PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Prolutex
Solution for injection

Each vial contains 25 mg progesterone.
Each 1 ml solution for injection contains 22.48 mg progesterone.
Inactive ingredients and allergens in the preparation – see section 6 and the "Important information regarding some of the ingredients of the medicine" section.
Read the entire leaflet carefully before using the medicine.
This leaflet contains concise information about the medicine.
If you have any other questions, refer to the doctor or the pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1. What is the medicine intended for?

Prolutex is intended for luteal support as part of fertility treatments in women with fertility problems who are unable to use or tolerate vaginal preparations.
Prolutex contains the active ingredient progesterone.
Progesterone is a sex hormone naturally occurring in women.
Prolutex works on the uterine lining and helps in becoming pregnant and in maintaining pregnancy.
Therapeutic class: progestogen hormones.

2. Before using the medicine:

Do not use this medicine if:

- You are sensitive (allergic) to progesterone or any of the additional components the medicine contains (see section 6).
- You suffer from vaginal bleeding (other than menstrual bleeding) that has not been checked by your doctor.
- You have experienced a miscarriage and your doctor suspects some tissue has remained in the womb.
- You have an ectopic pregnancy.
- You suffer or have suffered from severe liver problems.
- You have or are suspected to have breast cancer or cancer of the reproductive system.
- You suffer or have suffered from blood clot(s) in the legs, lungs, eyes or elsewhere in the body.
- You suffer from porphyria (a group of inherited or acquired enzymatic disorders).
- During pregnancy you have suffered from jaundice (yellowing of the eyes and skin due to liver problems), severe itching and/or skin blisters.
- You are under the age of 18 years.

Special warnings regarding the use of the medicine:
Before treatment with Prolutex, tell the doctor if you suffer or have suffered from:
- Liver problems (mild or moderate)
- Epilepsy
- Migraine
- Asthma
- Heart and/or kidney problems
- Diabetes
- Depression

If you suffer from any of the conditions listed above, the treating doctor will monitor you closely during treatment.
Additional warnings:
Inform the treating doctor immediately if any of the effects listed below appear during treatment; you may need to discontinue the treatment. In addition, contact the treating doctor immediately if any of the effects listed below appear a few days after the last dose of Prolutex:
- Heart attack (chest pain and/or back pain and/or pain and throbbing pain in the arm(s), sudden shortness of breath, sweating, dizziness, light-headedness, nausea, palpitations)
- Stroke (severe headache or vomiting, dizziness, feeling faint or changes in vision or speech, weakness or numbness in the arm or leg)
- Blood clot(s) in the eyes or elsewhere in the body (pain in the eyes or pain and swelling of the ankle, hands and feet)
- Worsening of depression
- Severe headache, changes in vision

Children and adolescents
Prolutex is not intended for use in children and/or adolescents.
Drug interactions:
If you are taking or have recently taken other medicines, including non-prescription medicines and food supplements, tell the doctor or the pharmacist. Especially if you are taking:
- Carbamazepine – medicine for treatment of seizures
- Rifampicin – an antibiotic
- Griseofulvin – an anti-fungal medicine
- Phenytoin and phenobarbital – antiepileptic medicines
- Hypericum plant (St. John's wort)
- Cyclosporine – a medicine given for treatment of certain types of inflammation and for use after organ transplantations
- Medicines for treatment of diabetes
- Ketoconazole – an anti-fungal medicine

Do not inject Prolutex at the same time with another medicine for injection.
Pregnancy and breastfeeding
Consult your doctor or pharmacist before using this medicine.
Pregnancy: Prolutex can be used during the first three months of pregnancy.
Breastfeeding: it has been found that the medicine is excreted into breast milk, therefore do not use Prolutex if you are breastfeeding.
Driving and operating machinery
Prolutex may impair your ability to drive or operate dangerous machinery, because you might feel drowsy and/or dizzy. If you feel these effects, you should not drive or operate dangerous machinery.
Important information regarding some of the ingredients of the medicine
Prolutex contains hydroxypropyl betadex. If you suffer from kidney problems, tell your treating doctor before using the medicine.

