

WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

*This patient information leaflet focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities (term to be revised).
The medicine may be authorised for additional or different uses by national medicines regulatory authorities.*

Information for the patient

[RH084 trade name] *
medroxyprogesterone acetate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have questions about the medicine, ask your health care provider.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness seem to be the same as yours.
- If you get any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [RH084 trade name] is and what it is used for
2. What you need to know before you are given [RH084 trade name]
3. How [RH084 trade name] is given
4. Possible side effects
5. How to store [RH084 trade name]
6. Contents of the pack and other information

1. What [RH084 trade name] is and what it is used for

[RH084 trade name] (DMPA) is used for long-term contraception in women aged over 18 years.

It can also be used for short-term contraception to cover specific periods when:

- your partner is awaiting vasectomy to become effective;
- you are awaiting sterilization;
- you are awaiting immunization against rubella to become effective.

[RH084 trade name] (DMPA) may be used in adolescents aged over 12 years if there is compelling reason for contraception and other methods are unsuitable or unacceptable.

Women who are living with HIV or are on antiretroviral (ARV) therapy can safely use DMPA.

2. What you need to know before you are given [RH084 trade name]

Do not use [RH084 trade name]:

- If you are allergic (hypersensitive) to medroxyprogesterone acetate or to any of the other ingredients (listed in section 6).
- If you think you may be pregnant.
- If you have had, or think you may have, hormone-dependent cancer of the breast or genital organs.

*Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

- If you have abnormal uterine bleeding.
- If you have liver disease.
- If you are hypertensive.
- If you have had diabetes for longer than 20 years.
- If you have a history of ischemic heart disease (e.g. myocardial infarction) or stroke
- If you have or have had arterial thrombosis
- If you have acute deep venous thrombosis or pulmonary embolism
- If you have systemic lupus erythematosus.

Warnings and precautions

Your health care provider will ask about you and your family's medical problems, check your blood pressure and exclude the likelihood of you being pregnant. You may also need a breast examination or other checks if you have any special concerns.

Tell your health care provider if you are using medicines such as steroids, antiepileptics and thyroid hormones. It is important that you tell your health care provider if you have or have had in the past any of the following conditions. Your health care provider will then discuss with you whether [RH084 trade name] is suitable for you or recommend a more suitable method of contraception.

- Migraine headaches.
- Diabetes or a family history of diabetes
- Severe pain or swelling in the calf
- Blood clotting disorders such as blood clot in the legs, lung or a stroke
- Problems with your eyesight for example a sudden partial or complete loss of vision or double vision
- Depression
- Problems with your liver or liver disease
- Problems with your kidneys or kidney disease
- Heart disease or cholesterol problems including any family history
- Abnormal pregnancy
- Asthma
- Epilepsy

Psychiatric disorders

Some women using hormonal contraceptives including [RH084 trade name] have reported depression or depressed mood. Depression can be serious and may sometimes lead to suicidal thoughts. If you experience mood changes and depressive symptoms contact your health care provider for further medical advice as soon as possible.

Cervical smear testing

The results of a cervical smear and some laboratory tests could be affected if you are using [RH084 trade name] so it is important that you tell your health care provider.

Protection against sexually transmitted infections

[RH084 trade name] does not protect against HIV infection, e.g. AIDS and other sexually transmitted infections. Safer sex practices, including correct and consistent use of condoms, reduce the transmission of sexually transmitted infections through sexual contact, including HIV. You should seek advice from your health care provider on how to decrease your risk of catching sexually transmitted infections including HIV.

Other medicines and [RH084 trade name]

Tell your health care provider:

- If you are taking, have recently taken or might take any other medicines.
- If you are taking a medicine called aminoglutethiamide or other medicines that thin your blood (anticoagulants).

Always tell your health care provider who treats you that you are using [RH084 trade name] as a contraceptive because medicines can sometimes interact with each other.

