Package leaflet: Information for the user

Qarziba 4.5 mg/mL concentrate for solution for infusion
dinutuximab beta

▼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 Qarziba is and what it is used for

Qarziba contains dinutuximab beta, which belongs to a group of medicines called 'monoclonal antibodies'. These are proteins, which specifically recognise and bind to other unique proteins in the body. Dinutuximab beta binds to the molecule known as disialoganglioside 2 (GD2), which is present on cancer cells, and this activates the body's immune system, causing it to attack the cancer cells.

Qarziba is **used to treat neuroblastoma** that has a high risk of coming back after a series of treatments, which include a stem cell transplantation for rebuilding the immune system. It is also used to treat neuroblastoma that has come back (relapsed) or could not be completely treated with previous therapies.

Prior to the treatment of relapsed neuroblastoma, your treating physician will stabilise any actively progressing disease by other suitable measures.

Your doctor will further decide whether the co-administration of a second medicine, interleukin-2, is necessary for the treatment of your cancer.

Neuroblastoma is a type of cancer that grows from abnormal nerve cells in the body, in particular in the glands above the kidneys. It is one of the most common cancers in infancy.

It is used for patients aged 12 months and above.

2. What you need to know before you use Qarziba

Do not use Qarziba if you

- are **allergic** to dinutuximab beta or any of the other ingredients of this medicine (listed in section 6)
- have acute grade 3 or 4, or extensive long-lasting graft-versus-host disease
  This disease is a reaction in which **cells of transplanted tissue attack cells of the recipient**.

Warnings and precautions

Before receiving Qarziba, you will have blood tests to check your liver, lung, renal and bone marrow functions.

You might notice the following when you first receive Qarziba and during the course of treatment:

- **pain**
  Pain is one of the most common side effects of Qarziba. It usually occurs at the beginning of infusion. Therefore, your doctor will give you an appropriate pain treatment starting 3 days before and continuing during use of Qarziba.
- **allergic reactions or other infusion-related reactions**
  Tell your doctor or nurse if you have any kind of reaction during or after the infusion, such as:
  - fever, shivering and/or low blood pressure
  - difficulties in breathing
  - skin rash, hives

  You will receive appropriate treatment to prevent these reactions and be closely monitored for these symptoms during infusion of Qarziba.
- **leakage from small blood vessels (capillary leak syndrome)**
  Leakage of blood components from small blood vessels may cause rapid swelling in arms, legs and other parts of the body. Rapid drop in blood pressure, light-headedness and breathing difficulties are further signs.
- **eye problems**
  You may notice changes to your vision.
- **problems with your nerves**
  You may notice numbness, tingling or burning in your hands, feet, legs or arms, reduced sensation or weakness with movement.
- **spinal cord and brain problems (central nervous system, CNS)**
  Tell your doctor or nurse if you have any kind of CNS symptoms, such as: substantial prolonged neurological deficit without apparent reason such as muscle weakness or loss of muscle strength in the legs (or arms), or mobility problems or unusual sensations and numbness, persistent or sudden onset of a headache, or progressive loss of memory and cognitive ability, subtle personality changes, inability to concentrate, lethargy, and progressive loss of consciousness

Tell your doctor immediately if you notice any of these problems.

Your doctor may decide to stop your treatment if you have any of the problems mentioned here. In some cases your treatment may be able to start again after a break or at a slower rate, but sometimes it may need to be stopped completely.

Your doctor will do blood tests and may do eye tests while you are taking this medicine.

Children

This medicine should not be given to children under 12 months because there is insufficient experience in this age group.

Other medicines and Qarziba

Tell your doctor if you are using, have recently used or might use any other medicines.

Do not use **medicines that suppress the immune system** from 2 weeks before the first dose of Qarziba until 1 week after the last treatment course, unless prescribed by your doctor. Examples of medicines that suppress the immune system are corticosteroids used to reduce inflammation or prevent organ transplant rejection.

Avoid **vaccinations** during treatment with Qarziba and for 10 weeks afterwards.

