



Module 1934

Non-oral hormonal contraceptives: long-acting reversible contraceptives

From this CPD module on non-oral hormonal contraceptives you will learn:

- How long-acting reversible contraceptives (LARCs) work
- When and how LARCs are used
- Side effects and when LARCs may not be appropriate
- Sources of advice and support to help women in their decision-making regarding alternatives to oral hormonal contraceptives

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Non-oral hormonal contraceptives can be classified as:

- Long-acting reversible contraceptives (LARCs), which are all progestogen-only based, and include the subdermal implant, intrauterine system (IUS) and injection. LARCs also include copper intrauterine devices, which are non-hormonal and not covered in this module.
- Intermediate-acting contraceptives, which are combined hormonal contraceptives containing both oestrogen and progestogen and include transdermal patches and vaginal rings (these will be covered in a separate module).

Around two thirds of women below 24 years of age in England are more likely to rely on a less effective, user-dependent form of contraceptive (eg oral contraceptives) over LARCs.¹ This could be because they are the most commonly known form of contraceptive, as they have been around the longest – since 1961.

However, the use of LARCs in the UK has doubled over the past 10 years, from about 14% to 30%.^{1,2}

Across the globe, the use of LARCs varies, partly due to the insertion method of some and partly due to belief systems, but also due to outdated knowledge. In the US, a lot of work is being done to increase public awareness and understanding of LARCs' advantages, by analysing the way advice regarding alternatives to oral hormonal contraceptives is offered to patients by healthcare providers.³

In Australia, a study has shown that the most significant reason for a lower uptake was due to healthcare provider beliefs and recommendations. The study involved training GPs to provide 'LARC first' structured counselling to women seeking contraception, and implementing rapid referral pathways for LARC insertion.⁴

Studies have shown that despite the cheaper purchase cost of oral contraceptives, LARCs are more cost-effective long term, as they are more effective. Subdermal implants and IUS devices are 99% effective. In contrast, oral contraceptives and other forms of hormonal contraceptives (injections, patches and rings), while all having a 99% efficacy rate with perfect use, are in reality only 91% effective, due to user error.³

Advantages of LARCs

All LARCs have the advantage of: not interrupting sexual intercourse; being safe in breastfeeding; not being affected by other medicines; reducing or stopping heavy or painful periods; and being good alternatives when oestrogen is contraindicated. In addition, each form has additional benefits.⁵

IUS advantages:⁶

- works for 3-5 years
- allows return to fertility as soon as the IUS is removed
- is one of the most effective forms of contraception available in the UK
- does not affect weight or increase the risk of cervical cancer, cancer of the uterus or ovarian cancer.

Implant advantages:⁷

- works for three years
- allows return to fertility as soon as the implant is removed.

Injection advantages:⁸

- each injection lasts for either eight or 13 weeks.

Intrauterine system

The IUS is a small, T-shaped plastic device that is placed into the uterus. It releases levonorgestrel, which thins the lining of the uterus to prevent a fertilised egg implanting and thickens cervical mucus to prevent sperm reaching an egg, as well as suppressing ovulation in some women (in some cycles).

More than 75% of women will continue to ovulate while using this method and this increases with the lower strength IUS.⁹ In addition to the progestogenic activity, the IUS itself may contribute slightly to the contraceptive effect.¹²

It is available as:

- Mirena – the first IUS; it is the largest and contains 52mg levonorgestrel¹⁰
- Kyleena – smaller than Mirena and containing 19.5mg levonorgestrel; the narrower insertion tube and smaller frame means it can be used if a woman has a narrow cervical canal or shorter uterine cavity¹¹
- Jaydess – the IUS with the lowest amount of

hormone; it is the same size as Kyleena, but contains only 13.5mg levonorgestrel and works for three years, as opposed to five years for the others¹²

- Levosert – is the same strength as Mirena, but has different licensing and insertion requirements; it has recently received a licence extension to five years of use for contraception and heavy menstrual bleeding.^{13,14}

