Prescribing Information

Cifoban 136mmol/l, solution for infusion

(Sodium Citrate)

please refer to the Summary of Product Characteristics for detailed information

Presentation and active ingredients: Solution bag with 1500ml ready-to-use solution. 1000 ml solution contains: Sodium Citrate 40.0g (Na^+ 408mmol and Citrate $^{3-}$ 136mmol).

Indications: Cifoban is used for regional citrate anticoagulation (RCA) in continuous venovenous haemodialysis (CVVHD), continuous venovenous haemodiafiltration (CVVHDF), sustained low efficiency (daily) dialysis (SLEDD) and therapeutic plasma exchange (TPE) via membrane plasma separation.

Posology and method of administration: Cifoban is to be infused into the extracorporeal blood circuit only. Cifoban should be prescribed only by a physician competent in the application of RCA in the specific treatment mode of CVVHD, CVVHDF, SLEDD and/or TPE and for the paediatric population, Cifoban should be prescribed and monitored by physicians competent in these treatment modes in children. ***Adults;*** The pre-filter infusion rate of Cifoban should be titrated proportional to the blood flow of the extracorporeal circuit to achieve a sufficient suppression of ionised calcium of the blood within the filter as per applied RCA protocol. Generally, a post-filter ionised calcium concentration below 0.3-0.35 mmol/l should be targeted, which is usually achieved with dosing of 4-5 mmol citrate per litre treated blood. The patient's systemic ionised calcium concentration should be maintained in the normal physiologic range, which commonly requires calcium supplementation. The application volume of Cifoban in adult patients should not exceed 10.4 litre/day. When used in combination with a calcium-free dialysis solution for CVVHD or CVVHDF having a sodium content of 133 mmol/l and bicarbonate content of 20 mmol/l, the citrate amount added to the blood before entering the dialysis filter should be targeted to 3 to 5 mmol/l blood during CVVHD and to 3 to 5.5 mmol/l blood during CVVHDF treatment modes. ***Special populations;*** *Patients with impaired citrate metabolism;* Cifoban can be applied in patients at risk of this (e.g., shock with severe lactic acidosis, severe liver failure). Treatment should be initiated with a sufficiently low citrate dose and intensified monitoring is recommended to prevent the development of citrate accumulation. *Geriatric population;* Elderly patients may be at risk of impaired citrate metabolism. No dose reduction is required. Frequent monitoring to detect citrate accumulation is recommended. ***Paediatric population;*** Cifoban can be applied in children of all age groups (term neonates up to adolescents), when the patient citrate load remains sufficiently low. The used equipment must support paediatric application for the given weight, including the required low blood flows. Blood flow and citrate dose guidance per age category: 2 to 11 years - blood flow should not exceed 5-6 ml/kg/min; citrate dosing can be initiated at appr. 4 mmol/l blood, as per protocol. 12 to 17 years - blood flow should be sufficient to reach the therapy targets, and generally not exceed blood flows in adults of similar weight. Citrate dosing same as 2-11 years. 0 to 23 months - if a blood flow of 7-8 ml/kg/min (or higher) is required, the citrate dosing should be initiated at appr. 3 mmol/l blood.

When treated with CVVHD or CVVHDF, a post-filter ionised calcium concentration below 0.3-0.35 mmol/l is preferably targeted, but this depends on the feasible citrate dose.

Contraindications: Hypersensitivity to the active substance, known severely impaired citrate metabolism.

Warnings: monitoring frequencies of impacted patient serum values - the indicated therapies call for the close monitoring of the patient's haemodynamic status, fluid balance, glucose level, electrolyte, and acid-base balance before and during treatment. *Additional Warnings;* citrate accumulation due to impaired metabolism, citrate overload, insufficient citrate load, prolonged patient immobilization and early clotting despite RCA.

Precautions: Intoxications that result in mitochondrial dysfunction, pre-existing hypocalcaemia, complexing and clearance of calcium and magnesium and blood product substitution (TPE).

Interactions with other medicinal products: No pharmacodynamic drug interactions among the constituents of Cifoban are to be expected. Interactions could only be expected by inadequate or incorrect therapeutic use of the solution. Interaction or compatibility studies with other medicinal products have not been performed. Thus, no other substance or solution must be added to Cifoban. Calcium containing solutions applied at the level of the filter (i.e. dialysis fluid) or upstream of the filter may reduce the effect of Cifoban. Interactions are conceivable with sodium-enriched products, which may increase the risk of hypernatraemia. Products containing hydrogen carbonate (or precursors metabolised yielding hydrogen carbonate, e.g., acetate) may increase the risk of metabolic alkalosis. Blood products containing citrate may increase the risk of hypocalcaemia, metabolic acidosis, and metabolic alkalosis.

Fertility, pregnancy, and lactation: ***Pregnancy and breast-feeding;*** There is no data from the use of Cifoban in pregnant or breast-feeding women. Animal studies are insufficient with respect to reproductive toxicity. Cifoban should not be used during pregnancy and breast-feeding unless the clinical condition of the woman requires treatment with RCA. ***Fertility;*** No human data on the effect of sodium and citrate on fertility are available.

Undesirable effects: Hypersensitivity, hypocalcaemia, hypernatraemia, metabolic alkalosis, severe hypocalcaemia, hypomagnesaemia, severe hypernatraemia, severe metabolic alkalosis, severe metabolic acidosis, fluid overload, headache, seizure, coma, arrhythmia, cardiac arrest, pulmonary oedema, hypotension, bronchospasm, respiratory arrest, tachypnoea (Kussmaul breathing), vomiting, muscle spasms/cramps.

Overdose: Inadvertent administration of too high volumes of Cifoban may lead to an overdose, which can cause a life-threatening situation for the patient such as acute hypocalcaemia, metabolic alkalosis, hypernatraemia and may expose the patient to neurological and cardiac complications.

Legal Category: POM

NHS list Price: £13.20 (excluding VAT)

Marketing authorisation number: PL13689/0027

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

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1. Cifoban SmPC 2021

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellowcard in the Google Play or Apple App Store. Adverse events should also be reported to Fresenius Medical Care UK Ltd on 0800 001 4499