PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

Gazyva®; concentrate for solution for infusion 1 000 mg/40 mL (or 25 mg/mL)

The active substance is obinutuzumab

Contains sugar (trehalose)

Read all of this leaflet carefully before you start receiving Gazyva

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist, nurse, or other health care provider.

What is in this leaflet

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

1. What Gazyva is and what it is used for

Gazyva contains the active substance obinutuzumab, which belongs to a group of medicines called “monoclonal antibodies”. Antibodies work by attaching themselves to specific targets in your body.

Gazyva kills certain cancer cells.

Gazyva can be used in adults to treat two different types of cancer:

- **Chronic lymphocytic leukaemia** (also called “CLL”)

Gazyva is used in patients who have not had any treatment for CLL before and who have other illnesses which make it unlikely that they would be able to tolerate a full dose of a different medicine used to treat CLL called fludarabine.

Gazyva is used together with another medicine for cancer called chlorambucil.

- **Follicular lymphoma** (also called “FL”)
  - Gazyva is used in patients who have not had any treatment for FL
  - Gazyva is used in patients who have had at least one treatment with a medicine called rituximab before and whose FL has come back or got worse after this treatment.
  - At the start of treatment for FL, Gazyva is used together with other medicines for cancer.
  - Gazyva can then be used on its own for up to 2 years as a “maintenance treatment”.

How Gazyva works

CLL and FL are types of cancer that affect white blood cells called “B-lymphocytes”. The affected “B-lymphocytes” multiply too quickly and live too long. Gazyva binds to targets on the surface of the affected “B lymphocyte” cells and causes them to die.

When Gazyva is given to patients with CLL or FL together with other medicines for cancer - this slows down the time it takes for their disease to get worse.

2. What you need to know before Gazyva is administered to you

You must not be given if:

- you are hypersensitive (allergic) to obinutuzumab or any of the other ingredients of this medicine.
- you have active infections.
- you have active hepatitis B infection.
- you require to have vaccinations with live vaccines prepared from microorganisms without their virulence altered. Examples include smallpox and adenovirus vaccines.
- you are pregnant or breastfeeding your baby.

Warnings and precautions

Talk to your doctor or nurse before you are given Gazyva if:

- you have an infection, or have had an infection in the past which lasted a long time or keeps coming back;
- you have ever taken, or been given, medicines which affect your immune system (such as chemotherapy or immunosuppressants);
- you are taking medicines for high blood pressure or medicines used to thin your blood – your doctor might need to alter how you take these;
- you have ever had heart problems;
- you have ever had brain problems (such as memory problems, difficulty moving or feeling sensations in your body, eyesight problems);
- you have ever had breathing problems or lung problems;
- you have ever had “hepatitis B” - a type of liver disease;
- you are due to have a vaccine or you know you may need to have one in the near future.

If any of the above apply to you (or you are not sure), talk to your doctor or nurse before you are given Gazyva.

Children and adolescents

Do not give Gazyva to children or young people under 18 years of age. This is because there is no information about its use in these age groups.

Other medicines and Gazyva

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

Pregnancy, Breastfeeding and Fertility

If you are pregnant or breastfeeding, please consult your doctor, pharmacist or other healthcare professional for advice before taking this medicine.

Pregnancy: Tell your doctor or nurse if you are pregnant, think you might be pregnant or are planning to have a baby. They will help you weigh up the benefit of continuing Gazyva against the risk to your baby. If you become pregnant during treatment with Gazyva, tell your doctor or

nurse as soon as possible. This is because treatment with Gazyva may affect yours or the baby's health.

***Breastfeeding*:** Do not breastfeed during treatment with Gazyva or for 18 months after stopping treatment with Gazyva. This is because small amounts of the medicine may pass into your breast milk.

***Contraception*:** Use an effective method of contraception while being treated with Gazyva. Continue to use effective contraception for 18 months after stopping treatment with Gazyva.

Driving and using machinery

Gazyva is not likely to affect your ability to drive, cycle or use any tools or machines. However, if you get an infusion related reaction (see Possible Side Effects), do not drive, cycle or use any tools or machines until the reaction stops.

