

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use JADELLE® safely and effectively. See full prescribing information for JADELLE.

JADELLE (levonorgestrel implants) for subdermal use
Initial U.S. Approval: 1996

-----RECENT MAJOR CHANGES-----
Drug Interactions (7) 12/2016

-----INDICATIONS AND USAGE-----
JADELLE is a progestin indicated for use by women to prevent pregnancy. (1)

-----DOSAGE AND ADMINISTRATION-----

- Mean daily *in vivo* release rate of levonorgestrel is approximately 100 µg/day at Month 1, 40 µg/day at 12 months, and 30 µg/day at 24 months and beyond. (2)
- Two implants each containing 75 mg of levonorgestrel are inserted subdermally using aseptic technique in the medial aspect of the non-dominant upper arm by a healthcare provider. Total administered (implanted) dose is 150 mg. (2)
- JADELLE must be removed no later than by the end of the fifth year. (2)

-----DOSAGE FORMS AND STRENGTHS-----
Two rod-shaped implants containing 75 mg levonorgestrel each. (3)

-----CONTRAINDICATIONS-----

- Known or suspected pregnancy. (4)
- Current thrombosis or thromboembolic disorders. (4)
- Acute liver disease, benign or malignant liver tumors. (4)
- Undiagnosed abnormal uterine bleeding. (4)
- Known or suspected breast cancer, personal history of breast cancer, or other progestin-sensitive cancer, now or in the past. (4)
- Hypersensitivity reactions to levonorgestrel or any of the components of the implants. (4)

-----WARNINGS AND PRECAUTIONS-----

- Insertion and removal complications: Pain, edema, bruising scarring and infection may occur. (5.1)
- Ectopic pregnancies: Consider ectopic pregnancy in women using JADELLE who become pregnant or have lower abdominal pain. (5.2)

- Thromboembolic disorders and other vascular problems: Remove JADELLE implants in the event of a thrombosis. (5.3)
- Elevated blood pressure: Remove JADELLE implants if blood pressure rises significantly and becomes uncontrolled. (5.4)
- Ovarian cysts: In some women, cysts may develop that could twist or rupture causing pain and possibly requiring surgery. (5.5)
- Menstrual changes: Counsel women regarding changes in bleeding frequency, intensity, or duration. (5.6)
- Liver function: Consider removing JADELLE implants if jaundice occurs. (5.7)
- Depressed mood: Consider removing JADELLE if depression occurs or recurs to a serious degree. (5.8)
- Idiopathic intracranial hypertension: Consider this diagnosis if persistent headache or visual disturbance occurs, and remove JADELLE if diagnosed. (5.9)
- Lipid and carbohydrate metabolism: Monitor diabetic women using JADELLE. (5.10)
- Effect on binding globulins: Sex hormone-binding globulin and thyroid-binding globulin concentrations are decreased by JADELLE use. (5.11)

-----ADVERSE REACTIONS-----
Most common (≥10%) adverse reactions in clinical trials were headache, leukorrhea, pelvic pain, weight increase, vaginitis, dizziness, breast pain/mastalgia, nausea and acne. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Bayer at drugsafety.gpv.us@bayer.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----DRUG INTERACTIONS-----
Drugs or herbal products that induce certain enzymes, such as CYP3A4, may decrease the serum concentration of progestins. (7.1)

-----USE IN SPECIFIC POPULATIONS-----

- Pregnant patients: Remove JADELLE implants if maintaining a pregnancy. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 12/2016

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

JADELLE is indicated for use by women to prevent pregnancy for up to 5 years.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing and Contraceptive Efficacy

JADELLE is a set of two flexible cylindrical implants, each containing 75 mg of the progestin levonorgestrel. The total administered (implanted) dose is 150 mg. The calculated mean daily *in vivo* release rate of levonorgestrel provided by the implants is about 100 µg/day at Month 1, followed by a decline to about 40 µg/day at 12 months and to about 30 µg/day at 24 months and beyond.

The two implants should be inserted during the first 7 days following the onset of menses by a healthcare professional familiar with JADELLE insertion technique. Insertion is subdermal in the mid-portion of the inner surface of the non-dominant upper arm about 8 cm to 10 cm above the medial epicondyle. The two implants should be placed in a “V” shape about 30 degrees apart. Proper insertion will facilitate removal [*see Insertion Procedure (2.3)*].

JADELLE implants provide up to 5 years of contraception.

2.2 Initiating Contraception with JADELLE

Table 1: Instructions for Initiating Contraception with JADELLE

IMPORTANT: Rule out pregnancy before inserting the implant. Timing of insertion depends on the woman’s recent contraceptive history, as follows:	
No Preceding Hormonal Contraceptive Use in the Past Month	<ul style="list-style-type: none"> • JADELLE implants may be inserted at any time during the cycle provided that the possibility of ovulation and conception has been considered, pregnancy has been excluded, and a non-hormonal contraceptive method is used for at least 7 days after the insertion. If possible, insert JADELLE within 7 days after onset of menstrual bleeding. • If JADELLE is inserted within 7 days after onset of menstrual bleeding, back-up contraception is not needed.
Switching from a Combined Oral Contraceptive, Vaginal Ring or Transdermal Patch	<ul style="list-style-type: none"> • Preferably, insert JADELLE the day after the last active tablet of the previous combined oral contraceptive but at latest on the day after the last day of the tablet-free interval or placebo tablet. • If a vaginal ring or transdermal patch has been used, it is preferable to insert JADELLE on the day of removal of the last ring or patch of a cycle pack, but at the latest when the next application would have been due.
Changing from Another Progestin-only Method (Minipill, Injection or Implant) or from a Progestin-releasing Intrauterine System (IUS)	The woman may switch: <ul style="list-style-type: none"> • Any day when switching from the minipill, • On the day of removal of another implant or the IUS, or • On the day when the next injection of an injectable contraceptive would have been due.
Following First- or Second-trimester Abortion	<ul style="list-style-type: none"> • JADELLE may be inserted immediately and no additional contraceptive measures are needed.
Following Delivery	<ul style="list-style-type: none"> • JADELLE may be inserted immediately after delivery and no additional contraceptive measures are needed. • If inserted later than 21 days after delivery, exclude pregnancy and instruct the woman to use additional non-hormonal contraception for a minimum of 7 days after insertion. • For women who are breastfeeding, see <i>Use in Specific Populations, Section 8.2, Lactation</i>.
Complete patient information for proper care and use of JADELLE is located in the FDA-approved Patient Labeling	

2.3 Insertion Procedure

Healthcare professionals who insert and remove JADELLE implants should be instructed and supervised in the procedures before they attempt them independently. During insertion, give special attention to the following:

- aseptic technique
- correct subdermal placement of the implants
- careful technique to minimize tissue trauma

This will help to avoid infections and excessive scarring at the insertion area and will help keep the implants from being inserted too deeply in the tissue. If the implants are placed too deeply, they will be more difficult to remove than correctly placed subdermal implants.

One JADELLE unit consists of two levonorgestrel implants in a sterile pouch. Perform the insertion under aseptic conditions using the trocar provided with the implants, to place the implants under the skin.

Determine if the woman has any allergies to the antiseptic or anesthetic to be used or any contraindications to the use of levonorgestrel or any of the components of the implants. If none are found, insert the implants according to the procedure outlined below.



Figure 1

Step 1: Assemble the following equipment in preparation for the insertion procedure (see [Figure 1](#)):

- an examination table for the patient to lie on
- sterile fenestrated surgical drapes, sterile gloves (free of talc), antiseptic solution
- local anesthetic, needles, and syringe
- scalpel, trocar, and forceps
- skin closure, sterile gauze, and compresses



Figure 2

Step 2:

- Instruct the patient to lie on her back on the examination table, with her non-dominant arm flexed at the elbow and externally rotated so that her hand is lying by her head (see [Figure 2](#)).
- The optimal insertion area is in the inner surface of the upper arm about 8 cm to 10 cm above the medial epicondyle of the humerus, avoiding the sulcus (groove) between the biceps and triceps muscles and the large blood vessels and nerves that lie in the neurovascular bundle deeper in the subcutaneous tissue. The implant should be inserted subdermally just under the skin.