Pregnancy, breast-feeding and fertility

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.

Talk to your doctor before you receive Qarziba if you are of childbearing age. It is recommended to use contraception for 6 months after discontinuation of treatment with Qarziba. You may only use Qarziba if your doctor assesses that benefits outweigh risks for a foetus.

Tell your doctor if you are breast-feeding. Do not breast-feed during treatment with Qarziba and for 6 months after the last dose. It is not known if the medicine can pass into breast-milk.

Driving and using machines

Qarziba has several side effects that may affect your ability to drive and use machines. Do not perform these activities if your ability to concentrate and react is affected.

3. How to use Qarziba

A doctor experienced in the use of medicines to treat cancer will supervise your treatment. It will be given to you by a doctor or nurse while you are in hospital. It is given into one of your veins (intravenous infusion) usually by using special tubes (catheters) and a pump. During and after the infusion, you will be checked regularly for infusion-related side effects.

Qarziba will be given to you in five treatment courses of 35 days and the infusion will last 5 or 10 days in the beginning of each course. The recommended dose is **100 mg** dinutuximab beta **per square metre of body surface per treatment course.** The doctor will calculate your body surface area from your height and weight.

If your doctor considers co-administration of interleukin-2, it will be given twice, by injection under the skin, each time for 5 consecutive days (before and during treatment with Qarziba).

4. Possible side effects

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

Tell your doctor or nurse immediately if you have any of the following:
Very common (may affect more than 1 in 10 people):
- rapid swelling of arms, legs and other body parts, rapid drop in blood pressure, light-headedness and breathing difficulties (capillary leak syndrome)
- pain in the stomach, throat, chest, face, hands, feet, legs, arms, back, neck, joint, or muscles
- allergic reactions and cytokine release syndrome with symptoms such as face or throat swelling, breathing difficulties, dizziness, hives, rapid or noticeable heartbeat, low blood pressure, hives, rash, fever, or nausea

Other side effects and their frequencies include:
Very common (may affect more than 1 in 10 people):
- fever, chills
- vomiting, diarrhoea, constipation
- inflammation of the mouth and lips (stomatitis)
- cough
- itching, rash
- low blood pressure, increased heartbeat
- oxygen deficiency
- tissue swelling (in the face, lip, around the eye, in the lower limbs)
- increased weight
- infection, in particular infection associated with the catheter that delivers the medicine
- headache
- dilated pupils or abnormal pupil reactions
- abnormal blood or urine tests (blood cells and other components, liver function, renal function)

Common (may affect up to 1 in 10 people):
- life-threatening infection (sepsis)
- fits
- agitation, anxiety
- nerve disorder in the arms and/or legs (with abnormal sensations or weakness), light-headedness, trembling, muscle spasms
- paralysis of eye muscles, blurred vision, light sensitivity, swelling in the retina
- high blood pressure
- cardiac failure, fluid around the heart
- respiratory failure, fluid in the lungs
- sudden constriction of the airways (bronchospasm, laryngospasm), rapid breathing
- decreased appetite, nausea, abdominal distension, accumulation of fluid in the abdominal cavity
- injection-site reactions, skin problems such as reddening, dry skin, eczema, excessive sweating, reaction to light
- unable to pass urine or passing reduced urine volume
- decreased weight, loss of fluids (dehydration)

Uncommon (may affect up to 1 in 100 people):
- shock due to decreased body fluid volume
- formation of blood clots in the small blood vessels (disseminated intravascular coagulation)
- a type of allergy (serum sickness) with fever, rash, joint inflammation
- a brain disorder characterised by headache, confusion, seizures and loss of vision (posterior reversible encephalopathy syndrome)
- inflammation of the intestine, injury to the liver
- kidney failure
- a condition in which some of the small veins in the liver are obstructed (veno-occlusive disease)

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Qarziba

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 label and the carton after EXP. The expiry date refers to the last day of that month.

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

Once opened, Qarziba is intended for immediate use.

