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SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 7: FAMILY PLANNING
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020-2024) REVIEW CYCLE-UPDATE

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the respective standard treatment guideline (STG) and supporting medicine reviews. All reviews and costing reports may be accessed at: https://www.health.gov.za/nhi-edp-stgs-eml/

A: AMENDMENTS

SECTION	MEDICINE/ MANAGEMENT	ADDED/DELETED/AMENDED/NOT ADDED/ RETAINED
Chapter Title		Not amended, an explanatory statement added at the beginning of chapter.
Introduction to contraception	Cross references to other clinical guidelines	Editorial amendments added, references to National and other guidelines added.
Contraceptive methods (Summary table)	Copper Intrauterine contraceptive device (IUCD)	-Editorial amendments added -The duration of use retained. -Guidance on use in women at very high risk of STIs added. -Guidance on use in active STIs added. -Advantages of use as emergency contraception added. -Safety during breastfeeding added.
	Levonorgestrel Intrauterine device (LNG-IUCD)	-Editorial amendments added -The duration of use retained. -Guidance for use at the time of caesarean section added.
	Hormonal subdermal: progestin-only implant	-Editorial amendments added.
	Hormonal injectable: progestin-only	-Editorial amendments added. -Possibility of Weight gain added.
	Hormonal oral: combined oral contraceptive (COC)	-Guidance on fertility after cessation of COC amended.
	Barrier: male and female condoms	-Emphasis on consistent and correct use added.
Effectiveness of family planning methods	Rates of unintended pregnancies	-Table amended
7.1 Intrauterine contraceptive copper device (IUCD)	Post choice termination of pregnancy (CTOP)	-Guidance added.
	Return for assessment	-Guidance added.
	Routine follow-up post insertion	-4 to 12 weeks follow-up after insertion added. -Annual visit not added. -Editorial amendments added.
	STI testing for women initiating contraception	Not added.
	Exclusion of IUCD in women with active or at high risk of STI	Guidance amended
	Use of Copper IUCD for women on enzyme-inducing medicines	Guidance editorially amended for clarity

7.2.1 Subdermal implant	Timing of insertion	Amended, editorial amendments also added.
	Concomitant use with Hepatic enzyme inducing medicines	Guidance amended.
	Concomitant use with dolutegravir	Guidance added.
	Insertion of etonogestrel 68 mg implant	Guidance amended with extensive editorial amendments.
7.2.2 Levonorgestrel intra-uterine device (LNG-IUD)	Title of section	Not amended and editorial amendments added.
7.2.3 Injectable	When to start the injection	Amended.
	Risk of HIV acquisition associated with progestin injectable contraceptives	Guidance removed.
	Late injection	-Guidance amended and cross reference to Section 7.4: Contraception, Emergency added -Editorial amendments added
	Medroxyprogesterone (long acting), SC	Added outside of Progestin-only Injectable therapeutic class and administration guidance added.
	Risk of meningiomas with long term use of DMPA	Caution box added
7.2. Oral	Triphasic preparations	Classification retained.
	When to start the pill	Guidance added.
	Non-liver enzyme inducing medicines (Lamotrigine)	Guidance amended and heading removed
7.3 Contraceptive, barrier methods	ICD 10 codes	Z30.4/Z30.5 removed, editorial amendments
7.4 Contraception, emergency	Description	Clinical editorial amendments
	Ulipristal acetate	Under consideration for review.
	Frequent use of emergency contraceptive	Guidance added.
	Double dose of levonorgestrel for patients on hepatic enzyme inducing drugs	Dosing guidance added.
	Use of levonorgestrel for patients on Enzyme inhibitor drugs (such as ketoconazole, fluconazole)	Guidance added.
	Referral	Cross reference to Section 21.3.6.2: Post exposure prophylaxis, rape and sexual assault added
7.6 Breakthrough bleeding with contraceptive use	Non-steroidal anti-inflammatory drugs (NSAIDS), Tranexamic Acid and Doxycycline	Under consideration for review.
	Breakthrough bleeding with Combined oral contraceptives (COCs)	Recommended dose of COCs containing ethinylestradiol amended to 30 mcg
Therapeutic interchange database /updates		See page 21

Chapter Title: *Not amended*

The family planning chapter currently provides guidance exclusively for contraception and does not include all aspects of family planning such as pre-conception care e.g. infertility. An external comment to rename the title of the chapter was not accepted at this time. A statement has been included at the beginning of the chapter to highlight the limitations of the guidance provided in the chapter in the context of family planning. A hyperlink to the National guidelines for safe conception and infertility has been included for additional guidance.

The STG has been amended as follows:

The guidance contained in this chapter is currently limited to contraception and does not cover all aspects of family planning such as pre-conception care. Refer to the National guidelines for safe conception and infertility for further guidance.

INTRODUCTION TO CONTRACEPTION

Cross references to other clinical guidelines: *Added*

For expanded guidance to supplement the recommendations included in the family planning chapter, the updated references for the NDoH National Contraception Clinical Guidelines[1], the WHO Medical eligibility criteria for contraceptive use[2],and the WHO family planning handbook for providers[3] have been added. It is to be noted that the STG is not a comprehensive clinical practice guideline document and therefore, additional guidance should be sought from the appropriate Programmatic guidelines.

The STG has been amended as follows:

Amended from: Consult the most recent National Contraception Clinical Guidelines (especially in women with medical conditions). Women should decide their own family planning method, in consultation with their health care professional, taking into consideration safety, efficacy, acceptability, and access. Always obtain a complete medical and sexual history and perform an appropriate physical examination in order to ensure that there are no contra-indications to using a particular method. Always exclude pregnancy before commencing contraception. Amended To: For comprehensive guidance, consult the most recent National Contraception Clinical Guidelines (especially for women with medical conditions) as well as the WHO Medical eligibility criteria for contraceptive use and the WHO family planning handbook for providers. Women should decide their own family planning method in consultation with their healthcare professional, taking into account the individual considerations of safety, efficacy, acceptability, and access. Always obtain a complete medical and sexual history and perform an appropriate physical examination in order to ensure that there are no contra-indications to using a particular method. Provide counselling and always exclude pregnancy before commencing contraception.

Contraceptive methods: Summary table

Copper Intrauterine contraceptive device (IUCD):
-Editorial amendments added
-The duration of use retained.
-Guidance on use in women at very high risk of STIs added.
-Guidance on use in active STIs added.
-Advantages of use as emergency contraception added.
-Safety during breastfeeding added.

The copper IUCD currently on the state contract HP-03 (ending 30 September 2026) Nova T 380®, is indicated for removal only after 5 years[4]-[5]. It was noted by NEMLC to investigate and encourage the sourcing copper IUCDs of longer duration for up to 10 years. In addition, the contraceptive methods summary table has been amended to include safety of the copper IUCD during breast feeding and an advantage for use as emergency contraception. An external comment to provide a recommendation as to whether the copper IUCD should be recommended in women who are at high risk of STIs was reviewed and not accepted. If a woman has a very high individual likelihood of exposure to STIs, she should generally not have a copper IUCD inserted unless other methods are not available or not acceptable[1].

[1] NDoH.National Contraception Clinical Guidelines.2019. https://knowledgehub.health.gov.za/elibrary/national-contraception-clinical-guidelines-2019

[2] World Health Organization. Reproductive Health. Medical eligibility criteria for contraceptive use. World Health Organization; 2015. https://iris.who.int/bitstream/handle/10665/181468/9789241549158_eng.pdf?sequence=9

[3] Family Planning: A Global Handbook for Providers (2022 update). Baltimore and Geneva: CCP and WHO, 2022. https://www.who.int/publications/i/item/9780999203705

[4] NDoH. Master Health product list (MHPL). January 2025

[5] Bayer Healthcare. Nova T 380®.Package insert.2011

The STG has been amended as follows:

Amended From:

Contraceptive method	Advantages include:	Disadvantages include:
Copper IUCD (see Section 7.1)	» Suitable for most women, including nulliparous women. » Provides long-term protection i.e. 5 years. » Convenient, does not require frequent follow up. » Works immediately on insertion. » Non-hormonal therefore no interaction with other medication and no hormonal side effects. » Fertility returns immediately on the removal of IUCD in women of child-bearing age.	» Some discomfort or cramping during and following insertion. » IUCD must be inserted or removed by a trained health care professional. » Should not be used in women with menorrhagia, active pelvic inflammatory disease (PID), purulent cervicitis, unexplained uterine bleeding, cervical and endometrial cancers or other uterine abnormalities.

Amended To:

Contraceptive method	Advantages include:	Disadvantages include:
» Copper IUCD (see Section 7.1)	» Suitable for most women, including nulliparous women. » Provides long-term protection i.e. 5 years. » Convenient, does not require frequent follow up. » Works immediately on insertion. » Non-hormonal therefore no interaction with other medication and no hormonal side effects. » Fertility returns on the removal of IUCD in women of childbearing age. » Can be used for emergency contraception (see section 7.4). » safe to use during breastfeeding.	» Some discomfort or cramping during and following insertion. » IUCD must be inserted or removed by a trained healthcare professional. » Should not be used in women with menorrhagia, high risk of STIs, active STIs and active pelvic inflammatory disease (PID), purulent cervicitis, unexplained uterine bleeding, cervical and endometrial cancers or other uterine abnormalities.

<u>Levonorgestrel Intrauterine device (LNG-IUD):</u>

-Editorial amendments added.