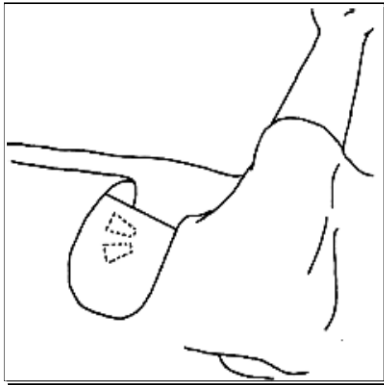


Figure 3

Step 3:

- Clean the patient's upper arm with antiseptic solution.
- Frame the insertion area with a sterile fenestrated drape (see [Figure 3](#)).

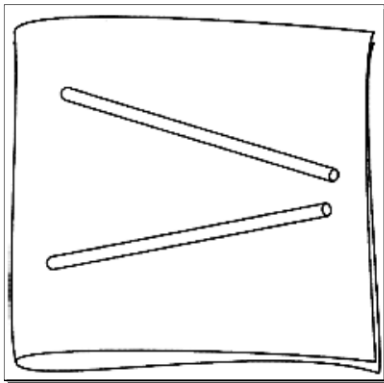


Figure 4

Step 4:

- Open the JADELLE package carefully by pulling apart the sheets of the pouch, allowing the two implants to fall onto a sterile drape (see [Figure 4](#)).

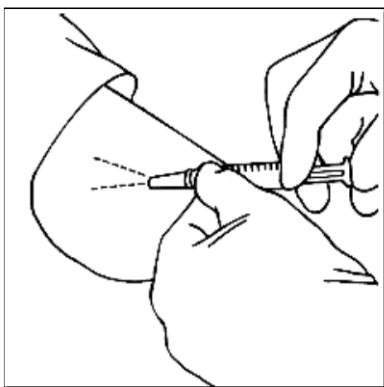


Figure 5

Step 5:

- After determining the absence of known allergies to the anesthetic agent or related drugs, fill a 5-mL syringe with the local anesthetic. Because blood loss is minimal with this procedure, it is not necessary to use epinephrine-containing anesthetics.
- Anesthetize the insertion area by first inserting the needle under the skin and injecting a small amount of anesthetic (see [Figure 5](#)). Injection of anesthetic just below the skin will raise the dermis above the underlying tissue.
- Anesthetize two areas about 4.5 cm long, to mimic the V shape of the implantation site.

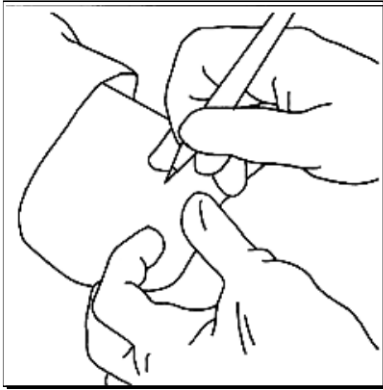


Figure 6

Step 6:

- Use the scalpel to make a small incision (about 2 mm) just through the dermis of the skin (see [Figure 6](#)).
- Alternatively, the trocar may be inserted directly through the skin without making an incision with the scalpel.
- The bevel of the trocar should always face up during the insertion.



Figure 7

Step 7:

The trocar provided with the implants has two marks on it (see [Figure 7](#)):

- The mark closest to the hub indicates how far to introduce the trocar under the skin to place the JADELLE implants.
- The mark closest to the tip indicates how much of the trocar should remain under the skin following placement of the first implant.

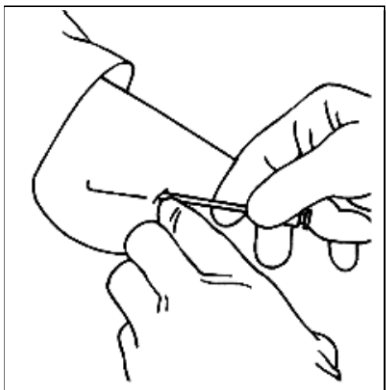


Figure 8

Step 8:

- Insert the tip of the trocar beneath the skin at a shallow angle (see [Figure 8](#)).
- Throughout the insertion procedure, the trocar should be oriented with the bevel up. Support the trocar with your index finger to raise the skin visibly during insertion. It is important to keep the trocar subdermal by tenting the skin with the trocar. Failure to do so may result in deep placement of the implants and could make removal more difficult.
- Advance the trocar provided with the implants gently under the skin to the mark **nearest** the hub of the trocar (see [Figure 7](#)). Be careful to use the appropriate mark. This will result in a distance of about 5 mm between the incision and the tip of the implant, which is necessary to avoid spontaneous expulsions.
- Do not force the trocar, and if resistance is encountered, try another direction.

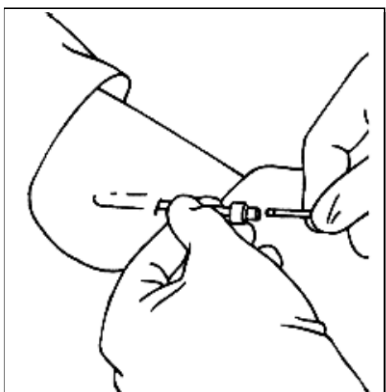


Figure 9

Step 9:

- When the trocar has been inserted the appropriate distance, remove the obturator and load the first implant into the trocar using your thumb and forefinger (see [Figure 9](#)).

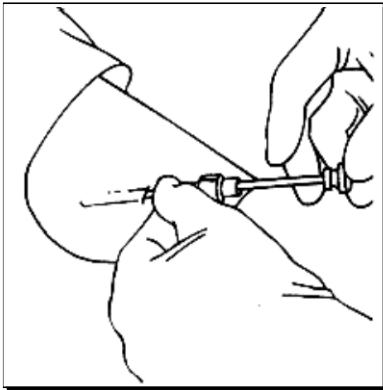


Figure 10

Step 10:

- Gently advance the implant with the obturator towards the tip of the trocar until you feel resistance (see [Figure 10](#)).
- Do not force the obturator.

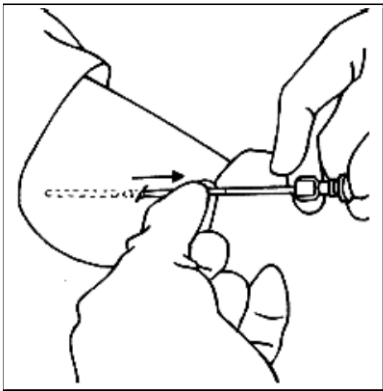


Figure 11

Step 11:

- Holding the obturator stationary, **withdraw the trocar** to the mark closest to the trocar tip. It is important to keep the obturator stationary and not to push the implant into the tissue.
- Do not completely remove the trocar until both implants have been placed. The trocar is withdrawn only to the mark closest to its tip (see [Figure 11](#)).

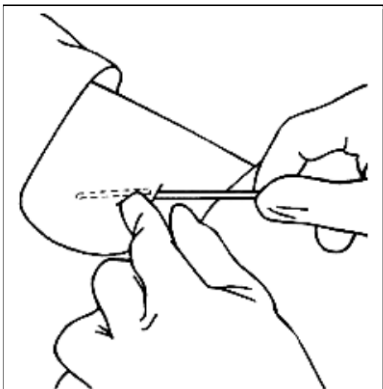


Figure 12

Step 12:

- The implant should have been released under the skin when the mark closest to the tip of the trocar is visible at the insertion point.
- Release of the implant can be checked by palpation (see [Figure 12](#)).

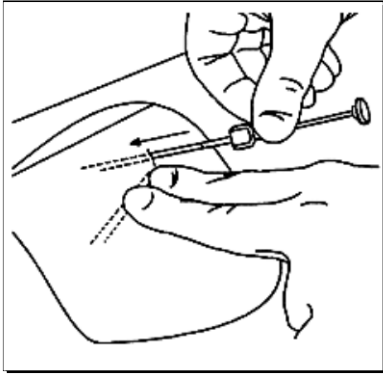


Figure 13a

Step 13a:

- To place the second implant, align the trocar so that the second implant will be positioned at about a 30-degree angle relative to the first.
- Fix the position of the previous implant with the forefinger and middle finger of your free hand, and advance the trocar along the tips of your fingers. This will ensure a suitable distance of about 30 degrees between implants and keep the trocar from puncturing the previously inserted implant (see [Figure 13a](#)).

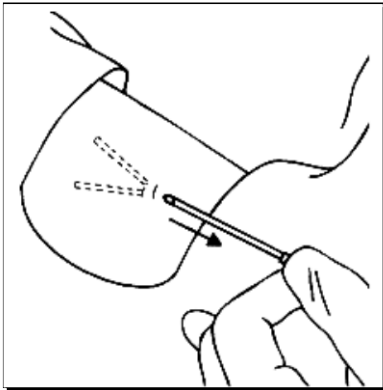


Figure 13b

Step 13b:

- Leave a distance of about 5 mm between the incision and the tips of the implants (see [Figure 13b](#)). This will help avoid spontaneous expulsions.

