Package leaflet: Information for the user

Pixuvri 29 mg powder for concentrate for solution for infusion
pixantrone

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Pixuvri is and what it is used for

Pixuvri belongs to a pharmacotherapeutic group of medicines known as 'antineoplastic agents'. These are used to treat cancer.

Pixuvri is used for the treatment of adult patients with multiply relapsed or refractory aggressive Non-Hodgkin Lymphomas. Pixuvri kills cancer cells by binding to DNA, resulting in cell death. It is used for patients whose cancer does not respond or has returned after they have received other chemotherapy treatments.

2. What you need to know before you use Pixuvri

Do not use Pixuvri:
- if you are allergic to pixantrone dimaleate or any of the other ingredients of this medicine (listed in section 6).
- if you have recently received a vaccine.
- if you have been told that you have persistent, long-term low numbers of red blood cells, white blood cells, and platelets.
- if you have very severe liver problems.

Warnings and precautions
Talk to your doctor before using Pixuvri:

- if you have been told that your white blood cell count is very low.
- if you have heart disease or uncontrolled high blood pressure, especially if you have ever been told you had heart failure or if you have had a heart attack within the last six months.
- if you have an infection.
- if you have ever been treated for cancer.
- if you follow a specific sodium restricted diet.
- if you are taking other medicines which could interact with Pixuvri (see 'Taking other medicines' below).

Skin sensitivity to sunlight
During treatment with pixantrone, you should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment). If you will be exposed to sunlight, you should wear sun-protective clothing and use sunscreen that strongly absorbs UV-A.

Children and adolescents
Do not give this medicine to children under the age of 18 years because there is no information about Pixuvri treatment in children and adolescents.

Other medicines and Pixuvri
Tell your doctor if you are taking, have recently taken or might take any other medicines. This is extremely important as using more than one medicine at the same time can strengthen or weaken their effect. Pixuvri must not be used with other medicines unless your doctor has told you it is safe to do so. In particular, make sure to tell your doctor if you are currently using, or have recently used, any of the following medicines:

Tell your doctor if you take medicines such as:

- Warfarin to prevent blood clot formation
- Theophylline to treat lung conditions like emphysema or asthma
- Amitriptyline to treat depression
- Olanzapine, Clozapine to treat schizophrenia or maniac depression
- Haloperidol to treat anxiety and sleeplessness
- Ondansetron to prevent nausea and vomiting during chemotherapy
- Propranolol to treat high blood pressure

Pixuvri with food and drink
You do not have to change your diet after treatment with Pixuvri unless instructed by your doctor.

Pregnancy, breast-feeding and fertility
Pixuvri must not be given to pregnant women as it may cause harm to unborn babies. If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before taking this medicine.

Adequate contraceptive precautions must be used when receiving Pixuvri and for up to 6 months after treatment. This applies to women who can become pregnant and men receiving Pixuvri who may be able to father a child.

Do not breast-feed while you are being treated with Pixuvri.

Driving and using machines
It is not known whether Pixuvri has an effect on your ability to drive a car or use machines.

Information for patients on a low salt diet
This medicinal product contains approximately 1000 mg (43 mmol) sodium per dose after dilution. To be taken into consideration by patients on a controlled sodium diet.

3. How to use Pixuvri

How much of Pixuvri is given
The amounts (dose) of Pixuvri that will be given to you will depend on your body surface area in square meters (m^2). This is determined by your height and weight. The results of blood tests and your medical condition will also be taken into account. The recommended dose is 50 mg/m^2. If necessary, your doctor will adjust the dose during treatment.

Your doctor will carry out some tests before you are given Pixuvri.

How often Pixuvri is given
Pixuvri is given on days 1, 8, and 15 of each 28-day cycle for up to 6 cycles.

Before the infusion is administered you may be given medicines to prevent or reduce possible reactions to Pixuvri, such as medicines to prevent sickness.

