PHC Chapter 7: Family planning

Introduction to contraception

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INTRODUCTION TO CONTRACEPTION

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.

Contraceptive methods

Hormonal contraception and IUCDs do not prevent sexually transmitted infections (STIs), including HIV. Dual protection i.e. the use of a condom in combination with another contraceptive method is recommended to reduce the risk of STIs, including HIV.

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 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.
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. » Can be inserted postpartum (within 48 hours after delivery). *LoE:II*[1]	» 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. *LoE:III*[2]
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.	» Frequent bleeding irregularities. » Implant must be inserted or removed by a trained health care professional under

	» 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.	aseptic conditions to prevent infection. » Incorrect insertion and removal technique may result in complications.
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). *LoE:III*[3]
Hormonal oral: progestin-only (see Section 7.2.3)	» Fertility returns within 3 months of discontinuing the pill. » 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.	» Daily adherence is required. » Interactions with other medicines can lower contraceptive effect. » Lower efficacy compared with COC. » Frequent bleeding irregularities.
Hormonal oral: combined oral contraceptive (COC) (see Sections 7.2.3 and 7.2.4)	» Non-contraceptive benefits, e.g.: alleviation of dysmenorrhoea, premenstrual syndrome, and menorrhagia. » Fertility returns within 3 months of discontinuing COC.	» Daily adherence is required. » Interactions with other medicines can lower contraceptive effect. » Cannot be used in women with venous thrombo-embolic disease. » Cannot be used immediately postpartum.
Barrier: male and female condoms (see Section 7.3)	» Protects against STIs, including HIV.	» Possibility of breakage or slipping off. » Possible allergic reaction to latex. » Lower efficacy than other contraceptive methods therefore advised as dual contraception.

(Refer to the most recent SAHPRA registered package inserts for detailed information).

Effectiveness of family planning methods

Rates of unintended pregnancies per 100 women:

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

LoE:III[4]

7.1 INTRAUTERINE CONTRACEPTIVE COPPER DEVICE (IUCD)

Z30.0/Z30.1/Z30.5

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.

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.

- 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:I*[5]

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). *LoE:III*[6]
» Routine follow-up after 3–6 weeks.

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.

For mild pain and discomfort after insertion:
- 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.

7.2 CONTRACEPTION, HORMONAL

CAUTION
Before starting hormonal contraception, advise women about the expected bleeding patterns, both initially and in the longer term.

7.2.1 SUBDERMAL IMPLANT
Z30.0/Z30.4/Z30.8

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.

- 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 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.

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.

LoE:III[7]

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**.

Insertion of etonogestrel 68 mg implant:

» 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.

Insertion of levonorgestrel 2 x 75 mg implants:

» 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 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.

For pain after insertion:

- Ibuprofen, oral, 400 mg 8 hourly with or after a meal as needed for up to 5 days.

Removal of progestin-only subdermal implants:

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.

7.2.2 LEVONORGESTREL INTRA-UTERINE DEVICE (LNG-IUD)

Z30.0/Z30.4/Z30.8

Dual protection with barrier methods is recommended to reduce the risk of STIs including HIV.

The LNG-IUD is an effective, safe, reversible, long-term contraceptive method that has minimal hormonal adverse effects and is not prone to drug interactions. It does not require daily adherence or frequent follow up.

- Progestin-only intrauterine device, e.g.:
- Levonorgestrel, intrauterine device, 52 mg. LoE:I[8]

HIV infection is NOT a contra-indication to the use of an LNG-IUD.

LoE:III[9]

The LNG-IUD is a T-shaped plastic device that steadily releases a small amount of levonorgestrel every day. It has the added benefit of reducing menstrual cramping and heavy menstrual bleeding. It can be inserted by specially trained health care professionals, 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 womant, and results in less discomfort and spotting. For use by women of any age, regardless of whether they had children before.

LNG-IUD may be inserted immediately postpartum or post miscarriage (within 48 hours) provided that no contra-indications are present (chorioamnionitis, ruptured membranes for more than 18 hours or postpartum haemorrhage). Provider require specific training in postpartum insertion by hand or using a ring forceps.

LNG-IUD may also be inserted at 4 or more weeks postpartum.

Advise women when to return:

» Expulsion of LNG-IUD or if strings of the LNG-IUD protrude.
» Complications (excessive bleeding, excessive pain, fever or foul smelling discharge). LoE:III[10]
» Routine follow-up after 3–6 weeks.
» First time migraine or severe headaches during use.

LNG-IUD is not recommended for women with acute venous thromboembolism, severe liver cirrhosis, active pelvic inflammatory disease (PID), purulent cervicitis, unexplained uterine bleeding, cervical- breast- ovarian- or endometrial cancers, or other uterine abnormalities.

For mild pain and discomfort after insertion:

- Ibuprofen, oral, 400 mg 8 hourly with or after a meal as needed for up to 3 days. LoE:IV

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.

LoE:III[11]

7.2.3 INJECTABLE

Z30.0/Z30.4

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. *LoE:I*[12]

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. *LoE:III*[13]

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:

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.

LoE:III[14]

There is uncertainty of the risk of HIV acquisition associated with progestin injectable contraceptives (Refer to the WHO MEC 2017 guidelines[15]). Dual protection is recommended.