-The duration of use retained.

-Guidance for use at the time of caesarean section added.

The LNG-IUD currently on the state contract HP-03 (ending 30 September 2026) Mirena® is indicated for removal only after 5 years[4-6]. It was noted by NEMLC to investigate the availability and encourage the sourcing LNG-IUDs of longer duration for up to 8 years. Similar to the copper IUCD, guidance has been added to highlight that LNG-IUD can be inserted during caesarian section as an advantage[1]. Editorial amendments also incorporated.

The STG has been amended as follows:

Amended From:

Levonorgestrel Intrauterine device (LNG-IUD) (see Section 7.2.2)	» Suitable for most women, including nulliparous women. » Provides long-term protection (up to 5 years). » Convenient, does not require frequent follow up. » Works immediately on insertion. » Immediate return to fertility on removal. » Reduces menstrual cramps, heavy menstrual bleeding, and symptoms of endometriosis.	» Bleeding changes are common but not harmful. Typically, lighter and fewer days of bleeding, or infrequent or irregular bleeding. » LNG-IUD must be inserted or removed by a trained health care professional. » Should not be used in women with active PID.

[6] Bayer Healthcare. Mirena®. Package insert.2019

	» Can be inserted postpartum (within 48 hours after delivery).	
Amended To:		
Levonorgestrel Intrauterine device (LNG-IUD) (see Section 7.2.2)	» Suitable for most women, including nulliparous women. » Provides long-term protection (up to 5 years). » Convenient, does not require frequent follow-up. » Works immediately on insertion. » Immediate return to fertility on removal. » Reduces menstrual cramps, heavy menstrual bleeding, and symptoms of endometriosis. » Similar to the Copper IUCD, can be inserted at the time of a caesarean section and postpartum (within 48 hours after delivery).	» Bleeding changes are common but not harmful. Typically, lighter and fewer days of bleeding, or infrequent or irregular bleeding. » LNG-IUD must be inserted or removed by a trained healthcare professional. » Should not be used in women with active PID.

Hormonal subdermal: progestin-only implant: *Editorial amendments added*

The STG currently recommends progestin-only subdermal implants as a therapeutic class. On the state contract HP-03 (ending 30 September 2026) Implanon NXT® containing etonogestrel; 68mg is available for use over a duration of 3 years. The NEMLC encourages the sourcing of other therapeutically equivalent alternatives with a longer duration of contraception e.g. levonorgestrel containing implants.

Minor editorial amendments have been added to the STG as follows:

Amended From:

Hormonal subdermal: progestin-only implant (see Section 7.2.1)	» Provides long-term protection i.e. 3 years (etonogestrel) or 5 years (levonorgestrel). » Convenient, does not require frequent follow up. » Can be used in women >35 years who are obese, who smoke, or who have diabetes, hypertension, or a history of venous thromboembolism. » Fertility returns on removal of implant in women of child-bearing age.	» Frequent bleeding irregularities. » Implant must be inserted or removed by a trained health care professional under aseptic conditions to prevent infection. » Incorrect insertion and removal technique may result in complications.

Amended To:

Hormonal subdermal: progestin-only implant (see Section 7.2.1)	» Provides long-term protection i.e. 3 years (etonogestrel) or 5 years (levonorgestrel). » Convenient, does not require frequent follow up. » Can also be used in women >35 years who are obese, who smoke, or who have diabetes, hypertension, or a history of venous thromboembolism. » Fertility returns on the removal of the implant in women of child-bearing age.	» Frequent bleeding irregularities. » Implant must be inserted or removed by a trained health care professional under aseptic conditions to prevent infection. » Incorrect insertion and removal techniques may result in complications.

Hormonal injectable: progestin-only:
-Editorial amendments added
-Possibility of weight gain added

Weight gain associated with the progestin-only injectable has been included as one of the undesirable effects[7]-[8]. In addition, the STG classification of progestin-only injectables as long-acting reversible contraception method has been retained.

The STG has been amended as follows with additional editorial amendments:

Amended From:

Hormonal injectable: progestin-only (see Section 7.2.2)	» Daily adherence is not required. » Long acting i.e. given every 8 or 12 weeks. » Interactions with other medicines do not lower contraceptive effect. » Can be used postpartum. » Can be used in women >35 years who are obese, who smoke, or who have diabetes, hypertension, or a history of venous thromboembolism.	» Delayed return to fertility of up to 9 months, after last injection. » Frequent bleeding irregularities (irregular, prolonged and/or heavy bleeding, or amenorrhoea).

Amended To:

Hormonal injectable: progestin-only (see Section 7.2.2)	» Daily adherence is not required. » Long acting i.e. given every 8 or 12 weeks. » Interactions with other medicines do not lower the contraceptive effect. » Can be used postpartum. » Can also be used in women >35 years who are obese, who smoke, or who have diabetes, hypertension, or a history of venous thromboembolism.	» Delayed return to fertility of up to 9 months, after the last injection. » Frequent bleeding irregularities (irregular, prolonged and/or heavy bleeding, or amenorrhoea). » Associated with a possible weight gain

Hormonal oral: combined oral contraceptive (COC): *Guidance on fertility after cessation of COC amended.*

For better clarity, the STG has been editorially amended to indicate that although fertility returns with the use of COCs, it may be delayed for up to 3 months.

The STG has been amended as follows:

Amended From:

» Non-contraceptive benefits, e.g.: alleviation of dysmenorrhoea, premenstrual syndrome, and menorrhagia.
» Fertility returns within 3 months of discontinuing COC.

Amended To:

» Non-contraceptive benefits, e.g.: alleviation of dysmenorrhoea, premenstrual syndrome, and menorrhagia.
» Fertility returns after discontinuation of COC but can take up to 3 months.

Barrier: male and female condoms: *Emphasis on consistent and correct use added.*

For emphasis, guidance has been added to the STG highlighting the importance of consistency and correct use of barrier methods to prevent pregnancies.

The STG has been amended as follows:

Amended From:

» Possibility of breakage or slipping off.
» Possible allergic reaction to latex.
» Lower efficacy than other contraceptive methods therefore advised as dual contraception.

Amended To:

» Possibility of breakage or slipping off.
» Possible allergic reaction to latex.
» Lower efficacy than other contraceptive methods therefore advised as dual contraception.

[7] Pfizer. Depo-Provera® 150mg inj. Package insert.2022

[8] Family Planning: A Global Handbook for Providers (2022 update). Baltimore and Geneva: CCP and WHO, 2022. https://www.who.int/publications/i/item/9780999203705

» Consistent and correct use is required to prevent pregnancy

Effectiveness of family planning methods: *Table amended*

Following clinical editorial review, in line with the WHO[9] guideline, the table comparing the rates of unintended pregnancies during the first year of typical vs consistent and correct use has been updated with the addition of a colour representation of the estimates of effectiveness of the various contraception methods. To make the table simpler for user interpretation, the historical column containing % of women continuing use of contraception at one year has been removed.

The STG has been amended as follows:

Contraceptive method	Failure rate in 1st year (%)		% of women continuing use at one year
	Consistent and correct use	As typically used	
Copper IUCD	0.6	0.8	78
LNG-IUD	0.2	0.2	80
Progestin-only subdermal implant	0.05	0.05	84
Progestin-only injectable	0.3	3	56
Progestin-only oral pill (not breastfeeding)	0.3	8	67
Progestin-only oral pill (during breast feeding)	0.5	1	n/a
Combined oral contraceptive (COC) pill	0.3	3	67
Barrier: female condoms	5	21	41
Barrier: male condoms	2	15	43
Sterilisation: male – vasectomy	0.1	0.15	100
Sterilisation: female - tubal ligation	0.5	0.5	100
No method	85	85	n/a

Key: 0-0.9: very effective 10-25: moderately effective
1-9: effective 26-32: less effective

Contraceptive method	Failure rate in 1st year (%)	
	Consistent and correct use	Typical use
Sterilisation: male – vasectomy	0.1	0.15
Sterilisation: female - tubal ligation	0.5	0.5
Progestin-only subdermal implant	0.1	0.1
LNG-IUD	0.5	0.7
Copper IUCD	0.6	0.8
Progestin-only injectable	0.2	4
Progestin-only oral pill (during breastfeeding)	0.3	7
Combined oral contraceptive (COC) pill	0.3	7
Progestin-only oral pill (not breastfeeding)	0.3	8
Barrier: male condoms	2	13
Barrier: female condoms	5	21
No method	85	85

Key:

0-0.9: very effective	1-9: effective
10-19: moderately effective	20+: less effective

7.1 Intrauterine contraceptive copper device (IUCD)

Routine follow-up post insertion:
-4 to 12 weeks follow-up after insertion added
-Annual visit not added
-Editorial amendments added

[9] Family Planning: A Global Handbook for Providers (2022 update). Baltimore and Geneva: CCP and WHO, 2022. https://www.who.int/publications/i/item/9780999203705

An external comment to recommend annual follow-up visits post insertion of the copper IUCD was considered but not accepted. The decision for the frequency of follow-up visits was considered in the context of programmatic implementation feasibility and capacity (National Contraception Clinical Guidelines current do not make this provision). The STG has also been amended to include re-examination at 4 to 12 weeks after insertion[10] in order to allow women to be trained on how to feel for the copper IUCD strings after each period.

