



DEVICE SAFETY INFORMATION (DSI)

Continuous renal replacement therapy (CRRT): Consider delayed administration of concurrent echinocandins, such as caspofungin, to reduce the risk of adsorption onto new polyacrylonitrile (PAN)-based filter membranes

***Specialisms:** Anaesthetics and intensive care, Cancer, Critical Care, Infection prevention, Infectious disease, Renal medicine, Urology and nephrology, Paediatrics and neonatology*

DEVICE DETAILS

All continuous renal replacement therapy devices

AFFECTED LOT SERIAL NUMBERS

All lots

MANUFACTURED BY

Various – check membrane compatibility and use

Summary

Continuous renal replacement therapy (CRRT) is used for managing severe acute kidney injury and fluid overload. Published evidence has shown that caspofungin can bind to polyacrylonitrile (PAN)-based membranes used in CRRT which may result in ineffective antifungal treatment with potentially life-threatening consequences in critically ill patients. It is considered that the potential risk is greatest when a new membrane or filter circuit has commenced. This is because adsorption reduces over time as the membrane becomes saturated¹. The same risk cannot be excluded for other membrane types used in CRRT or other drugs with similar properties. Where possible, it is recommended that echinocandins such as caspofungin, and similar drugs, are administered at least six hours¹ after initiation of PAN-based filter use, and after filter circuit set changes.

Advice for Healthcare Professionals:

- echinocandins, such as caspofungin, may adsorb onto PAN-based membranes used in CRRT which may result in ineffective antifungal treatment

- adsorption risk reduces over time as the membrane becomes saturated
- where possible, administration of antifungal treatments, including with echinocandins and similar drugs, should be at least 6 hours after CRRT has been initiated or following routine filter circuit set changes. CRRT should proceed as clinically indicated and should not be delayed or paused solely to facilitate drug administration, unless otherwise deemed necessary by the responsible clinician
- all healthcare professionals involved in the CRRT process and set up, as well as the prescribing, dispensing and administration of caspofungin, should be made aware of this recommendation
- seek specialist pharmacist, infectious disease, medical microbiology or mycology input if you are concerned about potential loss of therapeutic efficacy
- filter adsorption should be considered as a potential reason for treatment non-responders, or sub-therapeutic responses, whilst patients are receiving any concurrent treatment during CRRT
- healthcare providers should review and update local protocols and standard operating procedures to reflect the potential for drug adsorption during CRRT, and to include recommendations for timing of medication administration in the context of this DSI

Advice for Healthcare Professionals to Provide to Patients:

The advice in this DSI is aimed at healthcare professionals in charge of treating and managing patients receiving CRRT. If you have any concerns about this advice, contact your healthcare professional.

Advice for Distributors:

There is no advice to distributors related to this DSI.

Explanation of identified safety issue

CRRT is a slow, 24-hour dialysis method which controls fluid levels via a semi-permeable membrane and mitigates risks associated with rapid solute changes. It is most often used in intensive care units in patients who are critically ill and hemodynamically unstable.

Caspofungin is an antifungal for the treatment of invasive fungal infections in adults and children. It is also used as an empirical therapy for presumed fungal infections in febrile, neutropenic patients. Ineffective antifungal treatment in critically ill patients can have fatal consequences.

The European Pharmacovigilance Risk Assessment Committee (PRAC) reviewed evidence that the polyacrylonitrile (PAN)-based membranes in CRRT can bind caspofungin and decrease its effectiveness. The PRAC recommended to avoid PAN-based membranes in CRRT patients who receive treatment with antifungals, either by swapping filter membranes or using an alternative antifungal. However, the MHRA recommendations for the UK differ following review of the available evidence.

The MHRA reviewed the PRAC recommendations along with additional studies which have since been published. Based on engagement with clinicians and the availability of CRRT machines at UK sites, the PRAC recommendations were not deemed to be feasible in the UK clinical setting. Avoiding caspofungin and other echinocandins is likely to have a serious clinical impact on patients, where this is a first line treatment for invasive candidiasis and ICU patients are likely to have increased susceptibility to fungal infections. Recommending use of alternative antifungals besides echinocandins may also be limited by sensitivities and drugs resistance to candida.

Studies into the adsorption potential of filter membranes indicate that adsorption is non-specific and likely highest immediately after treatment with a new membrane, or when a filter circuit has commenced, and reduces over time as the membrane becomes saturated^{1, 2}. By scheduling drug administration to occur after filter circuit changes, loss of drug may be mitigated.

Where clinically appropriate, the MHRA recommends that echinocandins such as caspofungin are administered at least six hours after CRRT has been initiated or following routine filter circuit set changes. If a patient is already receiving treatment with echinocandins prior to requiring CRRT, a delay in administering the next treatment dose or starting the patient on CRRT should only be considered if clinically viable. Healthcare professionals are advised to monitor for lack of efficacy when CRRT treatment initiation overlaps with the half-life of the concurrent drugs administered.

Whilst PAN-based membranes lend themselves to being more susceptible to drug adsorption, comparative studies with other membrane types have not been conducted, and adsorption cannot be conclusively excluded for other membrane types.

As adsorption is not specific to caspofungin, if a patient is not responding to their therapy whilst receiving concurrent CRRT, interactions with the filter (i.e. binding to the filter) should be considered. Alternatively, different treatment options taking into account potential filter retention, may be sought.

Healthcare professionals who are concerned about the potential loss of therapeutic efficacy are recommended to seek advice from local specialists about the availability of fungal antigen testing to allow close monitoring of clinical progression. Specialist infectious disease, medical microbiology and mycology input is available nationally.

A [DHPC](#) has been issued which communicates the key safety messages of this DSI.

Reporting advice

Healthcare professionals should report incidents:

- in England and Wales to the [Yellow Card website](#) or via the Yellow Card app
- in Scotland to [Incident Reporting & Investigation Centre \(IRIC\)](#) and their local incident recording system
- in Northern Ireland to the Yellow Card website in accordance with your organisations medical device policies and procedures.

Additional information:

You can [sign up](#) to receive email updates on alerts and device safety information from the MHRA.

You can [sign up](#) to receive our monthly roundup of safety communications.

For any enquiries, please contact info@mhra.gov.uk

Stakeholder engagement:

- UK Kidney Association
- NHS England National Patient Safety team and Devolved Administrations
- Medical Devices and Estates Safety (MDES) for Department of Health N. Ireland
- Incident Reporting & Investigation Centre (IRIC) for Scotland

References:

1. Massol J and others. [Letter to the Editor regarding 'Impact of Continuous Renal Replacement Therapy with Polyacrylonitrile-Derived Filter on Caspofungin Concentration: A Retrospective Study'](#). Infectious Disease Therapy. 2026: volume 15(3), pages 915 to 919.
2. Arrestier R and Razazi K. [A Response to: "Letter to the Editor regarding 'Impact of Continuous Renal Replacement Therapy with Polyacrylonitrile-Derived Filter on Caspofungin Concentration: A Retrospective Study'"](#). Infectious Disease Therapy. 2026: volume 15(3), pages 911 to 914.