Package leaflet: Information for the patient

Cifoban 136 mmol/l solution for infusion

sodium citrate

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.
- 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 Cifoban is and what it is used for

Cifoban is a solution for infusion, which contains the active substance sodium citrate.

For infusion in the extracorporeal (outside the body) circuit only.

This medicine is used as an anticoagulant (to make your blood thinner) during regional citrate anticoagulation in the following kidney replacement and plasma exchange therapies:
- continuous venovenous haemodialysis (CVVHD)
- continuous venovenous haemodiafiltration (CVVHDF)
- sustained low efficiency (daily) dialysis (SLEDD)
- therapeutic plasma exchange (TPE) (removes and replaces a patient´s blood plasma).

This medicine is intended to be used in adults and children of all age groups (except premature babies).

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

You must not be given Cifoban
- if you are allergic to sodium citrate
- if a recent treatment with Cifoban was stopped because your body was insufficiently able to break down the required dose of Cifoban and as a result citrate accumulated in your blood.

Warnings and precautions
Talk to your doctor before you are given Cifoban.

Your doctor will:
- ensure that any reduced liver function, a decrease of oxygen in the blood, or a disturbed oxygen utilisation in the body tissues are known before starting the treatment and start the treatment with an adapted dose or another anticoagulation method, if necessary.
- ensure that any existing hypocalcaemia (low concentration of ionised calcium in the blood) will be treated before starting the therapy.
- ensure that the calcium, sodium and magnesium levels, as well as the acid-base balance (deviation in the blood pH) are correct and closely monitored during your treatment.
- ensure that the anticoagulant effect is monitored during treatment, and that any unexpected clotting of the filter will be detected.
- ensure that, if you have been immobilised for a longer period, unusual changes in calcium dose are noted, and that the status of calcium and other minerals in your bone (bone mass) are monitored.
- stop, if necessary, the regional citrate anticoagulation with Cifoban in case you have developed citrate accumulation.

Children
This medicine is not recommended in premature babies because there is insufficient experience in this group of patients.

Other medicines and Cifoban
Tell your doctor if you are taking, have recently taken or might take any other medicines.

The following interactions are possible with medicines containing:
- Calcium given at the wrong position in the extracorporeal (outside the body) circuit, which may reduce the anticoagulant effect of citrate.
- Sodium-enriched products, which may increase the risk of hypernatremia (high concentration of sodium in the blood).
- Hydrogen carbonate (or precursors such as acetate), which may increase the risk of metabolic alkalosis (a high concentration of bicarbonate in the blood).
- Blood products, which are another source of citrate, may increase the risk of hypocalcaemia (a low ionised calcium concentration in the blood) and metabolic acidosis (a high concentration of (citrate) acid in the blood), when citrate is insufficiently broken down, or may increase the risk of metabolic alkalosis (a high concentration of bicarbonate in the blood) once citrate is broken down to bicarbonate.

This medicine must not be mixed with other medicines, as there are not enough data on compatibility available.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before starting treatment with this medicine.
There are no documented clinical data on the use of Cifoban during pregnancy and breast-feeding. Therefore, this medicine should only be used during pregnancy and breast-feeding if your doctor considers treatment necessary.

3. How Cifoban is given

Extracorporeal use. To be infused into the extracorporeal (outside the body) blood circuit only.

This medicine must be administered using a dedicated extracorporeal (outside the body) blood purification device, appropriate anticoagulation protocol and, if possible, matching applied dialysis and volume replacement fluids.

Dose
The dose of Cifoban will be determined by your doctor. In brief, Cifoban is given in a specific dose to the blood flow in the extracorporeal (outside the body) circuit to induce locally very low ionised calcium levels, to make your blood thinner (regional citrate anticoagulation). The blood flow used, and the dose of this medicine will depend on your condition and treatment. More information about dosage can be found in the information for healthcare professionals below.

This medicine is given in hospitals and administered by trained medical professionals only and can be applied in an intensive care setting where it will be given under close medical supervision.

Use in children
The used equipment must support treatment in children and must support low blood flows when neonatal application is desired. Your doctor will ensure that a low blood flow in relation to your child's weight is selected and prescribe an accordingly reduced dose of Cifoban. This medicine is prescribed by your doctor only if your doctor has experience with the prescribed kidney replacement or plasma exchange therapy in children.