Pregnancy, breast-feeding and fertility

Pregnancy

Your health care provider will check that you are not pregnant before giving you the first injection and also if any following injection is delayed beyond 12 weeks. You should not take [RH084 trade name] if you are pregnant as hormonal medicines can affect the developing baby.

Breast-feeding

[RH084 trade name] does not prevent the breast from producing milk so nursing mothers can use it, however, it is better for the baby that for the first few weeks after birth its mother's milk contains no traces of any medicines, including [RH084 trade name]. Your health care provider may advise that you wait until at least 6 weeks after your baby has been born before you start using [RH084 trade name] for contraception.

Fertility

Your usual level of fertility should return when the effect of the injection has worn off. This takes different amounts of time in different women, and does not depend on how long you have been using [RH084 trade name]. Some women have become pregnant as early as 14 weeks after their last injection.

Driving and using machines

[RH084 trade name] may cause headaches and dizziness. Do not operate machines or drive if you feel dizzy after taking [RH084 trade name].

[RH084 trade name] contains methyl paraben, propyl paraben and sodium

Each vial contains methyl paraben and propyl paraben which may cause allergic reactions (possibly delayed), and exceptionally bronchospasm (difficulty breathing caused by narrowing of the airways).

This medicinal product also contains less than 1mmol sodium, i.e., is essentially 'sodium-free'.

3. How [RH084 trade name] is given

[RH084 trade name] will be given to you by your health care provider.

(The last section of this leaflet contains instructions for your health care provider on how they should do this.)

[RH084 trade name] is given every 12 weeks as a single intramuscular injection of 1 mL (150mg medroxyprogesterone acetate) into the buttock or upper arm. The injection is given during the first 5 days after the beginning of a normal menstrual period.

Following childbirth, the first [RH084 trade name] can be given within 5 days after childbirth if you are **not** breastfeeding.

Provided that the injection is given at the times stated above, then you are protected from pregnancy straight away and there is no need to take extra precautions.

[RH084 trade name] works as a contraceptive for 12 weeks in your body. There is no way of reversing the injection once it is given.

For effective contraceptive cover, [RH084 trade name] **MUST** be given every 12 weeks. Make sure that you or your health care provider makes your next appointment for 12 weeks' time.

The risk of heavy or prolonged vaginal bleeding may be increased if [RH084 trade name] is used immediately following childbirth or termination of pregnancy.

If you forget an injection of [RH084 trade name]

If you forget your injection or are late getting your next injection (i.e. wait longer than 12 weeks between injections), there is a greater risk that you could become pregnant. Ask your health care provider when you should receive your next injection of [RH084 trade name] and which type of contraception you should use in the meantime.

Switching from other methods of contraception

When you switch from other contraceptive methods, your health care provider will make sure you are not at risk of becoming pregnant by giving you your first injection of [RH084 trade name] at the appropriate time. If you switch from oral contraceptives, you should have your first injection of [RH084 trade name] within 7 days after taking your last pill.

If you have any questions on the use of this medicine, ask your health care provider.

4. Possible side effects

Like all medicines, this medicine can cause side effects although not everybody gets them.

Seek medical help immediately if you notice any of the following side effects:

- Hypersensitivity (allergic) reaction (It is not known how frequently this occurs). Symptoms include sudden skin rash, swelling of the face, lips, tongue or throat, wheezing or difficulty in breathing.
- A blood clot in the lungs (this occurs rarely—may affect up to 1 in 1000 people)
Symptoms include
 - Shortness of breath
 - Breath-related chest pains
 - Coughing up blood
- A blood clot in the leg (this occurs rarely—may affect up to 1 in 1000 people)

Deep vein thrombosis (DVT) is a condition in which blood clot forms in one of your deep veins, usually in your leg.