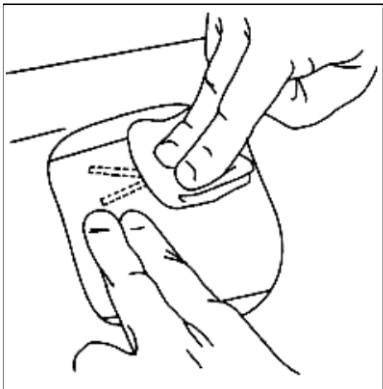


Figure 14

Step 14:

- After placement of the second implant, sterile gauze may be used to apply pressure briefly to the insertion site and ensure hemostasis.
- Palpate the distal ends of the implants to make sure that both have been properly placed (see [Figure 14](#)).

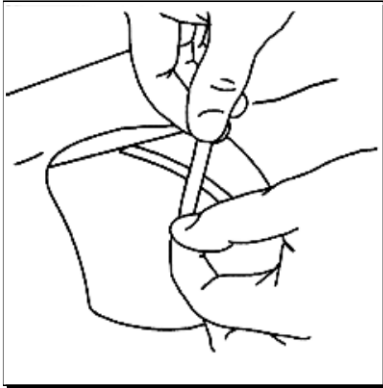


Figure 15

Step 15:

- Press the edges of the incision together, and close the incision with a skin closure (see [Figure 15](#)).
- Suturing the incision should not be necessary.

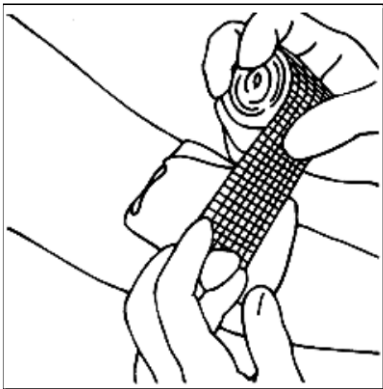


Figure 16

Step 16:

- Cover the placement area with a dry compress, and wrap gauze snugly around the arm to ensure hemostasis (see [Figure 16](#)).

- To aid removal, it is helpful to include a drawing showing location of the implants in the patient's file, and to describe any variations in placement.
- Observe the patient for a few minutes for signs of syncope or bleeding from the insertion site before she is discharged.
- Advise the patient to keep the insertion area dry and avoid heavy lifting for 2 to 3 days. The gauze may be removed after 1 day, and the skin closure as soon as the insertion area has healed, typically in 3 days.

2.4 Removal Procedure

Remove the implants very gently. This procedure will take more time than insertion. Implants are sometimes nicked, cut, or broken during removal.

The position of the patient and the need for aseptic technique are the same as for insertion.



Figure 17

Step 1: Assemble the following equipment in preparation for the removal procedure (see [Figure 17](#)):

- an examination table for the patient to lie on
- sterile fenestrated surgical drapes, sterile gloves (free of talc), antiseptic solution
- local anesthetic, needles, and syringe
- scalpel, forceps (straight and curved mosquito)
- skin closure, sterile gauze, and compresses

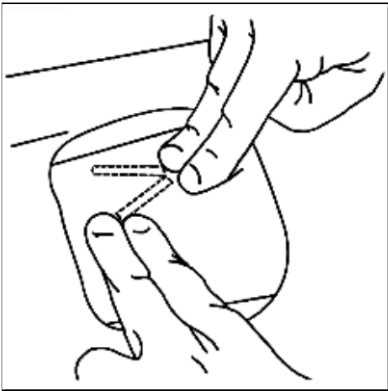


Figure 18

Step 2:

- Palpate the area to locate both implants (see [Figure 18](#)). If the implants cannot be palpated, they may be located by ultrasound or X-ray.
- Once both implants are located, clean the patient's upper arm with antiseptic solution and then frame the area with a fenestrated drape.
- You may mark the position of the JADELLE implants with a sterile marker.

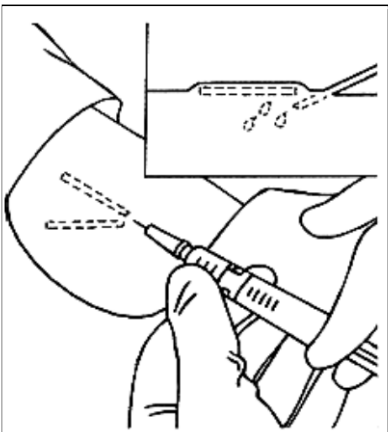


Figure 19

Step 3:

- Once both implants are located, apply a small amount of local anesthetic at the skin and *under* the ends of the implants nearest the original incision site. This will serve to raise the ends of the implants (see [Figure 19](#)).
- Do not inject anesthetic above the implants. Anesthetic injected over the implants will obscure them and make removal more difficult.
- Additional small amounts of the anesthetic can be used for removal of the second implant, if required.

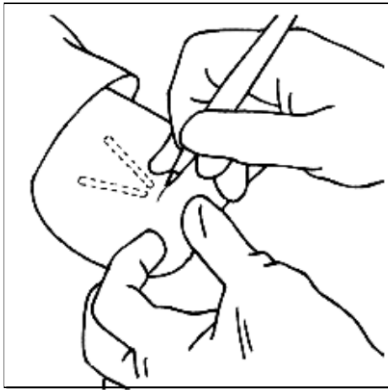


Figure 20

Step 4:

- Make a 4-mm incision with the scalpel close to the proximal ends of the implants (below the bottom of the “V”). Do not make a large incision (see [Figure 20](#)).

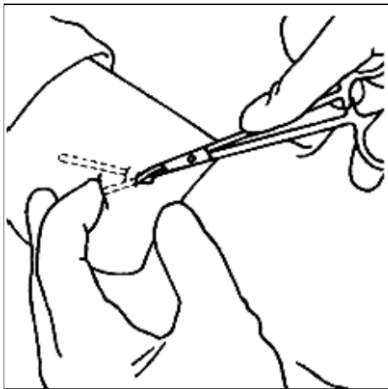


Figure 21

Step 5:

- Push each implant gently towards the incision with your fingers.
- When the tip is visible or near to the incision, grasp it with a mosquito forceps (see [Figure 21](#)).

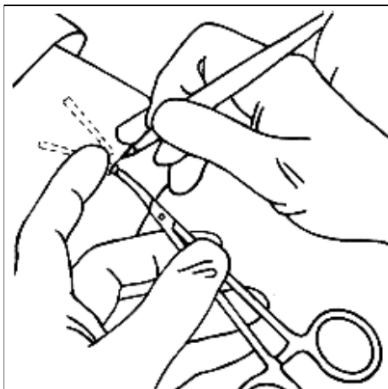


Figure 22

Step 6:

- Use the scalpel, the other forceps, or gauze to very gently open the tissue sheath that has formed around the implant (see [Figure 22](#)).

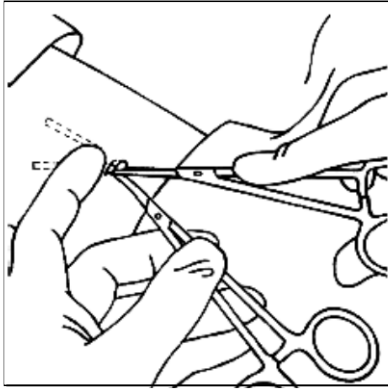


Figure 23a

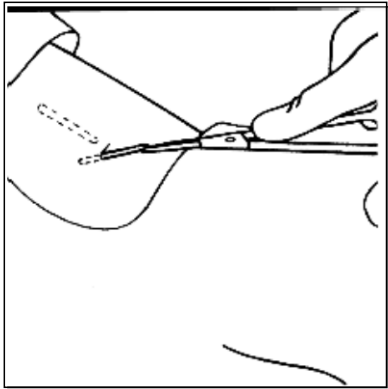


Figure 23b

Steps 7a and 7b:

- Grasp the proximal end of the implant with the second forceps and gently remove it.
- Repeat the procedure for the second implant (see [Figure 23a](#) and [Figure 23b](#)).
- Check both implants to ensure that you have removed the entire implant.