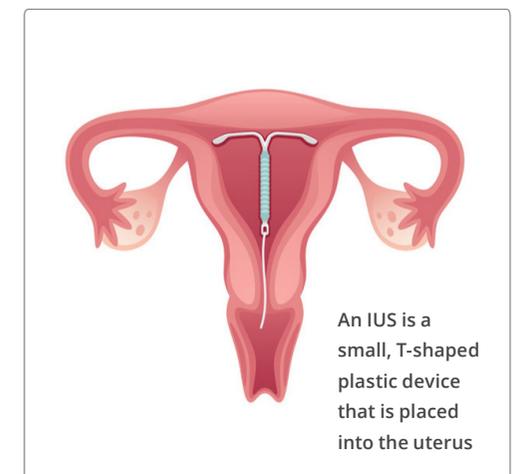
Insertion of Kyleena and Jaydess has been reported to be significantly easier and associated with significantly less pain than insertion of Mirena. Both of these products are licensed for contraception only.^{10,12}

Due to the variety of IUS brands, which have different licences and methods of insertion, it is important for pharmacists and pharmacy technicians to check that prescriptions specify the brand of IUS is being prescribed.¹⁴

How is an IUS used?

A trained healthcare professional will insert an IUS. The process takes about five minutes and can be uncomfortable or painful, so local anaesthetic can be offered. The IUS has two foldable arms that are bent back and the IUS is inserted inside its tube into the vagina to a set plunger level.

Once the IUD is in place in the uterus, the plunger is removed, the arms unfold, and it hangs



in place with two threads that pass through the cervix and sit at the top of the vagina. Patients should use these threads to check that the IUS is still in place, but can be reassured they should not obstruct intercourse. The IUS should be removed using these threads by the trained healthcare professional. The manufacturer's information for each device provides specific insertion information that will help when talking patients through the process.¹³

Pharmacy professionals can advise women having an IUS fitted to take ibuprofen ahead of their appointment, as well as to take any analgesic following the insertion if they experience cramping shortly afterwards. The patient should return to have the positioning checked after four to six weeks to ensure it has not moved and should use a barrier method of contraception during this time to be safe. They should also be counselled on the signs, symptoms and risks of perforation and ectopic pregnancy.

Although non-hormonal copper IUDs are used for emergency contraception, the levonorgestrel IUS is not licensed for this.

How does the IUS affect periods?

For the first 3-6 months, women may notice that their period becomes irregular and may also have frequent spotting or light bleeding. A few women have heavy bleeding during this time. After this, as the body adjusts, the number of bleeding and spotting days is likely to decrease, but may remain irregular. After a year, many women may have no period at all.¹⁵

How long can the IUS be used for?

The IUS works for five years (Mirena, Levosert, Kyeena) or three years (Jaydess), but can be taken out sooner. If fitted after the age of 45 years, Mirena can stay in place for contraception until after the menopause, when contraception is no longer needed.

The IUS is over 99% effective once fitted, and fertility returns to normal as soon as the IUS is taken out.

Side effects associated with IUS use

Although some patients report adverse effects, there is no good evidence that the IUS significantly increases the risk of:^{9,16}

- reduced libido
- weight gain
- breast cancer
- venous thromboembolism
- myocardial infarction.

Side effects that may occur include:

- pain on insertion
- perforation of the wall of the uterus (although this is rare and depends on the clinician's skill)
- The most important risk factors for uterine perforation are insertion in breastfeeding women (where the risk of perforation is six times higher) and insertion within 36 weeks of giving birth
- acne, breast tenderness, headache – these usually settle with time
- ectopic pregnancy
- expulsion, which normally occurs within the first three months of insertion
- hypersensitivity
- ovarian cysts; although these do not usually

need to be treated as they tend to be asymptomatic and resolve spontaneously

- pelvic inflammatory disease (PID)
- unscheduled bleeding.

Pharmacy professionals should make women aware that there is a risk of seizures during the time of insertion or removal, although this is rare and the risk is low. Women should let their practitioner know if they have epilepsy before they have an IUS inserted.

In which situations may an IUS not be suitable?

