PROPOSED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

Columvi 2,5 mg/2,5 mL; Concentrate for solution for infusion

Columvi 10 mg/10 mL; Concentrate for solution for infusion

The active substance is glofitamab

Contains sugar (sucrose) 205,4 mg for 2,5 mg/2,5 mL vial,

and 821,5 mg for 10 mg/10 mL vial

Read all of this leaflet carefully before you are given Columvi

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

What is in this leaflet

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

1. What Columvi is and what it is used for

What Columvi is

Columvi is a cancer medicine that contains the active substance glofitamab.

What Columvi is used for

Columvi is used to treat adults with a cancer called “diffuse large B-cell lymphoma” (DLBCL). Columvi can be given alone (monotherapy) or with chemotherapy medicines.

- Columvi is used alone when the cancer has come back (relapsed) or did not respond to previous treatments (refractory) and when you have received two or more prior treatments.
- Columvi is used with the medicines gemcitabine and oxaliplatin when the cancer has come back (relapsed) or did not respond to previous treatments (refractory) and when you cannot receive a stem cell transplant.

Diffuse large B-cell lymphoma is a cancer of a part of your immune system (the body’s defences).

- It affects a type of white blood cell called ‘B-cells’.
- In DLBCL, B cells multiply in an uncontrolled manner and build up in your tissues.

How Columvi works

Columvi binds to the surface of these cancerous B cells and also to the surface of T cells (another type of white blood cell). This binding on two targets activates T cells which causes them to multiply and causes the rapid breakdown of the cancerous B cells.

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

Columvi should not be administered to you:

- if you are allergic (hypersensitive) to glofitamab or any of the other ingredients of Columvi (see Section 6 for a complete list of ingredients in Columvi).

If you are not sure, talk to your doctor or nurse before you are given Columvi.

Warnings and precautions

Tell your doctor or health care provider before being given Columvi if:

- you have an infection
- you have had a long-lasting infection (chronic) or an infection which keeps coming back (recurring)
- you have or had any kidney, liver, or heart problems

Special care should be taken with Columvi: Pay attention to the following serious side effects. These can sometimes be life-threatening and may happen any time during Columvi treatment.

Tell your doctor immediately if you experience any of the following side effects while receiving Columvi:

- if you experience fever, fast heartbeat, feeling dizzy or lightheaded, chills, or shortness of breath. These may be symptoms of a condition known as cytokine release syndrome, a serious condition.
- if you experience confusion, disorientation, sleepiness, or change in consciousness level. These symptoms could be a sign of a problem with your nervous system caused by your immune cells. This is known as neurologic toxicity including immune effector cell-associated neurotoxicity syndrome.

- if you develop fever, chills, difficulty breathing, or burning sensation while passing urine. These may be signs of an infection. Some infections may be life-threatening or fatal.
- if you experience kidney problems (weakness, shortness of breath, fatigue, and confusion), heart problems (fluttering of the heart or a faster or slower heartbeat), vomiting or diarrhoea, and tingling in the mouth, hands, or feet. These may be signs of a condition called tumour lysis syndrome.
- your cancer appears to become worse and you develop tender swollen lymph nodes, chest pain, cough, inability to breathe easily, or pain at the site of the tumour. These may be symptoms of tumour flare.

If you have any of the above symptoms tell your doctor straight away.

Your doctor may:

- give you other medicines to reduce symptoms and prevent complications
- stop your treatment for a short time, or
- stop your treatment completely

Children and adolescents (< 18 years)

Columvi should not be used in children or adolescents under 18 years of age. This is because Columvi has not been studied in this age group.

Other medicines and Columvi

Tell your doctor or nurse if you are taking, have recently taken, or might start taking any other medicines. This includes medicines obtained without a prescription and herbal medicines.

Pregnancy and breastfeeding

Pregnancy and contraception

- Tell your doctor if you are pregnant, think you might be pregnant, or are planning to become pregnant.
- You should not be given Columvi if you are pregnant. This is because it is possible that Columvi could harm your unborn baby.
- If you could become pregnant, you must use effective contraception while you are being treated with Columvi and for 2 months after the last dose.
- If you become pregnant while you are being treated with Columvi tell your doctor immediately.

Breastfeeding

Do not breast-feed while receiving Columvi and for at least 2 months after the last dose. This is because it is not known if this medicine can pass into breast milk and harm your baby.

Driving and using machines Columvi is not likely to affect your ability to drive, cycle, or use any tools or machines.