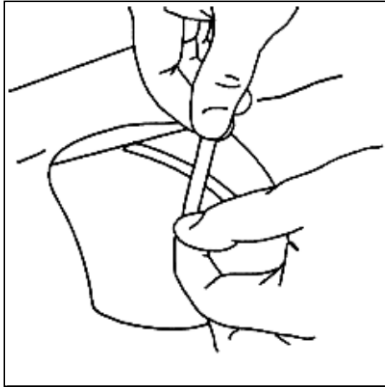


Figure 24a

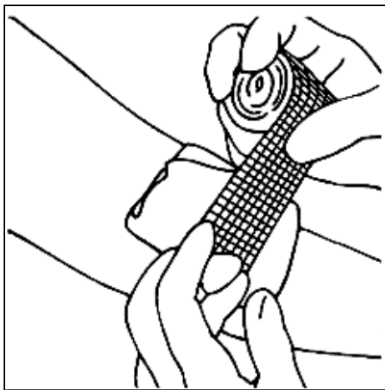


Figure 24b

Steps 8a and 8b:

- After the procedure is completed, close and bandage the incision, as with insertion (see [Figure 24a](#) and [Figure 24b](#)).
- Instruct the patient to keep the upper arm dry for a few days.

Difficult Removal

The overall incidence of removal difficulties in the clinical trials, including damage to the implants, was 7.5%. If removal of the implant(s) proves difficult, close the incision and bandage the wound, and have the patient return for another visit. The remaining implant(s) will be easier to remove after the area is healed. It may be appropriate to seek consultation or provide referral for patients in whom initial attempts at implant removal prove difficult. Advise the patient to use a non-hormonal method of contraception until both implants are completely removed.

Following Removal of JADELLE Implants

Following removal, if the woman does not desire pregnancy, she should initiate a new contraceptive method immediately. If the patient wishes to continue using the method, a new set of JADELLE implants can be inserted through the same incision.

2.5 Identification of the JADELLE Implant

JADELLE packaging contains stick-on labels identifying the lot number for both the provider's and the patient's records. Retain one stick-on label in the provider's records in case a need arises to determine which lot is being used by the patient. Affix the patient's stick-on label to her copy of the patient information materials.

3 DOSAGE FORMS AND STRENGTHS

JADELLE is a set of two flexible cylindrical implants consisting of a dimethylsiloxane/methylvinylsiloxane copolymer core enclosed in thin-walled silicone tubing. Each implant contains 75 mg of the progestin levonorgestrel.

4 CONTRAINDICATIONS

JADELLE is contraindicated in patients who have:

- Known or suspected pregnancy
- Current thrombophlebitis or thromboembolic disorders
- Liver tumors, benign or malignant, or active liver disease
- Undiagnosed abnormal uterine bleeding
- Known or suspected breast cancer, personal history of breast cancer, or other progestin-sensitive cancer, now or in the past
- Hypersensitivity

5 WARNINGS AND PRECAUTIONS

5.1 Insertion and Removal Complications

Complications related to insertion may include pain, edema and bruising. In clinical trials, removal complications and difficulties, including damage to the implants, were reported in 7.5% of the more than 1,100 JADELLE removals. Complications of insertion or removal included deep placement, multiple or long incisions, bruising, displacement, pain, prolonged removal, incomplete removal requiring an additional visit or visits, broken implants, and fibrous pericapsular tissue.

Infection (including cellulitis), ulcerations, excessive scarring/keloid, phlebitis and hyperpigmentation have been reported with JADELLE implants. During clinical trials of JADELLE implants, infection at the insertion site occurred in 0.4% of women. Attention to aseptic technique and proper insertion and removal of JADELLE implants reduces the likelihood of infection. If infection occurs, initiate suitable treatment. If infection persists, remove the implants.

Arm pain, numbness and tingling may occur following the insertion and removal procedures. Nerve injury, most commonly associated with deep placement and removal, may also occur. Expulsion of one or more implants has been reported with JADELLE implants. Replace an expelled implant with a new

sterile implant. If infection is present, ensure that it is resolved before another implant is inserted. Protection against pregnancy is likely to be inadequate if only a single implant is in place.

Implant displacement (i.e., movement) has been reported with JADELLE implants. While displacement most commonly involves minor changes in the position of the implants, reports of significant displacement (up to several inches) have been received. Some instances of displacement have been associated with pain or discomfort. When implant displacement occurs, the removal technique may have to be modified, for example, by an additional incision or visit.

Advise women that JADELLE implants can be removed for any reason whenever the woman wishes, and must be removed by the end of five years. The removal should be done by personnel familiar with the removal techniques.

5.2 Ectopic Pregnancies

Consider the possibility of an ectopic pregnancy among women using JADELLE implants who become pregnant or complain of lower abdominal pain. Ectopic pregnancy occurs with levonorgestrel implants at a rate less than 0.5 per 1,000 woman-years. In clinical studies on JADELLE used for up to 5 years with more than 4,100 woman-years of exposure, 8 pregnancies occurred, one of which was ectopic. However, pregnancy is more likely to be ectopic if it occurs in a woman using JADELLE compared to a woman using no contraception. In case of contraceptive failure with JADELLE, exclude ectopic pregnancy.

5.3 Thromboembolic Disorders and Other Vascular Events

Thromboembolic disorders (e.g., pulmonary embolism and deep vein thrombosis) have been reported with JADELLE implants; stroke and cardiovascular problems (e.g., myocardial infarction) have been reported with levonorgestrel implant use.

If thromboembolic disorders or cardiovascular problems occur in JADELLE users, remove the implants. Consider removal in women who will be subjected to prolonged immobilization because of surgery or other illnesses. Use of JADELLE in women with active thrombophlebitis or thromboembolic disorders is contraindicated [*see Contraindications (4)*].

Evaluate patients for retinal thrombosis immediately if there is an unexplained loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions.

Superficial phlebitis has been reported in clinical trials of JADELLE, more commonly in the arm of insertion. Some of these cases have been associated with trauma to the arm.

5.4 Elevated Blood Pressure

Discourage women with a history of hypertension-related diseases or renal disease from using hormonal contraception.

For women with well-controlled hypertension, use of JADELLE can be considered. Closely monitor women with hypertension who use JADELLE. If sustained hypertension develops during the use of JADELLE, or if a significant increase in blood pressure does not respond adequately to antihypertensive therapy, remove JADELLE.

5.5 Ovarian Cysts

If follicular development occurs with JADELLE implants, atresia of the follicle may be delayed, and the follicle may continue to grow beyond the size it would attain in a normal cycle. In the majority of women, enlarged follicles (cysts) will spontaneously disappear and should not require surgery. In some cases, they may twist or rupture, sometimes causing abdominal pain, and surgical intervention may be required.

5.6 Menstrual Changes

Most women using JADELLE implants can expect some variation in menstrual bleeding patterns. Irregular menstrual bleeding, prolonged episodes of bleeding and spotting, heavy bleeding, intermenstrual spotting and amenorrhea occur in some women. Altered bleeding patterns associated with JADELLE implants could mask symptoms of cervical or endometrial cancer. Because some levonorgestrel implant users have periods of amenorrhea, missed menstrual periods cannot serve as the only means of identifying early pregnancy. Perform a pregnancy test whenever a pregnancy is suspected. Six weeks or more of amenorrhea after a pattern of regular menses may signal pregnancy.

In case of abnormal bleeding, conduct appropriate diagnostic testing to rule out malignancy and pregnancy. If pregnancy occurs, remove JADELLE implants.

During clinical trials, JADELLE implants were used by 1,393 subjects, including 1,243 subjects at fully compliant sites. Table 2 displays menstrual complaints reported by more than 1.0% of the 1,243 subjects at compliant sites in the first year of JADELLE use, and the percent of patients with those events in Years 1 to 5 of use. About 14% of subjects discontinued the trial prematurely because of unacceptable menstrual bleeding patterns.

Table 2: Menstrual Conditions Reported by >1.0% of Subjects Using JADELLE (N=1,243)

Menstrual Condition	Year 1	Years 1-5
Reports of Increased Bleeding		
Menorrhagia (increased duration)	13.9%	27.0%
Menometrorrhagia	9.7%	20.9%
Long spotting duration or length unclear	9.0%	15.8%
Polymenorrhea	2.7%	5.1%
Menorrhagia (increased amount)	1.4%	4.3%
Metrorrhagia	0.4%	3.6%
Reports of Decreased Bleeding		
Amenorrhea	7.9%	12.3%
Oligomenorrhea	7.8%	11.2%
Hypomenorrhea	1.7%	2.6%

5.7 Liver Disease

Steroid hormones may be poorly metabolized in patients with impaired liver function. Use of JADELLE in women with acute liver disease is contraindicated [see Contraindications (4)].

