

## CASPOFUNGIN

### Use

Caspofungin is very expensive but it is probably the anti-fungal drug of choice when systemic infection with a *Candida* organism proves resistant to treatment with fluconazole (q.v.), and when aspergillus infection proves resistant to conventional management with amphotericin B (q.v.).

### Pharmacology

Caspofungin is the first of a new class of antifungals (the echinocandins), first licensed for clinical use in 2001, that works by inhibiting the synthesis of  $\beta$ -(1,3)-D-glucan, an integral component of fungal cell walls. Caspofungin demonstrates good *in vitro* and *in vivo* activity against *Aspergillus* and a range of *Candida* species, including *C albicans*, *C prapsilosis*, *C tropicalis* and *C glabrata*, and in a controlled trial published in 2002 adults with invasive candidiasis responded to caspofungin better than they did to amphotericin. There were also fewer side effects. There are, however, very few published reports as yet of this drug's use in very young children, and the manufacturer is not yet ready to recommend use in children less than 12 years old. The drug was found to be embryotoxic and to interfere with fetal bone formation when given, in a standard dose, to pregnant rats and rabbits but nothing, understandably, is yet known about the effect of its use in women during pregnancy or lactation.

Caspofungin blood levels decline in a polyphasic manner, the brief  $\alpha$ -phase in adults being followed by a 9–11 hour  $\beta$ -phase and a 40–50 hour  $\gamma$ -phase as widespread tissue redistribution is followed by slow hydrolysis, acetylation and chemical degradation before the resultant metabolites are finally excreted in the urine and faeces. Little pharmacokinetic data in neonates has yet been published, but the volume of distribution in infancy would seem to be even higher than it is in adult life while the  $\beta$ -phase half life shorter, making a rather higher dose necessary.

### Drug interactions

Patients taking any of the hepatic enzyme-inducing drugs, such as carbamazepine, dexamethasone, nelfinavir, nevirapine, phenytoin and rifampicin, probably need to be given a rather higher daily dose because of enhanced drug elimination.

### Treatment

Relatively little is known about treatment in the first year of life. The most appropriate IV dose is probably 2 mg/kg once a day, given as a 1-hour infusion. Treatment was continued for 2–3 weeks in most reports published to date. The dose given does not normally need to be reduced in patients in renal failure, but it is probably not wise to continue giving high dose treatment to patients showing signs of liver failure.

### Supply and administration

Caspofungin comes as a powder ready for reconstitution in 50 mg vials that cost £328 each. Vials should be stored at 4°C, but brought to room temperature before the powder is dissolved using 10.5 ml of sterile 0.9% sodium chloride. The resultant solution (containing 5 mg/ml of caspofungin) should then be used within 24 hours. Caspofungin is incompatible with dextrose, and has to be given into a line that only contains 0.9% sodium chloride, or compound sodium lactate.

### References

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