Package leaflet: Information for the patient

Columvi 2.5 mg concentrate for solution for infusion
Columvi 10 mg concentrate for solution for infusion
glofitamab

▼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 are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
  - Your doctor will give you a Patient Card. Read it carefully and follow the instructions on it. Keep this Patient Card with you at all times.
  - Always show the Patient Card to the doctor or nurse when you see them or if you go to hospital.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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). It is used when the cancer:
- has come back (relapsed), or
- did not respond to previous treatments.

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

- The active substance in Columvi, glofitamab, is a bispecific monoclonal antibody, a type of protein that attaches to two specific targets in the body. It attaches to a specific protein on the surface of B cells, including cancerous B cells, and also to another protein on the surface of T cells (another type of white blood cell). This activates T cells and causes them to multiply. This, in turn, results in the destruction of the B cells, including the cancerous cells.

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

You must not be given Columvi

- if you are allergic to glofitamab or any of the other ingredients of this medicine (listed in section 6)
- if you are allergic to obinutuzumab, which is another medicine given before starting Columvi treatment (see also section 3 'How Columvi is given'), or any of the other ingredients of this medicine

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

Warnings and precautions

Talk to your doctor before you are 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
- you are planning to have a vaccine in the near future

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

Pay attention to serious side effects.

Some side effects of Columvi are serious and can be life-threatening. These may happen any time during Columvi treatment.

Tell your doctor straight away if you experience any of the following side effects while receiving Columvi. The symptoms of each side effect are listed in section 4.

- **Cytokine release syndrome:** an exaggerated inflammatory condition associated with medicines that stimulate T cells, characterized by fever and impairment to multiple organs in the body. Cytokine release syndrome is more likely to occur during Cycle 1 after Columvi is given (see section 3 'How Columvi is given'). Close monitoring is needed. Before each infusion, you may be given medicines, which help reduce possible side effects of cytokine release syndrome.
- **Tumour lysis syndrome:** some people may get unusual levels of some salts in the blood (such as potassium and uric acid) – caused by the fast breakdown of cancer cells during treatment. Your doctor or nurse will do blood tests to check for this condition. Before each infusion, you should be well-hydrated and may be given medicines that can help reduce high levels of uric acid. These may help reduce possible side effects of tumour lysis syndrome.
- **Tumour flare:** a reaction to certain medicines that act on the immune system which is/appears similar to worsening of the cancer.
- **Infections:** you may get signs of infection, which can vary depending on where in the body the infection is.

If you have, or think you may 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

This medicine should not be given to children and adolescents below 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 contraception

- If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.
- 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.

Breast-feeding

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 has minor influence on your ability to drive, cycle or use any tools or machines.

If you feel any symptoms that may affect your ability to drive, including symptoms of cytokine release syndrome (such as fever, fast heartbeat, feeling dizzy or lightheaded, chills or shortness of breath) – do not drive, cycle or use any tools or machines until you feel better. See section 4 for more information about side effects.

3. How Columvi is given

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 reduce the number of B cells in your blood.
- **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 may be given up to 12 treatment cycles of Columvi. Each cycle lasts 21 days. During the first two cycles, 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
- 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. Your doctor will monitor you carefully during the first infusion and for 24 hours after completion of infusion. 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 cytokine release syndrome 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.

Before stopping Columvi treatment

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

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

4. Possible side effects

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

Serious side effects

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

- **Cytokine release syndrome (very common):** symptoms may include, but are not limited to, fever, fast heartbeat, feeling dizzy or lightheaded, nausea, headache, rash, confusion, chills, shortness of breath
- **Infections (very common):** symptoms may include, but are not limited to, fever, chills, difficulty breathing, burning pain when passing urine

- **Tumour flare (very common):** symptoms may include, but are not limited to, tender swollen lymph nodes, chest pain, inability to breathe easily, pain at the site of the tumour
- **Tumour lysis syndrome (common):** symptoms may include, but are not limited to, weakness, shortness of breath, feeling confused, irregular heartbeat, muscle cramps

Other side effects

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

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

- lowered levels, as measured in blood tests, of:
  - neutrophils (a type of white blood cell; neutropenia), 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; thrombocytopenia), which may cause bruising or bleeding
- fever
- low levels, as measured in blood tests, of phosphate, magnesium, calcium or potassium
- rash
- constipation
- diarrhoea
- feeling sick (nausea)
- viral infections, such as lung infection, shingles
- headache

Common (may affect up to 1 in 10 people)

- low sodium levels, as measured in blood tests, which may cause tiredness, muscle twitching or cramps
- increased levels, as measured 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, infection in or around the stomach
- fungal infection
- nose and throat infections (upper respiratory tract infections)
- infections of the lungs such as bronchitis or pneumonia (lower respiratory tract infections), which may cause fever, cough, and difficulty breathing
- blood poisoning (sepsis), which may cause fever, chills and confusion
- low levels, as measured in blood tests, of lymphocytes (a type of white blood cell; lymphopenia)
- fever with low levels of neutrophils (febrile neutropenia)
- 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

If you notice any of the side effects above or if they get worse, tell your doctor straight away.

