

Package leaflet: Information for the user

Benlysta 120 mg powder for concentrate for solution for infusion Benlysta 400 mg powder for concentrate for solution for infusion

belimumab

▼ 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 Benlysta is and what it is used for
2. What you need to know before you are given Benlysta
3. How Benlysta is used
4. Possible side effects
5. How to store Benlysta
6. Contents of the pack and other information

1. What Benlysta is and what it is used for

Benlysta as an infusion is a medicine used to treat lupus (systemic lupus erythematosus, SLE) in adults and children (5 years of age and older) whose disease is still highly active despite standard treatment.

Lupus is a disease in which the immune system (the system that fights infection) attacks your own cells and tissues, causing inflammation and organ damage. It can affect almost any organ in the body, and is thought to involve a type of white blood cells called *B cells*.

Benlysta contains **belimumab** (*a monoclonal antibody*). It reduces the number of B cells in your blood by blocking the action of BLYS, a protein that helps B cells to live longer and is found in high levels in people with lupus.

You will be given Benlysta as well as your usual treatment for lupus.

2. What you need to know before you are given Benlysta

Do not receive Benlysta

- if you are **allergic** to belimumab or any of the other ingredients of this medicine (*listed in section 6*).

➔ **Check with your doctor** if this may apply to you.

Warnings and precautions

Talk to your doctor before you are given Benlysta

- if you have a current or long-term **infection** or if you often get infections (*see section 4*). Your doctor will decide if you can be given Benlysta
- if you are planning to have a **vaccination** or have had a vaccination within the last 30 days. Some vaccines should not be given just before or during treatment with Benlysta
- if your lupus **affects your kidneys** or **nervous system**
- if you are **HIV positive** or have **low immunoglobulin** levels
- if you have, or have had, **hepatitis B or C**
- if you have had an **organ transplant** or a **bone marrow** or **stem cell transplant**
- if you have had **cancer**.

→ **Tell your doctor** if any of these may apply to you.

Depression and suicide

There have been reports of depression, suicidal thoughts, and suicide attempts including suicide during treatment with Benlysta. Tell your doctor if you have a history of these conditions. If you experience new or worsening symptoms at any time:

→ **Contact your doctor or go to a hospital straight away.**

If you feel depressed or have thoughts of harming yourself or committing suicide, you may find it helpful to tell a relative or close friend and ask them to read this leaflet. You might ask them to tell you if they are worried about changes in your mood or behaviour.

Look out for important symptoms

People taking medicines that affect their immune system may be more at risk of infections, including a rare but serious brain infection called progressive multifocal leukoencephalopathy (PML).

→ **Read the information ‘Increased risk of brain infection’ in section 4 of this leaflet.**

To improve the traceability of this medicine, your healthcare provider should record the Benlysta lot number in your patient file. You may also wish to make a note of this information in case you are asked for it in the future.

Children

This medicine is not intended for use in children younger than 5 years of age.

Other medicines and Benlysta

Tell your doctor if you are taking any other medicines, if you have recently taken or might take any other medicines.

In particular tell your doctor if you are being treated with medicines that affect your immune system:

- cyclophosphamide (a medicine to treat some cancers and autoimmune disorders)
- any medicine that affects your B cells (to treat cancer or inflammatory diseases).

→ **Tell your doctor.** Using such medicines in combination with Benlysta may make your immune system less effective. This could increase your risk of a serious infection.

Pregnancy and breast-feeding

Contraception in women of childbearing potential

- **Use an effective method of contraception** while you are being treated with Benlysta and for at least 4 months after the last dose.

Pregnancy

Benlysta is not usually recommended if you are pregnant.

- **Tell your doctor if you are pregnant**, think you may be pregnant, or are planning to have a baby. Your doctor will decide if you can be given Benlysta.
- **If you become pregnant** while being treated with Benlysta, tell your doctor.

Breast-feeding

Tell your doctor if you are breast-feeding. It is likely that Benlysta can pass into breast milk. Your doctor will discuss with you whether you should stop treatment with Benlysta while you are breast-feeding, or if you should stop breast-feeding.

Driving and using machines

Benlysta can have side effects which may make you less able to drive or use machines.

Important information about the contents of Benlysta

This medicine contains less than 1 mmol sodium (23 mg) per dose, so it is essentially sodium-free.

3. How Benlysta is used

A nurse or doctor will give you Benlysta through a drip in your vein (intravenous infusion) over one hour.