Post choice termination of pregnancy (CTOP):
-Guidance added

An external comment to add post choice termination of pregnancy (CTOP) to the STG as an indication for copper IUCD insertion has been accepted.

Return for assessment:
-Guidance added

An additional criterion to return for assessment has been added to the STG, highlighting that when strings of the inserted copper IUCD cannot be felt, the woman should be advised to return for assessment. In addition, an editorial review comment to clarify that women should be advised to return for assessment if there is an expulsion of IUCD or if strings of the IUCD become visible was accepted. Furthermore, The STG advises women to return for assessment if the strings of the IUCD cannot be felt, the Committee accepted the clinical editor recommendation for guidance to be added advising women to check the strings of the IUCD monthly to ensure that the device is still in place.

STI testing for women initiating contraception:
-Not added

An external comment recommending routine STI testing for women initiating copper IUCD contraception based on the outcomes of the ECHO trial[11] was not accepted. The NEMLC noted that although the ECHO trial demonstrated a high baseline rate of STIs in African women, the authors did not specifically recommend testing before initiating the contraception method. It was felt that the decision to recommend STI testing should be pragmatically implemented from the National programme based on capacity and resource considerations.

Exclusion of IUCD in women with active or at high risk of STI
-Guidance amended

In line with the National guidelines[12], the STG has been amended to highlight that Copper IUCD is not recommended if a woman has a very high individual likelihood of exposure to STIs, unless other methods are not available or not acceptable.

Interaction of IUCD with antiretrovirals: *Caution text amended*

Following clinical editorial review, for better clarity to the reader, the caution box has been amended indicating that IUCDs are often the most suitable contraceptive for women on enzyme-inducing medicine, because of the absence of drug interactions.

The STG has been amended including editorial amendments as follows:

Amended From:	Amended To:

[10] Bayer. Nova-T 380®. Package insert.2011

[11] Evidence for Contraceptive Options and HIV Outcomes (ECHO) Trial Consortium. HIV incidence among women using intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: a randomised, multicentre, open-label trial. Lancet. 2019;394(10195):303–13. doi: 10.1016/S0140-6736(19)31288-7.

[12] NDoH.National Contraception Clinical Guidelines.2019. https://knowledgehub.health.gov.za/elibrary/national-contraception-clinical-guidelines-2019

Dual protection with barrier methods is recommended to reduce the risk of STIs including HIV. The IUCD is a long-term contraceptive method that is effective, safe and reversible. It has no hormonal effects or drug interactions..It does not require daily adherence or frequent follow up.	Dual protection with barrier methods is recommended to reduce the risk of STIs including HIV. The copper IUCD (also known as the Copper T) is a long-term contraceptive method that is effective, safe and reversible. It has no hormonal effects or drug interactions. It does not require daily adherence or frequent follow up.
HIV infection is NOT a contra-indication to the use of an IUCD. **IUCDs are often the most suitable contraceptive for women on antiretrovirals and other enzyme-inducing medicines, because of the absence of drug interactions.**	**HIV infection is NOT a contra-indication to the use of an IUCD.** **IUCDs are often the most suitable contraceptive for women on enzyme-inducing medicines, because of the absence of drug interactions.**
Copper IUCD, e.g.: Cu T380A, 380mm² copper device. Devices with lower copper surface area are not recommended. The IUCD can be inserted at any time during the menstrual cycle, once pregnancy has been excluded (by clinical history or with a pregnancy test if required). Insertion at menstruation may be easier for the woman and results in less discomfort and spotting. Copper IUCDs may be inserted immediately postpartum or post miscarriage (within 48 hours) by specially trained health care professionals, provided that no contra-indications are present (chorioamnionitis, ruptured membranes for more than 18 hours, or postpartum haemorrhage). Alternatively, an IUCD may be inserted at least 4 weeks postpartum. *LoE:IIb*[i] Advise women when to return: Expulsion of IUCD or if strings of the IUCD protrude. Complications (excessive bleeding, excessive pain, fever, or foul-smelling discharge). Routine follow-up after 3–6 weeks. *LoE:IVb*[ii] Copper IUCD is not recommended for women with menorrhagia, active pelvic inflammatory disease (PID), purulent cervicitis, unexplained uterine bleeding, cervical and endometrial cancers or other uterine abnormalities. <u>For mild pain and discomfort after insertion:</u> Ibuprofen, oral, 400 mg 8 hourly with or after a meal as needed for up to 3 days. **REFERRAL** Excessive pain or bleeding after insertion. Signs of infection within 7 days of insertion (e.g. fever, abdominal pain and/or foul-smelling discharge). Abnormal bleeding for > 3 months.	Copper IUCD, e.g.: Cu T380A, 380mm² copper device. Devices with lower copper surface area are not recommended. The IUCD can be inserted at any time during the menstrual cycle, once pregnancy has been excluded (by clinical history or with a pregnancy test if required). Insertion at menstruation may be easier for the woman and results in less discomfort and spotting. Copper IUCDs may be inserted immediately postpartum or post miscarriage and post choice termination of pregnancy (CTOP) (within 48 hours) by specially trained healthcare professionals, provided that no contra-indications are present (chorioamnionitis, ruptured membranes for more than 18 hours, or postpartum haemorrhage). Alternatively, an IUCD may be inserted at least 4 weeks postpartum. *LoE:IIb*[iii] Advise women to check the strings of the IUCD monthly to ensure that the device is still in place. Advise women when to return: Expulsion of IUCD or if strings of the IUCD become visible. Complications (excessive bleeding, excessive pain, fever, or foul-smelling discharge). Routine follow-up at 4–12 weeks after insertion. *LoE:IVb*[iv] If the strings of the IUCD cannot be felt. Copper IUCD is not recommended for women with menorrhagia, active STI, active pelvic inflammatory disease (PID), purulent cervicitis, unexplained uterine bleeding, cervical and endometrial cancers or other uterine abnormalities. If a woman has a very high individual likelihood of exposure to STIs, she should generally not have a Copper IUCD inserted unless other methods are not available or not acceptable. <u>For mild pain and discomfort after insertion:</u> Ibuprofen, oral, 400 mg 8 hourly with or after a meal as needed for up to 3 days. **REFERRAL** Excessive pain or bleeding after insertion. Signs of infection within 7 days of insertion (e.g. fever, abdominal pain and/or foul-smelling discharge). Abnormal; or heavy menstrual bleeding for > 3 months.

7.2.1 Subdermal implant

<u>Timing of insertion:</u>

-Amended

<u>Concomitant use with Hepatic enzyme inducing medicines:</u>

-Guidance amended

<u>Concomitant use with dolutegravir:</u>

Guidance added

<u>Insertion of etonogestrel 68 mg implant:</u>

Guidance amended with extensive editorial amendments

The timing of insertion of the subdermal implant has been revised. The implant should be inserted between Day 1 (first day of menstrual bleeding) and Day 5 of the menstrual cycle[13] with the contraceptive effect being achieved within 24 hours of placement.
For better clarity, the STG has also been amended to highlight that subdermal implants are not contraindicated when using drugs which induce the metabolism of progestins[14]-[15]. However, it is emphasised that patients should be advised to use non-hormonal contraceptive methods during the time of concomitant use.
Additionally, the STG has been amended to highlight that subdermal implants may effectively be combined with dolutegravir-based ART regimens[16].
In line with the revised package insert[17] of the product currently on the state contract, the guidance for the safe insertion and removal of the etonogestrel implant has been revised extensively with editorial amendments. In addition, an editorial comment to consider revising the product specific guidance included in the STG in the event that a different product is procured was reviewed, the STG text has been amended to indicate that readers should refer to the specific professional information for detailed guidance on the product available on the National contract.

The STG has been amended as follows:

Amended From:	Amended To:
SUBDERMAL IMPLANT Z30.0/Z30.4/Z30.8	**SUBDERMAL IMPLANT** Z30.0/Z30.4/Z30.8
Dual protection with barrier methods is recommended to reduce the risk of STIs, including HIV.	Dual protection with barrier methods is recommended to reduce the risk of STIs, including HIV.
The subdermal implant is an effective, safe, reversible, and convenient long-term contraceptive method that does not require daily adherence or frequent follow-up.	The subdermal implant is an effective, safe, reversible, and convenient long-term contraceptive method that does not require daily adherence or frequent follow-up.
Progestin-only subdermal implant contraceptive, e.g.: Etonogestrel, subdermal, 68 mg, single-rod implant.	Progestin-only subdermal implant contraceptive, e.g.: Etonogestrel, subdermal, 68 mg, single-rod implant.
The progestin-only subdermal implant can be inserted at any time during the menstrual cycle, once pregnancy has been excluded. If the implant is inserted within 7 days of the onset of the menstrual cycle the contraceptive effect is achieved on the day of insertion.	The progestin-only subdermal implant can be inserted at any time during the menstrual cycle, once pregnancy has been excluded. If the implant is inserted within day 1 and day 5 of the onset of the menstrual cycle the contraceptive effect is achieved within 24 hours of placement.
The main reason for discontinuation of the implant is irregular bleeding. This requires good counselling before the implant is inserted to inform women that this side effect can occur and can be treated. See Section 7.6: Breakthrough bleeding with contraceptive use.	The main reason for discontinuation of the implant is irregular bleeding. This requires good counselling before the implant is inserted to inform women that this side effect can occur and can be treated. See Section 7.6: Breakthrough bleeding with contraceptive use.
Progestin-only hormonal contraceptives are contraindicated in certain conditions e.g. unexplained vaginal bleeding, active liver disease. Consult the package insert in this regard.	The progestin-only subdermal implant is contraindicated in certain conditions e.g. unexplained vaginal bleeding, active liver disease. Consult the package insert in this regard.
LoE:IIIb[v]	*LoE:IIIb*[vi]
CAUTION Medicines that induce the metabolism of progestins could reduce contraceptive efficacy. These medicines include efavirenz, rifampicin, phenytoin, carbamazepine, and phenobarbital. Women on these medicines should be advised to use alternate contraceptive methods such as the copper IUCD or DMPA. If the client chooses to use the implant, then she should be advised to use dual contraception.	**CAUTION** Medicines that induce the metabolism of progestins could reduce contraceptive efficacy. These medicines include efavirenz, rifampicin, phenytoin, carbamazepine, and phenobarbital. Women receiving any of the above listed hepatic enzyme-inducing medicines should be advised that the efficacy of the subdermal implant may be reduced. If it is decided to continue using the subdermal implant, women should be advised to also use a non-hormonal contraceptive method dur-