6. Contents of the pack and other information

What Qarziba contains

- The active substance is dinutuximab beta.
  1 mL concentrate contains 4.5 mg dinutuximab beta. Each vial contains 20 mg dinutuximab beta in 4.5 mL.
- The other ingredients are histidine, sucrose, polysorbate 20, water for injections, hydrochloric acid (for pH adjustment).

What Qarziba looks like and contents of the pack

Qarziba is colourless to slightly yellow liquid, provided in a clear glass vial with a rubber stopper and aluminium seal.
Each carton contains 1 vial.

- **Marketing Authorisation Holder**
  EUSA Pharma (UK) Limited
  Breakspear Way,
  HP2 4TZ Hemel Hempstead
  United-Kingdom

- **Manufacturer**
  Millmount Healthcare Ltd
  Block 7, City North Business Campus
  Stamullen, Co. Meath
  K32 YD60
  Ireland

This leaflet was last revised in 01/2023

The following information is intended for healthcare professionals only:

Qarziba is restricted to hospital-use only and must be administered under the supervision of a physician experienced in the use of oncological therapies. It must be administered by a healthcare professional prepared to manage severe allergic reactions including anaphylaxis in an environment where full resuscitation services are immediately available.

Posology
Treatment with dinutuximab beta consists of 5 consecutive courses, each course comprising 35 days. The individual dose is determined based on the body surface area and should be a total of 100 mg/m^2 per course.

Two modes of administration are possible:
- a continuous infusion over the first 10 days of each course (a total of 240 hours) at the daily dose of 10 mg/m^2
- or five daily infusions of 20 mg/m^2 administered over 8 hours, on the first 5 days of each course

If IL-2 is combined with dinutuximab beta, it should be given as subcutaneous injections for 5 consecutive days twice during each course. First 5-day treatment should start 7 days prior to first dinutuximab beta infusion. Second 5-day treatment with IL-2 should start concurrently with dinutuximab beta infusion (days 1 to 5 of each course). IL-2 is administered as 6×10^6 IU/m^2/day, resulting in an overall dose of 60×10^6 IU/m^2/course.

Preparation of the infusion
The solution for infusion must be prepared under aseptic conditions. The solution must not be exposed to direct sunlight or heat.

The patient-specific daily dose of Qarziba is calculated based on body surface area. Qarziba should be diluted aseptically to the patient-specific concentration/dose with sodium chloride 9 mg/mL (0.9%) solution for infusion, containing 1% human albumin (e.g. 5 mL of human albumin 20% per 100 mL sodium chloride solution).

- For continuous infusions, the solution for infusion can be prepared freshly on a daily basis, or sufficient for up to 5 days of continuous infusion. The daily dose is 10 mg/m^2. The amount of solution to be infused per day (within a treatment course of 10 consecutive days) should be 48 mL; with 240 mL for a 5-day dose. It is recommended to prepare 50 mL solution in a 50 mL syringe, or 250 mL in an infusion bag suitable for the employed infusion pump, i.e. an overfill of 2 mL (syringe) or 10 mL (infusion bag) to allow for dead volumes of the infusion systems.

- For repeated daily infusions, the daily dose is 20 mg/m^2 and the calculated dose should be diluted in 100 mL sodium chloride 9 mg/mL (0.9%) containing 1% human albumin.

Administration of the infusion
The solution for infusion should be administered via a peripheral or central intravenous line. Other intravenously co-administered agents should be delivered via a separate infusion line. The container should be inspected visually for particulates prior to administration. It is recommended that a 0.22 micrometre in-line filter is used during infusion.

For continuous infusions, any medical device suitable for infusion at a rate of 2 mL per hour can be applied, e.g. syringe infusion pumps/infusors, electronic ambulatory infusion pumps. Note that elastomeric pumps are not considered suitable in combination with in-line filters.

Storage of the diluted solution

Chemical and physical in-use stability has been demonstrated for up to 48 hours at 25 °C (50 mL syringe) and for up to 7 days at 37 ºC (250 mL infusion bag), after cumulative storage in a refrigerator (2 °C – 8 °C) for 72 hours.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not normally be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.