REFERRAL

Heavy or prolonged bleeding, despite adequate treatment with combined oral contraceptives. See Section 7.6: Breakthrough bleeding with contraceptive use.

7.2.4 ORAL

Z30.0/Z30.4

Dual contraception with barrier methods, are recommended to reduce the risk of STIs, including HIV.

Monophasic preparations:

- Progestin only pills, e.g.:
- Levonorgestrel, oral, 30 mcg daily. *LoE:III*[16]
- Progestins and estrogen, fixed combinations, e.g.:
- Ethinylestradiol/ levonorgestrel, oral, 30 mcg/150 mcg:
  - 21 tablets ethinylestradiol/levonorgestrel, 30 mcg/150 mcg and
  - 7 tablets placebo. *LoE:III*[17]

Triphasic preparations:

- Progestins and estrogen, sequential preparations, e.g.:
- Ethinylestradiol/levonorgestrel, oral:
  - 6 tablets ethinylestradiol/levonorgestrel, 30 mcg/50 mcg

- 5 tablets ethinylestradiol/levonorgestrel, 40 mcg/75 mcg and
- 10 tablets ethinylestradiol/levonorgestrel, 30 mcg/125 mcg and
- 7 tablets placebo.

LoE:III[18]

Counselling:

» Hormonal oral pills must be taken at the same time every day without interruption.
» Taking the hormonal oral pill with food or at bedtime may alleviate nausea.
» If the woman is not using dual contraception with barrier methods and vomits within 2 hours, or has severe diarrhoea within 12 hours of taking the hormonal oral pill, repeat the dose as soon as possible. Recommend condom use.
» Women who have persistent vomiting or severe diarrhoea resulting in two or more missed pills must follow instructions for missed pills - see section 7.2.4. Recommend condom use.

Contraindications and guidance to starting the hormonal oral pill

	Progestin only	**Combined estrogen/progestin**
Contra-indications	Progestin only preparations are contraindicated in certain conditions (Consult the package insert in this regard). Contraindications include: » Abnormal uterine bleeding of unknown cause. » Myocardial infarction/stroke. » Liver disease. » Cancer of the breast/ genital tract. » Known or suspected pregnancy. *LoE:III*[19]	Combination preparations contraindicated in certain conditions (Consult the package insert in this regard). Contraindications include: » Women >35 years of age who smoke ≥15 cigarettes a day or have risk factors for cardiovascular disease: – heart disease – liver disease – thromboembolism – certain cancers
When to start the pill	» 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.	

Medicine interactions

Enzyme-inducing medicines interacting with oral contraceptives		**Recommendation**
Therapeutic class	**Examples**	
Anti-tuberculosis	Rifampicin	Use copper IUCD or alternatively use dual contraception e.g. condoms in combination with COCs.
Anti-epileptics	Phenobarbital	
	Phenytoin	
	Carbamazepine	
Antiretrovirals	Nevirapine	
	Lopinavir/ritonavir	
	Efavirenz	

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.

Breastfeeding

» Women who are intending to breastfeed should delay initiation of COCs until cessation of breastfeeding or at 6 months postpartum, whichever occurs earlier.

REFERRAL

Abnormal vaginal bleeding for >3 months.

7.2.5 MISSED PILLS

Progestin only pills

Efficacy is rapidly lost if one pill is forgotten or taken >3 hours late. Recommend dual contraception for all scenarios for at least 7 days.

LoE:III[20]

Scenario	Action
One pill forgotten or if pill taken >3 hours late and unprotected sexual intercourse has not occurred in the past 5 days.	Take pill as soon as remembered and continue taking one pill daily at the same hour.
One pill forgotten or if taken 3 hours late and unprotected sexual intercourse has occurred in the past 5 days.	Give emergency contraception (see Section 7.4). Take one pill the next day and continue taking one pill daily at the same hour.

Combination of progestin and estrogen in each pill

Missing active pills and extending hormone free interval leads to decreased contraceptive efficacy. Recommend dual contraception for all scenarios for at least 7 days.

LoE:III[21]

LoE:III[22]

Scenario	Action
One active pill forgotten.	Take pill as soon as remembered and take next one at usual time.
≥ Two pills forgotten during the first 7 active pills of the pack and sexual intercourse has occurred in the past 5 days.	Give emergency contraception (see Section 7.4). Restart active pills 12 hours later.
≥ Two pills forgotten during the middle 7 active pills of the pack.	Take the most recent missed pill immediately (discard the other missed pills). Continue taking remaining pills as usual. No emergency contraception required.
≥ Two pills forgotten in the last 7 active pills of the pack and sexual intercourse has occurred in past 5 days.	Continue active pills of current pack. Omit the inactive pills and immediately start the active pills of the next pack.

7.3 CONTRACEPTION, BARRIER METHODS

Z30.0/Z30.4/Z30.5

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 STIs and HIV infection.

Condoms (male and female) or other barrier methods may be an option for contraception where other methods are contraindicated.

7.4 CONTRACEPTION, EMERGENCY

Z30.0/Z30.4

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

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

OR

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

Advise women that their period should be on time; very rarely it is 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 be given double the standard dose.

LoE:III[23]

REFERRAL

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

7.5 VOLUNTARY STERILISATION, MALE AND FEMALE

Z30.2

Female sterilisation

Also known as tubal occlusion or tubal ligation. This is a permanent, surgical contraceptive method for women who do not intend to have more children.