[13] Organon SA. Implanon NXT® 68 mg Implant ®. Package insert.2019

[14] Stalter RM, Amorim G, Mocello AR, Jakait B, Shepherd BE, Musick B, Bernard C, Bukusi EA, Wools-Kaloustian K, Cohen CR, Yiannoutsos CT, Patel RC; Implant/Efavirenz Study Group and the East Africa IeDEA regional consortium. Contraceptive implant use duration is not associated with breakthrough pregnancy among women living with HIV and using efavirenz: a retrospective, longitudinal analysis. J Int AIDS Soc. 2022 Sep;25(9):e26001. doi: 10.1002/jia2.26001. PMID: 36073977; PMCID: PMC9454412.

[15] Todd CS, Lorenzetti L, Mussa A, Ridgeway K, Morroni C, Nanda K. Drug-drug interactions between antiretrovirals and hormonal contraception: An updated systematic review. Contraception. 2024 Oct;138:110490. doi: 10.1016/j.contraception.2024.110490. Epub 2024 May 16. PMID: 38762199.

[16] Bishop IJ, Gertz AM, Simon B, Tawe L, Lechiile K, Liu S, Teodoro N, Mussa A, Avalos A, Malima S, Maotwe T, Mokganya L, Westhoff CL, Morroni C. Etonogestrel concentrations among contraceptive implant users in Botswana using and not using dolutegravir-based antiretroviral therapy. Contraception. 2020 Sep;102(3):174-179. doi: 10.1016/j.contraception.2020.04.019. Epub 2020 May 7. PMID: 32387328.

[17] Implanon NXT® 68mg Implant.Package insert.South Africa.Revision:27 August 2019

Insertion and removal procedures Participation in a training session is strongly recommended to become familiar with the use of the subdermal implants and techniques for insertion and removal. Only health care professionals familiar with these procedures should insert and remove subdermal implants, under aseptic conditions. Insert the implant **subdermally just under the skin of the upper non-dominant arm.** **Important: Refer to the package inserts for detailed information**. <u>Insertion of etonogestrel 68 mg implant:</u> Insertion should only be performed with the preloaded applicator. Have the woman lie on her back on the examination table with her non-dominant arm flexed at the elbow and externally rotated so that her wrist is parallel to her ear and her hand is positioned next to her head. Identify anatomical surface markings to establish the area of insertion, which is the inner side of the non-dominant upper arm about 8–10 cm above the medial epicondyle of the humerus, avoiding the sulcus (groove) between the biceps and triceps muscle and the large blood vessels and nerves situated in the neurovascular bundle deeper in the subcutaneous tissue. Clean the insertion site with an antiseptic solution. Anaesthetise the insertion area. Mark the insertion site with a marker. Insert the implant subdermally:. Remove the transparent protection cap by sliding it horizontally in the direction of the arrow, away from the needle. Puncture the skin with the tip of the needle slightly angled less than 30° relative to the skin surface. Lower the applicator to a horizontal position. While lifting the skin with the tip of the needle, slide the needle to its full length. You should be able to see the applicator just below the skin. Be seated, looking at the applicator from the side and NOT from above to clearly see the insertion and positioning of the needle just under the skin. While keeping the applicator in the same position and the needle inserted to its full length, unlock the purple slider by pushing it slightly down. Move the slider fully back until it stops. The implant is now in its final subdermal position. Remove the applicator. Always verify the presence of the implant in the woman's arm immediately after insertion by palpation and allow her to feel the implant as well. Apply sterile gauze with a pressure bandage to minimise bruising. The woman may remove the pressure bandage in 24 hours and the small bandage over the insertion site after 3–5 days. <u>Insertion of levonorgestrel 2 x 75 mg implants:</u> Clean the woman's upper arm with an antiseptic solution. The optimal insertion area is in the medial aspect of the upper arm about 6-8 cm above the fold of the elbow. Use the scalpel to make a small incision (about 2 mm) just through the dermis of the skin. Alternatively, the trocar may be inserted directly through the skin without making an incision. The implants will be inserted subdermally, in the shape of a narrow V, opening towards the armpit. Anesthetise two areas about 4.5 cm long, to mimic the V shape of the implantation site. Mark the insertion site with a marker. Open the implant pouch by pulling apart the film of the pouch and let the two implants drop on a sterile cloth. Note: Always use sterile gloves or forceps when handling the implants. If an implant is contaminated, e.g. falls on the floor leave it for later disposal. Open a new package and continue with the procedure. The implant is provided with a disposable trocar that is sharp enough to penetrate the skin directly. Thus the disposable trocar can be used to puncture the skin and insert the rods, without the need for an incision. The trocar has two marks. One mark is close to the handle and one close to the tip. When inserting the implants, the mark closest to the handle indicates how far the trocar should be introduced under the skin before loading each implant. The mark closest to the tip indicates how much of the trocar should be left under the skin after the insertion of the first implant. When inserting the trocar, avoid touching the part of the trocar that will go under the skin. Once the tip of the trocar is beneath the skin it should be directed along the subdermal plane horizontally by pointing it slightly upwards and raising the skin (tenting). Failure to keep the trocar in the subdermal plane may	ing the time of concomitant use (the subdermal implant is not contra-indicated when using the above medicines). Dolutegravir, however, can be effectively be used in combination with subdermal implants. **Insertion and removal procedures** Participation in a training session is strongly recommended to become familiar with the use of the subdermal implants and techniques for insertion and removal. Only health care professionals familiar with these procedures should insert and remove subdermal implants, under aseptic conditions. Insert the implant **subdermally just under the skin of the upper non-dominant arm.** **Important: Refer to the specific professional information for detailed guidance on the product available on the National contra** <u>Insertion of etonogestrel 68 mg implant:</u> Insertion should only be performed with the preloaded applicator. Have the woman lie on her back on the examination table with her non-dominant arm flexed at the elbow and externally rotated, so that her hand is underneath her head (or as close as possible). Identify the insertion site, which is at the inner side of the non-dominant upper arm. The insertion site is overlying the triceps muscles about 8 to10 cm from the medial epicondyle of the humerus and 3 to 5 cm posterior to the sulcus (groove) between the biceps and triceps muscles). This location is intended to avoid the large blood vessels and nerves lying within and surrounding the sulcus. If it is not possible to insert the implant in this location (e.g. in women with thin arms), it should be inserted as far posterior from the sulcus as possible Make two marks with a surgical marker: First, mark the spot where the implant will be inserted, and second, mark a spot at 5 centimetres proximal (toward the shoulder) to the first mark This second mark (guiding mark) will later serve as a direction guide during insertion (guiding mark). *LoE:IVb*[vii] Clean the insertion site with an antiseptic solution. Anaesthetise the insertion area. Insert the implant subdermally:. - Hold the applicator just above the needle at the textured surface area. Remove the transparent protection cap by sliding it horizontally in the direction of the arrow away from the needle Puncture the skin with the tip of the needle slightly angled less than 30° relative to the skin surface. If you insert the needle past the bevel, withdraw it until only the bevel is beneath the skin. Lower the applicator to a horizontal position. To facilitate subdermal placement, lift the skin with the needle, while sliding the needle to its full length. You should be able to see the applicator just below the skin. Be seated, looking at the applicator from the side and NOT from above to clearly see the insertion and positioning of the needle just under the skin. While keeping the applicator in the same position and the needle inserted to its full length. The purple slider should be unlocked by pushing it slightly down). The slider should be moved fully back until it stops. The implant is now in its final subdermal position. Remove the applicator. Always verify the presence of the implant in the woman's arm immediately after insertion by palpation and allow her to feel the implant as well. Apply sterile gauze with a pressure bandage to minimise bruising. The woman may remove the pressure bandage in 24 hours and the small bandage over the insertion site after 3–5 days. <u>Insertion of levonorgestrel 2 x 75 mg implants:</u> Clean the woman's upper arm with an antiseptic solution. The optimal insertion area is in the medial aspect of the upper arm about 6-8 cm above the fold of the elbow. The implants will be inserted subdermally, in the shape of a narrow V, opening towards the armpit. Anesthetise two areas about 4.5 cm long, to mimic the V shape of the implantation site. Mark the insertion site with a marker.

