

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.¹

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

¹ https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

Patient information leaflet: Information for the user

[RH028 trade name]²

Levonorgestrel

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

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your health care provider.
- This medicine has been prescribed for you only. Do not pass it on to others.
- If you get any side effects, talk to your health care provider.
This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What [RH028 trade name] are and what they are used for
2. What you need to know before you use [RH028 trade name]
3. How to use [RH028 trade name]
4. Possible side effects
5. How to store [RH028 trade name]
6. Contents of the pack and other information

1. What [RH028 trade name] are and what they are used for

[RH028 trade name] are used for the prevention of pregnancy (contraception). The implants consist of two thin, flexible rods made of a rubber-like material, that are inserted by a minor surgical procedure just beneath the skin on the inside of your upper arm.

The implants slowly release a small amount of the hormone levonorgestrel, which is one of the active ingredients in many oral contraceptives. [RH028 trade name] are long-acting and are effective for up to three years. Immediately after insertion, low doses of the hormone start to be released continuously into your body.

[RH028 trade name] work by a combination of factors. The most important of these are prevention of regular egg release and thickening of the cervical mucus, making it more difficult for sperm to reach the egg.

² Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

2. What you need to know before you use [RH028 trade name]

General notes

Before you decide to use [RH028 trade name] or any other contraceptive method, you should compare it to other available methods. If you want to learn more about other methods, ask your health care provider. One of these other methods may be better for you than [RH028 trade name]. Each woman who considers using [RH028 trade name] should understand the benefits and risks of using this contraceptive method compared with other methods. This leaflet will give you much of the information you will need to make this decision but you will still need to discuss the matter thoroughly with your health care provider. You should discuss the information provided in this leaflet, when choosing whether to use [RH028 trade name] and on check-up visits. Follow your health care provider's advice with regard to check-ups while using [RH028 trade name].

Some women should not use [RH028 trade name]. To find out whether you are one of them, talk to your health care provider and read the sections entitled: "Do not use [RH028 trade name]" and "Warnings and precautions".

Some women who use [RH028 trade name] will experience side effects. You should know the warning signs. To learn about them, talk to your health care provider and read the sections below entitled "Warnings and precautions" and "Possible side effects".

Contraceptive effectiveness of [RH028 trade name] implants

[RH028 trade name] are among the most effective reversible contraceptive methods. However, no contraceptive is 100 percent effective. The average annual pregnancy rate for [RH028 trade name] over a 3-year period is less than 1%. This means less than one pregnancy for every 100 women during the first year of use.

Protection against HIV infection or other sexually transmitted diseases

[RH028 trade name] do not protect against HIV infection (AIDS) or other sexually transmitted diseases.

Do NOT use [RH028 trade name] if you:

- are allergic to levonorgestrel or any of the other ingredients in [RH028 trade name] (listed in section 6)
- have abnormal vaginal bleeding
- have, or are suspected of having, breast cancer or cancer of the lining of the womb
- have, or have ever had, severe illness involving your liver, as long as your liver is not working properly again as judged by laboratory
- have, or have ever had, a liver tumour (benign or malignant)
- have a blood clot in a blood vessel (thrombosis) in, for instance, your leg, lung or eye.

Warnings and precautions

Talk to your health care provider before using or while you are using [RH028 trade name], if any of the following symptoms occur:

- migraines or increase in the frequency of migraine attacks

- persistent headaches or problems with vision, particularly if you are overweight or have recently gained weight
- sudden headaches or vomiting, dizziness or fainting, disturbances of vision or speech, weakness, or numbness in an arm or leg
- pain in the calf of the leg or unusual swelling of arms or legs
- sharp pain in the chest or sudden difficulty in breathing, or coughing blood
- unbearable pain or a feeling of pressure in the chest
- severe abdominal pain or tenderness in the abdominal area
- suspect you may be pregnant
- heavy vaginal bleeding
- skin or eyes become yellow
- lump or lumps in the breast
- pain, pus or bleeding at the insertion site of the implants
- sleeping problems, weakness, lack of energy, tiredness or mood swings
- implant is expelled
- fluid retention

