PATIENT INFORMATION LEAFLET

OCLADRA 2 mg/ml Vial Containing Injectable Solution

Sterile, cytotoxic

Administrated subcutaneously.

**** Active ingredient:*** Each vial contains 10 mg cladribine.

**** Excipients:*** sodium chloride, sodium hydroxide, hydrochloric acid, water for injection.

Before using medicine, read this PATIENT INFORMATION LEAFLET carefully, because it contains important information for you.

- *Keep this patient information leaflet. You may need to read it again later.*
- *If you have any further questions, consult your doctor or pharmacist.*
- *This medicine is prescribed for you individually, do not pass it on to others.*
- *During usage of this medicine, when you go to a doctor or a hospital tell your doctor that you are using this medicine.*
- *Follow these instructions exactly. Do not use **higher or lower dosages** of this medicine except for recommended dosages.*

In this patient information leaflet;

Heads are available.

1.What is OCLADRA and what is used for?

* OCLADRA contains 10 mg cladribine in 5 ml solution as active ingredient.

* OCLADRA is a clear, colorless solution and presented in package of one vial of 5 ml containing injectable solution.

*OCLADRA is a cytostatic agent (particularly preventing the reproduction of cancer cells). It affects the reproduction of malign leucocytes (with cancer) which has a role in the disease of hairy cell leukemia. OCLADRA is used for the treatment of this disease.

2.Precautions before using of OCLADRA:

Please DO NOT USE OCLADRA at following conditions:

- If you have hypersensitivity to cladribine or another contents of this medicine,
- If you are pregnant or lactating,
- If you are below age 18,
- If you have renal or liver insufficiencies at moderate or severe levels,
- If you are using other medicines which affects the manufacturing of blood cells in bone marrow (myelosupression).

Please USE OCLADRA CAREFULLY at following conditions:

If you have or had one of the facts below in past, please tell your doctor:

- Liver or renal problems,
- Infections:
  - If you have infection, it will be treated before using OCLADRA,
  - If you notice any symptoms of infections during treatment with OCLADRA or after treatment with OCLADRA (flu-like symptoms or fever, etc.), inform your doctor immediately.
- Fever
- Blurred vision, double vision or loss of vision, difficulty speaking, weakness in the arm or leg, difficulty in walking or balance problems, permanent numbness, reduced or lost sensation, memory loss or unconsciousness. All of these symptoms may indicate a serious and fatal brain disorder called progressive multifocal leukoencephalopathy (PML). If these symptoms are present before you are treated with cladribine, tell your doctor if there has been a change in the symptoms.

Before or while using OCLADRA, regular blood tests will be performed to you in order to control whether continuing the treatment is safe for you or not. Your doctor may decide to transplant blood in order to recover the levels of blood cells. In addition, liver and renal functions will be controlled.

If you are a male planning to have children, before starting treatment with OCLADRA, please speak to your doctor. Do not become father or mother during treatment of OCLADRA or until 6 months later from treatment with OCLADRA. Your doctor will give information to you about possibilities of storing your sperms after freezing. (criopreservation).

If these precautions are valid now or were valid also in the past, please consult your doctor.

Using OCLADRA with food and drinks:

Because of subcutaneous administration of product, it has no interactions with foods and drinks.

Pregnancy

Before using this medicine, please consult your doctor or pharmacist.

If you are pregnant, do not use OCLADRA. You must use proper birth control methods during treatment or the next 6 months after the last dose of OCLADRA.

If you notice that you are pregnant during treatment, please consult your doctor.

Lactation:

Before using this medicine, please consult your doctor or pharmacist.

Do not lactate during treatment with OCLADRA or the next 6 months after the last dose of cladrabine.

Driving and machinery usage:

There is an important effect of OCLADRA on driving and machinery usage. If you are feeling a lack of energy or dizziness due to lowered leucocytes caused by OCLADRA, do not drive or use machines.

Important information on excipients in contents of OCLADRA:

Any negative effects are not expected due to substances in its contents.