Women who opt for sterilisation should be adequately counselled and referred.

Male sterilisation

Also known as vasectomy. This is a permanent surgical contraceptive method for men who do not intend to have more children.

Men who opt for this method should be adequately counselled and referred.

CAUTION

Sterilisation does not protect against sexually transmitted infections (STIs), including HIV. If there is a risk of STI/HIV, the correct and consistent use of condoms is recommended.

LoE:III[24]

7.6 BREAKTHROUGH BLEEDING WITH CONTRACEPTIVE USE

N92.0/N92.1/N92.4

DESCRIPTION

Breakthrough bleeding refers to unscheduled or irregular vaginal bleeding, which often presents as spotting, or prolonged or frequent bleeding in women using hormonal contraception. The pattern and duration of these unscheduled bleedings vary with the contraceptive method used.

GENERAL MEASURES

Before starting hormonal contraception, counsel women regarding possible bleeding patterns, both initially and in the longer term.

Clinical assessment:

» Current method of contraception and duration of use.
» Drug interactions.
» Cervical screening history.
» Risk of sexual transmitted infections (e.g. Chlamydia trachomatis).
» Menstrual and break though bleeding history prior to current method being initiated.
» Exclude pregnancy.

Hormonal contraceptives causing breakthrough bleeding	Treatment
Progestin-only injectables	• COC containing 30 mcg ethinylestradiol, oral, for 14 days. *LoE:III*[25]
Progestin subdermal implants	• Ethinylestradiol/levonorgestrel, oral, 30/150 mcg, daily for 20 days.
Progestin intrauterine devices	Refer – see Section 7.2.2.
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 a COC containing the lowest dose of ethinylestradiol, oral, daily. <u>If bleeding persists:</u> • Change COC to a COC containing 35 mcg ethinylestradiol, oral, daily. *LoE:IV*

REFERRAL

» Pelvic pain.
» Pelvic mass.
» Heavy bleeding.
» Abnormal cervix on speculum examination (e.g. polyps).
» Bleeding not controlled by treatment above.

References:

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[14] Progestin-only injectables (late injection): National Contraception and Fertility Planning and Service Delivery Guidelines, 2019 (Draft format).

[15] World Health Organisation. Guidance statement: Hormonal contraceptive eligibility for women at high risk of HIV, 2019. https://www.who.int/reproductivehealth/publications/contraceptive-eligibility-women-at-high-risk-of-HIV/en/

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[22] Dual contraception for at least 7 days (missed pills): South African Medicines Formulary. 13th Edition. Division of Clinical Pharmacology. University of Cape Town. 2020.

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Chapter 8

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 7: FAMILY PLANNING
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020 -2023 REVIEW CYCLE)

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).

A: NEW SECTIONS/ SUB-SECTIONS

SECTION	CONDITION	MEDICINE MANAGEMENT	MEDICINE ADDED
7.2.2	Levonorgestrel intra-uterine device (LNG-IUD)	Yes	Progestin-containing IUD (added as a therapeutic group)
			LNG-IUD, 52 mg (added as an example of progestin-containing IUD group)
			LNG-IUD, 16 mg (added as an alternative of progestin-containing IUD group on the therapeutic interchange database)

7.2.2 LEVONORGESTREL INTRA-UTERINE DEVICE (LNG-IUD)

Progestin-containing IUD: *added as a therapeutic group*
LNG-IUD, 52 mg: *added as an example of progestin-containing LNG -IUD group*
LNG-IUD, 16 mg: *added as an alternative of progestin-containing LNG-IUD group on the therapeutic interchange database*

REVIEW OF PRICE OFFER FOR LNG-IUD, 52 MG

Background: Long-acting, reversible contraceptive methods (LARCs) are the most attractive option for contraception, especially in adolescents, as they are highly effective and does not require daily or monthly monitoring. The LNG-IUD has many benefits apart from effective contraception (see below), but its widespread use is inhibited by its higher cost. Previously, NEMLC had recommended that standard-dose LNG-IUD, 52mg not be recommended for contraception, as despite comparable effectiveness and safety with copper IUD, standard-dose LNG-IUD, 52mg is not affordable for contraception[1]. Subsequently, following a health economic analysis, NEMLC recommended standard-dose LNG-IUD, 52mg for refractory abnormal uterine bleeding as third-line treatment option at Tertiary and Quaternary Level of Care[2]. More recently, NEMLC recommended that the low-dose LNG-IUD, 19.5mg not be included on the PHC EML, as it is expensive relative to other contraceptive agents currently included on the EML[3].

The supplier of low-dose and standard-dose LNG-IUD recently offered a reduced price for standard-dose LNG-IUD, 52mg, and the PHC/Adult Hospital Level Committee reviewed this for inclusion as a contraceptive option.

CONSIDERATIONS:

- ***Supply challenges:*** With the continuous supply challenges of contraceptives over the past few years, it would be feasible to consider an additional agent.
- ***New contraceptive modalities****:* In 2019, the Adult Hospital Level Committee undertook a review of the evidence for consideration of additional contraceptive modalities on the EML, noting that 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.
- ***Uptake of contraceptives:*** However, uptake of contraceptives in the public sector has to date, not increased since 2014, as per the South African Demographic Health Survey, 2016[4] (a nationally representative sample of persons aged 15-49). Below is the contraceptive use method uptake.