An IUS may not be suitable in the following conditions:

- acute malignancies affecting the blood or leukaemias, except when in remission
- cervical dysplasia
- cervicitis
- conditions associated with increased susceptibility to infections
- confirmed or suspected hormone-dependent tumours, including breast cancer
- congenital or acquired abnormality of the uterus, including fibroids if they distort the uterine cavity



The subdermal implant is a small, flexible rod that is inserted by a trained healthcare professional

- current genital infection
- current or recurrent pelvic inflammatory disease
- hypersensitivity to the active substance or to any of the excipients
- known or suspected pregnancy
- liver tumour or other acute or severe liver disease
- postpartum endometritis, infection following an abortion during the past three months
- recent trophoblastic disease while human chorionic gonadotrophin levels remain elevated
- undiagnosed abnormal genital bleeding
- uterine or cervical malignancy.¹⁵

Subdermal implant

How does the progestogen-only subdermal implant work?

The subdermal implant is available as Nexplanon. It is a small, flexible rod that is inserted, by a trained healthcare professional, under the skin of the upper arm. It contains 68mg of etonogestrel. The release rate is approximately 60-70mcg/day in weeks five and six, which decreases to approximately 35-45mcg/day at the end of the first year, to approximately 30-40mcg/day at the end of the second year and to approximately 25-30mcg/day at the end of the third year.

It is radio-opaque, containing barium sulphate to enable detection by x-ray, whereas its predecessor, Implanon, was not. The progestogen not only stops ovulation, it also thickens cervical mucus to stop sperm reaching an egg and thins the lining of the uterus to prevent a fertilised egg implanting. In clinical trials, ovulation was not observed at all in the first two years, and only rarely in the third year of use.^{17,18}

How is the implant used?

Local anaesthetic is applied to the skin in the inner area of the upper arm and the implant inserted. It takes a few minutes and feels like having an injection. To confirm a successful insertion, the implant is depressed at one end to feel the other

end pop up, so it is important it is not inserted too deep.

A correctly inserted implant should be clearly palpable by the healthcare professional as well as by the patient – where both ends of the implant can be felt between thumb and finger. Regular checks can be made by patients to observe the implant pop up and confirm it is present. To remove it, a small incision is made under local anaesthetic and the implant gently pulled out.

How do implants affect periods?

The implant has a marked effect on periods. Fewer than a quarter of women using the progestogen-only implant will have regular bleeds. Infrequent bleeding is the most common pattern (approximately one third); around a fifth of women experience no bleeding; and approximately a quarter have prolonged or frequent bleeding. Periods are likely to remain irregular while using the device.¹⁷

How long can the implant be used for?

The implant is licensed for three years, but can be taken out sooner if needed. After three years of use, there is a potential risk of pregnancy and additional contraceptive precautions should be advised.

It is over 99% effective once fitted and, as long as it is replaced immediately, and after no longer than three years since the previous insertion, it will continue to remain effective. The implant does not delay fertility, which returns to normal as soon as it is removed.

What side effects are associated with use of the implant?

Pharmacists and pharmacy technicians should ensure patients are aware that skin atrophy is recognised as a potential adverse effect of steroid hormone use with the implant and consideration may be given to switching arms after two consecutive implants. Reiterate that women can use implants throughout their reproductive years and there is no maximum number of implants a woman can have.¹⁷

Occasionally the implant can become impalpable. If this occurs, the patient should be advised to use additional precautions or avoid intercourse until the implant's presence is confirmed. An impalpable or deep implant should be located, possibly by x-ray, before exploratory surgery. The patient should also be advised to speak to their GP if the implant has changed shape, they notice any skin changes or pain around the site of the implant, or they become pregnant.¹⁷

Changes in menstrual bleeding are expected, and bleeding patterns are likely to remain irregular while using the device.

It is essential that healthcare professionals administering implants keep their training up to date, as there have been litigation cases due to non-insertion of an implant, deep insertion and nerve injury.¹⁸

There is no evidence that the progestogen-only implant causes:¹⁹

- depression and mood changes
- headache
- loss of libido
- weight changes.

In which situations are implants not suitable?

Contraceptive efficacy is likely to be reduced in women using liver enzyme-inducing drugs. These patients should be advised to switch to a method unaffected by enzyme-inducing drugs or to use additional contraception until 28 days after stopping the treatment.

