INJECTABLE CONTRACEPTION

Sal Roberts

Injectables

- progestogen-only injectable is a long acting, reversible contraceptive (LARC)
- slow release of a synthetic progestogen into the systemic circulation following administration
- 3 forms of progestogen-only injection available in the UK:

Depot medroxyprogesterone acetate (DMPA): intramuscular or subcutaneous (Depo Provera and Sayana Press)

Norethisterone Enanate (NET-EN) (Noristerat)

DepoProvera™

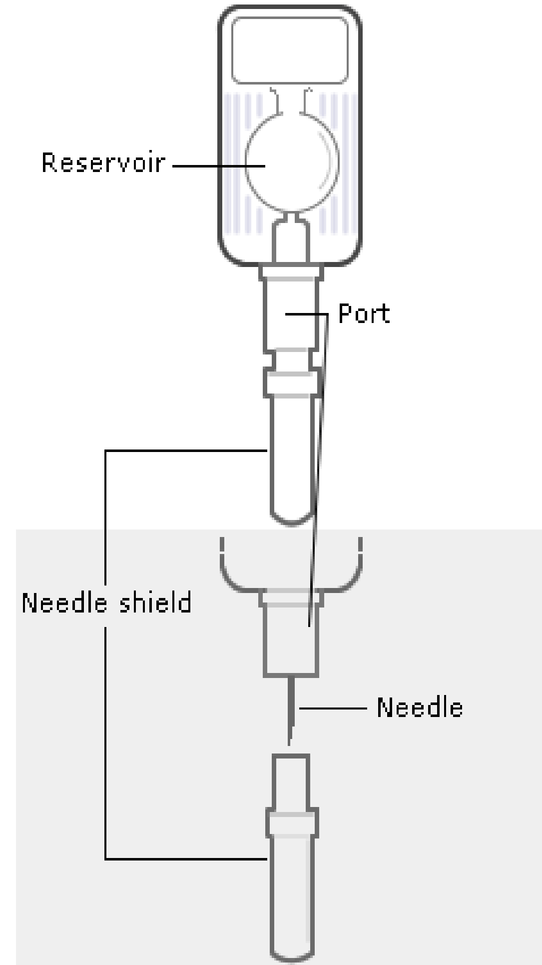
- DMPA is formulated for deep intramuscular (IM) injection as Depo-Provera™: 150mg medroxyprogesterone acetate in 1ml
- usually administered into the UOQ of gluteal muscle (do not massage)
- kept at room temperature
- given every 13 weeks (this is CEU guidance and outside the product licence for Depo-Provera™ which states every 12 weeks)
- UK guidance states that can be given late: up to 14 weeks without the loss of contraceptive cover or the need for extra contraceptive precautions

Sayana Press™

- 104mg MPA in 0.65ml in a pre-filled injector for subcutaneous (SC) injection
- injected into the anterior thigh or the abdomen avoiding boney areas or the umbilicus
- kept at room temperature
- given every 13 weeks
- women can self-administer after the first dose following training (resources to support this are available http://www.sayanaanswers.co.uk/guide-to-self-injection) under the supervision of an appropriate healthcare professional
- can be given up to 14 weeks without the loss of contraceptive cover or the need for extra contraceptive precautions

Sayana Press^{TM}

- single dose container which is activated by squeezing the needle shield and the injector port together
- before use shake vigorously.



Noristerat™

- Norethisterone enanate, or NET-EN 200mg intramuscular injection
- lasts for 8 weeks (given up to 10 weeks without extra precautions)
- licensed for short term contraception but may be used long term (unlicensed)

POI - Efficacy

- inhibits ovulation and changes cervical mucus (limits sperm penetration)
- very low typical user failure rate of 6% in real life and 0.2% in the first year of perfect use

Progestogen-only injectable failure could occur if:

- DMPA (IM and SC) later than 14 weeks since last injection
- NET-EN later than 10 weeks since last injection
- The woman was already pregnant when the first injection was given

POI – Starting?

- A full medical history should be taken
- consideration of the UKMEC guidelines to assess the appropriateness of progestogen-only injectables
- they are safe for most women

POI - Starting

UKMEC 3 conditions include:

- Multiple risk factors for cardiovascular disease
- Vascular disease
- Stroke
- Current and history of ischaemic heart disease
- Diabetes with complications of nephropathy, neuropathy, retinopathy or other vascular disease
- Breast cancer - past, and no evidence of current disease for last five years
- Cirrhosis - severe (decompensated)
- Malignant liver tumour or hepatocellular adenoma
- Unexplained vaginal bleeding
- SLE with positive or unknown antiphospholipid antibodies

UKMEC 4: current breast cancer (within last five years).

POI - Benefits

- Reduction in menorrhagia and dysmenorrhoea
- improvement in endometriosis symptoms
- possible reduction in risk of endometrial and ovarian cancer
- up to 70% of DMPA users are amenorrhoeic at one year of use, which may help with anaemia
- may reduce the severity of sickle crisis pain in women with sickle cell disease

POI – Drug Interactions

- no effect on the efficacy of progestogen-only injectables by liver enzyme-inducing drugs
- may reduce the efficacy of Ulapristal emergency contraception (UPA) so DO NOT start for 5 days and then use extra precautions until Depo effective (extra 7 days)

POI – Side Effects

Common:

- altered bleeding pattern
- weight gain for DMPA use (adolescents with a BMI ≥ 30kg/m^2 and women who gain more than 5% baseline body weight in the first six months of DMPA use)
- injection site reactions for both IM and SC DMPA, more common with SC DMPA

Rare:

- galactorrhoea is a recognised side effect and serum prolactin should be checked if it occurs
- acne
- no evidence of headache, mood change, breast tenderness, vaginitis or loss of libido

POI - Bones

- small loss of bone mineral density (BMD) associated with DMPA
- maximal at 1-2 years recovering after discontinuation
- with prolonged use, the loss may be greater and take longer to recover
- no evidence of the development of osteoporosis or increased fracture risk
- caution is needed in women ≥45 years and those younger than 18 years of age (UKMEC 2)
- women aged under 18 years progestogen-only injectable contraception can be used after consideration of alternative methods
- advised that the risks and benefits of progestogen-only injectables should be assessed every two years
- switch to another method at age 50 years

POI - Bones

Problems:

- Women on long term anti-epileptic medication (carbamazepine, phenytoin, primidone or sodium valproate) particularly if they are immobilised for long periods or have inadequate sun exposure – NICE recommends Vitamin D supplementation
- HIV+ women prone to having a lower BMD and osteopenia

POI – Return of Fertility

- Delay of up to one year
- no evidence of reduced fertility long term

POI – Problem Bleeding

- Rule out STI's and gynae pathology
- COC (cyclically or continuously) for 3/12
- or mefenamic acid 500 mg TDS for five days
- ??? how long for…….
- potentially bring forward date of next injection (up to 2 weeks)
- give in correct place for IM DMPA

POI - Risks

- current stroke, ischaemic heart disease or such a history is UKMEC 3
- limited evidence of an association between POI use and myocardial infarction or stroke
- no association between DMPA and venous thrombosis
- weak association between current use of DMPA and breast cancer
- prolonged use of DMPA (over five years) = weak association with occurrence of cervical cancer

POI - Starting

General:

- 1-5 of cycle (no additional contraception required)
- can be started at any time in the cycle if certain that the woman is not pregnant (additional contraception should be used for seven days)

Postnatal:

- up to day 21 with immediate effect
- after day 21 use additional contraception
- SPC = delay 1st injection for breast feeding by 6 weeks BUT only UKMEC 2 (benefits outweigh the risks) as no adverse effects on breast milk quality or volume, or on infant growth and development

Post Miscarriage/Abortion:

- days 1-5 afterwards (no additional contraception required)
- later than day 5 afterwards (additional contraception or abstinence is required for seven days)

POI - Starting

After EHC:

- a temporary bridging with an oral contraceptive is advised
- BUT can give after levonorgestrel (LNG) EHC or after five days following UPA EHC if bridging methods are not appropriate or acceptable
- if quick starting - a pregnancy test should be performed after 3 weeks following the last UPSI (unprotected sexual intercourse)
- additional precautions for 7 days
- if pregnant not harmful to fetus

POI - Changing from another method

CHC

Starting	Additional contraceptive protection required?	Additional information
Immediately after the last day of pill/patch/ring (i.e. Day 1 of the hormone-free interval)	No additional precautions required	Could be started up to Day 3 of the hormone-free interval without the need for additional precautions as ovulation would not be expected until Day 10
Week 1 following the hormone-free interval	7 days of additional precautions required. If UPSI has occurred after Day 3 of the hormone-free interval advise restarting the CHC method for at least 7 days	When switching after a 7-day hormone-free interval there are no data to confirm that suppression of ovulation is maintained
Week 2–3 of pill/ring/patch	No additional precautions required providing the CHC method has been used consistently and correctly for 7 consecutive days before switching	There is evidence to suggest that taking hormonally active pills for seven consecutive days prevents ovulation. Therefore as long as there have been 7 days of CHC use, seven hormone-free days can occur without any effect on contraceptive efficacy

POI - Changing from another method

POP or LNG-IUS

Starting	Additional contraceptive protection required?	Additional information
Any time	Yes for 7 days or continue method for 7 days	The continuing method provides contraceptive cover while the effects of the injectable are established

Cu-IUD

Starting	Additional contraceptive protection required?	Additional information
Day 1–5 of menstrual cycle	No additional precautions required	
Any other time	Yes for 7 days or continue method for 7 days	The continuing method provides contraceptive cover while the effects of the injectable are established

POI - Changing from another method

Implant

Starting	Additional contraceptive protection required?	Additional information
≤3 years since implant insertion	No additional precautions required	
>3 years since implant insertion	Yes (7 days)	If there has been a risk of pregnancy consider the need for EC and a pregnancy test no sooner than 3 weeks after the most recent incidence of UPSI

Barrier Methods

Starting	Additional contraceptive protection required?	Additional information
Can be started immediately if the previous method was used consistently and correctly	Yes (7 days) unless the injectable is given within Day 1-5 of the menstrual cycle	

POI – What to do if she's late????

Over 2+ weeks late:

- **Assess risk of pregnancy** (timing of sexual intercourse (SI), use of condoms, assuming contraceptive cover until 14 weeks)
- Does she need a pregnancy test?
- Assess need for emergency contraception
- If there is a low risk of pregnancy, check how she would feel about either of the following options:
- Being given DMPA (+/- emergency contraception) now and returning for a pregnancy test (PT) in three weeks
- Waiting and abstaining from SI until three weeks after last unprotected sexual intercourse (UPSI) and then having PT and DMPA
- **Amenorrhoea/timing of DMPA injection**
- Is she amenorrhoeic? Was last DMPA given on time? Is that information recorded?
- **Medical history**
- Are there any changes in her medical history?

POI - Checks

- Every 2 years discuss osteoporosis risks (heavy smoking, history of anorexia, low BMI, family history, diet, sunlight/vit D, oesteo-arthritis etc)
- No need for BP or weight checks at every visit unless predisposing issues – opportunity for healthy lifestyle discussion instead!!