africa supports the option of self administration of DMPA - SC. A local acceptability and feasibility study may be required to determine if the self-administration option is a viable option for South Africa.

Low dose DMPA- SC:

Level of Evidence: I Systematic review, RCT

Self administration of low dose DMPA-SC:

Level of Evidence: II Systematic Review (moderate quality RCTs); cohort studies

Review indicator: *Availability of SAHPRA registered product on the South African market, affordable price*

NEMLC MEETING OF 26 SEPTEMBER 2019:
NEMLC accepted the proposal as recommended by the Adult Hospital Level Committee, noting that SAHPRA registration and a reasonable price is required for this contraceptive to be considered for inclusion on the national EML.

Transdermal contraceptive patch: *not recommended for inclusion to EML*
Refer to medicine review below:

TransdermalContraceptivePatch_Adults

http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/404-phc-medicines-reviews

Recommendation: Based on the evidence reviewed, the Adult Hospital Level Committee does not recommend inclusion of norelgestromin/ethinyl estradiol 6/0.6mg patches on the national Essential Medicine List. Contraceptive patches containing other progestins are being investigated in clinical trials and further assesment of this contraceptive modality is reccomended for review, pending SAHPRA registeration and product is locally accesible.

Rationale: Risk benefit assesment favours combined oral contraceptive (containing the same progestin) in terms of associated veno-thromboembolic events. More clear data of the risk of VTE for the difeferent progestins, on adherence and acceptability of the contraceptive patch in local context and a more affordable price would further contribute to decision-making. (Authors of a systematic review concluded that there is limited evidence of low to moderate quality that showed conflicting results of VTE risk associated with patch or ring compared to COCs (7).

Level of Evidence: II Moderate quality clinical trials and a Systematic Review (for safety)

Review indicator: Safety data

NEMLC MEETING OF 26 SEPTEMBER 2019:
NEMLC accepted the proposal as recommended by the Adult Hospital Level Committee, above.

THERAPEUTIC INTERCHANGE DATABASE AMENDMENT – PRIMARY HEALTH CARE LEVEL OF CARE

Monophasic-progestin only pills: *only agents of low VTE risk included in therapeutic group*
Monophasic preparations: combination of estrogen and progestin in each pill: *available agents categorised according to VTE risk*
Triphasic preparation: combination of estrogen and progestin: *only agents of low to moderate VTE risk included in therapeutic group*

Background: Query received from the Northern Cape Provincial PTC not to consider therapeutic class tendering of oral contraceptives as:

i) Health care worker and patients will be confused as the different therapeutic agents will look different and requires different stock codes;
ii) Extra contraceptive measures would be required for 7-14 days that would lead to unwanted pregnancies and possible litigation.