However, if you experience symptoms of cytokine release syndrome (such as fever, fast heartbeat, feeling dizzy or lightheaded, chills or shortness of breath) or neurologic toxicity including immune effector cell-associated neurotoxicity syndrome – do not drive, cycle, or use any tools or machines until you feel better.

3. How to use Columvi

You will be given Columvi under the supervision of a doctor experienced in cancer treatment, in a hospital or clinic.

Medicines given before Columvi treatment

- Seven days before starting Columvi treatment, you will be given another medicine, obinutuzumab, to deplete the B cells in your blood in order to prevent cytokine release syndrome.
- During the 30 to 60 minutes before you are given Columvi, you may be given other medicines (pre-medication) to help reduce reactions associated with cytokine release syndrome. These medicines may include:
  - A corticosteroid such as dexamethasone
  - A fever-reducing medicine such as paracetamol
  - An antihistamine such as diphenhydramine

How much and how often you will receive Columvi

You will be given 12 treatment cycles of Columvi.

- Each cycle lasts 21 days.

Your doctor will begin Columvi treatment with a low-dose and will gradually increase it to the full dose.

A typical schedule is shown below.

Cycle 1: This will include a pre-treatment and 2 low doses of Columvi during the 21 days:

- Day 1 – Pre-treatment with obinutuzumab
- Day 8 – 2,5 mg starting dose of Columvi dose
- Day 15 –10 mg intermediate dose of Columvi Cycle 2 to Cycle 12: This will be just one dose in the 21 days:

- Day 1 – 30 mg full dose of Columvi

How Columvi is given and monitoring

Columvi is given as a drip into a vein (an intravenous infusion). Your doctor will adjust the time required for infusion depending on how you respond to treatment.

- Your first infusion will be given over 4 hours.
- When Columvi is given alone, your doctor will monitor you carefully during the first infusion and for 10 hours after completion of infusion.
- When Columvi is given with the medicines gemcitabine and oxaliplatin, your doctor will monitor you carefully during and after completion of the first infusion for a combined total of 8 hours.
- This is to watch for any signs or symptoms of cytokine release syndrome.
- For following infusions, your doctor may require to monitor you after completion of infusion. This will be necessary if you have had moderate or severe CRS with your previous dose.
- If you do not have any cytokine release syndrome after 3 doses, your doctor may give the following infusions over 2 hours.

If you miss a dose of Columvi

If you miss an appointment, make another one straight away. For the treatment to be fully effective, it is very important not to miss a dose.

If you stop using Columvi

Speak with your doctor before stopping treatment. This is because stopping treatment may make your condition worse.

Ask your doctor if you have any further questions on the use of this medicine.

4. Possible side effects

Columvi can cause side effects

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

The following side effects have been reported with this medicine:

Serious side effects

Tell your doctor immediately if you get any of the serious side effects listed below – you may need urgent medical treatment.

- Cytokine release syndrome; symptoms include fever, fast heartbeat, feeling dizzy or lightheaded, chills, and shortness of breath
- Neurologic toxicity including immune effector cell-associated neurotoxicity syndrome; symptoms include confusion, disorientation, sleepiness, and change in consciousness level
- Infection; symptoms include fever, chills, difficulty breathing, and burning pain when passing urine
- Tumour flare; symptoms include tender swollen lymph nodes, chest pain, inability to breathe easily, and pain at the site of the tumour
- Tumour lysis syndrome; symptoms include weakness, shortness of breath, feeling confused, irregular heartbeat, and muscle cramps

Other side effects

Columvi monotherapy

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

Very common (may affect more than 1 in 10 people)

- Reduced levels in blood tests of:
  - neutrophils (a type of white blood cell), which may cause fever or any symptoms of an infection
  - red blood cells (anaemia), which may cause tiredness, feeling unwell, and pale skin
  - platelets (a type of blood cell), which may cause unusual bruising or bleeding
- fever
- Low levels in blood tests of:
  - phosphate, magnesium, calcium, or potassium
- rash
- constipation
- diarrhoea
- feeling sick (nausea)
- headache
-

Common (may affect up to 1 in 10 people)

- low sodium levels in blood tests, which may cause tiredness, muscle twitching, or cramps
- increased levels in blood tests of liver enzymes and bilirubin (yellow substance in blood) which may cause yellowing of skin or eyes and dark urine
- bacterial infections, such as urinary tract infection and infection in or around the stomach
- respiratory tract infections, such as runny nose, sore throat, sinus infections, and chest colds
- reduced levels in blood tests of lymphocytes (a type of white blood cell), that may affect the body's ability to fight infection
- infection in blood (sepsis), which may cause fever, chills, and confusion