If jaundice develops in any woman using JADELLE implants, consider removing the implants.

5.8 Depressed Mood

Carefully observe women with a history of depression and consider removal of JADELLE if depression recurs to a serious degree. Consider removing JADELLE implants in women who become significantly depressed, because depression may be drug-related.

5.9 Idiopathic Intracranial Hypertension

Idiopathic intracranial hypertension has been reported on rare occasions in users of levonorgestrel implants. Consider this diagnosis if persistent headache and/or visual disturbances occur in a woman with JADELLE, particularly if the patient is obese or has recently gained weight. Remove JADELLE if idiopathic intracranial hypertension is diagnosed.

5.10 Lipid and Carbohydrate Metabolism

Follow women who are being treated for hyperlipidemias closely if they elect to use JADELLE implants, as serum lipoprotein levels may be altered.

Changes in carbohydrate tolerance and insulin sensitivity following oral glucose loads have been reported in some studies among healthy users of JADELLE implants. These changes include modest elevations of serum insulin concentrations as well as increases in serum glucose levels. Consider more frequent blood glucose monitoring in diabetic patients who use JADELLE implants.

5.11 Effect on Binding Globulins

Sex hormone-binding globulin and thyroid-binding globulin concentrations are decreased by JADELLE use. Thyroxine concentrations may be slightly decreased and triiodothyronine uptake increased. The dose of replacement thyroid hormone therapy may need to be decreased.

6 ADVERSE REACTIONS

The following adverse reactions reported with the use of progestin-only contraception are discussed elsewhere in the labeling:

- Ectopic pregnancies [*see Warnings and Precautions (5.2)*]
- Menstrual changes [*see Warnings and Precautions (5.6)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

JADELLE was evaluated in three clinical trials. Two of these trials were randomized, multi-center comparisons of JADELLE and another levonorgestrel implant that were conducted at sites in and outside of the US. The third trial was an open-label, multi-center study conducted primarily at sites in the US. A total of 1,393 women used JADELLE in these studies, including 1,243 women who participated at fully compliant study sites.

Of the 1,243 women treated with JADELLE at compliant sites, 460 women completed 5 years of JADELLE use. The total experience with JADELLE in Years 1 through 5 was 4,138 woman-years. The mean experience with JADELLE per woman was 3.3 years.

Subjects in the clinical studies of JADELLE were healthy women between 18 and 40 years of age who were at risk of becoming pregnant. Exclusion criteria included major diseases (e.g., diabetes mellitus, cancer, severe cardiovascular disease, thromboembolism), receipt of injectable contraceptives within the previous year, receipt of oral contraceptives within the previous month, and being less than 6 weeks postpartum.

In the clinical trials of JADELLE, the average weight change over 5 years of use was a gain of about 9 pounds. Approximately 20% of women gained at least 10 pounds in the first year, and 50% gained at least 10 pounds by the end of the fifth year of use.

Adverse reactions reported by $\geq 5\%$ of subjects during 5 years of JADELLE use in clinical trials are listed in [Table 3](#).

Table 3: Adverse Reactions Reported in $\geq 5\%$ of Subjects during 5 Years of JADELLE Use in Clinical Trials

Adverse Reaction	Percent of Subjects N=1,243
Headache	30.5%
Leukorrhoea	30.3%
Pelvic pain	24.4%
Weight increase	22.4%
Vaginitis ^a	16.3%
Dizziness	14.5%
Breast pain, mastalgia	12.6%
Nausea	11.6%
Acne	10.9%
Ovarian cysts or follicle	9.8%
Nervousness	8.6%
Dermatitis, contact	8.2%
Application site reaction ^b	6.7%
Alopecia	5.6%
Benign breast neoplasm	5.3%
Weight decrease	5.0%

^a Includes also genital pruritus, infections and vaginal problems not elsewhere classified

^b Includes application site reaction, pain at (application) site, and other related terms

Non-menstrual adverse reactions that led to discontinuation in $\geq 1\%$ were recorded for the 1,393 subjects with JADELLE implants at all study sites in the clinical studies during Years 1 through 5, and are shown in Table 4.

Table 4: Adverse Reactions that Led to Discontinuation in $\geq 1\%$ of Subjects During 5 Years of JADELLE Use in Clinical Trials

Adverse Reaction Leading to Discontinuation	Percent of Subjects N=1,393
Headache	4.2%
Weight increase	3.4%
Acne	1.0%
Depression	1.0%

The most common serious adverse reactions (leading to hospitalization) in subjects using JADELLE were gallbladder or biliary disorders (cholecystitis, cholelithiasis, biliary lithiasis; 7 subjects), ovarian disorders (cyst, mass, enlargement; 6 subjects), cervical disorders (cervicitis, dysplasia, biopsy, polyp; 4 subjects), breast cancer (2 subjects), other breast disorders and surgeries (4 subjects), uterine disorders (fibroid, prolapse, adenomyosis; 4 subjects), and depression (2 subjects).

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of JADELLE. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Blood and lymphatic system disorders: anemia, coagulopathy, hemoconcentration, leukocytosis, hemoglobin decreased

Endocrine disorders: increased serum prolactin, thyroid disorder

Eye disorders: blurred vision, ocular icterus, papilledema, visual impairment

Gastrointestinal disorders: abdominal discomfort, distension or pain, constipation, diarrhea, flatulence, gastritis, pancreatic cyst, vomiting

Hepatobiliary disorders: cholelithiasis, cholestatic jaundice

Immune system disorders: Anaphylactic shock, hypersensitivity, mouth swelling

Implant site skin disorders: abscess, bruising, cellulitis, discharge, discoloration, discomfort, edema, erosion, erythema, fibrosis, furuncle, hematoma, hemorrhage, hypersensitivity, hypoesthesia, impaired healing, induration, infection, inflammation, irritation, pain, pruritus, rash, swelling, urticaria, vesicles, warmth

Infections: bronchitis, cystitis, fungal infection, influenza, pharyngitis, pneumonia, urinary tract infection, vaginal infection, vulvovaginal mycotic infection

Metabolism and nutrition disorders: changes in weight and appetite, changes in glucose, hypoglycemia, increased body temperature, pyrexia

Musculoskeletal and connective tissue disorders: arthralgia, arthropathy, asthenia, joint swelling, limb discomfort, muscle atrophy, spasms, tightness or weakness, musculoskeletal pain, musculoskeletal stiffness, systemic lupus erythematosus

Nervous system disorders: benign intracranial hypertension, brain edema, burning sensation, cerebrovascular stenosis, dysesthesia, hypersomnia, hypoesthesia, loss of consciousness, migraine, monoplegia, peripheral neuropathy, paresthesia, peripheral nerve lesion, somnolence, syncope

Neoplasms benign, malignant and unspecified: fibroadenoma of breast, melanocytic nevus

Psychiatric disorders: anxiety, apathy, depressed mood, fear of eating, hallucination, insomnia, irritability, libido decrease or loss, altered mood, mood swings, nervousness, panic attack, personality change, stress, tearfulness, tension

Renal and urinary disorders: dysuria, urine abnormality, urine output decreased

Reproductive system and breast disorders: alterations in bleeding and menstrual patterns, adnexa uteri pain, breast discharge, engorgement, enlargement, swelling or mass, cervical dysplasia, dyspareunia, endometriosis, galactorrhea, genital discharge, nipple pain, genital pruritus, suppressed lactation, uterine cyst, vaginal discharge or odor

Respiratory: dyspnea

Skin and subcutaneous tissue disorders: chloasma, dermatitis ecchymosis, eczema, erythema, abnormal hair growth, hirsutism, nail discoloration, night sweats, pain, palmar-plantar erythema, pruritus, rash, scarring, seborrheic dermatitis, discoloration, discomfort, striae, ulcer, urticaria

Vascular disorders: deep vein thrombosis, pulmonary embolism, intracranial venous sinus thrombosis, hot flush, hypertension, hypotension, peripheral coldness, varicose vein, thrombosis, vasodilation

7 DRUG INTERACTIONS

Consult the labeling of concurrently-used drugs to obtain further information about interactions with hormonal contraceptives or the potential for enzyme alterations.