This medicine contains more than 1 mmol sodium in each vial. This situation must be considered in patients with controlled sodium diet.

Usage with other medicines:

If you are taking medicines containing followings, inform your doctor:

- Corticosteroids commonly used in inflammation treatment (inflammation with pain),
- Antiviral agents used in treatment of viral infections.

OCLADRA must not be used in combination with other medicines which affects the reproduction of blood cells in bone marrow (myelosupression).

If you are taking or have taken any prescribed or non-prescribed medicines now or recently, inform your doctor or pharmacist about these.

3. How to use OCLADRA?

Instructions for suitable usage and dosage/ administration frequency:

Always use OCLADRA as described by your doctor. If you are not sure, please consult your doctor or pharmacist.

Your doctor will decide the dosage of medicine according to your body weight and explain about the treatment program in detail. Recommended daily dosage is 0.14 mg/kg body weight for 5 days (single treatment cycle).

In order to decrease excessive uric acid quantity, you can take another medicine containing allopurinol as active ingredient.

Administration route and method:

OCLADRA is administered by subcutaneously (subcutaneous injection) every day at the same hours. If you are injecting OCLADRA by yourself, you must take enough education from your doctor or nurse. You can find detailed instructions about injection at the end of this patient information leaflet.

Different age groups:

Usage on chidren:

Do not use OCLADRA in children under age 18.

Usage in geriatrics:

Geriatric patients must be treated with carefully monitoring renal and liver functions, blood counts and individual evaluations

Special usage situations:

Renal/liver insufficiencies:

Patients with known or suspicious renal or liver insufficiencies must be treated carefully. In all patients treated with cladribine, liver and renal functions must be evaluated periodically as mentioned clinically.

If you notice that effects of OCLADRA is too strong or too weak, please speak to your doctor or pharmacist.

If you have used more OCLADRA than you should:

If you have used OCLADRA more than you should, speak to your doctor or pharmacist.

If you have forgotten to take OCLADRA:

If you have missed a dose of OCLADRA, immediately speak to your doctor.

Do not take double dosage to balance the forgotten dosage.

Effects which may occur after the treatment with OCLADRA ends:

Do not stop your treatment unless your doctor tells you to do so. If you face any problem while using this medicine, consult your doctor.

4. What are the possible side effects?

Like all medicines, side effects can be seen in patients who have hypersensitivity to substances in contents of OCLADRA.

If any of the followings occur, stop using OCLADRA and IMMEDIATELY inform your doctor or go to the emergency service of the nearest hospital:

- Serious allergic reaction, sudden pruritus, urticaria, inflation at hands, foots, wrist, face, lips, mouth or throat (difficulties for breathing and gulping) and feeling like fainting.

These are very serious side effects. If you have any of side effects above, you are seriously allergic to OCLADRA. Intermediate medical care or hospitalization may be required. These serious side effects are seen very rarely.

If you notice followings, tell your doctor:

- Any infection symptoms (flu-like symptoms),
- Fever.

Repetition of cancer disease most not be ignored. This means that you have slightly higher risks of getting malign diseases than healthy patients. The reason why the risk is higher may depend on leukemia disease with hairy cell and the medicines which are used to treat this disease including OCLADRA.

Side effects are ordered according to following categories:

Very common : it can be seen minimum one patient of 10 patients.

Common : it can be seen less than 10 patients but, on patient of 100 patients or more than one patient.

Non-common : it can be seen in less than one patient of 100 patients but one patient of 1000 patients or more than one patient.

Rare : it can be seen less than one patient of 1000 patients but, one patient of 10,000 patients or more than one patient.

Very rare : it can be seen less than one patient of 10,000 patients.

Not known : According to the available data available.

Very-common:

- Infections,
- Fever,
- Low numbers of thrombocytes or low leucocytes in blood tests (neutrophils or lymphocytes),
- Low red blood cells that may lead to anemia symptoms with symptoms like tiredness, numbness,
- Decreased immune system function,
- Headache, dizziness,
- Abnormal breathing sounds, abnormal chest sounds, cough,
- Nausea, vomiting, constipation and diarrhea,
- Urticaria, edema, pruritus, pain at injection site, perspiration. Skin reactions are generally medium and light degrees and recovery within one-two days.
- Tiredness, tremor, loss of apetite,
- Weakness.

