PRODUCT MONOGRAPH

Pr GAZYVA®

obinutuzumab

25 mg/mL Concentrate for Solution for Infusion

Professed Standard

Antineoplastic

Hoffmann-La Roche Limited
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Date of Approval:
August 9, 2018

Submission Control No: 208089

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PART III: CONSUMER INFORMATION

[Pr]GAZYVA®
obinutuzumab
(pronounced: ga zye' vah)

This leaflet is part III of a three-part "Product Monograph" published when GAZYVA was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about GAZYVA. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
GAZYVA contains obinutuzumab, which belongs to a group of medicines called monoclonal antibodies and is used to treat two different types of cancer.

- Chronic Lymphocytic Leukaemia (CLL)
  - GAZYVA is used in adults who have not had any treatment before. It is used together with another medicine for cancer called chlorambucil.
- Follicular Lymphoma (FL) - a type of Non-Hodgkin Lymphoma. GAZYVA is used:
  - in combination with other cancer medications to treat patients with stage II bulky, III or IV follicular lymphoma (FL) who have not been treated for FL before.
  - with another medicine for cancer, called bendamustine, 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.
    - Patients who respond to treatment with GAZYVA in combination with other cancer medications can continue to be treated with GAZYVA on its own (monotherapy) for up to 2 years.".

CLL and FL are types of cancers of the blood which affect a type of white blood cell called "B lymphocytes". The affected B lymphocytes multiply too quickly and live too long. This means that there are too many of them circulating in your blood. CLL can also make your lymph nodes get larger; they are part of a network of vessels running round your body that is filled with clear watery fluid called "lymph".

What it does:
GAZYVA binds to the surface of the "B lymphocyte" cells and causes them to die.

When it should not be used:
If you are allergic to obinutuzumab, any of the other ingredients of this medicine, or the container it is in.

What the medicinal ingredient is:
obinutuzumab.

What the non-medicinal ingredients are (alphabetical order):
L-histidine, L-histidine hydrochloride, poloxamer 188, trehalose, water for injection.

What dosage forms it comes in:
Each 50 mL single-use glass vial contains a single 1000 mg dose of obinutuzumab in 40 mL of liquid concentrate (25 mg/mL), to be diluted in 0.9% aqueous sodium chloride solution, for intravenous administration. GAZYVA is available in a pack containing 1 vial.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions
In patients treated with GAZYVA, the following serious side effects have occurred and were fatal in some cases:

- Severe and life-threatening infusion reactions.
- Recurrence of hepatitis B virus infection can occur with GAZYVA treatment.
- Serious and life threatening brain condition called progressive multifocal leukoencephalophathy (PML).
- Tumour Lysis Syndrome (TLS) that is caused by breakdown of tumour cells and may lead to kidney damage.
- Serious, including fatal, cardiovascular events could occur in patients with GAZYVA treatment.
- Serious and life-threatening infections, some of which resulted in death.
- Serious and life-threatening thrombocytopenia (low level of cells that help to stop bleeding). This may result in bleeding or promote bleeding caused by other factors.
- See below for signs and symptoms of these serious side effects. Immediately report to your doctor if you notice any of the described symptoms.

BEFORE you use GAZYVA talk to your health professional if:

- You have an infection
- You have ever taken medicines which affect your immune system (such as chemotherapy or immunosuppressants)
- You are taking medicine which may increase bleeding risk (platelet inhibitors, anticoagulants)
- You are taking medicines for high blood pressure; your doctor might need to change how you take these.
- You have ever had heart problems
- You have ever had breathing problems or lung problems
- You have ever had a liver disease called hepatitis
- You are due to have a vaccine or may need one in the near future

GAZYVA has not been studied in pregnant or breastfeeding women. If you are pregnant, could become pregnant or are breastfeeding, be sure to discuss with your doctor whether GAZYVA is right for you. Women should avoid pregnancy and use effective birth control methods during treatment with GAZYVA and for 18 months after the last dose GAZYVA. Women should avoid breastfeeding during treatment and for 18 months after the last dose of GAZYVA. If you have given birth while on GAZYVA treatment, your newborn will be monitored for reduced immunity. Postponing your child's vaccinations, that use live virus vaccines, may be considered until your child's immunity levels are acceptable.

What are the possible side effects from using GAZYVA:

Infusion related reactions: GAZYVA is an infusion ("drip") which is given intravenously (into your veins). Very commonly patients being given GAZYVA have some side effects while the infusion is being given. Most patients are also given medication such as acetaminophen, antihistamines, and steroids (such as prednisone) for allergic reactions before the infusion to prevent these reactions. If you notice any trouble breathing, feel hot or shivery, have hives or an itchy rash, tell the person giving you the infusion immediately; these side effects are more common with the first infusions of GAZYVA, and decreased with subsequent infusions of GAZYVA. If you develop any of these symptoms, the infusion will be slowed down or stopped for a while. Once these symptoms go away, or improve, the infusion can be continued.

Heart Disease: If you have ever had heart disease, your doctor will take special care of you during therapy with GAZYVA.

Hepatitis B infection: Tell the doctor if you had or think you had hepatitis; you will be carefully checked for signs of active hepatitis B virus.

Infection: While you 're taking GAZYVA, you may develop infections. Some of these infections may be fatal and severe, so be sure to talk to your doctor if you think you have an infection. The symptoms of infection can include one or more of the following: fever of 38ºC or greater, chills, cough, sore throat, or pain on urination. Patients administered GAZYVA in combination with chemotherapy, followed by GAZYVA alone are at a high risk of infections during and after treatment. Patients with a history of recurring or chronic infections may be at an increased risk of infection. Patients with an active infection should not be treated with GAZYVA. Patients taking GAZYVA plus bendamustine may be at higher risk for fatal or severe infections compared to patients taking GAZYVA plus CHOP or CVP.

Progressive multifocal leukoencephalopathy (PML): Cases of PML have been observed in patients treated with GAZYVA. PML is a condition that causes nerve damage within the brain. Tell your doctor immediately if you have memory loss, trouble thinking, and difficulty with walking, clumsiness, falls or weakness on one side of the body, changes in mood or loss of vision. Your doctor will check if you need to see a neurologist.

Tumour Lysis Syndrome (TLS): Cases of TLS have been reported during the use of GAZYVA. TLS is a condition that causes sudden kidney failure and abnormal heart rhythms due to changes in blood chemistry, which may be fatal. Tell your doctor immediately if you have palpitations/irregular heartbeats; vomiting; fatigue/weakness; difficulty concentrating/trouble thinking; swelling, numbness or tingling in hands, face or feet; back pain; muscle cramps; fainting or trouble breathing. Some patients with TLS in its early stages have no symptoms, and your doctor will be performing blood tests for this and other side effects.

Low White Blood Cell Count: When you have an abnormally low count of infection-fighting white blood cells, it is called neutropenia. While you are taking GAZYVA, your doctor will do blood work to check your white blood cell count. Severe and life-threatening neutropenia can develop during or after treatment with GAZYVA. Some cases of neutropenia can last for more than one month. If your white blood cell count is low, your doctor may prescribe medication to help prevent infections.

Low Platelet Count: Platelets help stop bleeding or blood loss. GAZYVA may reduce the number of platelets you have in your blood; having low platelet count is called thrombocytopenia. This may affect the clotting process. While you are taking GAZYVA, your doctor will do blood work to check your platelet count. Severe and life-threatening thrombocytopenia can develop during treatment with GAZYVA. Fatal bleeding events have occurred in patients treated with GAZYVA. If your platelet count gets too low, your treatment may be delayed or reduced.

Gastrointestinal perforation (a hole in the stomach or intestines): Gastrointestinal perforation has been reported in patients treated with GAZYVA. Most cases occurred in patients with Non-Hodgkin Lymphoma. One patient died of gastrointestinal perforation. Some patients experienced serious events.

Allergic reactions: Immediate (e.g. anaphylaxis) and delayed (e.g. serum sickness) allergic reactions have been reported in patients treated with GAZYVA. If an allergic reaction is suspected during or after an infusion (e.g. symptoms typically occurring after previous exposure and very rarely with the first infusion), your doctor will permanently take you off treatment.

INTERACTIONS WITH THIS MEDICATION

Before starting treatment, please tell your health professional if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription and herbal medicines.

PROPER USE OF THIS MEDICATION

Usual dose:
A health professional in a healthcare facility will give you GAZYVA as prescribed by your doctor. It is given into a vein (intravenously) as a drip (infusion) over several hours.

Chronic Lymphocytic Leukaemia
You will be given 6 treatment cycles of GAZYVA. Each cycle lasts 28 days. A typical schedule is shown below.

Your first cycle:
- Day 1 – 100 mg
- Day 1 (continued) or Day 2 – 900 mg
- Day 8 – 1000 mg
- Day 15 – 1000 mg

If you are able to tolerate the first 100 mg of the infusion on Day 1 without any changes to the infusion rate or interruptions to the

infusion, the second 900 mg infusion may be given on Day 1 as well.

Your next cycles 2, 3, 4, 5, and 6:
- Day 1 – 1000 mg.

Follicular Lymphoma (that has returned)
You will be given 6 treatment cycles of GAZYVA with bendamustine (each cycle lasts 28 days) followed by GAZYVA only treatment (infusion every 2 months) for up to 2 years. A typical schedule is shown below.