Adults and children (5 years of age and older)

Your doctor will decide on the correct dose depending on your body weight. The recommended dose is 10 mg for each kilogram (kg) of your body weight.

You are usually given Benlysta on the first day of treatment then again 14 and 28 days later. After this, Benlysta is usually given once every 4 weeks.

Medicine given before an infusion

Your doctor may decide to give you medicines which help to reduce any infusion reactions before you are given Benlysta. These may include a type of medicine called an anti-histamine and a medicine to prevent a high temperature. You will be checked closely and if you do have any reactions these will be treated.

Stopping treatment with Benlysta

Your doctor will decide if you need to stop being given Benlysta.

4. Possible side effects

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

Allergic reactions — get medical help immediately

Benlysta can cause a reaction to the infusion, or an allergic (*hypersensitivity*) reaction.

These are common side effects (may affect up to 1 in 10 people). They can occasionally be severe (uncommon, affecting up to 1 in 100 people), and could be life-threatening. These severe reactions are more likely to happen on the day of your first or second treatment with Benlysta, but can be delayed and occur several days afterwards.

Tell your doctor or nurse immediately, or go to the Emergency department of your nearest hospital, if you get any of the following symptoms of an allergic or infusion reaction:

- swelling of the face, lips, mouth or tongue
- wheezing, difficulty in breathing or shortness of breath
- rash
- itchy raised bumps or hives.

Rarely, less severe delayed reactions to Benlysta can also occur, usually 5 to 10 days after an infusion. They include symptoms such as rash, feeling sick, tiredness, muscle aches, headache, or facial swelling.

If you experience these symptoms, particularly if you get two or more of them together:

→ Tell your doctor or nurse.

Infections

Benlysta can make you more likely to get infections, including infection of the urinary tract and airways, younger children may be at increased risk. These are very common and may affect more than 1 in 10 people. Some infections can be severe and can uncommonly cause death.

If you get any of the following symptoms of an infection:

- Fever and/or chills
- cough, breathing problems
- diarrhoea, vomiting
- burning sensation while passing urine; urinating often
- warm, red or painful skin or sores on your body.

→ Tell your doctor or nurse immediately.

Depression and suicide

There have been reports of depression, suicidal thoughts, and suicide attempts during treatment with Benlysta. Depression can affect up to 1 in 10 people, suicidal thoughts and suicide attempts can affect up to 1 in 100 people. If you feel depressed, have thoughts about harming yourself or other distressing thoughts, or if you are depressed and notice that you feel worse or develop new symptoms:

→ Contact your doctor or go to a hospital straight away.

Increased risk of brain infection

Medicines that weaken your immune system, such as Benlysta, may put you at higher risk of getting a rare but serious and life-threatening brain infection called *progressive multifocal leukoencephalopathy* (PML).

Symptoms of PML include:

- memory loss
- trouble in thinking
- difficulty with talking or walking
- loss of vision.

→ Tell your doctor immediately if you have any of these symptoms, or similar problems that have lasted over several days.

If you already had these symptoms before you started treatment with Benlysta:

→ **Tell your doctor immediately** if you notice any changes in these symptoms.

Other possible side effects:

Very common side effects

These may affect **more than 1 in 10** people:

- bacterial infections (*see 'Infections' above*)
- feeling sick, diarrhoea.

Common side effects

These may affect **up to 1 in 10** people:

- high temperature or fever
- low white blood cell count (can be seen in blood tests)
- nose, throat or stomach infection
- pain in hands or feet
- migraine.

Uncommon side effects

These may affect **up to 1 in 100** people:

- itchy, bumpy rash (hives), skin rash.

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 Benlysta

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

Store in a refrigerator (2°C to 8°C).

Do not freeze.

Store in the original package in order to protect from light.

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

6. Contents of the pack and other information

What Benlysta contains

- The active ingredient is belimumab.
 - Each 5 ml vial contains 120 mg belimumab.
 - Each 20 ml vial contains 400 mg belimumab.

After reconstitution, the solution contains 80 mg belimumab per ml.

- The other ingredients are citric acid monohydrate (E330), sodium citrate (E331), sucrose and polysorbate 80. See 'Important information about the contents of Benlysta' in section 2 for further information.

What Benlysta looks like and contents of the pack

Benlysta is supplied as a white to off-white powder for solution for infusion, in a glass vial with a siliconised rubber stopper and a flip-off aluminium seal.