Although there are no weight restrictions for the implant to be effective and no increased risk of pregnancy has been demonstrated in women weighing up to 149kg, Nexplanon's manufacturer advises to consider earlier replacement in heavier women, which is considered around 70kg.¹⁹ The implant should not be used in the following circumstances:

- active venous thromboembolic disorder
- hypersensitivity to the active substance or to any of the excipients
- known or suspected sex steroid-sensitive malignancies



Contraceptive injections are usually administered into the gluteus maximus by a healthcare professional

- presence or history of liver tumours (benign or malignant)
- presence or history of severe hepatic disease if liver function values have not returned to normal
- undiagnosed vaginal bleeding.

Injection

How does the progestogen-only injection work?

The long-acting contraceptive injection is available as Depo-Provera (depot medroxyprogesterone acetate (DMPA) 150mg) or Sayana Press (DMPA 104mg). Noristerat (norethisterone enantate 200mg), is rarely used and is licensed only for short-term use (two injections). Of all the LARCs, injections have the most similar efficacy profile to combined oral contraceptives.¹⁷

Progestogen stops ovulation, thickens cervical mucus to prevent sperm reaching an egg, and

thins the lining of the uterus to prevent a fertilised egg implanting.

It is important to clearly counsel patients about the risks, as the injection cannot be removed from the body, so any side effects may continue for as long as it works and for some time afterwards.

How are the injections used?

Depo-Provera and Noristerat are injected into a muscle by a healthcare professional, usually in the gluteus maximus, although Depo-Provera can sometimes be given in the deltoid. Noristerat is a thicker solution, so it may be slightly more painful. Sayana Press is a newer formulation and can be injected subcutaneously at the front of the thigh or abdomen. Women may be able to self-administer this at home, after the first injection, once they have received training in injection technique and the administration schedule from a healthcare professional.¹⁹

How do the injections affect periods?

The injections commonly result in amenorrhoea or reduced bleeding, which means they can be used to benefit women with menstrual problems by helping with endometriosis and heavy menstrual bleeding. If it becomes a problem, women with unscheduled bleeding during the use of an injectable contraceptive can be offered 500mg mefenamic acid up to three times daily for five days. Alternatively, they can be offered a combined oral contraceptive (COC) for three months. This can be taken in the usual cyclic manner or continuously without a hormone-free interval.

How long can the injections be used for?

Depo-Provera or Sayana Press are effective for 13 weeks, while Noristerat is only effective for eight weeks, so the latter is most likely to be used as short-term interim contraception (eg before a partner's vasectomy becomes effective). Noristerat can only be used twice, while the others may be used until the age of 50 years, as long as use is reviewed every two years for Depo-Provera, and yearly for Sayana Press.

With perfect use, the injection is more than 99% effective. However, this form has a shorter duration

of action than the IUS or patch and it depends on the user returning for their next dose. So, with typical use, where users may be late to receive their supply, it is around 94% effective.

How does the injection affect future fertility?

It is important to counsel women that fertility may take up to one year to return after stopping the injection, although it may take longer for some people. Menstruation can take several months to return to normal.

What side effects are associated with use of the injection?

- Breast cancer – the risk is small compared with the overall risk of developing breast cancer and gradually disappears within 10 years after stopping the progestogen-only injectable; cervical cancer is also a risk if using DMPA for five years or longer (pharmacy professionals can encourage women to undertake regular smear tests)
- Injection site reactions, mostly with the subcutaneous injection
- Menstrual irregularities
- Small loss of bone mineral density after use for more than a year

- Weight gain – DMPA is associated with weight gain of up to 2-3kg in weight over the first year of use (pharmacy professionals can offer diet and exercise advice if this side effect occurs).

There is little evidence that the use of the progestogen-only injectable causes the following reported adverse effects:

- acne
- headache
- hot flushes
- loss of libido
- mood changes
- vaginitis.

In which situations are injections not suitable?

As a contraceptive choice in adolescents, Depo-Provera and Sayana Press should be used only when other methods of contraception are inappropriate. In all women, the benefits of using medroxyprogesterone acetate beyond two years should be evaluated against the risks. This does not mean it should be stopped, but use should be reviewed and should be stopped at age 50 years. The risk of bone mineral density loss should be considered and women with risk factors for osteoporosis should consider an alternative method of contraception.