If you, or someone in your family, has certain diseases, you must discuss with your health care provider if you should have the implants. Tell the health care provider if you:

- have had an ectopic pregnancy (where the embryo is known or suspected to grow outside the uterus; see section on “Pregnancy, breast-feeding and fertility”)
- or someone in your family has a history of formation of blood clots (thrombosis) or a blood clotting (coagulation) disorder, stroke, heart attack, high blood pressure, very high lipid or cholesterol levels or coronary artery disease (see section “Blood clots (thrombosis)”)
- have or have had migraines or frequent headaches
- are breast-feeding
- have or have had a lump or lumps in your breast, mastopathy (which may show as breast aching or breast tenderness) or an abnormal mammogram (breast X-ray) or someone in your family has had breast cancer
- have problems with your gall bladder, liver disorders or a kidney disease
- have diabetes
- have depression
- have impaired hearing due to a condition called otosclerosis
- have had itchy, red hives or small bumps during pregnancy (herpes gestationis)

Your health care provider may decide that you will be able to use [RH028 trade name], even if any of the above applies to you.

Blood clots (thrombosis)

As with oral contraceptives, there have been reports of blood clots, heart attacks and strokes in connection with the use of levonorgestrel implants.

If you develop a clot, for instance in your leg, lung or eye, [RH028 trade name] must be removed.

If you are bedridden after **surgery**, or have limited movement for a long time because of an illness or an accident, the risk of blood clots may increase. In that case, your health care provider may decide to remove the [RH028 trade name].

Blood pressure

Even though studies have not shown a considerable increase in blood pressure in users of [RH028 trade name], blood pressure may still increase in some women. You should therefore have your blood pressure checked regularly whilst the implants are present.

Increased pressure around the brain (intracranial pressure)

Increased pressure around the brain has been reported rarely in users of levonorgestrel implants. Contact your health care provider if you experience frequent, severe or persistent headaches or have problems with your vision.

Enlarged ovarian follicles (ovarian cysts)

These may occur in some women with [RH028 trade name]. Such follicles will be detected in a physical examination and usually disappear on their own. In rare cases, however, they may twist or rupture, causing abdominal pain, and may require surgery. If you feel any pain or discomfort, contact your health care provider.

Children and adolescents

The safety and effectiveness of [RH028 trade name] have not been established in females below 18 years of age.

Other medicines and [RH028 trade name]

Always tell your health care provider if you are taking, have recently taken or might take any other medicines. Also tell any other health care provider that you are using [RH028 trade name]. They can tell you if you need to take additional contraceptive precautions (for example condoms) and if so, for how long (see section on “Extra “backup” contraceptive precautions”), or, whether the use of another medicine you need must be changed.

Some medicines: - can have an influence on the blood levels of [RH028 trade name]
- can make [RH028 trade name] **less effective in preventing pregnancy**
- can cause unexpected bleeding.

These include medicines used for the treatment of:

- HIV infection; so-called non-nucleoside reverse transcriptase inhibitors (e.g. efavirenz, nevirapine, etravirine)
- tuberculosis (e.g. rifampicin)
- fungal infections (griseofulvin, azole antifungals, e.g. itraconazole, voriconazole, fluconazole).
- epilepsy (e.g. primidone, phenytoin, barbiturates, carbamazepine, oxcarbazepine, topiramate, felbamate)
- pulmonary artery hypertension (e. g. bosentan)
- bacterial infections; so-called macrolide antibiotic (e.g. clarithromycin, erythromycin)
- certain heart diseases, high blood pressure, so-called calcium channel blockers, e.g. verapamil, diltiazem)

Mid-cycle bleeding and unintended pregnancies have been reported. You need to take additional reliable non-hormonal contraceptive precautions such as condoms while you are taking the other medicine and for **28 days** afterwards. Read carefully the section on “Extra “backup” contraceptive precautions”.

In case you have a long-term treatment using the medicines mentioned above, you should consider using another method of contraception instead of [RH028 trade name].