result in deep placement of the implants, causing a more difficult removal. Throughout the insertion procedure, the trocar should be oriented with the bevel up. Advance the trocar beneath the skin about 5.5 cm from the incision to the mark closest to the handle of the trocar. Do not force the trocar, and if you feel any resistance, try another direction. Remove the plunger when the trocar is advanced to the correct mark. Load the first implant into the trocar with either tweezers or fingers. Push the implant gently with the plunger to the tip of the trocar until you feel resistance. Never force the plunger. Hold the plunger steady and pull the trocar back along it until it touches the handle of the plunger. It is important to keep the plunger steady and not to push the implant into the tissue. Do not completely remove the trocar until both implants have been placed. The trocar is withdrawn only to the mark closest to its tip. When you can see the mark near the tip of the trocar in the incision, the implant has been released and will remain in place beneath the skin. You can check this by palpation. Insert the second implant next to the first one, to form a V shape. Fix the position of the first implant with the left fore-finger and advance the trocar along the side of the finger. This will ensure a suitable distance between implants. To prevent expulsions, leave a distance of about 5 mm between the incision and the ends of the implants. You can check their correct position by cautious palpation of the insertion area. After inserting the second implant, press the edges of the incision together, close with a skin closure and dress the wound. Advise the woman to keep the insertion area dry for 3 days. The gauze and the bandage may be removed as soon as the incision has healed, usually after 3–5 days. <u>For pain after insertion:</u> Ibuprofen, oral, 400 mg 8 hourly with or after a meal as needed for up to 5 days. <u>Removal of progestin-only subdermal implants:</u> Remove etonogestrel implants at the end of 3 years and levonorgestrel implants at the end of 5 years. Locate the implant/s by palpation. If impalpable refer for ultrasound removal. Clean the removal site with an antiseptic solution. Anaesthetise the removal area. Push down the proximal end of the implant and a bulge may appear to indicate the distal end of the implant. Make a 2-4 mm vertical incision with the scalpel close to the distal end of the implant, towards the elbow. Remove the implant very gently, using a small forceps (preferably curved mosquito forceps). Where an implant is encapsulated, dissect the tissue sheath to remove the implant with the forceps. Confirm that the complete implant has been removed by measuring the length (etonogestrel rod: 40 mm; levonorgestrel rods: 43 mm). Close the incision with a steristrip or plaster and dress. Advise the woman to keep the arm dry for a few days. **REFERRAL** Heavy or prolonged bleeding, despite treatment with COCs. Infection at insertion site, inadequately responding to initial course of antibiotic treatment. See Section 5.4.3: Cellulitis. Failure to locate an implant (in the arm) by palpation.	Use the scalpel to make a small incision (about 2 mm) just through the dermis of the skin. Alternatively, the trocar may be inserted directly through the skin without making an incision. Open the implant pouch by pulling apart the film of the pouch and let the two implants drop on a sterile cloth. Note: Always use sterile gloves or forceps when handling the implants. If an implant is contaminated, e.g. falls on the floor leave it for later disposal. Open a new package and continue with the procedure. The implant is provided with a disposable trocar that is sharp enough to penetrate the skin directly. Thus, the disposable trocar can be used to puncture the skin and insert the rods, without the need for an incision. The trocar has two marks. One mark is close to the handle and one close to the tip. When inserting the implants, the mark closest to the handle indicates how far the trocar should be introduced under the skin before loading each implant. The mark closest to the tip indicates how much of the trocar should be left under the skin after the insertion of the first implant. When inserting the trocar, avoid touching the part of the trocar that will go under the skin. Once the tip of the trocar is beneath the skin it should be directed along the subdermal plane horizontally by pointing it slightly upwards and raising the skin (tenting). Failure to keep the trocar in the subdermal plane may result in deep placement of the implants, causing a more difficult removal. The trocar should be oriented with the bevel up throughout the insertion procedure.. Advance the trocar beneath the skin about 5.5 cm from the incision to the mark closest to the handle of the trocar. Do not force the trocar; if you feel any resistance, try another direction. Remove the plunger when the trocar is advanced to the correct mark. Load the first implant into the trocar with either tweezers or fingers. Push the implant gently with the plunger to the tip of the trocar until you feel resistance. Never force the plunger. Hold the plunger steady and pull the trocar back along it until it touches the handle of the plunger. It is important to keep the plunger steady and not to push the implant into the tissue. Do not completely remove the trocar until both implants have been placed. The trocar is withdrawn only to the mark closest to its tip. When you can see the mark near the tip of the trocar in the incision, the implant has been released and will remain in place beneath the skin. You can check this by palpation. Insert the second implant next to the first one, to form a V shape. Fix the position of the first implant with the left fore-finger and advance the trocar along the side of the finger. This will ensure a suitable distance between implants. To prevent expulsions, leave a distance of about 5 mm between the incision and the ends of the implants. You can check their correct position by cautious palpation of the insertion area. After inserting the second implant, press the edges of the incision together, close with a skin closure and dress the wound. Advise the woman to keep the insertion area dry for 3 days. The gauze and the bandage may be removed as soon as the incision has healed, usually after 3–5 days. <u>For pain after insertion:</u> Ibuprofen, oral, 400 mg 8 hourly with or after a meal as needed for up to 5 days. <u>Removal of progestin-only subdermal implants:</u> Remove etonogestrel implants at the end of 3 years and levonorgestrel implants at the end of 5 years. Locate the implant/s by palpation. If impalpable refer for ultrasound guided removal. Mark the distal end (end closest to the elbow) e.g. with a surgical marker Clean the removal site with an antiseptic solution. Anaesthetise the removal area. Inject the local anaesthetic under the implant to keep the implant close to the skin surface Push down the proximal end of the implant and a bulge may appear to indicate the distal end of the implant. Make a longitudinal (parallel to the implant) incision of approximately 2 mm towards the elbow . Very gently remove the implant, using a small forceps (preferably curved mosquito forceps). Where an implant is encapsulated, dissect the tissue sheath to remove the implant with the forceps. Confirm that the complete implant has been removed by measuring the length (etonogestrel rod: 40 mm; levonorgestrel rods: 43 mm). Close the incision with a steristrip or plaster and dress. Advise the woman to keep the arm dry for a few days.

	REFERRAL Heavy or prolonged bleeding, despite treatment with COCs. Infection at the insertion site, inadequately responding to an initial course of antibiotic treatment. See Section 5.4.3: Cellulitis. Failure to locate an implant (in the arm) by palpation.

7.2.2 LEVONORGESTREL INTRA-UTERINE DEVICE (LNG-IUD)

Title of section: *Not amended and editorial amendments added.*

An external comment to rename this section Levonorgestrel containing intra-uterine device (LNG-IUD) to allow for other progestin-containing devices that may be used in future was considered but not accepted at this stage. Minor editorial amendments to the referral criteria have also been made to include heavy menstrual bleeding as an indication for referral. ICD 10 code Z30.5 (Z30.5 - Surveillance of (intrauterine) contraceptive device) has been added and ICD 10 code Z30.4 (Surveillance of contraceptive drugs) removed.

The STG has been amended as follows:

Amended From:

REFERRAL
Excessive pain or bleeding after insertion.
Signs of infection within 7 days of insertion (e.g. fever, abdominal pain and/or foul-smelling discharge).
Abnormal bleeding for > 3 months.
First time migraine or severe headaches.

Amended To:

REFERRAL
Excessive pain or bleeding after insertion.
Signs of infection within 7 days of insertion (e.g. fever, abdominal pain and/or foul-smelling discharge).
Abnormal or heavy menstrual bleeding for > 3 months.
First time migraine or severe headaches.

7.2.3 INJECTABLE

When to start the injection: *Amended*

The STG guidance for initiation of the progestin-only injectable contraceptive has been amended, recommending treatment to be started immediately postpartum in both breastfeeding and non-breastfeeding women if no other method is acceptable or available. It was noted that progestin-only injectable are classified as WHO Medical eligibility criteria for contraceptive use (MEC) category 3[18], whereas classified as MEC category 2 under the National contraceptive guidelines[19].

Risk of HIV acquisition associated with progestin injectable contraceptives: *Removed*

The previous STG recommendation advised for dual contraception with barrier methods in view of the uncertainty of the risk of HIV acquisition associated with using the progestin injectable contraceptives at the time of chapter review. This recommendation has been removed. In line with the ECHO trial results, there is no substantial difference in HIV acquisition among the various contraceptive methods evaluated (DMPA-IM, a copper IUD, or a LNG implant) in the trial, all methods were safe and highly effective[20].

[18] World Health Organization. Reproductive Health. Medical eligibility criteria for contraceptive use. World Health Organization; 2015.

[19] NDoH.National Contraception Clinical Guidelines.2019. https://knowledgehub.health.gov.za/elibrary/national-contraception-clinical-guidelines-2019

[20] Evidence for Contraceptive Options and HIV Outcomes (ECHO) Trial Consortium. HIV incidence among women using intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: a randomised, multicentre, open-label trial. Lancet. 2019 Jul 27;394(10195):303-313. doi: 10.1016/S0140-6736(19)31288-7. Epub 2019 Jun 13. Erratum in: Lancet. 2019 Jul 27;394(10195):302. doi: 10.1016/S0140-6736(19)31408-4. PMID: 31204114; PMCID: PMC6675739.