3. How Gazyva is given

Gazyva is given under the supervision of a doctor experienced in such treatment. It is given into a vein as a drip (intravenous infusion) over several hours. Your doctor will tell you how long your treatment with Gazyva will last.

The Gazyva treatment

Chronic lymphocytic leukaemia

You will be given 6 treatment cycles of Gazyva in combination with another medicine for cancer called chlorambucil. Each cycle lasts 28 days.

Follicular lymphoma

You will be given 6 or 8 treatment cycles of Gazyva in combination with other medicines for cancer - each cycle lasts 28 or 21 days. depending on which other cancer medicines are given together with Gazyva.

This induction phase will be followed by a "maintenance phase" - during this time you will be given Gazyva every 2 months for up to 2 years as long as your disease does not progress. Based on your disease status after the initial treatment cycles your doctor will decide whether you will receive treatment in the maintenance phase.

Induction phase

Cycle 1 - this will include three doses of Gazyva in the 28 or 21 days depending on which other cancer medicines are given together with Gazyva.

Cycles 2-6 or 2-8 - this will be just one dose of Gazyva in the 28 or 21 days depending on which other cancer medicines are given together with Gazyva.

Maintenance phase

Full dose once every 2 months for up to 2 years as long as your disease does not progress.

Medicines given before each infusion

Before each infusion of Gazyva, you will be given medicines to lessen the chance of getting infusion related reactions or tumour lysis syndrome. These may include:

- fluids
- medicines to reduce a fever;
- medicines to reduce pain (analgesics);
- medicines to reduce inflammation (corticosteroids);
- medicines to reduce an allergic reaction (anti-histamines);
- medicine to prevent tumour lysis syndrome (such as allopurinol).

Do not share medicines prescribed for you with any other person.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Since a healthcare professional will administer this medicine, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you miss a Gazyva treatment

If you miss your appointment, make another one as soon as possible. This is because for this medicine to be as effective as possible, it is important to follow the dosing schedule.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Gazyva can have side effects.

Not all side effects reported for Gazyva are included in this leaflet. Should your general health worsen or if you experience any untoward effects while on Gazyva, please consult your health care provider for advice.

Gazyva can cause some serious side effects that you need to tell your doctor or nurse about immediately. These include:

- *Infusion related reactions*

Tell your doctor or nurse straight away if you get any of the infusion related reactions listed below. Infusion reactions can happen during the infusion or any time in the 24 hours after the infusion.

If you get infusion reactions, you may require additional treatment, or the infusion may need to be slowed down or stopped. When these symptoms go away, or improve, the infusion can be continued. These reactions are more likely to happen with the first infusion. Your doctor may decide to stop treatment with Gazyva treatment if you have a severe infusion related reaction. Before each infusion of Gazyva, you will be given medicines which help to reduce possible infusion reactions or “tumour lysis syndrome”. Tumour lysis syndrome is a potentially life-threatening complication, caused by chemical changes in the blood due to the breakdown of dying cancer cells.

Tell your doctor or nurse straight away if you get any of the following symptoms during your infusion or up to 24 hours after having your infusion.

Most frequently reported:

- nausea
- fatigue
- dizziness
- headache
- diarrhoea
- fever, flushing or chills
- vomiting
- shortness of breath

- low or high blood pressure
- heart beating very fast
- chest discomfort

Less frequently reported:

- irregular heartbeat
- swelling of the throat or airway
- wheezing, difficulty breathing, tight chest or throat irritation

If you get any of the above, tell your doctor or nurse straight away.

- *Progressive multifocal leukoencephalopathy (also called "PML")*

Progressive multifocal leukoencephalopathy (PML) is a very rare and life-threatening brain infection that has been reported in very few patients having treatment with Gazyva.

Tell your doctor or nurse straight away if you have memory loss, trouble speaking, difficulty walking or problems with your eyesight. If you had these symptoms before treatment with Gazyva, tell your doctor straight away if you notice any changes in them. You may need medical treatment.

- *Infections*

Tell your doctor or nurse straight away if you get any signs of infection after your Gazyva treatment. You may be more likely to get an infection after treatment with Gazyva. Often these are colds, but there have been cases of more severe infections. A type of liver disease called "hepatitis B" has also been reported to reoccur in patients who have had hepatitis B in the past.