If you have been given more Cifoban than you should
As Cifoban will only be given to you by a doctor, it is unlikely that you will be given too little or too much. However, if you think you have been given too much of this medicine, please tell your doctor or nurse.

The signs of an overdose may be symptoms of a low calcium level (such as muscle cramps, and abnormal or irregular heartbeat) and symptoms of changes in your acid-base balance and sodium balance (such as confusion, lightheadedness, headache, vomiting).

If you get any of the above mentioned symptoms please tell your doctor or nurse immediately.

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.

The following more common side effects may occur:
- imbalances in the level of electrolytes in the blood (e.g. low blood calcium level, low blood magnesium level, high blood sodium level)
- disorders in the blood acid-base status (too high or too low blood pH)

The following less common side effects may occur (the exact frequency is unknown):
- allergic reactions leading to e.g. low blood pressure, feeling of sickness, back and abdominal pain, local reaction (itching, rash, reddening of the skin)
- too much fluid in your body
- headache, seizures, unconscious state
- abnormal heartbeat, cardiac arrest
- excess fluid in the lungs
- low blood pressure
- breathing difficulty, respiratory arrest
- abnormally rapid breathing
- vomiting (being sick)
- muscle cramps

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

HPRA Pharmacovigilance
Website: www.hpra.ie

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Cifoban

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 label after EXP. The expiry date refers to the last day of that month.

Do not refrigerate or freeze.

Keep the bags in the outer carton in order to protect from light.

The content of the bag must be used immediately after opening.

The solution is for single use only. Any unused solution and damaged container must be discarded.

6. Contents of the pack and other information

What Cifoban contains
- The active substance is sodium citrate. Each 1000 ml of solution contains 40.0 g of sodium citrate corresponding to 408 mmol sodium and 136 mmol citrate.
- The other ingredients are water for injections and hydrochloric acid.

What Cifoban looks like and contents of the pack
Cifoban is provided in a bag with 1500 ml ready-to-use solution.
The solution is clear and colourless and practically free from particles.
This medicine is provided pairwise as two identical solution bags which can be separated by a tear seam in the protective overwrap. Each bag is equipped with a connective tubing and a connector.

Cifoban is provided in the following connector systems and pack sizes per carton:

SecuNect	Safe●Lock
8 bags of 1500 ml	8 bags of 1500 ml

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Fresenius Medical Care Deutschland GmbH,
Else-Kröner-Straße 1,
61352 Bad Homburg v.d.H.,
Germany

Manufacturer
Fresenius Medical Care Deutschland GmbH,
Frankfurter Straße 6-8,
66606 St. Wendel,
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:
Fresenius Medical Care (UK) Ltd,
Tel.: 0800 001 4499

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:
AT: Citravyl
BE, LU, PT: Civastyn
BG: Цифобан
BG, CY, DK, EL, ES, FI, HU, IE, IT, NL, NO, PL, RO, SK, UK(XI): Cifoban
CZ, EE, LT, SI: Cigenta
DE, FR, HR, LV, SE: Civaron

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The following information is intended for healthcare professionals only:

1000 ml solution contains:

Sodium citrate	40.0 g
Na^+	408 mmol
$Citrate^{3-}$	136 mmol

Theoretical osmolarity: 544 mOsm/l
pH: 7.1 – 7.5

Posology
Extracorporeal dosing of Cifoban is to be titrated proportional to the blood flow of the extracorporeal circuit (e.g. 4 mmol of citrate per litre treated blood) to achieve a sufficient suppression of ionised calcium, where generally a post-filter ionised calcium concentration below 0.3-0.35 mmol/l is to be targeted. The application volume in adult patients must not exceed 10.4 litre/day. The extracorporeal blood flow must be sufficient to reach the therapy targets but be kept low enough to avoid unnecessary citrate infusion and promote clearance of citrate within the applied filter. In kidney replacement and plasma exchange therapies composition and applied volumes of other solutions must be considered with the prescription of Cifoban. Further recommendations and limitations apply for use in patients with impaired citrate metabolism, as well as the geriatric and paediatric populations. For details, please refer to the Summary of Product Characteristics.

Method of administration
Extracorporeal use. To be infused into the extracorporeal blood circuit only.

Infusion only by an integrated pump within the extracorporeal blood purification device, which is intended by its manufacturer for the infusion of a concentrated citrate solution in the pre-pump segment of the access tubing system ("blood access line").

Please observe the special warnings and precautions in the Summary of Product Characteristics.

Additionally:
- Cifoban must only be used in accordance with an appropriate protocol for regional citrate anticoagulation (RCA). It shall only be used by, or under the direction of, a physician competent in the application of RCA and by health care professionals who are sufficiently trained in the indicated therapies and in the application of the involved products.
- Handling instructions of the used extracorporeal blood purification device and the tubing system provided by the manufacturer must be adhered to.
- Cifoban can be used for RCA in an intensive care unit or under similar conditions, where it must be used under close medical supervision and continuous monitoring.

Disposal
The solution is for single use only. Any unused solution and damaged container must be discarded.

Handling
The solution bags are equipped either with a **SecuNect connector** or with a **Safe●Lock connector**.

The following points prior to the use of the solution bag have to be considered:

Aseptic technique must be used throughout administration to the patient. The solution must be used immediately after opening to avoid microbiological contamination.

Extracorporeal use. To be infused into the extracorporeal blood circuit only.

The solution is not intended to be used for the addition of any drugs.

For solution bags equipped with a **SecuNect connector (transparent with a green ring)**:
1. Separate the two bags at the tear seam without damaging the integrity of the overwrap.
2. Remove the overwrap only immediately before using the solution. Check the solution bag (label, expiry date, clearness of the solution, bag and overwrap not damaged).
   Plastic containers may occasionally be damaged during transport from the manufacturer to the dialysis clinic or hospital clinic or within the clinic itself. This can lead to contamination and the growth of bacteria or fungi in the solution. Therefore, careful inspection of the bag and the solution before use is essential. Particular attention must be paid to even the slightest damage to the closure of the bag, the welding seams and the corners of the bag. The solution must only be used if colourless and clear and if the bag and connector are undamaged and intact.
3. Put the bag on the dedicated attachment by its hanger hole.
4. Remove the protection cap from the **SecuNect connector with its green ring** and attach the connector only to its corresponding counterpart with same colour to prevent misconnection. Do not touch any inner parts especially do not touch on top of the connector. The inner part of the connector is delivered sterile and is not intended to be further treated with chemical disinfectants. Connect the bag connector with a twisting motion to the tubing line connector by hand, overcoming a guarding force until a "click" is audible and connection is established.
5. Before start of treatment and in case of bag changes break the frangible pin of the bag connector and make sure that the pin is completely broken.
6. Proceed with the further steps as indicated in the treatment applied RCA protocol.

For solution bags equipped with a **Safe●Lock connector (transparent)**:

1. Separate the two bags at the tear seam without damaging the integrity of the overwrap.
2. Remove the overwrap only immediately before using the solution. Check the solution bag (label, expiry date, clearness of the solution, bag and overwrap not damaged).
   Plastic containers may occasionally be damaged during transport from the manufacturer to the dialysis clinic or hospital clinic or within the clinic itself. This can lead to contamination and the growth of bacteria or fungi in the solution. Therefore, careful inspection of the bag and the solution before use is essential. Particular attention must be paid to even the slightest damage to the closure of the bag, the welding seams and the corners of the bag. The solution must only be used if colourless and clear and if the bag and connector are undamaged and intact.
3. Put the bag on the dedicated attachment by its hanger hole.
4. Remove the protection cap from the **transparent Safe●Lock connector** and attach the connector only to its corresponding counterpart to prevent misconnection. Do not touch any inner parts especially do not touch on top of the connector. The inner part of the connector is delivered sterile and is not intended to be further treated with chemical disinfectants. Connect the bag connector with the appropriate counterpart and twist together.
5. Before start of treatment and in case of bag changes break the frangible pin of the bag connector and make sure that the pin is completely broken.
6. Proceed with the further steps as indicated in the treatment applied RCA protocol.