- fungal infection
- fever with low levels of neutrophils (a type of white blood cell)
- lung infection (pneumonia) which may cause fever, cough, and difficulty breathing
- vomiting
- bleeding in the stomach or gut (gastrointestinal haemorrhage), which may cause black stools or blood in vomit
- confusion
- trembling
- sleepiness

Uncommon (may affect less than 1 in 100 people)

- swelling of the spinal cord (myelitis), which may cause muscle weakness or numbness
- inflammation of the large bowel, which may cause abdominal pain, bloody stools and urge to have a bowel movement

Columvi in combination with gemcitabine and oxaliplatin

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

Very common (may affect more than 1 in 10 people)

- reduced levels in blood tests of:
  - platelets (a type of blood cell), which may cause unusual bruising or bleeding
  - neutrophils (a type of white blood cell), which may cause fever or any symptoms of an infection
  - red blood cells (anaemia), which may cause tiredness, feeling unwell, and pale skin
  - lymphocytes (a type of white blood cell), that may affect the body's ability to fight infection
- feeling sick (nausea)

- numbness, tingling, a burning sensation, pain, discomfort or weakness and/or difficulty walking (peripheral neuropathy)
- diarrhoea
- increased levels in blood tests of liver enzymes
- rash
- fever
- vomiting
- pain in the muscles and bones
- abdominal (belly) pain
- constipation
- low levels in blood tests of potassium (hypokalaemia) or sodium (hyponatremia)
- COVID-19 infection caused by a virus called coronavirus (SARS-CoV-2)
- respiratory tract infections, such as runny nose, sore throat, sinus infections, and chest colds
- lung infection (pneumonia) which may cause fever, cough, and difficulty breathing

Common (may affect up to 1 in 10 people)

- headache
- low levels in blood tests of magnesium, calcium, or phosphate
- new or recurring viral infections, such as shingles and cytomegalovirus infection
- bacterial infections, such as urinary tract infection
- infection in blood (sepsis), which may cause fever, chills, and confusion
- fungal infection
- increased level of bilirubin in the blood which may cause yellowing of skin or eyes

- fever with low levels of neutrophils (a type of white blood cell)
- inflammation of the large bowel, which may cause abdominal pain, bloody stools and urge to have a bowel movement
- inflammation of the pancreas
- inflammation of the lungs (pneumonitis), which may cause cough and difficulty breathing

Uncommon (may affect less than 1 in 100 people)

- trembling
- elevated liver enzymes (shown in tests), which may be a sign of an inflamed liver
- lung infection (pneumocystis jirovecii pneumonia)

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 Columvi.

5. How to store Columvi

Columvi will be stored by your doctor at the hospital or clinic. The storage details are as follows:

- 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 carton and label 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.
- Keep the vial in the outer carton in order to protect from light.
- Do not use this medicine if it appears cloudy, discoloured, or contains particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away any medicines you no longer use. These measures will help protect the environment.

Columvi is for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.

6. Contents of the pack and other information

What Columvi contains

- The active substance is glofitamab.
- Columvi 2,5 mg/2,5 mL: Each vial contains 2,5 milligrams of glofitamab (in 2,5 mL).
- Columvi 10 mg/10 mL: Each vial contains 10 milligrams of glofitamab (in 10 mL).
- The other ingredients are:
    - L-Histidine,
    - L-Histidine Hydrochloride monohydrate,
    - L-Methionine,
    - Polysorbate 20,
    - D-Sucrose,
    - Water for Injection

What Columvi looks like

Columvi 2,5 mg/vial: Pack of 1 vial. Colourless 6 mL, Type I, borosilicate glass vial with a flouroresin laminated grey rubber stopper, sealed with an aluminium seal with pink plastic flip-off cap.

Columvi 10 mg/vial: Pack of 1 vial. Colourless 15 mL, Type I, borosilicate glass vial with a flouroresin laminated grey rubber stopper, sealed with an aluminium seal with avocado plastic flip-off cap.

Holder of Certificate of Registration

Roche Products (Pty) Ltd

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South Africa

Roche Ethical Assistance Line toll-free: 0800 21 21 25

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Columvi 2,5 mg/2,5 mL: 57/30.5/0287

Columvi 10 mg/10 mL: 57/30.5/0288