The herbal remedy St. John's wort is a substance that increases the clearance of levonorgestrel.

[RH028 trade name] may **influence the effect** of other medicines. Accordingly, the concentration of these other medicines in the blood and tissues may either increase (e. g. cyclosporine, a medicine used to prevent rejection of transplanted organs) or decrease (e.g., lamotrigine, a medicine used to treat epilepsy).

Laboratory tests

If you need a blood test or other laboratory tests tell your doctor or the laboratory staff that you are using [RH028 trade name] because these can affect the results of some tests.

Pregnancy, breast-feeding and fertility

Pregnancy

[RH028 trade name] must not be used during an existing or suspected pregnancy.

Ectopic pregnancy has sometimes occurred in users of levonorgestrel implants.

Symptoms of ectopic pregnancy include:

- spotting (a very light vaginal bleed)
- abdominal cramping, pain

These usually begin shortly after the first missed period. Contact your health care provider if you miss a period or have abdominal pain.

If, after the insertion of the implants, you first have a regular bleed and then your period is more than 6 weeks late, you should make sure that you are not pregnant.

If you become pregnant with [RH028 trade name] in place, you must have the implants removed. There are no studies available for [RH028 trade name] regarding an effect on the baby if used before or during pregnancy. However, contraceptive pills containing levonorgestrel used prior or during pregnancy have not caused harmful effects on the baby.

If you want to become pregnant [RH028 trade name] can be removed at any time by your health care provider (see section 3 “When should [RH028 trade name] be removed?”), after which pregnancy may be possible.

Breast-feeding

If you are breast-feeding and want to use these implants, you should discuss this with your health care provider. Small amounts of levonorgestrel (the hormone in [RH028 trade name]) will be excreted in breast milk. Studies have not shown any significant effects on the growth or other development of breast-fed babies whose mothers used other levonorgestrel implants from the sixth week after childbirth. However, it is not known if levonorgestrel is found in breast milk in the first 6 weeks after giving birth.

Fertility

Your usual level of fertility will return after the implants are removed.

Driving and using machines

[RH028 trade name] have no influence on ability to drive or use machines.

3. How to use [RH028 trade name]

[RH028 trade name] are different from other contraceptive methods. They must be inserted and removed by a health care provider familiar with the minor surgical procedure.

Before inserting the implants your health care provider will:

- ask you about your medical history
- perform a physical examination
- make sure that you are not pregnant.

Placement of [RH028 trade name]

[RH028 trade name] should be placed within seven days from the start of your menstrual bleed (your monthly period). In this case you will not need to take any additional contraceptive precautions.

If insertion is done after the 7th day (from the first day of bleeding) you will have to use other non-hormonal contraception (e.g. condoms) for at least the next 7 days. Read carefully the section on "Extra "backup" contraceptive precautions".

Changing from a combined hormonal contraceptive (combined oral contraceptive /COC), vaginal ring or transdermal patch)

[RH028 trade name] should preferably be inserted on the day after you have taken the last active tablet of your combined oral contraceptive but at the latest on the day after the 7th day of the tablet free interval or placebo tablet.

If you have previously used a vaginal ring or a transdermal patch, [RH028 trade name] should preferably be inserted on the day of removal of the last ring or patch of a cycle pack, but at the latest when the application of the next ring or patch would have been due.

Changing from another progestogen-only method (minipill, injection, implant) or from a progestogen-releasing or other intrauterine system (IUS)

[RH028 trade name] may be inserted

- on any day if you have previously taken the minipill,
- on any day once your previous implant or IUS has been removed,
- when the next injection would have been due.

Use of [RH028 trade name] after giving birth, or after miscarriage or abortion

- [RH028 trade name] may be inserted immediately after childbirth.
- If [RH028 trade name] is inserted within 3 weeks of delivery, you will not need other contraceptive precautions.
- If [RH028 trade name] is inserted later than 3 weeks after giving birth, your health care provider will make sure that you are not pregnant, and you must use other non-hormonal methods of contraception for a minimum of 7 days after the insertion.
- If you have just had a miscarriage or an abortion the implants can be inserted immediately. Your health care provider will tell you more about this.