[1] Minutes of the NEMLC meeting of 25 April 2013
[2] Minutes of the NEMLC meeting of 27 September 2018
[3] Minutes of the NEMLC meeting of 17 September 2020
[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

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**

Table 1. South African Demographic Health Survey, 2016 – uptake of contraceptives

In the Western Cape, where there is good access to family planning services, the Couple Year protection rate is 74.2% (from the 2019 annual report[5]). This means that almost 75% of women aged 15-49 in the public sector are using a contraceptive method.
According to the UN Contraceptive Use by Method 2019[6], the OC pill is used by 16% of women worldwide, injectables 8%, IUD 17% and implants 2%.
The 2020 StatsSA report 'Unwanted fertility in SA, 2016[7]' showed that 20% of women sampled experienced a birth when they were no longer planning a baby.

Proven strategies to expand contraceptive options include introducing new contraceptive technologies, expanding access to existing methods, and expanding the provider base.[8] [9] [10] [11] Currently, there are 5 pharmacological contraceptive options recommended in the STGs and EML.[12] Increasing the contraception options would provide a broader base to choose from. In an analysis of data estimating contraceptive use from representative national surveys between 1982 and 2009, use of modern contraception increased when more methods became available, both cross-sectionally and over time.[13]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.

- ***Advantages of LNG-IUD over the copper IUCD:***

Although both the LNG-IUD and copper IUCD are intra-uterine devices and LARCs, there mechanism of action (and therefore recommendations for usage) is different and the LNG-IUD should really be discussed in the same class as the other progesterone-only contraceptive methods (injectable and the progesterone-only OC ('mini pill').
For LNG-IUD vs copper IUCD, LNG-IUD has the additional advantage of decreasing menstrual blood after 3 months of use with amenorrhea in about 20% of women. The LNG-IUD also decreases menstrual pain and the risk of pelvic infection and endometrial cancer. The decrease in menstrual bleeding reduces the risk of anaemia. These non-contraceptive benefits of the LNG-IUD makes it ideal for women with heavy menstrual bleeding and/or severe menstrual pain. It is an attractive option for adolescents and for women who cannot tolerate estrogen or where estrogen is contra-indicated. The copper IUCD is also an attractive option for women with contra-indications to hormones, but it's main side effect is

[5] Western Cape, Department of Health. Quarterly performance reports: 2018/19
https://www.westerncape.gov.za/assets/departments/premier/QPR/2018-2019/Q1/publication_template_v06_.pdf
[6] United Nations – Department of Economic and Social Affairs. Contraceptive Use by Method, 2019.
https://www.un.org/en/development/desa/population/publications/dataset/contraception/wcu2019.asp
[7] Maluleka R. Unwanted fertility in South Africa / Statistics South Africa. Pretoria: Statistics South Africa, 2020.
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[9] Charyeva Z, Oguntunde O, Orobaton N, Otolorin E, Inuwa F, Alalade O, Abegunde D, Danladi S. Task Shifting Provision of Contraceptive Implants to Community Health Extension Workers: Results of Operations Research in Northern Nigeria. Glob Health Sci Pract. 2015 Sep 15;3(3):382-94.
https://pubmed.ncbi.nlm.nih.gov/26374800/
[10] Christofield M, Lacoste M. Accessible Contraceptive Implant Removal Services: An Essential Element of Quality Service Delivery and Scale-Up. Glob Health Sci Pract. 2016 Sep 29;4(3):366-72. https://pubmed.ncbi.nlm.nih.gov/27577239/
[11] Hoke T, Brunie A, Krueger K, Dreisbach C, Akol A, Rabenja NL, Olawo A, Stanback J. Community-based distribution of injectable contraceptives: introduction strategies in four sub-Saharan African countries. Int Perspect Sex Reprod Health. 2012 Dec;38(4):214-9. https://pubmed.ncbi.nlm.nih.gov/23318171/
[12] PHC STGs and EML, 2018. https://www.knowledgehub.org.za/
[13] Ross J, Stover J. Use of modern contraception increases when more methods become available: analysis of evidence from 1982-2009. Glob Health Sci Pract. 2013 Jul 26;1(2):203-12. https://pubmed.ncbi.nlm.nih.gov/25276533/

menstrual cramping and irregular or prolonged and heavy menstrual bleeding.[14] [15]

- ***Standard-dose LNG-IUD, 52mg:*** The national EML currently recommends standard-dose LNG-IUD, 52mg for refractory menorrhagia[16]. The proposed reduced offer for LNG-IUD, 52 mg is R720.36.
- ***Low-dose LNG-IUD, 19.5mg****:* Low-dose LNG-IUD, 19.5mg is smaller and may be more acceptable to adolescents, and more suitable for nulliparous or nulligravid women. The supplier has also been requested to consider a lower price for this preparation.
- ***Training:*** The importance of training for healthcare workers on the correct insertion and removal of the LNG-IUD, 52 mg was emphasized. Thus, the Programme needs to be actively involved with supplier support for training to ensure successful implementation.

Additional information that informed NEMLC's decision:

A. CONTRACEPTIVE EFFICACY BETWEEN THE VARIOUS CONTRACEPTIVE AGENTS:

Failure rates: The PHC STGs and EML, 2020 edition includes the following information:

Effectiveness of family planning methods

Rates of unintended pregnancies per 100 women:

Contraceptive method	Failure rate in 1st year (%)	
	Consistent and correct use	As typically used
Copper IUCD	0.6	0.8
Progestin-only subdermal implant	0.05	0.05
Progestin-only injectable	0.3	3
Progestin-only oral pill (not breastfeeding)	0.3	8
Progestin-only oral pill (during breast feeding)	0.5	1
Combined oral contraceptive (COC) pill	0.3	3
Barrier: female condoms	5	21
Barrier: male condoms	2	15
Sterilisation: male – vasectomy	0.1	0.15
Sterilisation: female - tubal ligation	0.5	0.5
No method	85	85

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

Level of Evidence: III Low to very low certainty evidence

For LNG-IUD, the failure rate for the first year reported by Trussel et al[17]:

Contraceptive method	Consistent and correct use	As typically used
LNG-IUD	0.2	0.2

Table 3. Failure rate for LNG-IUD the first year (Trussel et al)

B. ACCEPTABILITY AMONGST END-USERS AND HEALTHCARE WORKERS:

Local data:

Knowledge and acceptability of IUCDs: Local studies show that there is a low uptake and lack of knowledge on IUCDs:

- A preprint of a systematic review and meta-analysis[18] assessing the knowledge, attitudes, and perceptions of long-acting reversible contraceptives (LARCs) amongst providers in sub-Saharan Africa showed that only 41% of providers received training on IUCD, whilst 63% expressed a desire for training. However, only 27% considered IUCD appropriate for use in the HIV-infected women; whilst minimum age were imposed by 56% and parity restrictions were observed among 29%.

[14] National Department of Health: Affordable Medicines, EDP- Primary Healthcare level. Medicine Review: Levonorgestrel-releasing intrauterine system for contraception, April 2013. https://www.knowledgehub.org.za/e-library

[15] National Department of Health: Affordable Medicines, EDP- Primary Healthcare level. Medicine Review: Low-dose levonorgestrel-releasing intrauterine system for contraception, August 2020. https://www.knowledgehub.org.za/e-library

[16] National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Economic analysis: Levonorgestrel-IUS for menorrhagia, Adult/Tertiary&Quatenary Review, June 2018. https://www.knowledgehub.org.za/

[17] Trussell J. Contraceptive failure in the United States. Contraception. 2011 May;83(5):397-404. https://pubmed.ncbi.nlm.nih.gov/21477680/

[18] Laura Rouncivell L, Takuva S, Ledibane N, Musekiwa A, Leong TD. Knowledge, attitudes, and perceptions of long-acting reversible contraceptive (LARC) methods among healthcare workers in sub-Saharan Africa: a systematic review and meta-analysis. medRxiv 2020.10.27.20220434; doi: https://doi.org/10.1101/2020.10.27.20220434

- A cross-sectional survey[19] of eight family planning clinics (216 clients and 30 providers) in Cape Town showed low awareness (41%; n=88) and low use of copper IUCD (4%; n=9). Three women were still using this method. Poor knowledge amongst users and providers with providers citing disadvantages of associated infection (47%; n=14) and increased menstrual bleeding (40%; n=12).
- A cross-sectional study[20] of pregnant teenagers in the Cape Town metropolitan area (n=314) showed that 76.4% felt their pregnancies had occurred at the "wrong time" but only 12.1% used contraception. 87.3% of participants had knowledge of the injectable hormonal contraception. Generally, contraceptive commonly used were the male condom (33.8%) and injectable contraception (31.2%). 61.1% reported that ease of access was acceptable, whilst 74.2% reported that information on contraception was readily available.

These studies conclude that there are unnecessary provider-imposed restrictions causing low uptake of IUCDs as a contraceptive option. Ongoing education of clients and providers, as well as strengthening of family-planning services may improve uptake of contraceptives. In a randomized controlled trial in Cape Town comparing the Copper-IUD or the LNG-IUD among women living with HIV, the LNG-IUD had significantly higher continuation during the study (96% for LNG-IUD versus 59% for Copper-IUD), suggesting the LNG-IUD to be a highly acceptable method in this setting if offered.[21]

Global data:

Of note is that in mostly higher-income countries, the satisfaction rate for LNG-IUD as a contraceptive method amongst users were reported to be high:

- Australian survey data from the ACCORd study[22] showed that: Satisfaction was highest among the LNG-IUD users; 86% were very/somewhat satisfied compared to 75% of implant users and 61% of oral contraceptive pill users ($p<0.001$).
- A 2020 systematic review of LNG-IUD as a contraceptive amongst nulliparous women (5 studies - United States, Germany, Sweden, Finland, Canada and China)[23] reported satisfaction rates of LNG-IUD users of greater than 90% (ranging from 76% to 96%)

[19] van Zijl S, Morroni C, van der Spuy ZM. A survey to assess knowledge and acceptability of the intrauterine device in the Family Planning Services in Cape Town, South Africa. J Fam Plann Reprod Health Care. 2010 Apr;36(2):73–8. https://pubmed.ncbi.nlm.nih.gov/20406549/

[20] Vollmer LR, van der Spuy ZM. Contraception usage and timing of pregnancy among pregnant teenagers in Cape Town, South Africa. Int J Gynaecol Obstet. 2016 Jun;133(3):334–7. https://pubmed.ncbi.nlm.nih.gov/26895740/

[21] Todd CS, Jones HE, Langwenya N, Hoover DR, Chen PL, Petro G, Myer L. Safety and continued use of the levonorgestrel intrauterine system as compared with the copper intrauterine device among women living with HIV in South Africa: A randomized controlled trial. PLoS Med. 2020 May 22;17(5):e1003110. https://pubmed.ncbi.nlm.nih.gov/32442189/

[22] Black KI, McGeechan K, Watson CJ, Lucke J, Taft A, McNamee K, Haas M, Peipert JF, Mazza D. Women's satisfaction with and ongoing use of hormonal long-acting methods compared to the oral contraceptive pill: Findings from an Australian general practice cluster randomised trial (ACCORd). Aust N Z J Obstet Gynaecol. 2021 Feb 18. https://pubmed.ncbi.nlm.nih.gov/33599984/

[23] Zgliczynska M, Kocaj K, Szymusik I, Dutsch-Wicherek MM, Ciebiera M, Kosinska-Kaczynska K. Levonorgestrel-Releasing Intrauterine System as a Contraceptive Method in Nulliparous Women: A Systematic Review. J Clin Med. 2020 Jul 3;9(7). https://pubmed.ncbi.nlm.nih.gov/32635369/

Table 4. Satisfaction rates.

Authors & Year	Assessment Time	Satisfaction Rate	Other
Suhonen et al. 2004 [45]	1st year	90% 'moderately' to 'very good'	88% would like to continue
Römer et al. 2009 [42]	Various	93% 'rather satisfied' (31%) to'very satisfied' (62%) at various times	86% would recommend to a friend; 87% would like to continue
Marions et al. 2011 [39]	12–16 weeks	76% 'very satisfied' or 'satisfied'; 10% 'neither satisfied or dissatisfied'; 5% 'dissatisfied' 9% data missing	
Zhao et al. 2014 [52]	3–4 months 1st year	92% 'very satisfied' or 'rather satisfied' 85% 'very satisfied' or 'rather satisfied'	
Gemzell-Danielsson et al. 2015 [35]	3rd year	LNG-IUS 8-94% 'very satisfied' or 'somewhat satisfied' LNG-IUS 13-96% 'very satisfied' or 'somewhat satisfied'	LNG-IUS 8 -73% would like to continue LNG-IUS 13-80% would like to continue

Abbreviations: LNG-IUS: levonorgestrel-releasing intrauterine system.

It is worth mentioning that Suhonen et al. reported that significantly more LNG-IUS users wanted to continue the method after the study than in case of OC group (88% vs. 68%) [45]. Marions et al. also noted that the satisfaction rate was better in the youngest age group (≤ 20 years) than in the oldest studied group (≥ 31 years; 75% and 59%, respectively) [39].

The global survey data should be interpreted with caution, as this may not be generalisable. Factors such as effective family planning services providing adequate education and training to providers, as well as adequate knowledge translation and counselling to clients in order to make informed choices, with the integration of health services should also be considered and strengthened wherever required.

C. <u>COSTING ANALYSIS:</u>

NEMLC had indicated that the direct medicine price comparison of LNG-IUD to other currently available contraceptive methods[24] was not sufficient[25], and the costing of LNG-IUD was further analysed.

- *Trussel et al, 2015[26]:* The economic model analysis estimated the average annual cost of no method, four short-acting reversible (SARC) methods (oral contraceptive, ring, patch and injection) and three LARC methods (implant, copper IUCD and LNG-IUD, 52mg) in 1000 women aged 20–29 years, over a 5-year time horizon in the United States. The analysis showed that copper IUD ($304 per women/year) and LNG-IUD 52 mg ($308) were the two least expensive contraceptive methods. Furthermore, LARC methods become cost-neutral in comparison to SARC methods within 3 years of use, and thereafter, continued use of LARC methods was shown to be cost saving. Use of LARC methods > 2.1 years was shown to be less costly than SARC methods despite the high capital layout, in this cohort of patients.

- *Costing analysis:* A costing analysis was conducted comparing current LARC methods in South Africa – IUDs, implants and injectables (2 and 3 month) taking direct medicine costs, as well as administration costs into account at primary level of care. As in the Trussel et al study mentioned above, costs if the LARC options are incurred primarily in the first year of initiation but then to decrease over time, and depending on the time horizon, may work out to be less expensive than initial price analysis suggests.
  As LNG-IUD is not currently used in the public sector for contraceptive purposes, its main comparator was assumed to be the current IUD, although overall in the population, utilization of IUDs is low.

  Estimating Resource Use
  Resources associated with long-acting, reversible contraceptive options in South Africa includes acquisition costs, health care staff costs associated with the administration and management of technology, and health care costs

[24] As listed in the PHC STGs and EML, 2020 edition. https://www.knowledgehub.org.za/
[25] Minutes of the NEMLC meeting of 25 February 2021.
[26] Trussell J, Hassan F, Lowin J, Law A, Filonenko A. Achieving cost-neutrality with long-acting reversible contraceptive methods. Contraception. 2015 Jan;91(1):49–56. https://pubmed.ncbi.nlm.nih.gov/25282161/

associated with the management of adverse events. Note that cost associated with the management of adverse events were not included in this costing analysis.