Late injection:

-Guidance amended and cross reference to Section 7.4: Contraception, Emergency added

-Editorial amendments added

The STG has been amended, allowing for a late reinjection grace period for up to 4 weeks for Depot medroxyprogesterone acetate (DMPA) and 2 weeks late reinjection grace period for norethisterone enanthate (NET-EN). Delayed reinjection for 4 weeks with DMPA and 2 weeks with NET-EN does not increase pregnancy risk and could increase contraceptive continuation[21] .This recommendation is also In line with the updated WHO Family planning handbook for providers[22]. In addition, an editorial review comment adding a cross reference to Section 7.4: Contraception, emergency in the event of a late injection was accepted.

An editorial review comment to incorporate the SAHPRA professional information for depot medroxyprogesterone SC, Sayana® 104 mg/0.65 ml, which recommends administration no later than 14 weeks after last injection was not accepted. For pragmatism, the Committee felt that the updated STG recommendation allowing up to 4 weeks late injection applies to both DMPA (long-acting) IM and SC formulations.

The STG has been amended as follows:

<table>
<tr>
<td>Amended From:
Late injection
If it has been <2 weeks since the missed injection, the next injection can be given without loss of protection. Continue with dual contraceptive method, i.e. condom in combination with the injection.
If it has been >2 weeks since the missed injection, exclude pregnancy:
<table>
<tr><th>Pregnancy test positive</th><th>Pregnancy test negative or unavailable</th></tr>
<tr><td>Refer for ante-natal care (See Section 6.4: Antenatal care).
or
TOP, see Section 6.3: Termination of pregnancy (TOP).</td><td>Provide emergency contraception, if indicated (see Section: 7.4 Contraception, emergency).
Administer the next injection.
Advise the woman to abstain from intercourse or use condoms to prevent pregnancy for the next 7 days.</td></tr>
</table>
</td>
<td>Amended To:
Late injection
The next injection can be as much as 4 weeks late if using the medroxyprogesterone acetate DMPA (long-acting),or 2 weeks late if using norethisterone enanthate (NET-EN).
» Injectable contraceptive may be administered later than recommended if more >4 weeks late for DMPA or >2 weeks late for NET-EN the next injection can receive, if:
• She has not had sex since 2 weeks after the scheduled date of her injection, or
• She has used a backup method or has taken emergency contraceptive pills after any unprotected sex since 2 weeks after the scheduled date of her injection, or
• She is fully or nearly fully breastfeeding and she gave birth less than 6 months ago.
However, in all three cases she will need a backup method for the first 7 days after the injection
» Assess the need for emergency contraception in the event of a late injection (See Section 7.4: Contraception, Emergency).</td>
</tr>
</table>

Depot medroxyprogesterone (long acting), SC: *Added outside of therapeutic class.*

Following the 2020 NEMLC review[23] conditionally recommending depot medroxyprogesterone acetate SC (DMPA-SC) as a therapeutic alternative in the progestin-only injectable contraceptive therapeutic class. The NEMLC felt at the time that there is no preference for either formulation as they seem to have similar therapeutic efficacy and safety profile. The recommendation was ratified by NEMLC pending the registration of a product by South African Health Products Authority (SAHPRA) which includes the self-injection label and additional local feasibility and acceptability studies to determine if the self-administration option is a viable option in the South African context. In 2024, a follow-up review was submitted and adjudicated by NEMLC providing further evidence on the SAHPRA registration, pricing and user acceptability studies for the consideration of DMPA-SC as an alternative choice of contraception method outside of the progestin-only injectable therapeutic class. NEMLC has recommended DMPA-SC as an EML

[21] Steiner MJ, Kwok C, Stanback J, Byamugisha JK, Chipato T, Magwali T, Mmiro F, Rugpao S, Sriplienchan S, Morrison C. Injectable contraception: what should the longest interval be for reinjections? Contraception. 2008 Jun;77(6):410-4. doi: 10.1016/j.contraception.2008.01.017. Epub 2008 Apr 10. PMID: 18477489

[22] Family Planning: A Global Handbook for Providers (2022 update). Baltimore and Geneva: CCP and WHO, 2022. https://www.who.int/publications/i/item/9780999203705

[23] NDoH Review. Medroxyprogesterone 104mg SC for prevention of pregnancy.2020

item in view of the updated approval by SAHPRA of DMPA-SC for self-administration along with updated evidence of feasibility, acceptability and affordability.

See NEMLC recommendation as tabulated below. A copy of the full review may be accessed on the NHI webpage.

	We recommend against the option and for the alternative **(strong)**	We suggest not to use the option **(conditional)**	We suggest using either the option or the alternative **(conditional)**	We suggest using the option **(conditional)**	We recommend the option **(strong)**
Type of recommendation				**X**	

NEMLC Recommendation: NEMLC suggests that either low dose DMPA-SC or intramuscular progestogen injectables may be used by women for preventing pregnancy. (Conditional recommendation, moderate certainty evidence).

Remarks:
This marks a change of DMPA-SC from a therapeutic interchange option to an EML item and is based on available evidence of efficacy and safety, the change in access given the updated approval of DMPA-SC by the South African Health Products Authority (SAHPRA) for self-administration, along with updated evidence of feasibility, acceptability and affordability.

Rationale: The current review found that there is evidence that DMPA-SC is acceptable to stakeholders, feasible to implement and access, and cost-effective. This is in addition to the previously appraised evidence of safety and efficacy which has not changed since first reviewed in 2020. NEMLC noted that the option for self-administration and expansion of contraceptive options may have important equity implications and public health benefit for women in the South African setting. This recommendation is conditional on the product being available at the indicative price provided herein (R29.63 incl VAT) or less.

Level of Evidence: Review indicator: *Increase in product price*

Monitoring and evaluation considerations:
Patients switching from another contraceptive option to DMPS-SC – has implications for forecasting.

Research priorities:
Acceptability and contraceptive adherence using self-administration in South Africa.

The STG has been amended as follows:

Amended From:	Amended To:
Dual protection with barrier methods is recommended to reduce the risk of STIs, including HIV. □ Progestin-only injectable contraceptive, e.g.: • Medroxyprogesterone (long-acting), IM, 150 mg, 12 weekly. Progestin-only hormonal contraceptives are contraindicated in certain conditions e.g. unexplained vaginal bleeding. Consult the package insert in this regard. When to start the injection » The injection can be started anytime within the menstrual cycle, provided pregnancy has been excluded. If the first injection is given within 7 days of the onset of the menstrual cycle, the contraceptive effect is achieved on the day of the first injection. » If started after day 7,advise the woman to abstain from intercourse or use condoms for the next 7 days. » Can be used postpartum. Late injection » If it has been <2 weeks since the missed injection, the next injection can be given without loss of protection. Continue with dual contraceptive method, i.e. condom in combination with the injection.	Dual protection with barrier methods is recommended to reduce the risk of STIs, including HIV. Progestin-only injectable contraceptive, e.g.: Medroxyprogesterone (long-acting), IM, 150 mg, 12 weekly. OR • Medroxyprogesterone (long-acting), SC,104mg, 12 weekly Progestin-only hormonal contraceptives are contraindicated in certain conditions e.g. unexplained vaginal bleeding. Consult the individual professional information in this regard. **Using the Progestin-only IM Injection** When to start the injection The injection can be started anytime within the menstrual cycle, provided pregnancy has been excluded. If the first injection is given within 7 days of the onset of the menstrual cycle, the contraceptive effect is achieved on the day of the first injection. If started after day 7, advise the woman to abstain from intercourse or use condoms for the next 7 days. Can be started immediately postpartum in both breastfeeding and non-breastfeeding women if no other method is acceptable or available.

» If it has been >2 weeks since the missed injection, exclude pregnancy

Pregnancy test positive	Pregnancy test negative or unavailable
Refer for ante-natal care (See Section 6.4: Antenatal care). ***or*** TOP, see Section 6.3: Termination of pregnancy (TOP).	Provide emergency contraception, if indicated (see Section: 7.4 Contraception, emergency). Administer the next injection. Advise the woman to abstain from intercourse or use condoms to prevent pregnancy for the next 7 days.

There is uncertainty of the risk of HIV acquisition associated with progestin injectable contraceptives (Refer to the WHO MEC 2017 guidelines). Dual protection is recommended.

Late injection

The next injection can be as much as 4 weeks late if using the medroxyprogesterone acetate DMPA (long-acting),or 2 weeks late if using norethisterone enanthate (NET-EN).

If more >4 weeks late for DMPA or >2 weeks late for NET-EN the next injection can receive, if:

- She has not had sex since 2 weeks after the scheduled date of her injection, or
- She has used a backup method or has taken emergency contraceptive pills after any unprotected sex since 2 weeks after the scheduled date of her injection, or
- She is fully or nearly fully breastfeeding and she gave birth less than 6 months ago.

However, in all three cases she will need a backup method for the first 7 days after the injection

Using the Progestin-only SC Injection

May be administered by a healthcare professional (HCP) or with adequate training when considered appropriate by the HCP, self-injected by the patient, with medical follow up as necessary.

When to start the injection

» The first injection of 104 mg SC should be given during the first 5 days of a normal menstrual cycle to ensure the client is not pregnant.

» The second and subsequent injections should be given at a 3 month interval (12 -14 weeks).