How Pixuvri is given
Pixuvri is given through a drip into a vein (by intravenous infusion). This will be done by a nurse or doctor.

How long the infusion will take
This will take approximately one hour unless otherwise stated.

4. Possible side effects

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

Infusion reactions
Pain/redness of the injection site may occur rarely during infusion of Pixuvri. Tell the person giving you the infusion immediately if you feel pain or if the injection site gets red. The infusion may need to be slowed down or stopped. When these symptoms go away or improve, the infusion can be continued.

Pixuvri has a deep blue colour and for several days after receiving Pixuvri, your skin and eyes may develop a bluish discolouration, and your urine may have a bluish discolouration. The skin discolouration generally disappears over a few days to weeks as the drug is cleared.

Infections
Tell your doctor if you get any symptoms of an infection (for example, fever, chills, trouble breathing, cough, sores in your mouth, trouble swallowing, or severe diarrhoea) after Pixuvri treatment. You might get infections more easily after you have been given Pixuvri.

Heart
There is a possibility that your heart pumping function could decrease as a result of the treatment or you might even develop a serious condition called heart failure, especially if your heart function was already compromised at the beginning of the treatment with Pixuvri. Your doctor will monitor your heart function if there is any sign or symptom of your heart being affected.

Tell your doctor if you think you have any of the following reactions

Very common: may affect more than 1 in 10 people
- nausea, vomiting
- skin discolouration
- thinning or loss of hair
- abnormal colouration of the urine
- physical weakness
- low number of white blood cells, low number of red blood cells (anaemia), and low number of platelets in the blood (may require transfusion).

Common: may affect up to 1 in 10 people
- infection such as lung infection, skin infections, infections with low white blood cells, thrush
- fever
- severe blood infection (sepsis)
- taste disturbances
- abnormal sensations of the skin such as numbness, tingling, pricking (paraesthesia)
- headache

- sleepiness
- tiredness
- inflammation of the eyes (conjunctivitis)
- diarrhoea
- pain in the abdomen
- inflammation and/or ulceration of the throat and the mouth
- dry mouth, constipation, indigestion, loss of appetite
- skin changes such as redness and itching of the skin, nail changes
- damage to the heart, decrease in heart's ability to pump blood, blockage of electrical signals in your heart, uneven or fast heartbeat.
- low blood pressure
- vein discolouration, pale skin
- shortness of breath, cough
- blood in urine
- excess protein in urine
- swelling of legs or ankles or other parts of the body
- bone pain
- chest pain
- low levels of phosphate in the blood
- abnormal blood test for liver or kidney function.

Uncommon: may affect up to 1 in 100people
- severe infections such as septic shock, bronchitis, pneumonia, candidiasis, cellulitis, meningitis, gastroenteritis
- viral infections such as shingles or reactivation of other virus such as herpes in the mouth
- nervousness, sleeplessness
- loss of energy
- dizziness, vertigo
- dryness of the eye
- numbness of the mouth
- infection of the cornea
- allergy to the medicine
- decrease in blood calcium and sodium level; increase in blood uric acid level
- inflammation or fluid accumulation around the lungs
- runny nose
- bleeding such as gut bleed, purple spots on body due to broken blood vessels
- vein irritation
- night sweats
- irregular heartbeat
- spontaneous erection
- skin rash and/or ulceration
- pain, swelling, weakness, stiffness in joints or muscles
- decreased urinary output
- loss of weight
- increased bilirubin in blood or urine
- inflammation of the gullet
- pain in neck, back, extremities
- nail infection
- neoplasm (tumour) progression
- new cancers of the bone marrow or blood, such as acute myeloid leukaemia (AML) or myelodysplastic syndrome (MDS)
- liver damage
- bone marrow failure
- increased eosinophils in blood.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL – Dublin 2
Tel: +353 1 6764971
Fax: + 353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

5. How to store Pixuvri

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

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

Store in a refrigerator (2°C to 8°C).
Keep the vial in the outer carton in order to protect from light.