Acquisition costs were sourced from the public sector contracts/tenders and a quote received from manufacturer on the new proposed price of LNG-IUD 52mg.

Healthcare resource use was estimated using District Health Barometer information for cost per PHC headcount. PHC expenditure per PHC headcount [South African average], 2019/20 = R529, and cost per visit to a community health clinic or centre = R278.73.

The estimated number of 21 visits over 5 years for injectable contraceptive administration was based on the assumption that 3-month injectables are more widely used than 2-month injectables locally.

Assuming the failure rate remains relatively constant for 5 years of use of each of the products, the overall 5-year failure rates can be determined and used to calculate an estimated additional cost per unwanted pregnancy prevented, of LNG-IUD 52mg versus other comparators.

Summary of medicine acquisition and administration costs are described below, using a time-horizon of 5 years:

	Intervention	Main comparator	Other long-term contraceptive options	
Time horizon: 5 years				
Contraceptive	**LNG-IUD 52mg**	**Copper IUCD**	**Etonogestrel implant**	**Norethisterone enanthate injection**
Acquisition costs	R720.36	R159.58	R443.02	R502.32
Health resource costs	R1 114.92	R1 114.92	R1 393.65	R5 853.33
Total costs	R1 835.28	R1 274.50	R1 836.67	R6 355.65
Average cost per year	R367	R254,9	367.33	R1271.13
Failure rate in the 1st year (as typically used)	0.2%	0.8%	0.05%	3%
Estimated failure rates over 5 years	3.36%	3.94%	0.25%	14.13%
Cost per additional pregnancy prevented over 5 years	N/A	R9514.9	R -44.76 (Implanon® more cost effective)	Injection Dominated – more expensive and least effective

Table 4. Total costs associated with LNG-IUD and comparator(s)

Administering LNG-IUD 52mg instead of a Copper IUCD (most relevant comparator) will result in an R560.78 increase in cost per patient over a five-year time horizon.

LNG-IUD is slightly more efficacious than the Copper IUD, however the difference is relatively small. The additional cost per pregnancy avoided for LNG-IUD versus IUD in 5 years is about R9500. LNG-IUD dominates the injectable option, however factors driving patients to select progestin-only implants and injectables as contraceptive methods might influence the utilization of the different modalities.

This analysis does not take into account discontinuation rates – which may render long-term methods relatively more expensive.

D: OTHER MATTERS

- *Drug-interactions with antiretroviral drugs:* A recent double-masked, randomized controlled non-inferiority trial from South Africa[27] investigated the risk of HIV transmission (by measuring genital tract viral load) between women on LNG-IUD vs Copper IUD. The LNG-IUD arm showed low levels of contraceptive failure, less anaemia (mean relative change in haemoglobin over 24 months 0.71 (95% CI 0.47 to 0.95;p=<0.001) and no increase in vaginal viral load. Additionally, the LNG group had less menorrhagia (5% vs 28.6% in the copper IUD group) and 48.5% of the LNG users had amenorrhea (11% in the copper IUD group). This makes the LNG-IUD an acceptable option for women living with HIV, as apart from the contraceptive benefits, there is a decreased risk for HIV transmission (lower genital viral load and less exposure to vaginal bleeding). LNG-IUS is not contra-indicated in those with WHO Stage 3 or 4 (severe or advanced HIV clinical disease). The WHO Medical Eligibility criteria category is 3, where use of the method is not usually recommended unless other, more appropriate methods are not available or acceptable.

[27] Todd CS, Jones HE, Langwenya N, Hoover DR, Chen PL, Petro G, Myer L. Safety and continued use of the levonorgestrel intrauterine system as compared with the copper intrauterine device among women living with HIV in South Africa: A randomized controlled trial. PLoS Med. 2020 May 22;17(5):e1003110. https://pubmed.ncbi.nlm.nih.gov/32442189/

- *Use with concomitant anticoagulants:* The WHO Medical Eligibility criteria for concomitant use of anticoagulants is category 2, where there is generally use of LNG-IUD with anticoagulants. Therefore, LNG-IUD is not contra-indication in patients with veno-thromboembolism on chronic anticoagulants from the STG.
- *Nomenclature for LNG-IUS*: To be corrected to LNG-IUD throughout the STG**,** aligned with the WHO Medical Eligibility criteria, 2015 edition.

The following STG was developed, based on the NEMLC-approved medicine reviews for LNG-IUD, 56mg and low-dose LNG-IUD, 16 mg; and the WHO Family planning global handbook for providers, 2018[28]

7.2.2 Levonorgestrel intra-uterine system (LNG-IUD)
Z30.0/Z30.4/Z30.8

Dual protection with barrier methods is recommended to reduce the risk of STIs including HIV.
The LNG-IUD is an effective, safe, reversible long-term contraceptive method requiring no patient effort to adhere to the method, has minimal hormonal adverse effects and is not prone to drug interactions.

- Progestin-only intrauterine device, e.g.:
- Levonorgestrel, intrauterine device, 52 mg.

HIV infection is NOT a contra-indication to the use of an LNG-IUD.