Common:

- Repeation of cancer disease,
- Low thrombocyte numbers causing non-spontoneous bleeding (exp; bleeding of nose and skin),
- İnsomnia, anxiety,
- İncreasing of heart rthym, abnormal heart sounds, lo blood pressure, providing low blood to heart muscle,
- Difficulties of breathing, oedema depending on oedema in lung tissues, inflamation in mounth and tongue with pain,

- Abdominal pain, flutulance in stomach and intestine, increasing of laboratory tests for liver which are returnes to normal after treatment (like bilirubine, transaminases),
- Pruritis, urticeria with pruritis,
- Odema at tissues, not-feeling well, pain (muscle, joints and bone),

Non-common:

- Anemia sourced from loosing of leucocytes,
- Somnia, pins and needless, tiredness, in-mobile status, deteriotion of peripheric nerves, mind confusion, difficulties on movement coordination,
- Inflamation in eyes with pain,
- Shore throat,
- Inflamation in superficial veins with pain,
- Serious loss of weight,

Rare:

- Decreased liver function,
- Decreased renal function,
- Complications depending on falling to pieces of cancer cells in treatment of cancer,
- Rejection answer for blood transplantation,
- Increasing numbers of leucocytes (eusonophilia),
- Paralyses,
- Difficulties of speaking and swalloving.
- Cardiac insufficiency,
- Abnormal heart rthym,
- Not enough circulation of hearth,
- Obstruction of intestine,
- Serious allergic skin reactions (Stevens-Johnson syndrome or Lyell syndrome).

Very-rare:

- Depression, epilepsia,
- Swalloving of eye lids,
- Blood coagulation in lungs,
- Inflamation with pain in gall bladder,
- Decresing of organ functions depending on increasing quantities of any substance which are produced by body (glycoprotein).

If you notice any side effects which are not mentioned in this leaflet, inform your doctor or pharmacist.

Reporting side effects:

Occuring of any side effects in patient information leaflet or not mentioned in patient information leaflet, speak to your doctor or pharmaciest. Furtermore, please inform to any seen side effects to Turkish Pharmacovigilance Association (TUFAM) by calling numbers of 0 800 314 00 08 or clicking of side effects noticing icon on web-site of www.titck.gov.tr. If you inform any side effects, you will add additional benefits for informing about your using medicine.

5.Storage of OCLADRA:

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

Store at 2-8^{0}C in refrigerator. Do not freeze.

Use suitable with its expiry date.

From a microbiological point of view, unless the opening precludes the risk of microbiological contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Do not use OCLADRA if you notice particulate matters in solution, notice that the solution is not clear or the vial is deteriorated.

Un-used products or waste materials must destruct according to guidelines of controls of medical wastes and controls of packaging and packaging wastes.

Do not use OCLADRA after the expiry date on box/ vial.

Registration holder: Biem İlaç San. ve Tic. A.Ş.

Anıttepe Mah., Turgut Reis Cad, No:21,

Tandoğan /Çankaya-Ankara.

Manufacturing site: Mustafa Nevzat Pharmaceuticals Co.A.Ş.

Yenibosna-İstanbul.

This patient information leaflet is approved on 28.08.2018.

FOLLOWING INFORMATION IS FOR MEDICAL PERSONELL WHO ADMINISTER OF THIS PRODUCT:

Instructions of injection:

This section contains information about how to administer OCLADRA injections. If you have not taken any education from your doctor or nurse, do not inject medicine by yourself. When you are going to inject medicine by yourself, your doctor will tell you about how much and how often you need OCLADRA. OCLADRA must be injected to subcutaneously. If you have any questions about making injections, please request help from your doctor or nurse.