These are symptoms of a **deep-vein thrombosis (DVT)**:

- You have pain, tenderness or swelling in your calf, ankle or foot
 - You have painful or inflamed veins in your leg
 - You find it difficult to put full weight on the affected leg
 - You have purple discolouration of the skin of the leg or the skin becomes red and warm to touch.
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- Jaundice (yellowing of the skin or the whites of the eyes).

Women who use [RH084 trade name] tend to have lower bone mineral density than women of the same age who have never used it. The side effects of [RH084 trade name] are greatest in the first 2-3 years of use. Following this, bone mineral density tends to stabilize and there appears to be some recovery when [RH084 trade name] is stopped. It is not yet possible to say whether [RH084 trade name] increases the risk of osteoporosis (weak bones) and fractures in later life.

Other side-effects include:

Very common: may affect more than 1 in 10 people

- nervousness
- headache
- stomach pain or discomfort
- weight increase or decrease

Common: may affect up to 1 in 10 people

- depression
- libido decreased (reduced sex drive)
- dizziness
- feeling sick
- feeling bloated
- hair loss
- acne
- back pain
- vaginal discharge
- breast tenderness
- difficult or painful period
- urinary tract infection
- oedema/fluid retention
- weakness

Uncommon: may affect up to 1 in 100 people

- appetite increased or decreased
- difficulty sleeping
- convulsions (fits)
- drowsiness
- tingling
- hot flush
- liver disorder
- facial hair growth
- nettle rash or hives
- itchy skin
- temporary brown patches
- difficult or painful period
- unexpected or unusual vaginal bleeding or spotting
- milky discharge from the breast when not pregnant or breast-feeding
- pelvic pain
- painful intercourse
- prevention of lactation

Rare: may affect up to 1 in 1,000 people

- breast cancer
- reduction in red blood cell
- blood disorder
- difficulty reaching orgasm
- behavior change
- mood change
- irritability
- anxiety
- migraine
- paralysis
- fainting
- feeling of dizziness or spinning
- heart beats more rapidly
- high blood pressure
- varicose veins
- rectal bleeding
- digestive disorder
- liver enzyme disorder
- accumulation of fat (at injection site)
- inflammation of the skin
- scar tissue formation
- stretch marks
- pain in a joint
- muscular cramps
- bone density decreased (osteoporosis)
- vaginal pain or inflammation
- stopping or extended break of your periods
- breast pain
- inflammation of the vagina
- stopping or extended break of your periods
- breast pain
- uterine bleeding or excessive bleeding
- periods with abnormally heavy or prolonged bleeding
- vaginal dryness
- change in breast size
- ovarian or vaginal cyst
- premenstrual syndrome
- excessive thickening of the lining of the womb
- breast lump
- nipple bleeding
- delayed egg release with longer menstrual cycles (periods)
- feel pregnant
- fever
- tiredness
- injection site pain or tenderness
- injection site lump or dimple
- feeling thirsty
- hoarseness

- facial nerve paralysis
- decreased sugar tolerance
- abnormal smear

Possible effect on your periods

After the first injection of [RH084 trade name] it is likely that you will have irregular, possibly lengthy bleeding or spotting. This is quite normal and nothing to worry about.

One third of women will not have any bleeding at all after the first injection. After 4 injections, most women find that their periods have stopped completely. Not having periods is nothing to worry about.

If you experience very heavy or prolonged bleeding you should talk to your health care provider. This happens rarely but can be treated.

When you stop taking [RH084 trade name] your periods will return to normal in a few months.

Possible effects on your bones

[RH084 trade name] works by lowering levels of oestrogen and other hormones. However, lower oestrogen levels can cause bones to become thinner (by reducing bone mineral density). Women who use [RH084 trade name] tend to have lower bone mineral density than women of the same age who have never used it. The effects of [RH084 trade name] are greatest in the first 2-3 years of use. Following this, bone mineral density tends to stabilise and there appears to be some recovery of bone density when [RH084 trade name] is stopped. It is not yet possible to say whether [RH084 trade name] increases the risk of osteoporosis (weak bones) and fractures in later life (after the menopause).