Procedure

1. The health care provider will insert the two thin [RH028 trade name] just beneath the skin on the inside of your upper arm. If you are right-handed, usually your left arm is used, and if you are left-handed, your right arm is used.
2. A small cut will be made to insert the implants, to do this a local anaesthetic will be used at the insertion site.
3. The implants are placed underneath the skin, one at a time, with a separate instrument (trocar). Since the insertion site is anaesthetised, you should not feel any pain.
4. After the procedure, the insertion site will be closed with skin tape and bandaged. Keep the wound dry and bandaged for 3 days. Do not bruise the insertion site during this time or lift anything heavy with that arm.

There may be some discolouration, bruising and swelling at the implant site for a few days after the insertion but these should not interfere with your normal activities. Occasionally, an infection may occur or there may be temporary pain, discomfort or itching.

The following skin reactions have been reported in connection with the insertion of other similar levonorgestrel implants:

- scarring, blistering, shedding of skin, ulceration, tingling and numbness.

Talk to your health care provider if you are worried – see also section 4.

Expulsion and displacement of implant

It is possible that an implant is expelled before the incision in your arm has healed, especially if the implants have been inserted very near the skin surface or too close to the incision or if the implant site is infected. If this happens contact your health care provider because an expelled implant must always be replaced with a new, sterile implant.

You also need to take additional reliable non-hormonal contraceptive precautions such as condoms, until you have seen your health care provider. Read carefully the section on “Extra “backup” contraceptive precautions”.

The implant may move position in your arm. This has been reported infrequently, however you may feel pain or discomfort. If you feel the implant has moved, contact your health care provider.

Extra “backup” contraceptive precautions

If you need extra contraceptive precautions

- use reliable non-hormonal contraception, such as condoms or
- do not have sex.

Do not use the rhythm or temperature method as additional contraceptive precautions. Changes in body temperature and cervical mucus that normally take place during the menstrual cycle may not occur during the use of [RH028 trade name].

When you should see your health care provider

After some time has elapsed from the insertion of the implants, your health care provider may want to check the implant site.

As with other hormonal contraceptives, you will need regular check-ups while you are using [RH028 trade name]. Your health care provider will tell you how often to go for check-ups.

When should [RH028 trade name] be removed?

You can decide to have your [RH028 trade name] removed at any time, after which pregnancy is possible. Therefore, if you do not want to have another set of [RH028 trade name] inserted and do not wish to become pregnant, you must start using another method of contraception immediately.

[RH028 trade name] **must be removed at the end of 3 years**. Do not put off removal after the 3 years have elapsed, as the implants will start to lose their effectiveness after that time. If you cannot see a healthcare provider in time to have them removed at the end of the third year, you must take additional contraceptive precautions and have the implants removed as soon as possible. Read carefully the section on “Extra “backup” contraceptive precautions”.

If you want to continue using the implants, a new set can be inserted when the existing implants are removed.

Removal procedure for [RH028 trade name]

The removal of [RH028 trade name] may be more difficult than their insertion. It may take longer and involve more pain. It may leave scars – a risk that does not exist with most other contraceptive methods.

1. As the implants are located beneath the skin on the inside of your upper arm, they must be removed by a health care provider. Do not try to remove them yourself.
2. The implant site will be anaesthetised and a small cut will be made in the skin.
3. After the removal, keep the wound clean, dry and bandaged for 3 to 5 days or until the skin has healed.

Bruising may occur at the site following removal. If the implants have been placed too deep, they may be more difficult to remove.

If both implants cannot be removed at the first attempt, you will need to see the health care provider again for a new attempt. You must use another method of contraception until both implants have been removed.

In cases where the removal of the implants has been difficult, there have been reports of pain, numbness, tingling and scarring in the upper arm.