3. How should you use the medicine?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the preparation. Remember that the treatment should only be done under the supervision of a specialist in treating fertility problems.
The generally accepted dosage is:
One daily injection that contains 25 mg progesterone.
Duration of treatment:
The treatment with Prolutex will be given until 12 weeks of confirmed pregnancy (10 weeks of treatment).
Do not exceed the recommended dose.
Method of administration
Prolutex can be given either as a subcutaneous or intramuscular injection. You will be able to inject yourself with 25 mg Prolutex as a subcutaneous injection after training by the treating doctor or a healthcare professional.
Subcutaneous injection
Before you inject Prolutex you should receive training that includes:
1. Practice giving subcutaneous injection
2. Where to inject
3. How to prepare the solution for injection
4. How to inject Prolutex

Method of administration
Please read the instructions below on preparing the medicine and how to inject:
- How to perform the steps required for self injection of Prolutex
  Important: each vial is intended for a single injection.
  Use the liquid immediately after opening the vial and do not store it inside the syringe.
  a. Preparation for injection
     It is important to keep the environment of the injection as clean as possible.
     First, wash your hands thoroughly and dry them with a clean towel.
     Choose a clean area to prepare Prolutex for administration.
     ○ Each vial contains Prolutex solution for injection.
     The following items are not supplied with Prolutex. The treating doctor and/or pharmacist should supply them:
     1. One syringe
     2. One large needle (usually the size of 21G) for intramuscular administration
     3. One small fine needle (usually the size of 27G) for subcutaneous administration
     4. Alcohol wipes

  b. Checking the package of the medicine, needles and syringes
     ○ Make sure the vial, syringe and needles all have a protective cover.
     ○ Check that the protective covers are not damaged and that they properly cover the syringe, needle and vial. If not, do not use them.
     ○ Make sure that Prolutex expiry date is valid before use. Do not use the medicine if it has expired.

  c. Preparing the syringe and vial

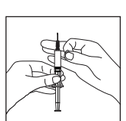
     ○ Remove the plastic cap from the top of the vial that contains Prolutex gently by pushing it upwards.
     ○ Using an alcohol wipe, wipe the rubber top that covers the vial's opening and allow to dry.
     ○ Unpack the syringe and hold it with one hand.
     ○ Take the package that contains the needle for intramuscular administration (21G), unpack the needle but keep the protective cover of the needle on.
     ○ Attach the syringe to the needle and only then remove the protective cover from the needle.

  d. Filling the syringe

     ○ Push the (21G) needle through the center part of the rubber that covers the vial.
     ○ Turn the syringe and vial upside down so that the needle is directed upwards. The vial should be firmly placed on the needle.
     ○ Make sure that the top of the needle is underneath the level of the liquid in the vial.
     ○ Gently draw all the liquid into the syringe.
     ○ Remove the needle from the vial.

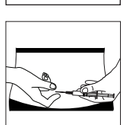
  e. Changing the injecting needle
     This step is only required if you are doing a subcutaneous injection. If your doctor is performing an intramuscular injection, he will prepare the dose and inject it.
     ○ Place the protective cover on the (21G) needle and gently remove the needle from the syringe.
     ○ Take the package that contains the (27G) needle for subcutaneous administration, remove the needle but keep the protective cover of the needle on.
     ○ Attach the syringe to the needle and only then remove the protective cover from the needle.

  f. Removing air bubbles



     ○ While holding the syringe with the (27G) needle pointing upwards, slightly draw back on the syringe plunger and tap on the syringe so that the air bubbles rise to the top.
     ○ Slowly push the syringe plunger so that all the air is out and until at least one drop of solution comes out of the tip of the needle.

  g. Subcutaneous injection



     ○ The doctor or healthcare professional has shown you where to inject Prolutex (e.g. in the abdomen or front of thigh).
     ○ Using an alcohol wipe, carefully clean the area intended for injection and allow to dry.
     ○ Hold the ready-to-inject syringe in one hand. With the other hand, gently pinch the skin in the area intended for injection between your thumb and index finger.
     ○ Insert the needle with a dart-like motion into the skin so the skin and the needle form a right angle.
     ○ Insert the needle all the way into the skin. **Do not inject directly into a vein.**
     ○ Inject the solution by gently pushing the plunger in a slow and steady motion until all the solution is injected under the skin. Inject the entire dose prescribed to you.
     ○ Release the skin and pull the needle out.
     ○ Wipe the injection area using an alcohol wipe in a circular motion.

  h. Disposing of used items
     ○ After finishing the injection, dispose of used vials, syringes and needles into a sharps container.
     ○ Throw away any solution that has not been used.

Administration by intramuscular injection should be performed by a doctor or healthcare professional only.
Prolutex intramuscular administration should be performed into the buttock or side of the thigh.
Your doctor or healthcare professional will clean the injection area using an alcohol wipe, and then allow the area to dry.
In a dart-like motion, the healthcare professional will insert the needle into the muscle and inject the solution by gently pushing the plunger in a slow and steady motion until all the solution is injected into the muscle.
He will pull the needle out and wipe the injection area using an alcohol wipe.
If you accidentally took a higher dosage of the medicine
Tell the doctor or pharmacist. Overdose symptoms include feeling drowsy.
If you accidentally took a higher dose or if a child accidentally swallowed the medicine, immediately refer to a doctor or to a hospital emergency room and bring the package of the medicine with you.
If you forgot to take the medicine
If you forgot one dose, inject it immediately as soon as you remember and continue using the medicine as usual. Do not inject a double dose in order to compensate for the forgotten dose. Refer to your doctor for further consultation.
Follow the treatment as recommended by the doctor.
If you stop taking the medicine
Do not stop using the medicine without a doctor's approval. Abrupt discontinuation of Prolutex may cause increased anxiety, depression and increased risk of experiencing seizures.
Do not take medicines in the dark! Check the label and the dose each time you use the medicine. Wear glasses if you need them.
If you have any other questions regarding the use of the medicine, consult the doctor or the pharmacist.

4. Side effects

As with any medicine, using Prolutex may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.
Stop using Prolutex and refer to the doctor immediately if you have one or more of the following symptoms:
- Overstimulation of the ovaries (the symptoms include lower abdominal pain, feeling thirsty, nausea and sometimes vomiting, passing reduced quantities of concentrated urine and weight gain)
- Depression
- Jaundice – yellowing of the skin and the whites of the eyes
- An acute allergic reaction that may cause breathing difficulties, swelling of the face and throat or a severe rash (anaphylactic reaction)

See also section 2 – "Additional warnings" above.
Very common side effects – effects that occur in more than 1 out of 10 users:
- Pain, redness, itch, irritation or swelling at the injection area
- Uterine spasms
- Vaginal bleeding

Common side effects – effects that occur in 1-10 out of 100 users:
- Headache
- Abdominal bloating
- Abdominal pain
- Constipation
- Nausea and vomiting
- Breast sensitivity and/or pain
- Vaginal discharge
- Tingling sensation or uncomfortable irritation or itching of the vaginal skin and the surrounding area
- Hardening of the area around the injection area
- Bruising at the injection area
- Fatigue (excessive tiredness, exhaustion, deep sleep)

Uncommon side effects – effects that occur in 1-10 out of 1,000 users:
- Mood swings
- Dizziness
- Drowsiness
- Digestive disturbances (including abdominal discomfort and/or tenderness in the abdomen, flatulence, painful spasms and retching)
- Skin rash (including red and warm skin or raised, itchy bumps or bruises or dry and cracked skin, blisters or swelling)
- Swelling of the breast/breasts and/or enlargement of the breasts
- Sensation of heat
- Discomfort sensation or general malaise
- Pain

Side effects with unknown frequency (frequency has not yet been determined) – these effects, although not reported in clinical studies using Prolutex, have been described with other preparations containing progesterone:
- Insomnia
- Symptoms of premenstrual syndrome (PMS)
- Menstrual disorders
- Hives (allergic skin reaction)
- Acne
- Excessive hairiness
- Alopecia (hair loss)
- Weight gain

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.
Reporting side effects
Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link: https://sideeffects.health.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date appearing on the carton package or the vial after the word EXP. The expiry date refers to the last day of that month.
- **Storage conditions:** store the medicine at a temperature below 25ºC.
  Do not store the medicine in a refrigerator or freezer.
  Store the medicine in the original package in order to prevent exposure to light.
  Use the vial immediately after opening.
  Do not use any remaining solution after use.
  Do not use the medicine if you notice particles in the solution or if the solution is not clear.

6. Additional information:

- In addition to the active ingredient, the medicine also contains:
  Hydroxypropylbetadex, Water for injection
- What does the medicine look like and what are the contents of the package?
  Prolutex is a clear, colorless solution that comes in a clear glass vial.
  The package includes: 1, 7, 14 vials. Not all package sizes may be marketed.
- Marketing authorization holder and address: CTS Ltd., 4 Haharash St., Hod Hasharon, Israel
- Name and address of the manufacturer:
  IBSA Institut Biochimique S.A
  Via Pian Scairolo 49, 6912 Pazzallo,
  Switzerland
- Registration number of the medicine in the national drug registry of the Ministry of Health:
  175-15-37196-99

This leaflet was revised in 03/2024 in accordance with the Ministry of Health guidelines.