The following are risk factors in the development of osteoporosis in later life. You should discuss with your health care provider before starting treatment if you have any of the following as an alternative contraceptive may be more suitable to your needs;

- Chronic alcohol or tobacco use
- Chronic use of drugs that can reduce bone mass, e.g. epilepsy medication or steroids
- Low body mass index or eating disorder, e.g. anorexia nervosa or bulimia
- Previous low trauma fracture that was not caused by a fall
- Strong family history of osteoporosis

Teenagers (up to 18 years)

Normally, the bones of teenagers are rapidly growing and increasing in strength. The stronger the bones are when adulthood is reached, the greater the protection against osteoporosis in later life. Since [RH084 trade name] may cause teenage bones to become thinner at a time when they should be growing, its effect may be particularly important in this age group. Bones start to recover when [RH084 trade name] is stopped, but it is not yet known whether the bone mineral density reaches the same levels as it would have if [RH084 trade name] had never been used. **You should therefore discuss whether another form of contraception might be more suitable for you with the person who provides your contraception before starting [RH084 trade name].**

If you use [RH084 trade name], it may help your bones if you take regular weight-bearing exercise and have a healthy diet, including an adequate intake of calcium (e.g. in dairy products) and vitamin D (e.g. in oily fish).

Possible risk of cancer

Studies of women who have used different forms of contraception found that women who used [RH084 trade name], for contraception had no increase in overall risk of developing cancer of the ovary, womb, cervix or liver.

Possible risk of breast cancer

Breast cancer is rare among women under 40 years of age whether or not they use hormonal contraceptives. Older women have a higher baseline risk of breast cancer and therefore the increase in the number of cases due to [RH084 trade name] is greater in older women than in younger women.

Possible risk of forming an abscess at the injection site

As with any intramuscular injection, there is a risk of an abscess forming at the site of injection. This may require medical or surgical attention.

Possible risk of weight gain

Some women gained weight while using [RH084 trade name]. Studies show that over the first 1-2 years of use, the average weight gain was 5-8 lbs. Women completing 4-6 years of therapy gained an average of 14-16.5 lbs.

Reporting of side effects

If you get any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. If available, you can also report side effects directly through the national reporting system. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store [RH084 trade name]

Keep this medicine out of the sight and reach of children.

Do not store above 30°C. Do not freeze.
Store vials in the cartons to protect from light.

This medicine must not be used after the expiry date stated on the vial label or carton after 'EXP'. The expiry date refers to the last day of that month.

This medicine must not be used if you notice description of the visible signs of deterioration.

Do not throw away any medicines in wastewater or household waste. Ask your health care provider how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [RH084 trade name] contains

The active substance in [RH084 trade name] is medroxyprogesterone acetate. Each dose (1 millilitre) contains 150 mg of medroxyprogesterone acetate.

The other ingredients of [RH084 trade name] are polyethylene glycol 3350, polysorbate 80 (tween 80), sodium chloride (injectable grade), methyl paraben, propyl paraben, sodium hydroxide (for pH adjustment), hydrochloric acid (for pH adjustment), nitrogen (injectable grade, for air displacement) and water for injection.

What [RH084 trade name] looks like and contents of the pack

[RH084 trade name] is a white to off-white sterile suspension for injection.

[RH084 trade name] is available in a 3mL type-1 clear glass vial, sealed with a 13mm grey chlorobutyl rubber stopper and a, red flip-off aluminium seal containing 1 ml white to off-white suspension. Each filled and sealed glass vial is packed in a printed unit carton.

