

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

[RH074 trade name]¹
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 [RH074 trade name] is and what it is used for
2. What you need to know before you take [RH074 trade name]
3. How to take [RH074 trade name]
4. Possible side effects
5. How to store [RH074 trade name]
6. Contents of the pack and other information

1. What [RH074 trade name] is and what it is used for

[RH074 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.

[RH074 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 take [RH074 trade name]

Do not use [RH074 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.
- If you have abnormal uterine bleeding.
- If you have liver disease.
- If you have not yet started your periods.

¹Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

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 [RH074 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 [RH074 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 [RH074 trade name] so it is important that you tell your health care provider.

Protection against sexually transmitted infections

[RH074 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 [RH074 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 [RH074 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 [RH074 trade name] if you are pregnant as hormonal medicines can affect the developing baby.

Breast-feeding

[RH074 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 [RH074 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 [RH074 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 [RH074 trade name]. Some women have become pregnant as early as 14 weeks after their last injection.

Driving and using machines

[RH074 trade name] may cause headaches and dizziness. Do not operate machines or drive if you feel dizzy after taking [RH074 trade name].

[RH074 trade name] contains methyl paraben (E218), propyl paraben (E216) and sodium

Each vial contains methyl paraben and propyl paraben which may cause allergic reactions (possibly delayed), and exceptionally bronchospasm. This medicinal product contains less than 1mmol sodium (23mg) per 150mg/mL, i.e essentially 'sodium-free'.

3. How to take [RH074 trade name]

[RH074 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.)

[RH074 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 within 7 days after the beginning of a normal menstrual period.

Following childbirth, the first [RH074 trade name] can be given up to 4 weeks 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.

[RH074 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, [RH074 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 [RH074 trade name] is used immediately following childbirth or termination of pregnancy.

If you forget an injection of [RH074 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 [RH074 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 [RH074 trade name] at the appropriate time. If you switch from oral contraceptives, you should have your first injection of [RH074 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.
-
- Jaundice (yellowing of the skin or the whites of the eyes).

Women who use [RH074 trade name] tend to have lower bone mineral density than women of the same age who have never used it. The side effects of [RH074 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 [RH074 trade name] is stopped. It is not yet possible to say whether [RH074 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 [RH074 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 [RH074 trade name] your periods will return to normal in a few months.

Possible effects on your bones

[RH074 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 [RH074 trade name] tend to have lower bone mineral density than women of the same age who have never used it. The effects of [RH074 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 [RH074 trade name] is stopped. It is not yet possible to say whether [RH074 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 [RH074 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 [RH074 trade name] is stopped, but it is not yet known whether the bone mineral density reaches the same levels as it would have if [RH074 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 [RH074 trade name].**

If you use [RH074 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 [RH074 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 [RH074 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 [RH074 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 [RH074 trade name]

Keep this medicine out of the sight and reach of children.
Do not store above 30°C. Do not freeze.

Do not use this medicine after the expiry date stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Do not use this medicine 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 [RH074 trade name] contains

The active substance is medroxyprogesterone acetate

The other ingredients of [RH074 trade name] are polysorbate 80, macrogol 3350, methyl paraben, propyl paraben, sodium chloride, water for injection, hydrochloric acid and/or sodium hydroxide for the pH adjustment.

What [RH074 trade name] looks like and contents of the pack

[RH074 trade name] is a white to off- white suspension, filled in 2 mL type I clear tubular glass vial with grey bromobutyl rubber stopper and white flip-off aluminium seal.

Pack size: 25 vials per carton

This injectable suspension is intended for intramuscular administration

Supplier and Manufacturer

Mylan Laboratories Limited
Plot No. 20 & 21, Parmez,
The Pharmaceutical Special Economic Zone,
Sarkhej – Bavla National highway No. 8-A,
Nr. Village – Matoda, Tal- Sanand,
Dist. - Ahmedabad -382213
India
Email: WHO.Regulatory@mylan.com

This leaflet was last revised in December 2019

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

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 [RH074 trade name] should be vigorously shaken just before use to ensure that the dose being given represents a uniform suspension of [RH074 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. The site is chosen according to the woman's preference.

Administration:

[RH074 trade name] is given intramuscularly every 12 weeks.

First injection

The first dose of [RH074 trade name] can be given:

- within 7 days of the start of the woman's monthly bleeding in women who are menstruating
- immediately if switching from an intra-uterine device (IUD)
- immediately if switching from a correctly used hormonal method
- immediately if switching when a repeat injection of another injectable method is due

If more than 7 days have passed since the start of her monthly bleeding, or the woman does not have monthly bleeding, or the woman has not been using another contraception method consistently, she can receive the injection at any time so long as it is reasonably certain she is not pregnant. In such a case she should use an additional (backup) method of contraception for the first 7 days.

First injection after birth

If the woman is *fully breast-feeding*, the first dose of [RH074 trade name] can be given:

- any time between 6 weeks and 6 months of birth if her monthly bleeding has not returned
- any time after more than 6 months of birth if her monthly bleeding has not returned and it is reasonably certain she is not pregnant; an additional (backup) method of contraception should be used for the first 7 days
- as for women who are menstruating (see above) if the woman's monthly bleeding has returned

If the woman is *partially breast-feeding*, the first dose of [RH074 trade name] can be given:

- 6 weeks after birth
- any time after more than 6 weeks of birth if her monthly bleeding has not returned and it is reasonably certain she is not pregnant; an additional (backup) method of contraception should be used for the first 7 days
- as for women who are menstruating (see above) if the woman's monthly bleeding has returned

If the woman is *not breast-feeding*, the first dose of [RH074 trade name] can be given:

- up to 4 weeks after birth
- any time after more than 4 weeks of birth if her monthly bleeding has not returned and it is reasonably certain she is not pregnant; an additional (backup) method of contraception should be used for the first 7 days
- as for women who are menstruating (see above) if the woman's monthly bleeding has returned

First injection after miscarriage or abortion

The first dose of [RH074 trade name] can be given:

- within 7 days of first- or second-trimester miscarriage or abortion
- any time after 7 days of first- or second-trimester miscarriage or abortion if it is reasonably certain she is not pregnant; an additional (backup) method of contraception should be used for the first 7 days

The injection may be given up to 2 weeks earlier, that is, after 10 weeks of the previous injection.

Managing Late Injections

As long as it is given within 4 weeks of the due dose, she can receive her next injection. No need for tests, evaluation or a backup method.

A client who is more than 4 weeks late for [RH074 trade name] can receive her next injection if it is reasonably certain she is not pregnant. She can receive her next injection if:

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

She will need to abstain from sex or use a backup method for the first 7 days after the injection.

Patients with renal impairment

No dose adjustment is necessary in women with renal impairment, since [RH074 trade name] is almost exclusively eliminated by hepatic metabolism.

Hepatic impairment

As [RH074 trade name] largely undergoes hepatic elimination it may be poorly metabolized in patients with severe hepatic impairment.