OCLADRA is cytotoxic and because of this, use carefully. If OCLADRA not administered by patient by himself, single usage gloves and protective clothes must be worn. If OCLADRA contacts with skin or eyes, related surface must be washed with plentiful water. Pregnant women must avoid from contact with OCLADRA.

What I need for injection?

For subcutanous injection by yourself, you need followings:

- One vial of OCLADRA (if you are going to inject more than 5 ml, you need two vials). Do not use the product if you notice particulate matters in solution, notice that the solution is not clear or the vial is deteriorated.
- One sterile syringe (exp; 10 ml syringe),
- One sterile injector needle (exp; 0.5 x 19 mm, 25G x3/4),
- Handkerchief with alcohol,
- Perforation resistant waste cap for destruction of syringe.

What I must do before subcutanous injection of OCLADRA?

- Before injection, temperature of OCLADRA must be brought to room temperature,
- Wash your hands properly,

- You must find suitable, comfortable and well-lighted place. You must place what you need on a place where you can easily find and reach.

How can I prepare injection?

Before injection of OCLADRA, you must perform followings:

1. Take off the protective cap of OCLADRA. Do not take off rubber cap. Swab the surface of rubber on vial with alcoholic handkerchief. Take off syringe from packaging not touching on tip. Take off injector needle from its packaging and insert to the tip of syringe. Take off the needle cap without touching the needle.

2. Pull needle to rubber closure of vial. Invert the syringe and vial up-side down. Be sure that the tip of needle is in solution.

3. Withdraw correct volume of OCLADRA with the help of the piston of syringe (your doctor will tell you about how much mL OCLADRA you will inject).

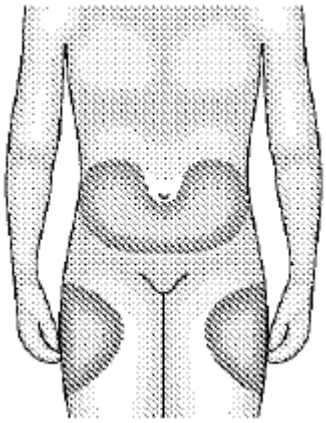
4. Take off the needle from vial.

5. Please be sure that syringe does not contain air. Hold the needle to up-right position to expel the air.

6. Control whether correct volume is withdrawn or not.

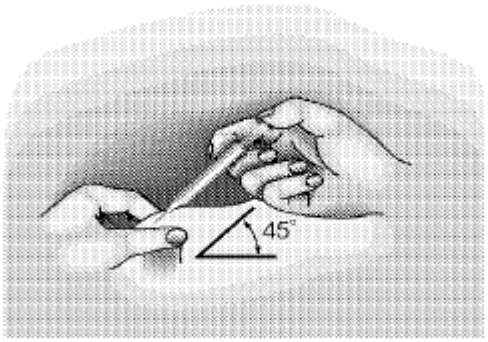
7. Inject immediately.

Which sites I must inject?



Most suitable place which you can inject OCLADRA is shown in figure: top site of your thigh or abdomen excluding enviromental area of belly. If another person will make the injection to you, he or she can use outer surface of upper arms or your hip.

How I must inject?



1. Disinfect your skin with alcoholic handkerchief. Wait for until drying of your skin. Compress your skin with your thumb and marking finger.
2. Please insert the needle on your skin with 45^0 angle as seen in figure.
3. Pull down piston of syringe lightly and control that if you are not-perforating a blood vein. If you see blood in syringe, withdraw needle and administer to another site.
4. You must inject liquid slowly and levelheaded within 1 minute by holding skin tightly.
5. Withdraw needle after injection of liquid.

6. Please put the syringe in waste cap which is resistant to perforating. For each new injection, you must use new syringes and new needles. Vials are for single use only. You must give un-used medicine to your doctor or pharmacist after usage for suitable destruction.

Destruction of used syringes:

Please put the syringes in perforation resistant waste cap and store at places where children can not to see or reach.
You must destruct the perforation resistant caps as explained by your doctor or your pharmacist.
Do not waste syringes with normal house wastes.