» Can be started immediately postpartum in both breastfeeding and non-breastfeeding women if no other method is acceptable or available

-Risk of meningiomas with long term use of DMPA: *Caution box added*

In line with the revised SAHPRA professional information for DMPA containing products[24], citing an observational case control study which showed an excess risk of meningioma with use of medroxyprogesterone acetate and other selected progestogens. (injectable medroxyprogesterone acetate, 9/18 061 (0.05%) vs 11/90 305 (0.01%) exposed controls, odds ratio 5.55 (95% confidence interval 2.27 to 13.56))[25]. The STG has thus been amended, adding a caution box to address this signal. In addition, the STG has been amended with guidance for the consideration of alternative contraceptive methods instead of the DMPA- injectable (taking into account client preferences and circumstances) when contraception is required for long term use (e.g., longer than 2 years).

The STG has been amended as follows:

CAUTION

» Alternative contraceptive options should be considered if the continued use of medroxyprogesterone acetate (IM or SC) is extended beyond 2 years. All effective contraceptive options should be considered, taking into account client preferences and circumstances.
» A small increased risk of meningiomas (rare, and mostly benign tumours) have been reported following long-term administration of Medroxyprogesterone acetate (long-acting),
» Medroxyprogesterone (long-acting) should be discontinued if a meningioma is diagnosed.
» Caution is advised when recommending Medroxyprogesterone (long-acting) to patients with a history of meningioma.

7.2.4 ORAL

[24] Depo-Provera®.Professional Information.South Africa.Revision:21 January 2025

[25] Roland N, Neumann A, Hoisnard L, Duranteau L, Froelich S, Zureik M, Weill A. Use of progestogens and the risk of intracranial meningioma: national case-control study. BMJ. 2024 Mar 27;384:e078078. doi: 10.1136/bmj-2023-078078. Erratum in: BMJ. 2024 Mar 28;384:q776. doi: 10.1136/bmj.q776. PMID: 38537944; PMCID: PMC10966896.

Triphasic preparations: *Classification retained*

An external comment to rename triphasic oral preparations to multiphasic preparation as triphasic preparations a generally considered as old generation was not accepted. The WHO still classifies oral contraceptives as monophasic, biphasic, and triphasic and in line, the STG has remained unchanged.

When to start the pill: *Guidance added*

The STG currently recommends that the pill, if started at any other time outside the menstrual cycle, has to be taken for at least 7 days to protect against pregnancy. Guidance has now been added recommending condom use during this time.

Non-liver enzyme inducing medicines (Lamotrigine): *Guidance amended, and heading removed*

The interaction between oral contraceptives and lamotrigine has been highlighted, recommending the use of a backup method (e.g. barrier contraception) if short term lamotrigine is required, or a change to IUCD or progesterone only methods if long term use of lamotrigine is required. A an external comment to include in the STG that the contraceptive effectiveness of COCs might be compromised when lamotrigine is taken concurrently has not be accepted due to insufficient supportive evidence. The lowering of contraceptive effect by the concurrent use of lamotrigine and oral contraceptives is not expected[26]-[27]. In addition, The Committee accepted an editorial review comment to remove the heading "*non-liver enzyme inducing medicines"* as the purported mechanism of the interaction between lamotrigine and COCs is that of liver enzyme induction.

The STG has been amended as follows:

Amended From:
» Exclude pregnancy.
» Start anytime within the menstrual cycle, but it is advisable to start during menses.
» If the first pill is given between days 1 and 5 of the menstrual cycle the contraceptive effect is achieved immediately.
» If the pill is started at any other time, it needs to be taken for at least 7 days before it protects against pregnancy.

Non-liver enzyme inducing medicines
Lamotrigine:
» Lowering of contraceptive effect not expected.
» Oral contraceptives may reduce lamotrigine concentration by 50%, increasing the risk of seizures. Consider alternative dual contraception method.

Amended To:
» Exclude pregnancy.
» Start anytime within the menstrual cycle, but it is advisable to start during menses.
» If the first pill is given between days 1 and 5 of the menstrual cycle the contraceptive effect is achieved immediately.
» If the pill is started at any other time, it needs to be taken for at least 7 days before it protects against pregnancy. The use of condoms is recommended

Lamotrigine:
» Lowering of contraceptive effect not expected.
» Oral contraceptives may reduce lamotrigine concentration, increasing the risk of seizures. Change to IUCD or progesterone only methods i.e (levonorgestrel implant or etonogestrel implant or LNG-IUD) if lamotrigine is going to be used long term.

7.3 CONTRACEPTION, BARRIER METHODS

ICD 10 codes Z30.4/Z30.5 removed, editorial amendments

Following clinical editorial review, the following ICD 10 codes were removed:
Z30.4 - Surveillance of contraceptive drugs

[26] Gaffield ME, Culwell KR, Lee CR. The use of hormonal contraception among women taking anticonvulsant therapy. Contraception. 2011 Jan;83(1):16-29. doi: 10.1016/j.contraception.2010.06.013. Epub 2010 Sep 15. PMID: 21134499.

[27] Family Planning: A Global Handbook for Providers (2022 update). Baltimore and Geneva: CCP and WHO, 2022. https://www.who.int/publications/i/item/9780999203705

Z30.5 - Surveillance of (intrauterine) contraceptive drugs

Including some editorial amendments, the STG Has been amended as follows:

Amended From	Amended To
Z30.0/Z30.4/Z30.5 Condoms (male and female) alone are not the most effective contraceptive method and should be used in combination with other contraceptive methods (e.g. copper IUCD). Condoms are recommended to reduce the risk of the acquisition of STIs and HIV infection. Condoms (male and female) or other barrier methods may be an option for contraception where other methods are contraindicated.	Z30.0 Condoms (male and female) alone are the least effective contraceptive method and should be used in combination with other contraceptive methods (e.g. copper IUCD). Condoms are recommended to reduce the risk of the acquisition of HIV infection and other STIs. Condoms (male and female) or other barrier methods may be an option for contraception where other methods are contraindicated.

7.4 CONTRACEPTION, EMERGENCY

Ulipristal acetate: *Under consideration for review*

Ulipristal acetate is currently proposed for consideration for NEMLC review in the next review cycle as an alternative for levonorgestrel for the management of emergency contraception.

Frequent use of emergency contraceptive: *Guidance added*

An external comment to include guidance for women who use emergency contraceptive frequently was accepted. Guidance to provide counselling for consideration of a longer acting and more effective family planning method has been added.

The STG has been amended as follows:

A woman who needs emergency contraception often should be counselled to consider a longer acting and more effective family planning method.

Double dose of levonorgestrel for patients on hepatic enzyme inducer drugs: *Guidance added*

Dosing guidance on doubling the dose of levonorgestrel in patients using hepatic enzyme inducer drugs has been added. To be taken as two x 1.5 mg tablets taken as a single dose, or if the dedicated product is not available, use COCs containing 30 µg ethinylestradiol + 150 µg levonorgestrel (e.g. Nordette/Oralcon). Six tablets followed by six tablets 12 hours later. A clinical editorial comment that the guidance for this section be incorporated outside of the caution box to avoid being missed by the reader which was accepted by the Committee.

Use of levonorgestrel for patients on Enzyme inhibitor drugs (such as ketoconazole, fluconazole): *Guidance added*

A recommendation to have a copper IUCD inserted or reduce the dose of levonorgestrel in patients on Enzyme inhibitor drugs requiring emergency contraception has been added. Enzyme inhibitors (such as ketoconazole, fluconazole) significantly increase the bioavailability of levonorgestrel thus potentiating nausea and vomiting.

Cross referral to Section 21.3.6.2: Post exposure prophylaxis, rape and sexual assault added

The STG has been amended, adding a cross referral to Section 21.3.6.2: Post exposure prophylaxis, rape and sexual assault for women who need of emergency contraception.Editorial amendments have been added and the STG amended as follows:

Amended From:

Emergency contraception is indicated to prevent pregnancy after unprotected intercourse in women not using contraception or where contraception is likely to be ineffective:

forgotten tablets (See Section 7.2.4: Missed pills)
slipped or broken condom
injectable contraception given >2 weeks late
sexual assault

Emergency contraception after pregnancy is excluded

Do a pregnancy test in all women and female adolescents. Children must be tested and given Emergency contraception from Breast Tanner Stage III.

Copper IUCD, e.g.:
Cu T380A, inserted as soon as possible after unprotected intercourse and not later than 5 days.

OR

Levonorgestrel 1.5 mg, oral, as a single dose as soon as possible after unprotected intercourse, and not later than 5 days.
If the client vomits within 2 hours, repeat the dose.

Advise women that their period should be on time; very rarely is it delayed but it should not be more than 7 days late. If this occurs, they should come back for a pregnancy test.

CAUTION

Emergency contraceptive tablets must be taken as soon as possible, preferably within 72 hours of unprotected intercourse, and not later than 5 days.

Enzyme inducers (including efavirenz and carbamazepine) cause a significant reduction in levonorgestrel concentrations. Women on these medicines should preferably have copper IUCD inserted ***or*** alternatively double the dose of levonorgestrel.

Women > 80 kg or BMI ≥ 30 should also preferably have copper IUCD inserted ***or*** alternatively double the dose of levonorgestrel.

REFERRAL
Women in need of emergency contraception must be referred for HIV counselling and testing and PEP

Amended To:

Emergency contraception is indicated to prevent pregnancy after unprotected intercourse in women not using contraception or where contraception is likely to be ineffective:

Forgotten tablets (See Section 7.2.45: Missed pills)
Slipped or broken condom
Injectable contraception given late (>2 weeks for NET-EN, >4 weeks for DMPA)
Sexual assault

A woman who needs emergency contraception often should be counselled to consider a longer acting and more effective family planning method.