7.1 Effect of Other Drugs on Hormonal Contraceptives

Substances decreasing the plasma concentrations of hormonal contraceptives (HCs) and potentially diminishing the efficacy of HCs:

Drugs or herbal products that induce certain enzymes, including cytochrome P450 3A4 (CYP3A4), may decrease the plasma concentrations of HCs and potentially diminish the effectiveness of HCs or increase breakthrough bleeding.

Some drugs or herbal products that may decrease the effectiveness of HCs include phenytoin, barbiturates, carbamazepine, bosentan, felbamate, griseofulvin, oxcarbazepine, rifampicin, topiramate, rifabutin, rufinamide, aprepitant, and products containing St. John's wort. Interactions between HCs and other drugs may lead to breakthrough bleeding and/or contraceptive failure. Counsel women to use an alternative method of contraception or a back-up method when enzyme inducers are used with HCs, and to continue back-up contraception for 28 days after discontinuing the enzyme inducer to ensure contraceptive reliability.

Substances increasing the plasma concentrations of HCs:

Co-administration of certain HCs and strong or moderate CYP3A4 inhibitors such as itraconazole, voriconazole, fluconazole, grapefruit juice, or ketoconazole may increase the serum concentrations of progestins, including levonorgestrel.

Human Immunodeficiency Virus (HIV)/Hepatitis C Virus (HCV) Antiretrovirals

When co-administered with sex hormones, many HIV/HCV protease inhibitors and non-nucleoside reverse transcriptase inhibitors can increase or decrease plasma concentrations of the progestin (decrease [e.g., nelfinavir, ritonavir, darunavir/ritonavir, (fos) amprenavir/ritonavir, lopinavir/ritonavir, and tipranavir/ritonavir, nevirapine, efavirenz] or increase [e.g., indinavir and atazanavir/ritonavir, etravirene]). These changes may be clinically relevant in some cases.

Efavirenz, a moderate CYP3A4 inducer, significantly decreased systemic exposure to levonorgestrel. Postmarketing reports of contraceptive failure with JADELLE in efavirenz-exposed patients have been received.

Consult the prescribing information of anti-viral and anti-retroviral concomitant medications to identify potential interactions.

7.2 Effect of Hormonal Contraceptives on Other Drugs

Hormonal contraceptives may affect the metabolism of other drugs. Consequently, plasma concentrations may either increase (for example, cyclosporine) or decrease (for example, lamotrigine). Consult the labelling of all concurrently-used drugs to obtain further information about interactions with hormonal contraceptives or the potential for enzyme alterations.

7.3 Interference with Laboratory Tests

The use of contraceptive steroids may influence the results of certain laboratory tests, such as coagulation factors, lipids, glucose tolerance, and binding proteins [see *Warnings and Precautions (5.11)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

JADELLE is contraindicated for use in pregnant women because there is no need for pregnancy prevention in a woman who is already pregnant [see *Contraindications (4)*]. Published studies report no harmful effects on fetal development associated with long-term use of contraceptive doses of oral progestins, including levonorgestrel, in pregnant women. Remove JADELLE if a woman wishes to continue her pregnancy.

8.2 Lactation

Risk Summary

Levonorgestrel is present in breast milk. Available data show no adverse effects on the breastfed infant or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for JADELLE and any potential adverse effects on the breastfed infant from JADELLE or from the underlying maternal condition.

8.4 Pediatric Use

Safety and efficacy of JADELLE implants have been established in women of reproductive age. Efficacy is expected to be the same for postmenarcheal adolescents under the age of 18 years and for patients 18 years and older. Use of this product before menarche is not indicated.

8.5 Geriatric Use

This product has not been studied in postmenopausal women and is not indicated in this population.

8.6 Obese Patients

Serum levonorgestrel concentrations were found to be inversely related to body weight [*see Pharmacokinetics (12.3)*]. Serum levonorgestrel concentrations in women weighing more than 70 kg were approximately half of those in women weighing less than 50 kg. Because of the range in serum concentrations and variation in individual response, serum concentrations alone are not predictive of the risk of pregnancy in an individual woman.

10 OVERDOSAGE

Remove all JADELLE implants before inserting a new set of implants or initiating use of any other hormonal contraceptive. If more than 2 JADELLE implants are *in situ*, uterine bleeding patterns may be altered.

11 DESCRIPTION

JADELLE is a set of two flexible cylindrical implants, consisting of a dimethylsiloxane/methylvinylsiloxane copolymer core enclosed in thin-walled silicone tubing. Each implant contains 75 mg of the progestin levonorgestrel. The implants are sealed with polydimethylsiloxane adhesive and sterilized. Each implant is approximately 2.5 mm in diameter and 43 mm in length. The implants are inserted in a superficial plane beneath the skin of the upper arm.

Levonorgestrel is a totally synthetic and biologically active progestin that exhibits no significant estrogenic activity and is highly progestational. The absolute configuration conforms to that of D-natural steroids.

The calculated mean daily *in vivo* release rate of levonorgestrel provided by the implants is about 100 µg/day at month 1 followed by a decline to about 40 µg/day at 12 months and to about 30 µg/day at 24 months with a stabilization thereafter at about 30 µg/day.

JADELLE implants are a progestin-only product and do not contain estrogen. The active ingredient in the implants is levonorgestrel, (-)-13-ethyl-17-hydroxy-18,19-dinor-17 α -pregn-4-en-20-yn-3-one. It has a molecular weight of 312.45 and the following structural formula (see [Figure 27](#)):

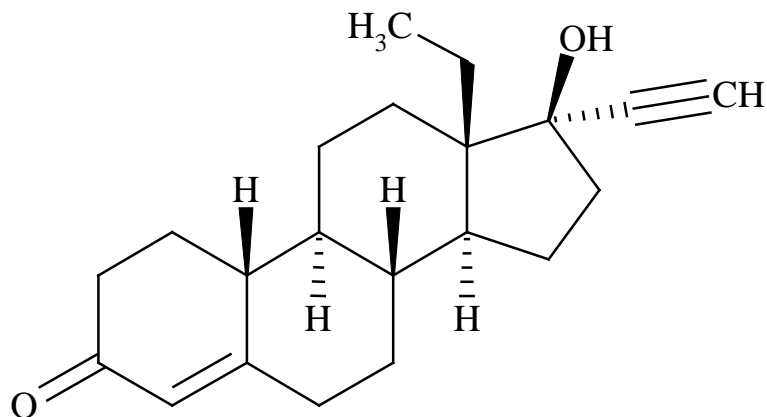


Figure 27: Structural Formula of Levonorgestrel

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The contraceptive effect of JADELLE implants is achieved by suppression of ovulation, increased viscosity of cervical mucus, and alterations in the endometrium.

12.3 Pharmacokinetics

Absorption

Levonorgestrel is delivered directly into interstitial fluids from the subdermal implants. However, the bioavailability of levonorgestrel after insertion of JADELLE implants compared with intravenous administration is not known. After placement of JADELLE implants, maximum levonorgestrel concentrations are reached in about 2 to 3 days, with the mean \pm standard deviation being 772 ± 414 pg/mL at 2 days. After the initial phase, mean levonorgestrel concentrations slowly decline to approximately 435 ± 172 pg/mL at 1 month, 357 ± 155 pg/mL at 6 months, and 280 ± 123 pg/mL at 3 years. Concentrations at 4 and at 5 years are similar to those at 3 years (see [Table 5](#)).

Table 5: Serum Concentrations during JADELLE Use

Time After Placement (months)	Mean \pm SD (pg/mL)	n
1	435 \pm 172	181
3	393 \pm 191	165
6	357 \pm 155	160
12	340 \pm 159	148
24	312 \pm 153	126
36	280 \pm 123	89
48	271 \pm 126	67
60	279 \pm 123	65

Serum levonorgestrel concentrations were found to be inversely related to body weight. Serum levonorgestrel concentrations in women weighing more than 70 kg were approximately half as high as in women weighing less than 50 kg.

Because of the range in serum concentrations and variation in individual response, serum concentrations alone are not predictive of the risk of pregnancy in an individual woman. Serum levonorgestrel concentrations in JADELLE users are substantially below those generally observed in users of oral contraceptives containing the progestins norgestrel or levonorgestrel.

Distribution

Levonorgestrel in serum is primarily protein bound, mainly to sex hormone-binding globulin (SHBG), and to a lesser extent to albumin. SHBG concentrations are depressed by levonorgestrel within a few days of administration, with resultant decreases in circulating levonorgestrel concentrations.