Tell your doctor or nurse straight away if you get any signs of infection after your Gazyva treatment. These include:

- fever
- cough
- chest pain
- fatigue
- painful rash

- sore throat
- burning pain when passing urine
- feeling weak or generally unwell.

If you had recurring or chronic infections before the start of Gazyva treatment, tell your doctor about it.

- *Disseminated Intravascular Coagulation (DIC)*

DIC is a rare but serious condition that causes abnormal blood clotting throughout the body's blood vessels. Talk to your health care provider if you experience bleeding from many places in the body, blood clots, bruising, drop in blood pressure, shortness of breath, confusion, memory loss or change of behaviour, fever.

These are all very serious side effects. If you have them, you may have had a serious reaction to Gazyva. You may need urgent medical attention or hospitalisation.

Other side effects:

Tell your doctor or nurse if you notice any of the following side effects:

More frequent side effects:

- fever
- lung infection
- headache
- joint pain, back pain
- feeling weak
- feeling tired
- pain in arms and legs
- diarrhoea
- constipation
- sleeplessness
- hair loss

- itchiness
- urinary tract infection
- nose and throat inflammation
- shingles
- changes in blood tests:
- anaemia (low levels of red blood cells),
- low levels of all types of white blood cells (combined)
- low levels of neutrophils (a type of white blood cell)
- a low level of platelets (a type of blood cell that helps your blood to clot)
- infection of upper airways (infection of nose, pharynx, larynx and sinuses), cough
- Pneumonia
- Insomnia (finding it difficult to sleep)

Frequent:

- cold sores
- depression, anxiety
- flu (influenza)
- weight increase
- runny or blocked nose
- eczema
- muscle and bone pain in your chest
- skin cancer (squamous cell carcinoma, basal cell carcinoma)
- bone pain
- irregular heart beat (atrial fibrillation)
- problems with urinating, urinary incontinence
- problems with digestion (e.g. heartburn), haemorrhoids
- changes shown in blood tests:

  - low levels of all types of white blood cells (combined), low levels of lymphocytes (a type of white blood cell), fever associated with low levels of neutrophils (a type of white blood cells)
  - increase in potassium, phosphate or uric acid - which can cause kidney problems (part of tumour lysis syndrome)
  - decrease in potassium.
- basal cell carcinoma (a type of skin cancer)
- febrile neutropenia - the development of fever, often with other signs of infection
- earache
- fatigue

Less frequent:

- a hole in the stomach or intestines (gastrointestinal perforation, especially in cases where the cancer affects the gastrointestinal tubes)

Tell your doctor or nurse if you notice any of the side effects listed above.
If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of Gazyva.

5. How to store Gazyva

Store all medicines out of reach of children.

Gazyva will be stored by the healthcare professionals at the hospital or clinic. The storage details are as follows: For single use only. Discard any unused concentrate after initial opening.

- Do not use this medicine after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.
- Store in a refrigerator (2 - 8 °C). Do not freeze. Do not shake.
- Keep the vial in the outer carton in order to protect from light.

Medicines should not be disposed of via wastewater or household waste. Your healthcare professional will throw away any medicines that are no longer being used. These measures will help protect the environment.

6. Contents of the pack and other information

What Gazyva contains

The active substance is obinutuzumab: 1 000 mg/40 mL per vial corresponding to a concentration before dilution of 25 mg/mL.

The other ingredients are L-histidine, L-histidine hydrochloride monohydrate, poloxamer 188, trehalose dihydrate, and water for injections.

What Gazyva looks like and contents of the pack

Gazyva is a concentrate for solution for infusion and is a colourless to slightly brown liquid, free from visible particulate matter, provided in sterile, preservative-free, non-pyrogenic, single dose vials.

Pack of 1 vial in a carton. Clear, colourless 50 mL Type I glass vial with a laminated grey butyl stopper. The two-piece crimp closure for the vial consists of a silver aluminium metal cap sealed with a red plastic flip-off disc.

Holder of Certificate of Registration

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This leaflet was last revised on

29 July 2025

Registration number

49/30.1/1142