Advice and support

Pharmacists and technicians can play a key role in supporting women with their contraceptive choices and provide appropriate counselling. Most notably, all of these methods do not provide protection from sexually transmitted infections, so it is important for pharmacy teams to be trained in providing advice on this and know where local sexual health services are for patients to be signposted to. Having local clinic access ages (some are specifically for young people) and opening times in a signposting folder can be useful.

Some resources, such as leaflets, can be printed for patients – see the list below.

Above all, it is important for pharmacy professionals to have access to up-to-date information and maintain their clinical knowledge

on the ever-changing topic of contraception.

Resources

It is important to have information about resources to signpost women to. The following is a list of websites for charities and NHS resources that can be accessed by all:

The Faculty of Sexual and Reproductive Healthcare (FSRH) has:

- clinical guidance on progestogen-only implants at tinyurl.com/contraceptive20.
- clinical guidance on progestogen-only injectable contraception at tinyurl.com/contraceptive21.
- clinical guidance on intrauterine contraception at tinyurl.com/contraceptive22.

The Family Planning Association (fpa):

- guide to LARC at tinyurl.com/contraceptive23.
- leaflets and booklets at tinyurl.com/contraceptive24.
- Which method of contraception is right for me? From the Sexwise section of the website at tinyurl.com/contraceptive25.

The National Institute for health and Care Excellence (NICE):

- Contraception: combined hormonal methods at tinyurl.com/contraceptive26.
- Contraception: progestogen-only methods at tinyurl.com/contraceptive27.
- Contraception: IUS/IUD at tinyurl.com/contraceptive28.
- Long-acting reversible contraception at nice.org.uk/guidance/cg30.

The NHS website:

- 'Your contraception' guide at tinyurl.com/contraceptive29.
- Find sexual health services at tinyurl.com/contraceptive30.

Brook Young People charity:

- My contraception tool at tinyurl.com/contraceptive31.



DMPA is associated with weight gain of up to 2-3kg in the first year of use – if this occurs, dietary advice can be offered

Take the 5-minute test online

1. The use of LARCs in the UK has doubled over the past 10 years.
True or false
2. Subdermal implants and IUS devices are 99% effective.
True or false
3. All of the IUSs work for five years.
True or false
4. Mirena, the first IUS to become available, contains 19.5mg levonorgestrel.
True or false
5. Fertility returns to normal as soon as the IUS is taken out.
True or false
6. The subdermal implant Nexplanon contains 68mg levonorgestrel.
True or false
7. Side effects of the progestogen-only implant include headache, loss of libido and weight gain.
True or false
8. There is no maximum number of implants a woman can have.
True or false
9. Depo-Provera and Sayana Press injections are effective for six months.
True or false
10. Side effects of the progestogen-only injection include increased risk of breast and cervical cancer.
True or false

Long-acting reversible contraceptives CPD planned learning

What are you planning to learn?

I want to learn more about long-acting reversible contraceptives (LARCs), including how they work, when and how they are used, side effects, and situations when they might not be suitable. I also want to improve my knowledge of reliable sources of advice and support that can help women decide about alternatives to oral hormonal contraceptives.

This learning will help me to confidently provide better, more effective advice to patients about LARCs and to signpost them to resources to help them make informed decisions about contraception.

How are you planning to learn it?

- I plan to find out more about the IUS on the Patient website at tinyurl.com/contraceptive32.
- I plan to find out more about the contraceptive implant on the Patient website at tinyurl.com/contraceptive33.
- I plan to read more about the contraceptive injection on the NHS website at tinyurl.com/contraceptive34.
- I plan to find out about reliable sources of information about contraception, such as the Sexwise website at tinyurl.com/contraceptive35 and the Brook website at tinyurl.com/contraceptive36.

Give an example of how this learning has benefited the people using your services

I was asked by a young woman in her twenties about alternatives to combined oral contraception. I was able to explain about the different types of LARCs, how they are used and their advantages and disadvantages. I suggested some websites where she might find more detailed information and also that she could make an appointment with the nurse at the local surgery to discuss further which contraceptive method would be most suitable for her.

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