Metabolism

Levonorgestrel is extensively metabolized. The most important metabolic pathways are the reduction of the Δ^4 -3-oxo group and hydroxylations at positions 2 α , 1 β and 16 β , followed by conjugation. CYP3A4 is the main enzyme involved in the oxidative metabolism of levonorgestrel. The available *in vitro* data suggest that CYP-mediated biotransformation reactions may be of minor relevance for levonorgestrel compared to reduction and conjugation.

Excretion

The elimination half-life of levonorgestrel is approximately 13 to 18 hours. Levonorgestrel and its metabolites are primarily excreted in the urine (40% to 68%) and about 16% to 48% are excreted in feces. After removal of the implants, levonorgestrel concentrations decrease below 100 pg/mL by 96 hours and below sensitivity of the assay by 5 days to 2 weeks.

14 CLINICAL STUDIES

The contraceptive efficacy of JADELLE was studied in three multicenter trials of women aged 18 to 40 years. Two of these trials were randomized trials conducted in and outside of the U.S., and one was an open-label trial conducted in the U.S. There were no restrictions on the basis of weight or body mass index (BMI). Exclusion criteria included major diseases (e.g., diabetes mellitus, cancer, severe cardiovascular disease, thromboembolism), receipt of injectable contraceptives within the previous year, receipt of oral contraceptives within the previous month, and being less than 6 weeks postpartum.

The 1,393 women treated with JADELLE in these studies were observed for 4,657 woman-years. The mean age of women treated with JADELLE was 26.3 years, mean weight was 59.9 kg, and mean parity at study admission was 1.8 births.

The pregnancy rate was calculated as the Pearl Index (PI) using data for subjects <36 years of age at the start of each treatment year. The PI was calculated based on the number of pregnancies divided by the months of exposure, then multiplied by 1200.

In women <36 years of age, 6 pregnancies occurred within 5 years of JADELLE placement. One of the 6 pregnancies was ectopic. Table 6 shows pregnancy rate as Pearl Indices for each year for JADELLE-treated women <36 years of age.

Table 6: Pearl Indices (Pregnancies per 100 woman-years) by Year for JADELLE Users <36 Years of Age

	Year 1	Year 2	Year 3	Year 4	Year 5
Number of Woman-Years	1217	998	795	584	455
Number of Pregnancies	1	1	1	0	5
Cumulative Pregnancies	1	2	3	3	6
Annual Pearl Index (95% Confidence Interval)	0.08 (0.01-0.24)	0.10 (0.01-0.29)	0.13 (0.01-0.37)	0.00 (0.01-0.03)	0.88 (0.30-1.73)

After removal of JADELLE, women return to fertility. Of 116 women who had JADELLE removed for planned pregnancy, 58% became pregnant within 3 months and 84% within one year, based on a prospective study of pregnancy after long-acting contraceptive use.

16 HOW SUPPLIED/STORAGE AND HANDLING

JADELLE implants are a set of two flexible cylindrical implants. Each implant contains 75 mg of the progestin levonorgestrel. The total administered (implanted) dose is 150 mg. Each implant is approximately 2.5 mm in diameter and 43 mm in length. JADELLE is supplied in a sterile package containing a set of two levonorgestrel-containing implants.

Store JADELLE at room temperature, between 15°C and 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Insertion Site Instructions

Advise the patient to keep the insertion area dry and avoid heavy lifting for 2 to 3 days. The gauze may be removed after 1 day, and the skin closure may be removed as soon as the insertion area has healed, typically in 3 days [see *Dosage and Administration (2.3)*].

Symptoms Related to Insertion and Infection

Advise patients to report symptoms related to insertion such as pain, edema and bruising. Advise patients to report symptoms of infection (including cellulitis and abscess formation) including blistering, ulcerations, sloughing, excessive scarring, phlebitis and hyperpigmentation [see *Warning and Precautions (5.1)*].

Removal of JADELLE

Advise the patient that JADELLE can be removed for any reason whenever she wishes and must be removed by the end of 5 years. Removal may cause more discomfort and scarring than the insertion procedure [see *Warnings and Precautions (5.1)*].

Changes in Normal Menses

Advise the patient that the use of JADELLE may be associated with changes in their normal menstrual bleeding pattern [see *Warnings and Precautions (5.6)*].

Sexually Transmitted Infections

Advise the patient that JADELLE does not protect against HIV infection or other sexually transmitted infections.

Manufactured by:

Bayer OY

Pansiontie 47

20210 Turku, Finland

Patient Information

JADELLE® (juh-DEL)

(levonorgestrel implants), for subdermal use

JADELLE does not protect against HIV infection (AIDS) or other sexually transmitted infections (STIs).

What is JADELLE?

- JADELLE is a set of 2 hormone-releasing birth control implants for use by women to prevent pregnancy for up to 5 years.
- JADELLE is a set of 2 flexible plastic rod-shaped implants about the size of a matchstick that contain a progestin hormone called levonorgestrel. Your healthcare provider will insert the implants just under the skin of the inner side of your upper arm. You can use JADELLE for up to 5 years. JADELLE does not contain estrogen.

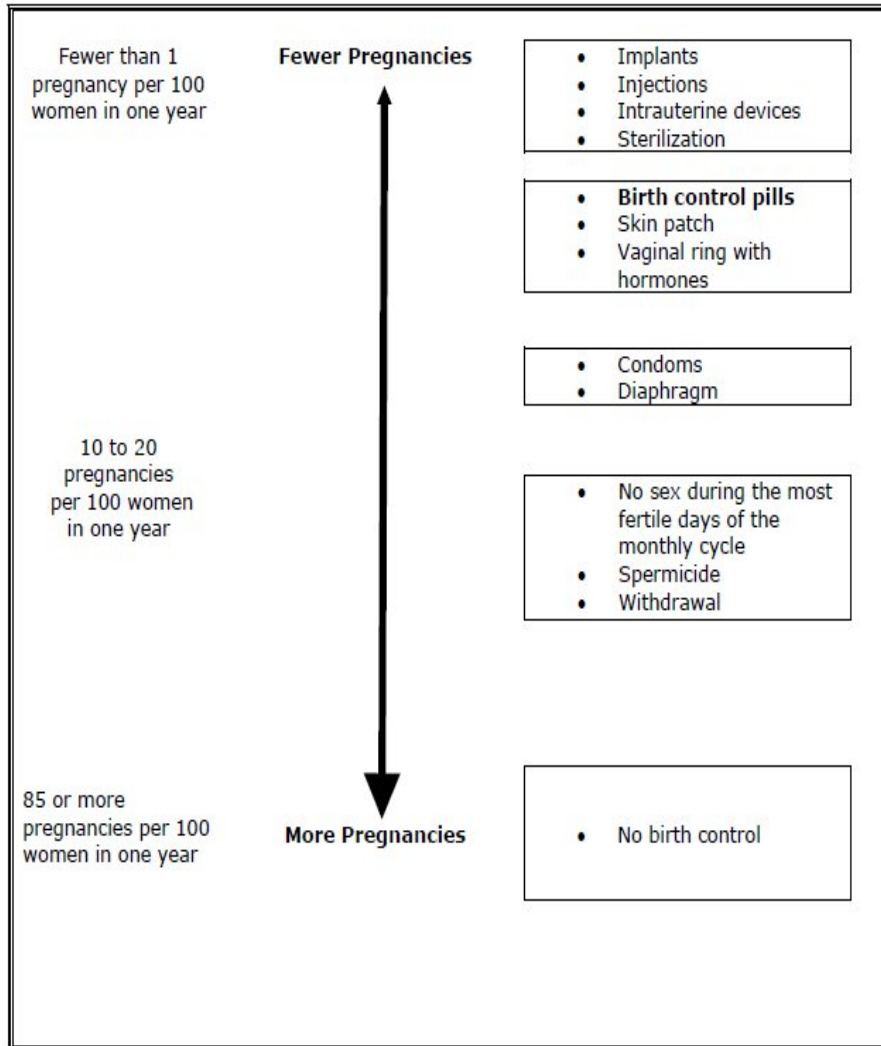
How does JADELLE work?

- JADELLE prevents pregnancy in several ways. JADELLE stops the release of an egg from your ovary. JADELLE also thickens mucus in your cervix, and this change may keep sperm from reaching the egg. JADELLE also thins the lining of your uterus.

How well does JADELLE work for contraception?