4. Possible side effects

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

The most frequently reported side effects include:

- irregularity of menstrual bleeding where periods may become prolonged (taking more days than usual), painful, lighter or heavier, more frequent or less frequent, or spotting may occur between periods. In some women, periods may stop altogether.
Such bleeding irregularities occur in the majority of users during the first year and often reduce with continuing use of [RH028 trade name]. Despite the increased number of bleeding days, monthly blood loss is usually no greater than from normal menstruation.
- Breakage of implant during removal

Blood sugar and fat (lipid) levels may also be altered during the use of these implants. Patients with diabetes or disorders of lipid metabolism should therefore be monitored closely during the use of these implants. Blood bilirubin levels reflecting liver function may rise at the start of using the implants.

If you wear **contact lenses**, you may have vision changes or you may no longer be able to wear your lenses. If this happens, you should contact your health care provider.

The following side effects have been reported in clinical studies:

Very common side effects: may affect more than 1 in 10 women

- breakage of implant during removal
- headache, nervousness, dizziness
- feeling sick (nausea)
- cervical inflammation, vaginal discharge, itching of the external genitals,
- lower abdominal pain,
- breast pain,
- weight gain
- back pain
- pain at implant site

- a vaginal infection

Common side effects: may affect up to 1 in 10 women

- mood swings, depression, decreased sexual drive, pain during sexual intercourse
- migraine
- palpitation, chest pain
- high blood pressure, varicose veins
- difficulty in breathing
- abdominal discomfort
- bilirubin, which is produced by your liver, may rise (this will show up in blood tests)
- acne, irritation of the skin (*contact dermatitis*), hair loss, excessive hairiness, rash, itching, skin discolouration
- urinary tract symptoms
- vaginal inflammation, ovarian cysts, benign breast lumps, breast discharge
- itching at the implant site, pain in general, tiredness,
- weight loss

Uncommon side effects: may affect up to 1 in 100 women

- bruising or infection at the implant site

Rare side effects: may affect up to 1 in 1,000 women

- expulsion of implant (see section 3“Expulsion and displacement of implant”), arm pain, numbness, tingling and scarring, difficulty in removal of the implants, nerve damage in the arm associated with removal of the implant, darkening of the skin over the implant site
- On rare occasions, ectopic pregnancies have been reported (see section 2 “Pregnancy, breast-feeding and fertility”).
- Darkened skin areas (hyperpigmentation) occurred in users of other levonorgestrel implants.

Reporting side effects

If you get any side effects, talk to your health care provider. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via your national medicines authority, or the manufacturer at safety.dahua@ddreg.in . By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store [RH028 trade name]

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

Do not store above 30°C. Keep the product in the provided outer carton to protect from light

[RH028 trade name] must not be inserted after the expiry date stated on the pouch or carton, after “EXP”. The expiry date refers to the last day of that month.

Do not use this medicine if you notice visible signs of deterioration or that it is different from the description below.

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 [RH028 trade name] contains

The product consists of two implants to be inserted subdermally.

The **active substance** is levonorgestrel. Each implant contains 75 mg levonorgestrel.

The **other ingredients** are: dimethylsiloxane/methylvinylsiloxane copolymer core; silicone tubing and polydimethylsiloxane adhesive

What [RH028 trade name] look like and contents of the pack

The set contains two flexible, sealed, white or off-white rod-like implants, about 44 mm in length and 2.4 mm in diameter.

The two sterile implants are packed into a bag made from specialist plastic/woven material. This pack is for single use only.

Supplier and Manufacturer

Shanghai Dahua Pharmaceutical Company Limited
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Changzheng Farm, Chongming County
Shanghai, China

Tel: +86-21-5931-1132

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Email: distribution@dahua-sh.com

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

This leaflet was last revised in October 2021.

Detailed information on this medicine is available on the World Health Organization (WHO) website:

<https://extranet.who.int/prequal/>.

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Patient Reminder Card for [RH028 trade name] sine inserter 2 x 75 mg

implants

Period of use: 3 years

Batch No.

The implants were inserted by:

Telephone number of the doctor or nurse:

Date:

Next visit:

Remarks:
