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IMPORTANT MEDICINE SAFETY INFORMATION

APPROVED BY THE HPRA An tÚdarás Rialála Táirgí Sláinte Health Products Regulatory Authority

09 October 2025

Caspofungin: Avoid use of polyacrylonitrile membranes during continuous renal replacement therapy.

Dear Healthcare Professional,

MSD, Clonmel Healthcare Ltd. and Pinewood Healthcare in agreement with the European Medicines Agency and the Health Products Regulatory Authority (HPRA) would like to inform you of the following:

Summary

- **In patients treated with caspofungin during continuous renal replacement therapy, the use of polyacrylonitrile-based membranes should be avoided.**
- **Cases describing caspofungin ineffectiveness in patients undergoing continuous renal replacement therapy using polyacrylonitrile filter membranes have been reported.**
- **The risk of antifungal treatment failure may lead to worsening of the systemic infection, which may ultimately lead to death.**
- **It is recommended to use an alternative extracorporeal membrane or an alternative antifungal.**

Background on the safety concern

Caspofungin is a sterile, lyophilized antifungal for intravenous infusion indicated for the treatment of invasive fungal infections in adult or paediatric patients and for the empirical therapy of presumed fungal infections in febrile, neutropenic adult or paediatric patients (see SmPC for the full indication).

The recommendation to avoid polyacrylonitrile (PAN)-based membranes in patients undergoing continuous renal replacement therapy (CRRT) and receiving treatment with caspofungin follows an analysis of reports of suspected ineffectiveness of caspofungin used in these conditions, and *in vitro* studies suggesting sequestration of this antifungal by PAN-based membranes:

- A literature case describing reversing candidemia when starting and stopping CRRT using PAN filter membrane[1] and four fatal cases describing caspofungin lack of efficacy in patients undergoing CRRT with the same membrane type.

- Two *in vitro* studies suggesting caspofungin adsorption by PAN membranes[2,3]. Sequestration persists even after increasing the caspofungin dose[3].

Any modification in caspofungin plasma concentrations may result in therapeutic failure. Ineffective treatment in these critically ill patients can have fatal consequences. It is recommended to use another extra-renal purification membrane in these patients, or another antifungal in accordance with the attending physician's clinical judgment and decision.

The product information of caspofungin-containing medicines will be updated to inform healthcare professionals of the suspected risk of sequestration.

Call for reporting

Healthcare professionals should report any suspected adverse reactions, lack of effectiveness and/or product quality complaints associated with the use of caspofungin, including batch/lot number, in accordance with the national spontaneous reporting system. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, website: www.hpra.ie. Healthcare professionals are encouraged to specify the type of membrane used in case of CRRT.

Company contact points

Further information can be obtained by contacting the relevant MAH below:

Marketing Authorisation Holder	**Medicinal Product Full Name**	**Marketing Authorisation Number**	**Email**	**Telephone**
MSD	CANCIDAS 50 mg powder for concentrate for solution for infusion	EU/1/01/196/001	medinfo_ireland@msd.com	+353 1 299 8700
MSD	CANCIDAS 70 mg powder for concentrate for solution for infusion	EU/1/01/196/003	medinfo_ireland@msd.com	+353 1 299 8700
Clonmel Healthcare Ltd	Caspofungin Clonmel 50 mg powder for concentrate for solution for infusion	PA0126/341/001	Medical Enquiries: medicalinformation@clonmel-health.ie Adverse Events: medicalinformation@clonmel-health.ie	Medical Enquiries: 052 617 7777 (Option 4) Adverse Events: 052 617 7777 (Option 4)
Clonmel Healthcare Ltd	Caspofungin Clonmel 70 mg powder for concentrate for solution for infusion	PA0126/341/002		
Pinewood Laboratories	Caspofungin 50 mg powder for concentrate for solution for infusion	PA 281/246/001	Medical Enquiries and Adverse Events drug.safety@pinewood.ie	+ 353 52 6186000 (Option 5)

Pinewood Laboratories	Caspofungin 70 mg powder for concentrate for solution for infusion	PA 281/246/002	Medical Enquiries and Adverse Events drug.safety@pinewood.ie	+ 353 52 6186000 (Option 5)

Yours sincerely,

Marketing Authorisation Holder	Person	Signature
MSD	Michael Higgins Associate Director Medical Affairs, MSD	Michael Higgins *Electronically signed by: Michael Higgins Reason: Approved Date: Oct 6, 2025 09:38:10 GMT+1*
Clonmel Healthcare Limited	Conor Booth Medical Affairs Manager	Conor Booth *Electronically signed by: Conor Booth Reason: Approved Date: Oct 6, 2025 09:46:48 GMT+1*
Pinewood Laboratories	Mary O'Meara Director Regulatory Affairs	Mary O Meara *Electronically signed by: Mary O Meara Reason: Approved Date: Oct 6, 2025 10:00:04 GMT+1*

List of literature references

1. Raphalen, J.-H., Marçais, A., Parize, P., Pilmis, B., Lillo-Lelouet, A., Lamhaut, L., & Baud, F. J. (2021). Is caspofungin efficient to treat invasive candidiasis requiring continuous veno-venous hemofiltration? A case report. Therapies, 76(5), 512–515.

2. Baud, F. J., Jullien, V., Secrétan, P.-H., Houzé, P., & Lamhaut, L. (2021). Are we correctly treating invasive candidiasis under continuous renal replacement therapy with echinocandins? Preliminary in vitro assessment. Anaesthesia Critical Care & Pain Medicine, 40(1), 100640.

3. Baud, F. J., Jullien, V., Desnos-Ollivier, M., Lamhaut, L., & Lortholary, O. (2023). Caspofungin sequestration in a polyacrylonitrile-derived filter: Increasing the dose does not mitigate sequestration. International Journal of Antimicrobial Agents, 62(6), 107007.