- The following chart shows the chance of getting pregnant for women who use different methods of birth control. Each box on the chart contains a list of birth control methods that are similar in effectiveness. The most effective methods are at the top of the chart. The box on the bottom of the chart shows the chance of getting pregnant for women who do not use birth control and are trying to get pregnant.

JADELLE, a set of 2 implants, is in the box at the top of the chart.



Do not use JADELLE if you:

- are or may be pregnant
- have unexplained vaginal bleeding
- have serious blood clots such as blood clots in your legs (deep vein thrombosis), lungs (pulmonary embolism), eyes (total or partial blindness), heart (heart attack), or brain (stroke)
- have liver disease or a liver tumor
- are allergic to levonorgestrel or any of the ingredients in JADELLE. See the end of this leaflet for a complete list of ingredients in JADELLE.

Before having JADELLE placed, tell your healthcare provider if you:

- have had a blood clot, heart attack, or stroke
- plan to have surgery
- have high blood pressure
- have or have had depression
- have diabetes
- have an allergy to numbing medicines (anesthetics) or medicines used to clean your skin (antiseptics). These medicines will be used when JADELLE is placed in or removed from your arm.
- have severe migraine headaches
- have any other medical conditions.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How are the JADELLE implants placed?

- The JADELLE implants are placed by your healthcare provider during an in-office visit. The implants are inserted just under the skin on the inner side of your upper arm.
- The timing of the insertion of the JADELLE implants is important. Your healthcare provider may:
 - do a pregnancy test before inserting the JADELLE implants
 - schedule the JADELLE implants insertion at a specific time of your menstrual cycle (for example, within the first 7 days of your regular menstrual bleeding)
- Right after the JADELLE implants are inserted, your healthcare provider should feel your arm to check that the implants are in the right place.
- If you and your healthcare provider cannot feel the JADELLE implants, you should use a non-hormonal birth control such as condoms and spermicide) until your healthcare provider confirms that the implants are in place. You may need special tests to check that the implants are in place or to help find the implant when it is time to take them out.
- Your healthcare provider will cover the site where JADELLE was placed with a gauze bandage. Keep the insertion site dry and avoid heavy lifting for 2 to 3 days. You may remove the gauze bandage after 1 day. You may remove the skin closure strip as soon as the insertion area has healed, usually in 3 days.
- Keep track of the date that the JADELLE implants are to be removed. Schedule an appointment with your healthcare provider to remove the JADELLE implants on or before the removal date.

What are the possible side effects of JADELLE?

- **Insertion and removal problems.** One or more JADELLE implants may fail to be inserted in your arm properly. If this happens, you may become pregnant. Right after JADELLE is inserted, and with help from your healthcare provider, you should be able to feel the JADELLE implants under your skin. If you cannot feel them, tell your healthcare provider.

In some cases, removal of the JADELLE implants may be difficult or impossible because the implants might have moved and are not where they should be. Special procedures, including surgery in the hospital, may be needed to remove the implants. Other problems with insertion and removal may include insertion site:

- pain
 - numbness and tingling
 - blisters
 - scarring
 - breakage of the implant(s) making it hard to remove
 - swelling
 - infection
 - ulcers
 - darkening of the skin
 - inflammation of blood vessels
 - bruising
 - abscess
 - peeling
 - nerve injury
- **Ectopic pregnancy.** If you get pregnant while using JADELLE, you may have an ectopic pregnancy. This means that the pregnancy is not in the uterus. Unusual vaginal bleeding or lower stomach-area (abdominal) pain may be a sign of ectopic pregnancy. Ectopic pregnancy is a medical emergency that may require surgery. Ectopic pregnancy can cause internal bleeding, infertility, and even death. Call your healthcare provider if you think you are pregnant or have unexplained lower abdominal pain.
 - **Serious blood clots and heart problems.** Serious heart problems (heart attack) and serious blood clots in your eyes (total or partial blindness) or brain (stroke) have happened with implants that contain levonorgestrel. Serious blood clots in your legs (deep vein thrombosis), or lungs (pulmonary embolism) have happened with JADELLE. It is possible to die from a problem caused by a blood clot, such as heart attack or stroke.

Tell your healthcare provider at least 4 weeks before if you are going to have surgery that will limit your ability to move around or if you will need to be on bed rest. You have an increased chance of getting blood clots when you are not moving around regularly.
 - **High blood pressure.** If you have high blood pressure that is controlled by medicine, your healthcare provider will check your blood pressure while you use JADELLE.
 - **Cysts on the ovary.** Some women using JADELLE develop a cyst on the ovary. These cysts usually disappear on their own, but sometimes they can cause pain. Sometimes surgery is needed to remove a cyst on the ovary.
 - **Changes in menstrual bleeding.** You may have changes in menstrual bleeding, including bleeding and spotting between menstrual periods, or your menstrual periods may stop. Tell your healthcare provider if you have irregular or heavy bleeding, bleeding or spotting that goes on for a long time, spotting in between your periods, or if you have not had a menstrual period for at least 6 weeks after having normal periods.

- **Liver problems.** Call your healthcare provider right away if you get any of these symptoms of liver problems while using JADELLE:
 - yellowing of the whites of your eyes
 - itchy skin
 - feeling tired
 - nausea or vomiting
 - flu-like symptoms
- **Depressed mood.** Tell your healthcare provider if you have problems sleeping, lack of energy, tiredness, or feel sad.
- **Increased pressure around the brain (idiopathic intracranial hypertension).** Tell your healthcare provider right away if you have vision problems or have headaches that happen often, are severe, or do not go away.
- **Changes in the level of fats (lipoprotein), insulin, and sugar in your blood.**
- **Effects on the thyroid gland.** If you take thyroid hormone replacement, your dose may need to be decreased during treatment with JADELLE.

The most common side effects of JADELLE include:

- headache
- nausea
- whitish discharge from the vagina (leukorrhea)
- acne
- pelvic pain
- ovarian cyst
- weight gain
- nervousness
- vaginal discharge, itching and pain (vaginitis)
- itchy rash
- dizziness
- injection site reaction and pain
- breast pain and tenderness
- hair loss
- benign breast lump
- weight loss

These are not all the possible side effects of JADELLE. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

After JADELLE has been placed, when should I call my healthcare provider?

Call your healthcare provider if you have any concerns about JADELLE.

Call your healthcare provider right away if you:

- think you might be pregnant
- have pain in your lower leg that does not go away
- have severe chest pain or heaviness in the chest
- have sudden shortness of breath, sharp chest pain, or coughing up blood
- have weakness or numbness in your arm, leg, or trouble speaking
- have sudden partial or complete blindness
- have very severe or migraine headaches
- have yellowing of the skin or whites of the eyes. These may be signs of liver problems.
- have unexplained fever, flu-like symptoms or chills
- have severe pain, swelling, or tenderness in the lower stomach-area (abdomen)
- feel a lump in your breast
- have problems sleeping, lack of energy, tiredness, or you have mood changes, such as you feel sad
- have heavy vaginal bleeding or bleeding that concerns you

General information about the safe and effective use of JADELLE

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about JADELLE that is written for healthcare professionals.

What if I need birth control for more than 5 years?

JADELLE must be removed after 5 years. Your healthcare provider can place a new JADELLE during the same visit if you choose to continue using JADELLE.

What if I want to stop using JADELLE?

JADELLE is meant for use for up to 5 years, but you can stop using JADELLE at any time by asking your healthcare provider to remove it. You could become pregnant as soon as JADELLE is removed, so you should use another method of birth control if you do not want to become pregnant. Certain birth control methods should be started 7 days before JADELLE is removed to ensure continued birth control.

What if I change my mind about birth control and want to stop using JADELLE before 5 years?

Your healthcare provider can remove JADELLE any time. You might become pregnant as soon as JADELLE is removed.

What if I become pregnant while using JADELLE?

Call your healthcare provider right away if you think that you are pregnant. If you get pregnant while using JADELLE, you may have an ectopic pregnancy. This means that the pregnancy is not in the uterus. Unusual vaginal bleeding or lower stomach area (abdominal) pain may be a sign of ectopic pregnancy.

Ectopic pregnancy is a medical emergency that may require surgery. Ectopic pregnancy can cause internal bleeding, infertility, and even death.

Is it safe to breastfeed while using JADELLE?

The hormone in JADELLE passes into your breast milk. The health of breastfed children whose mothers used contraceptive implants containing levonorgestrel has been studied. No effects on the growth and development of the children or on breast milk were seen.

This Patient Information has been approved by the US Food and Drug Administration.

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