Pack sizes

1 vial in an inner carton
20 vials in an inner carton

Supplier

Incepta Pharmaceuticals Limited
40, Shahid Tajuddin Ahmed Sarani
Tejgaon I/A, Dhaka-1208
Bangladesh
e-mail: ira@Inceptapharma.com

Manufacturer

Incepta Pharmaceuticals Limited
Unit-1, Injectable Potent Drug (IPD),
Krishnapura, Sahabelishor
Dhamrai, Dhaka
Bangladesh
e-mail: ira@Inceptapharma.com

For any information about this medicine, contact the local representative of the supplier:

This leaflet was prepared in May 2020

Sections 5 and 6 were updated in September 2020

Detailed information on this medicine is available on the World Health Organization (WHO) web site:
<https://extranet.who.int/prequal/>.

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The following information is intended for health care providers only: (For further information, consult the Summary of Product Characteristics.)

Dosage:

Each mL of suspension contains 150 mg medroxyprogesterone acetate. The sterile aqueous suspension of [RH084 trade name] should be vigorously shaken just before use to ensure that the dose being given represents a uniform suspension of [RH084 trade name]. Doses should be given by deep intramuscular injection into the buttock or arm.

Care should be taken to ensure that the depot injection is given into the muscle tissue, preferably the gluteus maximus, but other muscle tissue such as the deltoid may be used and the site of injection should be cleansed using standard methods prior to administration of the injection.

Assembly of syringe for single use:

1. Remove tip cap.
2. Position needle using aseptic technique.
3. Remove needle shield. The syringe is now ready for use.

Further doses: These should be given at 12 week intervals, however, as long as the injection is given no later than five days after this time, no additional contraceptive measures (e.g. barrier) are required.

(NB For partners of men undergoing vasectomy a second injection of 150 mg i.m. 12 weeks after the first may be necessary in a small proportion of patients where the partner's sperm count has not fallen to zero.) If the interval from the preceding injection is greater than 12 weeks for any reason, then pregnancy should be excluded before the next injection is given and the patient should use additional contraceptive measures (e.g. barrier) for fourteen days after this subsequent injection.

Administration:

Adults

First injection: To provide contraceptive cover in the first cycle of use, an injection of 150 mg i.m. should be given during the first five days of a normal menstrual cycle. If the injection is carried out according to these instructions, no additional contraceptive cover is required.

Postpartum: To increase assurance that the patient is not pregnant at the time of first administration, this injection should be given within 5 days postpartum if not breast-feeding.

There is evidence that women prescribed [RH084 trade name] in the immediate puerperium can experience prolonged and heavy bleeding. Because of this, the drug should be used with caution in the puerperium. Women who are considering use of the product immediately following delivery or termination should be advised that the risk of heavy or prolonged bleeding may be increased.

Health care providers are reminded that in the non-breast-feeding postpartum patient, ovulation may occur as early as week 4. If the puerperal woman will be breast-feeding, the initial injection should be given no sooner than six weeks postpartum, when the infant's enzyme system is more fully developed. Further injections should be given at 12 week intervals.

Paediatric population (12-18 years): [RH084 trade name] is not indicated before menarche. Data in adolescent females (12-18 years) is available. Other than concerns about loss of BMD, the safety and effectiveness of [RH084 trade name] is expected to be the same for adolescents after menarche and adult females.

Switching from other Methods of Contraception: [RH084 trade name] should be given in a manner that ensures continuous contraceptive coverage. This should be based upon the mechanism of action of other methods (e.g. patients switching from oral contraceptives should have their first injection of [RH084 trade name] within 7 days of taking their last active pill).

Hepatic Insufficiency: The effect of hepatic disease on the pharmacokinetics of [RH084 trade name] is unknown. As [RH084 trade name] largely undergoes hepatic elimination it may be poorly metabolised in patients with severe liver insufficiency (see Contraindications).

Renal Insufficiency: The effect of renal disease on the pharmacokinetics of [RH084 trade name] is unknown. No dosage adjustment should be necessary in women with renal insufficiency, since [RH084 trade name] is almost exclusively eliminated by hepatic metabolism.