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store Columvi

Your doctor, pharmacist or nurse is responsible for storing this medicine and disposing of any unused product correctly. The following information is intended for healthcare professionals.

- 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 the vial label after EXP. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C - 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.

Any unused medicine 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: Each vial contains 2.5 milligrams of glofitamab (in 2.5 mL concentrate) at a concentration of 1 mg/mL
- Columvi 10 mg: Each vial contains 10 milligrams of glofitamab (in 10 mL concentrate) at a concentration of 1 mg/mL
- The other ingredients are: L-histidine, L-histidine hydrochloride monohydrate, L-methionine, sucrose, polysorbate 20 (E432) and water for injections.

What Columvi looks like and contents of the pack

Columvi concentrate for solution for infusion (sterile concentrate) is a colourless, clear solution provided in a glass vial.

Each pack of Columvi contains one vial.

Marketing Authorisation Holder and Manufacturer

Roche Products Limited
6 Falcon Way, Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

This leaflet was last revised in August 2023.

This medicine has been given 'conditional approval'. This means that there is more evidence to come about this medicine.

The following information is intended for healthcare professionals only:

Columvi must be administered as an intravenous infusion through a dedicated infusion line. It must not be administered as an intravenous push or bolus.

For instructions on dilution of Columvi before administration, see below.

Instructions for dilution

- Columvi contains no preservative and is intended for single use only
- Columvi must be diluted by a healthcare professional using aseptic technique, prior to intravenous administration.
- Do not shake the vial. Visually inspect the Columvi vial for particulate matter or discoloration prior to administration. Columvi is a colorless, clear solution. Discard the vial if the solution is cloudy, discolored or contains visible particles.
- Withdraw the appropriate volume of sodium chloride 9 mg/mL (0.9%) solution for injection or sodium chloride 4.5 mg/mL (0.45%) solution for injection, as described in Table 6, from the infusion bag using a sterile needle and syringe and discard.
- Withdraw the required volume of Columvi concentrate for the intended dose from the vial using a sterile needle and syringe and dilute into the infusion bag (see Table 6 below). Discard any unused portion left in the vial.
- The final glofitamab concentration after dilution must be 0.1 mg/mL to 0.6 mg/mL.
- Gently invert the infusion bag to mix the solution in order to avoid excessive foaming. Do not shake.
- Inspect the infusion bag for particulates and discard if present.
- Prior to the start of the intravenous infusion, the content of the infusion bag should be at room temperature (25°C).

Table 6. Dilution of Columvi for infusion

Dose of Columvi to be administered	**Size of infusion bag**	**Volume of sodium chloride 9 mg/mL (0.9%) or 4.5 mg/mL (0.45%) solution for injection to be withdrawn and discarded**	**Volume of Columvi concentrate to be added**
2.5 mg	50 mL	27.5 mL	2.5 mL
	100 mL	77.5 mL	2.5 mL
10 mg	50 mL	10 mL	10 mL
	100 mL	10 mL	10 mL
30 mg	50 mL	30 mL	30 mL
	100 mL	30 mL	30 mL

Only sodium chloride 9 mg/mL (0.9%) or 4.5 mg/mL (0.45%) solution for injection should be used to dilute Columvi, since other solvents have not been tested.

When diluted with sodium chloride 9 mg/mL (0.9%) solution for injection, Columvi is compatible with intravenous infusion bags composed of polyvinyl chloride (PVC), polyethylene (PE),

polypropylene (PP) or non-PVC polyolefin. When diluted with sodium chloride 4.5 mg/mL (0.45%) solution for injection, Columvi is compatible with intravenous infusion bags composed of PVC.

No incompatibilities have been observed with infusion sets with product-contacting surfaces of polyurethane (PUR), PVC or PE, and in-line filter membranes composed of polyethersulfone (PES) or polysulfone. The use of in-line filter membranes is optional.

Diluted solution for intravenous infusion

Chemical and physical in-use stability have been demonstrated for a maximum of 72 hours at 2 °C to 8 °C and 24 hours at 30 °C followed by a maximum infusion time of 8 hours.

From a microbiological point of view, the diluted solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Disposal

Columvi vial is for single use only.

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