The LNG-IUD is a T-shaped plastic device that steadily releases a small amount of levonorgestrel every day. It has the added benefit of reducing menstrual cramping and heavy menstrual bleeding. It can be inserted by specially trained heath care professionals, 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 patient resulting in less discomfort and spotting. For use by women of any age, regardless if they had children before.
LNG-IUD may be inserted immediately postpartum or post miscarriage (within 48 hours) providing that no contra-indications are present (chorioamnionitis, ruptured membranes for more than 18 hours or postpartum haemorrhage). A provider requires specific training in postpartum insertion by hand or using a ring forceps.
Counsel women to return if they experience complications (excessive bleeding, excessive pain, fever or foul smelling discharge).
LNG-IUD may also be inserted at 4 or more weeks postpartum.

Advise the patient when to return:

- Expulsion of LNG-IUD or if strings of the LNG-IUD protrude.
- Complications (see below).
- Routine follow-up after 3–6 weeks.

LNG-IUD is not recommended for women with acute venous thromboembolism, severe liver cirrhosis, active pelvic inflammatory disease (PID), purulent cervicitis, unexplained uterine bleeding, cervical- breast- ovarian- or endometrial cancers or other uterine abnormalities.

For mild pain and discomfort after insertion:

- 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.

Level of Evidence: I Moderate to high certainty evidence

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NEMLC MEETING OF 29 JULY 2021:
The NEMLC recommended that LNG-IUD 52 mg be included in the PHC STG and EML at the reduced proposed price of R720.36 as a contraceptive option. Low-dose LNG IUD 19 mg was recommended for inclusion to the therapeutic interchange database as an alternative option of a progestin-containing IUD.
NEMLC also recommended the monitoring of discontinuation rates (by Provinces) and implementation with adequate training (by the NDoH Programme).

B: MEDICINE AMENDMENTS

SECTION	MEDICINE	ADDED/DELETED/AMENDED
Introduction to contraception	LNG-IUCD	Directions for use (advantages) added
7.2.5 Missed pills	Dual contraception	Directions for use amended (duration)

[28] World Health Organization Department of Reproductive Health and Research (WHO/RHR) and Johns Hopkins Bloomberg School of Public Health/Center for Communication Programs (CCP), Knowledge for Health Project. Family Planning: A Global Handbook for Providers (2018 update). Baltimore and Geneva: CCP and WHO, 2018. https://www.who.int/reproductivehealth/publications/fp-global-handbook/en/

INTRODUCTION TO CONTRACEPTION

LNG-IUD: *Directions for use (advantages) added*

Duration of contraceptive use: *duration of contraceptive use listed as 5 years*
An external comment was received advising that in 2020 the USA Federal Drug Agency (FDA) approved the label of LNG-IUD, extending contraceptive use from 5 years to 6 years. However, the FDA approval was based on preliminary results of the Mirena Extension Trial (an open-label, uncontrolled study enrolling 362 women). The trial data is still unpublished and recruitment ended May 2021 – clinictrials.gov registry number NCT02985541[29]. The duration for contraceptive use of LNG-IUD will be retained as 5 years, pending publication of new data.

Postpartum-use: *guidance added for insertion within 48 hours after delivery*
Evidence:

- For immediate postpartum insertion for breastfeeding women, LNG-IUD is categorised as WHO medical eligibility criteria, category 2, where the benefits of using the method generally outweigh the risks[30].
- A systematic review[31] of 11 RCTs of low to moderate quality suggests that contraceptives (including LNG-IUD) may be used post-partum. Studies had inconsistent results for various methods, but the better quality RCTs showed that hormonal progestin-containing contraceptive have *"little effect on breastfeeding or infant growth".*
- Systematic review[32] of 12 RCTs of moderate to high quality, showed that *"early LNG-IUS insertion is similar to delayed LNG-IUS insertion in terms of breastfeeding continuation after delivery*" (RR 0.99; 95% CI 0.84, 1.16; p=0.88).

Level of Evidence: Moderate quality evidence

Other external comments:

- An external comment to include the indication of endometrial hyperplasia for LNG-IUD was not accepted, as the chapter specifically relates to family planning at primary level of care.
- External comments were received regarding the current pricing of LNG-IUCD which varies in the two-tiered healthcare system (namely tender prices for public sector and single exit prices for private sector). Addressing this discrepancy does not fall in the remit or mandate of the NEMLC, and will hopefully be clarified once National Health Insurance is implemented.

7.2.5 MISSED PILLS

Dual contraception: *Directions for use amended (duration)*

Dual contraception recommended for a period of at least 7 days, when a pill (either combined oral contraceptive or progestin-only pill) is missed. This is aligned with the SAMF, 2020 edition[33].

[29] Mirena Extension Trial - Tabular View - ClinicalTrials.gov [Internet]. [cited 2021 Jul 23]. Available from: https://clinicaltrials.gov/ct2/show/record/NCT02985541
[30] World Health Organization. Medical eligibility criteria for contraceptive use, Fifth edition (2015). https://www.who.int/publications/i/item/9789241549158
[31] Abdelhakim AM, Sunoqrot M, Amin AH, et al. The effect of early vs. delayed postpartum insertion of the LNG-IUS on breastfeeding continuation: a systematic review and meta-analysis of randomised controlled trials. Eur J Contracept Reprod Health Care. 2019 Oct;24(5):327-336. https://pubmed.ncbi.nlm.nih.gov/31517549/
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[33] South African Medicines Formulary. 13th Edition. Division of Clinical Pharmacology. University of Cape Town. 2020.