Your first cycle:
- Day 1 – 1000 mg
- Day 8 – 1000 mg
- Day 15 – 1000 mg

Your next cycles 2, 3, 4, 5, and 6, as well as monotherapy:
- Day 1 – 1000 mg.

Follicular Lymphoma (previously untreated)

You will be given 6 treatment cycles of GAZYVA with bendamustine (each cycle lasts 28 days) or 6 treatment cycles of GAYZVA with CHOP (each cycle lasts 21 days) followed by 2 additional cycles of GAZYVA alone, or 8 treatment cycles of GAZYVA with CVP (each cycle lasts 21 days). If your lymphoma responds to the treatment, you will be given GAZYVA-only treatment (infusion every 2 months) for up to 2 years or until your cancer returns. A typical schedule is shown below.

Your first cycle:
- Day 1 – 1000 mg
- Day 8 – 1000 mg
- Day 15 – 1000 mg

Your next cycles 2-6 or 2-8, as well as monotherapy:
- Day 1 – 1000 mg.

Before each infusion of GAZYVA, you will be given medicines which help to reduce possible infusion reactions or tumour lysis syndrome. These may include
- Fluids
- Medicines to reduce an allergic reaction (anti-histamines)
- Medicines to reduce inflammation (corticosteroids)
- Painkillers (analgesics)
- Medicines to reduce a fever
- Medicines to prevent "tumour lysis syndrome"

Overdose:
It is unlikely that you will receive too much GAZYVA as you will be closely monitored by health professionals during your infusion. However, if you suspect you received too much GAZYVA, contact your doctor and poison control centre immediately.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:
If you miss a dose of GAZYVA, contact your doctor immediately. Your doctor will decide when you should receive your next dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Unwanted effects are possible with all medicines. Talk to your doctor, nurse or pharmacist if you are worried about side effects or find them very bothersome, and report any new or continuing symptoms to your doctor immediately. Your doctor will be able to tell you what to do and may be able to help you with these side effects.

Very common (may affect more than 1 in 10 patients):
- Infusion reactions (symptoms include skin rash, trouble breathing, feel hot or shivery, have hives)
- Decreased number of white blood cells (symptoms could include fever, sore throat, infection)
- Decreased number of platelets in the blood (symptoms could include fatigue, weakness)
- Nausea
- Decreased number of red blood cells in the blood that carry oxygen (symptoms include feeling of weakness or fatigue in general or during exercise, poor concentration)
- Diarrhoea
- Fever
- Constipation
- Hair loss
- Headache
- Vomiting

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Very Common (occurring in at least 1 of every 10 patients)	Infusion reaction (e.g. trouble breathing, feel hot or shivery, have hives or an itchy rash)		✓	
Common (occurring between 1 and 10 of every 100 patients)	Decreased number of white blood cells (symptoms could include fever, sore throat, infection)		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
	Symptoms of tumour lysis syndrome, which causes kidney problems, such as producing less urine than normal and muscle spasms.		✓	
	Symptoms of gastrointestinal perforations (a hole in the stomach or intestines) such as abdominal pain, constipation and vomiting.		✓	
Uncommon (occurring between 1 and 10 of every 1000 patients)	Symptoms of infection that include: -fever, temperature at 38ºC or higher. -Sore throat -Cough -Any redness or swelling -Pain when you pass your urine		✓	
	Decreased number of platelets in the blood (symptoms could include fatigue, weakness)		✓	
	Chest pain, fast heart rate or an irregular or uneven heart rate		✓	
	Symptoms of PML, such as memory loss, difficulty with walking or loss of vision.		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Rare (occurring between 1 and 10 of every 10,000 patients)	Symptoms of Hepatitis B virus, such as mild fever, feeling of sickness, fatigue, loss of appetite, joint and/or abdominal pain and yellowing of whites of the eyes, skin and tongue.		✓	

This is not a complete list of side effects. For any unexpected effects while taking GAZYVA, contact your doctor or pharmacist.

HOW TO STORE IT

GAZYVA will be stored by the health professionals at the hospital or clinic. The storage details are as follows:

- Store in a refrigerator (2 – 8 ^{o}C)
- Do not use this medicine after the expiry date shown on the vial and carton
- Keep vial in outer carton to protect from light.
- Do not freeze or shake.

Do not throw away any medicines via wastewater or household waste. Your health professional will properly discard any medicines that are no longer being used.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at: www.rochecanada.com or by contacting the sponsor, Hoffmann-La Roche Limited, at: 1-888-762-4388.

This leaflet was prepared by Hoffmann-La Roche Limited.

Last revised: July 5, 2018

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