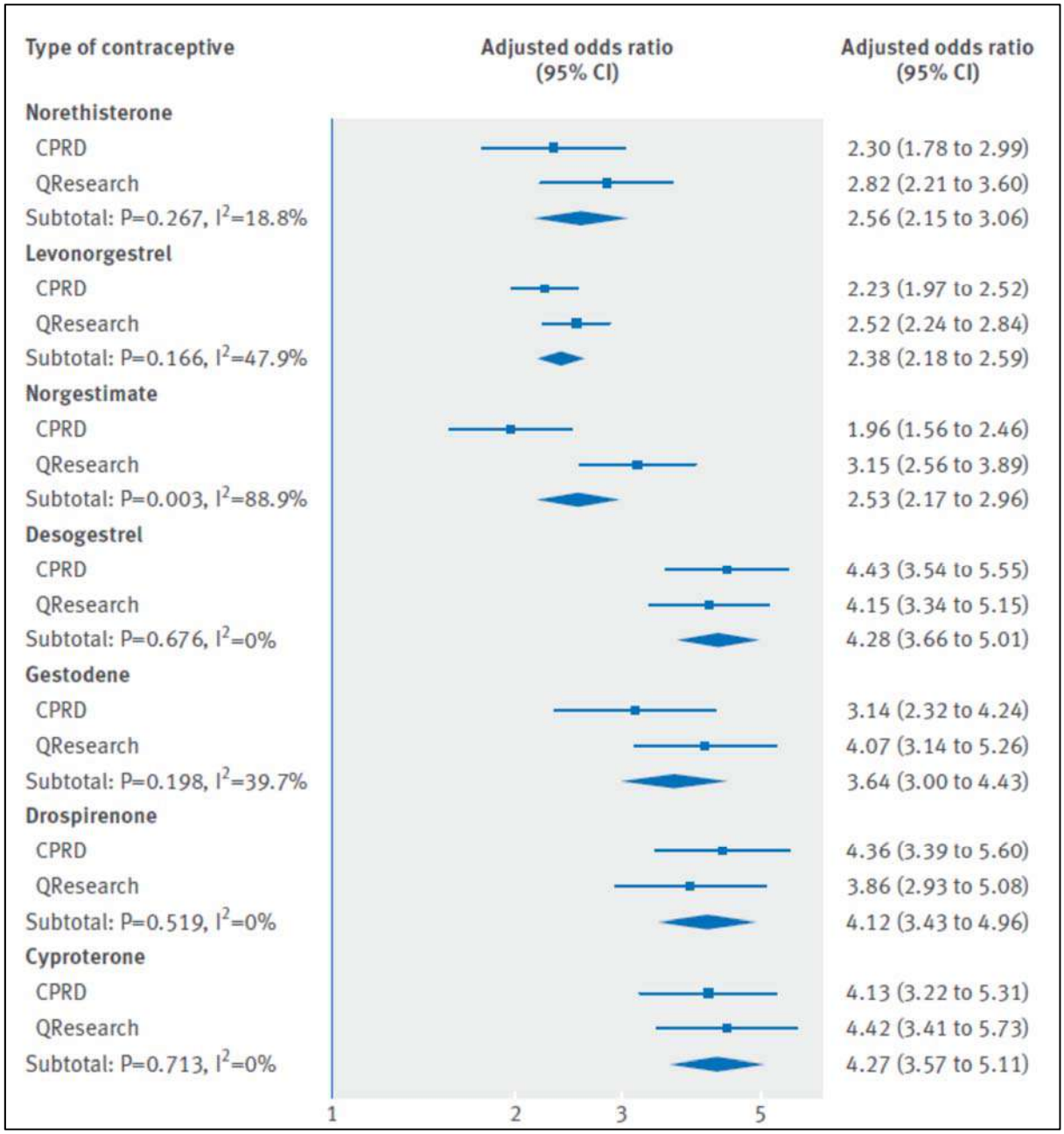
Uptake of contraceptive pills: Estimated to be only 4.3%, as reported by the South Africa Demographic and Health Survey, 2016[4].
Stock-outs: From February 2019 to October 2019 there has been consistent stockouts of all contraceptive pills that has been awarded a contract on contract circular RT283-2017 (RSAPharmadatabase).
Switching of contraceptives: Dual contraception with condoms are recommended in the PHC STGs and EML, 2018 edition - but it is noted that guidance on switching between pills could assist the healthcare worker – for consideration for inclusion to the PHC family planning chapter.
Safety concerns regarding venous thromboembolism (VTE): Adult Hospital Level Committee reviewed the evidence and recommends that due to the varying risk of VTE with different progestins, that the PHC therapeutic interchange database be updated to stratify the various oral contraceptives according to risk of VTE, as suggested by Vinogradava et al (2015)[5] and Tepper et al (2016)[6], below:

Amendment:

THERAPEUTIC CLASS	INN
Monophasic-progestin only pills - low VTE risk	**Levonorgestrel (2)**
Monophasic-progestin only pills - low VTE risk	Norethisterone (2)
Monophasic preparations: combination of estrogen and progestin in each pill - low to moderate VTE risk	**levonorgestrel and ethinylestradiol (3)**
Monophasic preparations: combination of estrogen and progestin in each pill - low to moderate VTE risk	gestodene and ethinylestradiol (3)
Monophasic preparations: combination of estrogen and progestin in each pill - high VTE risk	desogestrel and ethinylestradiol (3)
Monophasic preparations: combination of estrogen and progestin in each pill - high VTE risk	drospirenone and ethinylestradiol (3)
Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk	**levonorgestrel and ethinylestradiol (3)**
Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk	norethisterone and ethinylestradiol (3)
Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk	norgestimate and ethinylestradiol (3)
Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk	gestodene and ethinylestradiol (3)

Vinogradova et al, 2015:
Figure 3: Adjusted odds ratio for VTE in patients currently exposed to combined oral contraceptives compared with no use in the last year, by database. Odds ratios and 95% confidence intervals are adjusted for body mass index, smoking status, alcohol consumption, ethnic group, chronic and acute conditions, and use of other hormonal contraceptives:

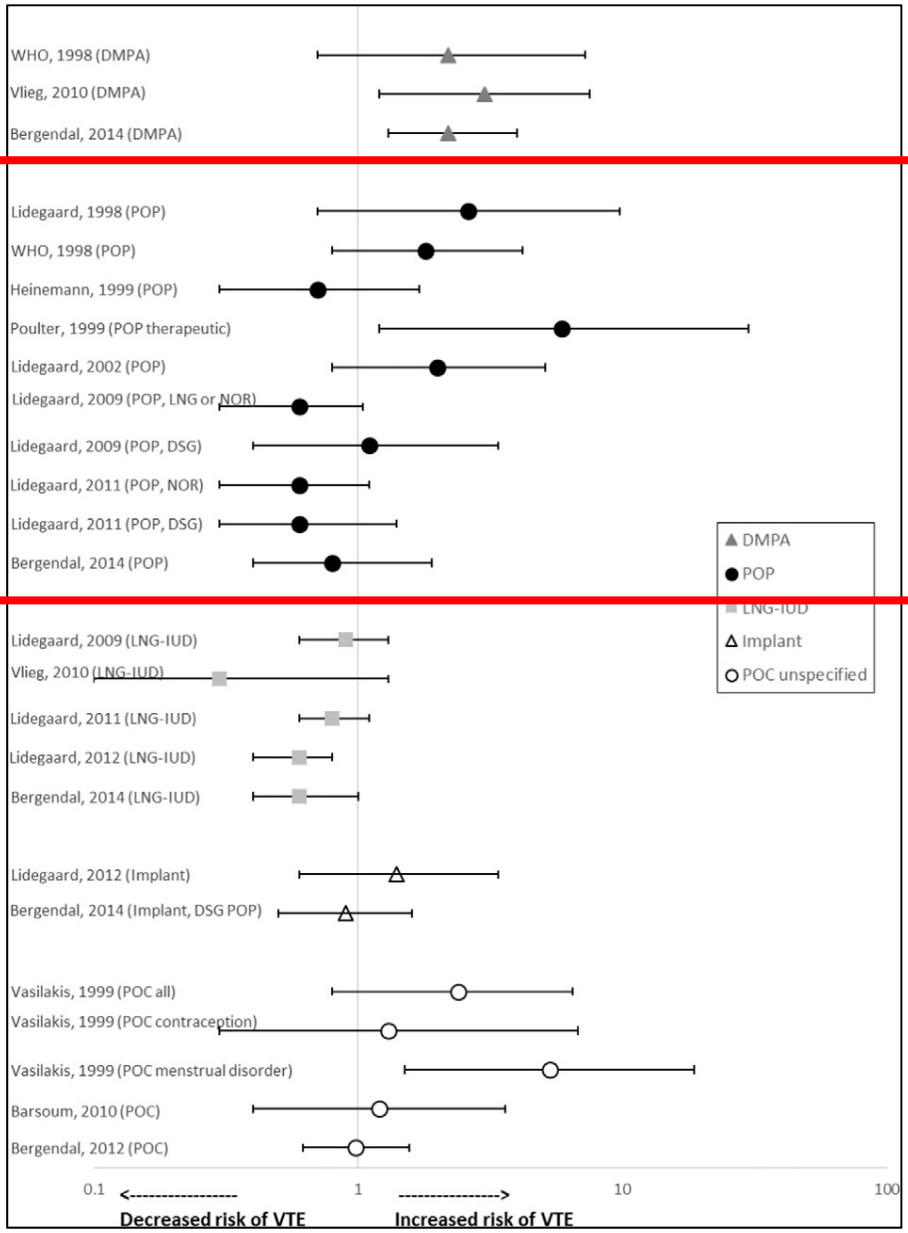
[4] National Department of Health and ICF. 2019. South Africa Demographic and Health Survey 2016. Pretoria: National Department of Health - NDoH - ICF. Available at http://dhsprogram.com/pubs/pdf /FR337/FR337.pdf
[5] Vinogradova Y, Coupland C, Hippisley-Cox J. Use of combined oral contraceptives and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases. BMJ. 2015 May 26;350:h2135. https://www.ncbi.nlm.nih.gov/pubmed/26013557
[6] Tepper NK, Whiteman MK, Marchbanks PA, James AH, Curtis KM. Progestin-only contraception and thromboembolism: A systematic review. Contraception. 2016 Dec;94(6):678-700. https://www.ncbi.nlm.nih.gov/pubmed/27153743



Tepper et al, 2016:

Fig. 5. Risk* of VTE among women in the general population using POCs. Abbreviations: *DMPA, depot medroxyprogesterone acetate; DSG, desogestrel; IUD, intrauterine device; LNG, levonorgestrel; NOR, norethindrone; POC, progestin-only contraceptive; POP, progestin-only pill; VTE, venous thromboembolism.*

*Reference group is nonusers.


WHO, 1998 (DMPA)
Vlieg, 2010 (DMPA)
Bergendal, 2014 (DMPA)
Lidegaard, 1998 (POP)
WHO, 1998 (POP)
Heinemann, 1999 (POP)
Poulter, 1999 (POP therapeutic)
Lidegaard, 2002 (POP)
Lidegaard, 2009 (POP, LNG or NOR)
Lidegaard, 2009 (POP, DSG)
Lidegaard, 2011 (POP, NOR)
Lidegaard, 2011 (POP, DSG)
Bergendal, 2014 (POP)
Lidegaard, 2009 (LNG-IUD)
Vlieg, 2010 (LNG-IUD)
Lidegaard, 2011 (LNG-IUD)
Lidegaard, 2012 (LNG-IUD)
Bergendal, 2014 (LNG-IUD)
Lidegaard, 2012 (Implant)
Bergendal, 2014 (Implant, DSG POP)
Vasilakis, 1999 (POC all)
Vasilakis, 1999 (POC contraception)
Vasilakis, 1999 (POC menstrual disorder)
Barsoum, 2010 (POC)
Bergendal, 2012 (POC)
DMPA
POP
LNG-IUD
Implant
POC unspecified
0.1
1
10
100
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Decreased risk of VTE
Increased risk of VTE