PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE

PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a physician's prescription only

Benlysta 120 mg

Powder for concentrate for solution for infusion

Each vial contains:

120 mg of belimumab (80 mg/ml after reconstitution)

Benlysta 400 mg

Powder for concentrate for solution for infusion

Each vial contains:

400 mg of belimumab (80 mg/ml after reconstitution)

For the list of inactive and allergenic ingredients, see section 2 – "Important information about some of the ingredients in this medicine" and section 6 "Further information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the physician or 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?

Benlysta is indicated as an add-on therapy in patients from the age of 5 years and up with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy.

Benlysta, in combination with immunosuppressive therapies, is intended for the treatment of adult patients with active lupus nephritis.

Therapeutic group: selective immunosuppressant.

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. The disease 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 human 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 in addition to your usual treatment for lupus.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are **sensitive (allergic)** to belimumab or any of the additional ingredients contained in the medicine (detailed in section 6).

→ **Check with your physician** if this may apply to you.

Special warnings regarding use of the medicine

Before the treatment with Benlysta, tell the physician if:

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

→ **Tell your physician** 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 physician if you have a history of these conditions. If you experience new or worsening symptoms at any time:

→ **Contact your physician 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 behavior.

<u>Look out for important symptoms</u>

Patients taking medicines that affect their immune system may be more at risk of

contracting infections, including a rare but serious brain infection called progressive multifocal leukoencephalopathy (PML).

→ **For further information, read "Increased risk of brain infection" in section 4 of this leaflet.**

Children and adolescents

This medicine is not intended for use:

- in children under 5 years of age with SLE (lupus).
- in children and adolescents (under 18 years of age) with active lupus nephritis.

Drug interactions:

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the physician or pharmacist. Especially if you are taking medicines that affect the immune system, including any medicine that affects your B cells (to treat cancer or inflammatory diseases).

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

Pregnancy and breast-feeding

Contraceptives in women of child-bearing potential

Use an effective method of contraception during treatment with Benlysta and for at least 4 months after the last dose.

Pregnancy

Benlysta is not usually recommended if you are pregnant.

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

Breast-feeding

Tell your physician if you are breast-feeding. It is likely that Benlysta can pass into breast milk. Your physician 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 operating machinery

Benlysta can cause side effects that may impair your ability to drive or operate machinery.

Important information about some of the ingredients in this medicine

Important information on the contents of Benlysta:

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

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the physician's instructions.

Check with the physician or the pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the physician only.

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

Instructions in English for preparation for healthcare professionals are in section "Instructions for use and handling" at the end of this leaflet.

Adults and children (from 5 years of age and up)

Your physician will determine the correct dose according to your body weight. The usual dosage is generally 10 mg for each kilogram (kg) of your body weight.

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

Medicines given before the infusion

Your physician may decide to give you medicines which help 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 closely monitored and if you do have any reactions, they will be treated.

Stopping treatment with Benlysta

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the physician.

Your physician will decide if you need to stop using Benlysta.

Do not exceed the recommended dose

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a physician or proceed to a hospital emergency room, and bring the package of the medicine with you.

Adhere to the treatment regimen recommended by the physician.

Do not take medicines in the dark! Check the label and dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the physician or the pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Benlysta may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Allergic reactions – refer for medical help immediately

Benlysta can cause an infusion reaction or an allergic (hypersensitivity) reaction. These side effects are common (may occur in up to one user in 10).

These effects can occasionally be severe (uncommon side effects, occur in up to one user in 100), and could be life-threatening. These severe effects are more likely to happen on the day of your first or second treatment, but they can be delayed and occur a few days later.

Tell your physician or nurse immediately, or proceed to the emergency room of the nearest hospital, if you experience 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 bumps on the skin or hives

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

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

→ **tell the physician or nurse.**

Infections

Benlysta can make you more likely to get infections, including infections of the urinary and respiratory tracts. Younger children may be at increased risk. These side effects are very common and occur in more than one user in 10. Some of the infections can be severe and infrequently, can cause death.

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

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

→ **Refer to your physician or nurse immediately.**

Depression and suicide

There have been reports of depression, suicidal thoughts, and suicide attempts during treatment with Benlysta. Depression can occur in up to 1 in 10 users, suicidal thoughts and suicide attempts can occur in up to 1 in 100 users. 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 physician 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 thinking
- difficulty talking or walking
- loss of vision

→ **Tell your physician** immediately if you experience any of these symptoms, or similar problems that lasted more than several days.

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

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

Additional side effects:

Very common side effects – occur in more than one user in 10:

- bacterial infections (see "Infections" section above)
- nausea, diarrhea.

Common side effects – occur in up to one user in 10:

- high temperature
- low white blood cell count (can be identified in a blood test)

- nose, throat, or stomach infection
- pain in hands or feet
- migraine

Uncommon side effects – occur in up to one user in 100:

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

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 with the physician.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the physician.

Do not use the medicine after the expiry date (exp. Date) that appears on the carton. The expiry date refers to the last day of that month.

Store in a refrigerator (between 2°C to 8°C).

Do not freeze.

For single use only.

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

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

sucrose, sodium citrate dihydrate, polysorbate and citric acid monohydrate.

For further information, see section 2 **"Important information about some of the ingredients in this medicine"**.

What the medicine looks like and the contents of the package:

Benlysta is supplied as a white to off-white powder for preparation of an infusion solution, in a glass vial, sealed with aluminum and a silicon cap.

Each package contains one vial.

License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.

Manufacturer: Glaxo Group Ltd., Brentford, UK.

Revised in November 2021 according to MoH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Benlysta 120 mg: 147-37-33499

Benlysta 400 mg: 147-38-33510

Ben PT v6