Pixuvri does not contain anything to prevent the growth of bacteria and it is, therefore, recommended that it be used immediately after reconstitution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should not be longer than 24 hours at 2°C to 8°C.

Reconstituted pixantrone solution is stable for up to 24 hours at room temperature (15°C to 25°C) in standard infusion bags.

Pixuvri is for single use only. Any unused medicinal product or waste material, including materials used for reconstitution, dilution, and administration should be disposed of in accordance with local requirements.

6. Contents of the pack and other information

What Pixuvri contains
- The active substance is pixantrone. Each vial contains 50 mg pixantrone dimaleate (equivalent to 29 mg pixantrone). The other ingredients are lactose monohydrate, sodium hydroxide, hydrochloric acid, and sodium chloride.

What Pixuvri looks like and contents of the pack
Pixuvri is a powder for concentrate for solution for infusion. It appears as a dark blue powder which comes in vials containing 29 mg of pixantrone. Pack size: 1 vial.

Marketing Authorisation Holder
CTI Life Sciences Limited
Highlands House
Basingstoke Road
Spencers Wood, Reading
Berkshire RG7 1NT
United Kingdom

Manufacturer
Les Laboratoires Servier Industrie
905 Route de Saran
45520 Gidy
France

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

Ireland
Servier Laboratories (Ireland) Ltd.
Tel: +353 (0)1 663 8110

United Kingdom
Servier Laboratories Ltd
Tel: +44 (0)1753 666409

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This medicine has been given 'conditional approval'.
This means that there is more evidence to come about this medicine.
The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

Detailed instructions for users

READ ENTIRE PREPARATION INSTRUCTIONS PRIOR TO RECONSTITUTION

Special precautions for use
Pixuvri is an anticancer medicinal product that is harmful to cells; caution should be exercised in handling. Avoid contact with eyes and skin. Use gloves, masks, and protective eyewear when handling and during decontamination procedures. If Pixuvri (lyophilised powder or reconstituted liquid solution) contacts the skin, wash the skin immediately and flush the membranes thoroughly with water.

Reconstitution/preparation for intravenous administration
Each single-use vial of Pixuvri contains pixantrone dimaleate equivalent to 29 mg pixantrone. After reconstitution with 5 ml sodium chloride 9 mg/ml (0.9%) solution for injection, each ml of concentrate contains pixantrone dimaleate equivalent to 5.8 mg pixantrone.

Using sterile procedures, reconstitute each 29 mg vial with 5 ml of sodium chloride 9 mg/ml (0.9%) solution for injection. The powder should completely dissolve in 60 seconds with agitation. This yields a dark blue solution with a pixantrone concentration of 5.8 mg/ml.

Using sterile procedures, withdraw the volume needed for the required dose (based on 5.8 mg/ml concentration) and transfer to a 250 ml infusion bag of sodium chloride 9 mg/ml (0.9%) solution for injection. Compatibility with other diluents has not been determined. After transferring, thoroughly mix the contents of the infusion bag. The mixture should be a dark blue solution.
Polyethersulfone 0.2 µm pore size in-line filters should be used during administration of the diluted Pixuvri solution.

In-use storage conditions
Pixuvri does not contain anything to prevent the growth of bacteria and it is therefore recommended that it be used immediately after reconstitution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should not be longer than 24 hours at 2°C to 8°C.

The reconstituted and diluted solution is stable for up to 24 hours at room temperature (15°C to 25°C) and daylight exposure in standard polyethylene (PE) infusion bags.

Special precautions for disposal and handling
Pixuvri is a cytotoxic agent. Any unused product or waste material should be disposed of in accordance with local requirements.

Devices and surfaces accidentally contaminated with Pixuvri must be treated with a solution of sodium hypochlorite (100 µl of water and 20 µl of sodium hypochlorite [7 ± 2% of available chlorine] for 0.58 mg of Pixuvri).

Equipment such as vials, needles and syringes used for Pixuvri administration should be handled as toxic waste.