Emergency contraception after pregnancy is excluded

Do a pregnancy test in all women and female adolescents. Children must be tested and given emergency contraception from Breast Tanner Stage III.

Copper IUCD, e.g.:
Cu T380A, inserted as soon as possible after unprotected intercourse and no later than 5 days.

OR

Levonorgestrel 1.5 mg, oral, as a single dose as soon as possible after ~~unprotected intercourse, and not later than 5 days~~.
If the client vomits within 2 hours, repeat the dose.

Advise women that their period should be on time. It is rarely delayed but it should not be more than 7 days late. If this occurs, they should come back for a pregnancy test.

If using enzyme inducing drugs or woman weighs > 80 kg / BMI ≥ 30:

- » It is recommended to have a copper IUCD inserted.
- » If this is not possible, double the dose of levonorgestrel administered:
  - Levonorgestrel, 1.5 mg, oral, 2 tablets taken as a single dose.
- » If the dedicated product is not available, use COCs containing 30 µg ethinylestradiol + 150 µg levonorgestrel (e.g. Nordette/Oralcon):
  - Ethinylestradiol/levonorgestrel, oral, 30 mcg/150 mcg, 6 tablets taken as a single dose, followed by 6 tablets 12 hours later.

CAUTION

- » Emergency contraceptive tablets must be taken as soon as possible, preferably within 72 hours of unprotected intercourse, and not later than 5 days.
- » Enzyme inhibitors (ketoconazole, fluconazole) significantly increase the bioavailability of levonorgestrel and may increase nausea and vomiting. Women taking these medicines should preferably have copper IUCD inserted or reduce the dose of levonorgestrel

REFERRAL
Women in need of emergency contraception must be referred for HIV counselling and testing and PEP (See Section 21.3.6.2: Post exposure prophylaxis, rape and sexual assault).

7.6 BREAKTHROUGH BLEEDING WITH CONTRACEPTIVE USE

Non-steroidal anti-inflammatory drugs (NSAIDS), tranexamic acid and doxycycline: *Under consideration for review*

The STG currently recommends combined oral contraceptives for the management of breakthrough bleeding with hormonal contraception. External comments to consider the addition of other treatment options such as NSAIDS, tranexamic acid and doxycycline in line with other clinical practice recommendations[28]-[29] were not considered at this stage. The requests have been proposed for consideration by NEMLC in the next review cycle.

Breakthrough bleeding with Combined Oral Contraceptives (COC)- *Recommended dose of COCs containing ethinylestradiol amended*

The STG currently recommends changing to a COC containing 35mcg ethinylestradiol if breakthrough bleeding on COC persists. Following market intelligence, it was confirmed that there is currently no commercially available product containing COC with 35mcg ethinylestradiol but only combinations containing 30 mcg ethinylestradiol. It was recommended for the STG to be amended, to recommend COC containing ethinylestradiol 30mcg for the management of breakthrough bleeding on COCs.

The STG has been amended as follows:

Amended From:		Amended To:	
Combined oral contraceptive pill **Unscheduled bleeding with COC usually settles with time.** **Changing to another COC in the first 3 months is not recommended.**	• **Change COC to another COC containing the lowest dose of ethinylestradiol, oral, daily.** **If bleeding persists:** • **Change COC to a COC containing 35 mcg ethinylestradiol, oral, daily.**	**Combined oral contraceptive pill** **Unscheduled bleeding with COC usually settles with time.** **Changing to another COC in the first 3 months is not recommended.**	• **Change COC to another COC containing the lowest dose of ethinylestradiol, oral, daily.** **If bleeding persists:** • **Change COC to a COC containing 30 mcg ethinylestradiol, oral, daily.**

[28] Abdel-Aleem H, d'Arcangues C, Vogelsong KM, Gaffield ML, Gülmezoglu AM. Treatment of vaginal bleeding irregularities induced by progestin only contraceptives. Cochrane Database Syst Rev. 2013 Oct 21;(10):CD003449. doi: 10.1002/14651858.CD003449.pub5. PMID: 24146298.

[29] Australia FP. Guidance for management of troublesome vaginal bleeding with progestogen-only long-acting reversible contraception (LARC). Manly, Qld: Family Planning Alliance Australia, 2015 [Internet].

B: Therapeutic interchange database

Section	Indication	Therapeutic class	INN	strength	unit	NEMLC Recommendation
Intrauterine contraceptive copper device (IUCD)						
7.1	Contraception	Intrauterine contraceptive copper device (IUCD)	IUCD	Cu T380A, 380mm² copper device	1	27 March 2025 Non-hormonal device. Not listed on the therapeutic Interchange database in a class. Market intelligence required for other similar devices and duration of insertion for competitive prices. The chapter has not been updated.
CONTRACEPTION, HORMONAL						
Progestin-only subdermal implant contraceptive						
7.2.1	Contraception	Progestin-only subdermal implant contraceptive	Etonorgestrel	68 mg	1	
7.2.1	Contraception	Progestin-only subdermal implant contraceptive	Levonorgestrel	75 x 2 mg	1	
Progestin-only intrauterine device						
7.2.2	Contraception	Progestin-only intrauterine device	Levonorgestrel	52 mg	1	
		Progestin-only intrauterine device	Levonorgestrel	19.5 mg	1	
Progestin-only injectable contraceptive						
7.2.3	Contraception	Progestin-only injectable contraceptive	Medroxyprogesterone	150mg	1 x IM inj	
7.2.3	Contraception	Progestin-only injectable contraceptive	Norethisterone	200mg	1X IM inj	
ORAL						
Progestin-only: Monophasic preparations (low VTE risk)						
7.2.4	Contraception	Monophasic-progestin only pills - low VTE risk	Levonorgestrel	30mcg	28 tabs	
7.2.4	Contraception	Monophasic-progestin only pills - low VTE risk	Norethisterone	350 mcg	28 tabs	
Monophasic preparations: combination of estrogen and progestin (low to moderate VTE risk)						
7.2.4	Contraception	Monophasic preparations: combination of estrogen and progestin in each pill - low to moderate VTE risk	Levonorgestrel and ethinylestradiol	150/30 mcg	28 Tabs	
7.2.4	Contraception	Monophasic preparations:	Gestodene and ethinylestradiol	75/30 mcg	28 Tabs	

		combination of estrogen and progestin in each pill - low to moderate VTE risk				
7.2.4	Contraceptio n	Monophasic preparations: combination of estrogen and progestin in each pill - low to moderate VTE risk	Desogestrel and Ethinylestradiol	150/30 mcg	28 Tabs	
7.2.4	Contraceptio n	Monophasic preparations: combination of estrogen and progestin in each pill - low to moderate VTE risk	Drospirenone and ethinylestradiol	3/30 mcg	28 Tabs	
Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk						
7.2.4	Contraceptio n	Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk	Levonorgestrel and ethinylestradiol	0.05/0.03mg (6); 0.075/0.04 mg (5); 0.125/0.03 mg (10)	28 Tabs	24 April 2025 Retained as the example of class item in the chapter.
7.2.4	Contraceptio n	Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk	Norethisterone/Norethinderone and ethinylestradiol	0.5/0.035mg (7); 0.75/0.035 mg (7); 1/0.035mg (7)	28 tabs	24 April 2025 No product identified in the SA market
7.2.4	Contraceptio n	Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk	Norgestimate and ethinylestradiol	0.18/0.035 mg (7); 0.215/0.035 mg (7); 0.25/0.035 mg (7)	28 tabs	24 April 2025 No product identified in the SA market
7.2.4	Contraceptio n	Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk	Gestodene and ethinylestradiol	0.05/0.03 mg	28 tabs	24 April 2025 No product identified in the SA market
Monophasic preparations: combination of estrogen and progestin (low to moderate VTE risk)						
7.6	Breakthrough bleeding with Progestin subdermal implants	Monophasic preparations: combination of estrogen and progestin in each pill - low to moderate VTE risk	Levonorgestrel and ethinylestradiol	150/30 mcg	28 Tabs	27 March 2025 Updated the chapter to include Ethinylestradiol/ levonorgestrel 150/30 mcg as a therapeutic class recommendation.
7.6	Breakthrough bleeding with Progestin subdermal implants	Monophasic preparations: combination of estrogen and progestin in each pill - low to	Gestodene and ethinylestradiol	75/30 mcg	28 Tabs	

		moderate VTE risk				
7.6	Breakthrough bleeding with Progestin subdermal implants	Monophasic preparations: combination of estrogen and progestin in each pill - low to moderate VTE risk	Desogestrel and Ethinylestradiol	150/30 mcg	28 Tabs	
7.6	Breakthrough bleeding with Progestin subdermal implants	Monophasic preparations: combination of estrogen and progestin in each pill - low to moderate VTE risk	Drospirenone and ethinylestradiol	3/30 mcg	28 Tabs	

Updates after NEMLC meeting 27 March 2025.

Amendments April 2025

Triphasic preparation: combination of estrogen and progestin - low to moderate VTE risk class- *Amendments to class*

Following market intelligence of available products recommended in this class, it was found that only the class example containing Levonorgestrel and ethinylestradiol 0.05/0.03mg is commercially available in the SA market. On the 24 April 2025, NEMLC electronically ratified to retain the oral Triphasic preparations as a class in the chapter pending the availably of the suggested alternative product in future.