There is 1 vial in each pack.

Marketing Authorisation Holder

GlaxoSmithKline UK Limited
980 Great West Road
Brentford
Middlesex
TW8 9GS
United Kingdom

Manufacturer

GlaxoSmithKline Manufacturing S.P.A.
Strada Provinciale Asolana No. 90
I-43056 San Polo di Torrile
Parma
Italy

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The following information is intended for healthcare professionals only:

Instructions for use and handling – reconstitution, dilution and administration

In order to improve traceability of biological medicinal products, the tradename and the batch number of the administered product should be clearly recorded.

1) How to reconstitute Benlysta

Reconstitution and dilution needs to be carried out under aseptic conditions.

Allow 10 to 15 minutes for the vial to warm to room temperature (15°C to 25°C).

It is recommended that a 21-25 gauge needle be used when piercing the vial stopper for reconstitution and dilution.

WARNING: The 5 ml and 20 ml vials are reconstituted with different volumes of diluent, see below:

120 mg vial

The 120 mg single-use vial of Benlysta is reconstituted with 1.5 ml of water for injections to yield a final concentration of 80 mg/ml belimumab.

400 mg vial

The 400 mg single-use vial of Benlysta is reconstituted with 4.8 ml of water for injections to yield a final concentration of 80 mg/ml belimumab.

Amount of Benlysta	Vial size	Volume of diluent	Final concentration
120 mg	5 ml	1.5 ml	80 mg/ml
400 mg	20 ml	4.8 ml	80 mg/ml

The stream of water for injections should be directed toward the side of the vial to minimize foaming. Gently swirl the vial for 60 seconds. Allow the vial to sit at room temperature (15°C to 25°C) during reconstitution, gently swirling the vial for 60 seconds every 5 minutes until the powder is dissolved. Do not shake. Reconstitution is typically complete within 10 to 15 minutes after the water has been added, but it may take up to 30 minutes. Protect the reconstituted solution from sunlight.

If a mechanical reconstitution device is used to reconstitute Benlysta it should not exceed 500 rpm and the vial should be swirled for no longer than 30 minutes.

2) Before diluting Benlysta

Once reconstitution is complete, the solution should be opalescent and colorless to pale yellow, and without particles. Small air bubbles, however, are expected and acceptable.

120 mg vial

After reconstitution, a volume of 1.5 ml (corresponding to 120 mg belimumab) can be withdrawn from each 5 ml vial.

400 mg vial

After reconstitution, a volume of 5 ml (corresponding to 400 mg belimumab) can be withdrawn from each 20 ml vial.

3) How to dilute the solution for infusion

The reconstituted medicinal product is diluted to 250 ml with sodium chloride 9 mg/ml (0.9%), sodium chloride 4.5 mg/ml (0.45%), or Lactated Ringer's solution for injection. For patients whose body weight is less than or equal to 40 kg, infusion bags with 100 ml of these diluents may be considered providing that the resulting belimumab concentration in the infusion bag does not exceed 4 mg/ml.

5% glucose intravenous solutions are incompatible with Benlysta and must not be used.

From a 250 ml (or 100 ml) infusion bag or bottle of sodium chloride 9 mg/ml (0.9%), sodium chloride 4.5 mg/ml (0.45%), or Lactated Ringer's solution for injection, withdraw and discard a volume equal to the volume of the reconstituted Benlysta solution required for the patient's dose. Then add the required volume of the reconstituted Benlysta solution into the infusion bag or bottle. Gently invert the bag or bottle to mix the solution. Any unused solution in the vials must be discarded.

Inspect the Benlysta solution visually for particulate matter and discoloration prior to administration. Discard the solution if any particulate matter or discoloration is observed.

The reconstituted solution, if not used immediately, should be protected from direct sunlight and stored refrigerated at 2°C to 8°C. Solutions diluted in sodium chloride 9 mg/ml (0.9%), sodium chloride 4.5 mg/ml (0.45%), or Lactated Ringer's solution for injection may be stored at 2°C to 8°C or room temperature (15°C to 25°C).

The total time from reconstitution of Benlysta to completion of infusion should not exceed 8 hours.

4) How to administer the diluted solution

Benlysta is infused over a 1 hour period.

Benlysta should not be infused concomitantly in the same intravenous line with other agents.

No incompatibilities between Benlysta and polyvinylchloride or polyolefin bags have been observed.
