ΕΤΑΙΡΕΙΑ: PHARMATHEN

ΠΡΟΪΟΝ: CASPOFU PD INF PHARMADYNAM ZA LEAFLET

ΚΩΔΙΚΟΣ: 2827753-3

ΑΡΧΙΚΗ ΔΙΑΣΤΑΣΗ: 170 x 620 mm

ΤΕΛΙΚΗ ΔΙΑΣΤΑΣΗ: 170 x 33 mm

ΔΙΠΛΩΜΑΤΑ: 5

ΒΑΡΟΣ Ά ΥΛΗΣ(gr/m²): 50gr

ΧΡΩΜΑΤΑ: black

ΕΚΔΟΣΗ:1η

ΗΜΕΡΟΜΗΝΙΑ: 18/03/2025

ΛΟΙΠΕΣ ΠΑΡΑΤΗΡΗΣΕΙΣ:

Laetus

Αριθ. Laetus: 8940

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Name / Date:

IVECAS IV

SCHEDULING STATUS S4

1. NAME OF THE MEDICINE
IVECAS 50 IV powder for solution for infusion
IVECAS 70 IV powder for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
IVECAS 50 IV:
Each 10 mL vial contains caspofungin acetate equivalent to caspofungin 50 mg.
The reconstituted solution contains caspofungin 5,2 mg per 1 mL solution.

Excipient with known effect:
Contains sugar (sucrose and the sugar alcohol, mannitol).
Each 50 mg vial contains sucrose 35,7 mg and mannitol 23,8 mg.

IVECAS 70 IV:
Each 10 mL vial contains caspofungin acetate equivalent to caspofungin 70 mg.
The reconstituted solution contains caspofungin 7,2 mg per 1 mL solution.

Excipient with known effect:
Contains sugar (sucrose and the sugar alcohol, mannitol).
Each 70 mg vial contains sucrose 50,0 mg and mannitol 33,3 mg.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Powder for concentrate for solution for infusion.
Before reconstitution, the powder is a white to off-white lyophilised powder.
Reconstituted solution:
- pH: 5,5 - 7,5
- osmolality: NMT 100 mOsm/kg.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
IVECAS is indicated in adults for:
- empirical therapy for presumed fungal infections in febrile, neutropenic patients
- treatment of invasive candidiasis, including candidaemia
- treatment of oesophageal candidiasis, where intravenous (IV) antifungal therapy is appropriate
- treatment of oropharyngeal candidiasis, where IV antifungal therapy is appropriate
- treatment of invasive aspergillosis in patients who are refractory to, or intolerant of other therapies, including amphotericin B, lipid formulations of amphotericin B and itraconazole.

Paediatric use
The safety and effectiveness of IVECAS in paediatric patients 3 months to 17 years of age are supported by evidence from adequate and well-controlled studies in adults, pharmacokinetic data in paediatric patients, and additional data from prospective studies in paediatric patients, 3 months to 17 years of age.
The efficacy and safety of IVECAS have not been adequately studied in prospective clinical trials involving neonates and infants under 3 months of age.
IVECAS has not been studied in paediatric patients with endocarditis, osteomyelitis and meningitis due to *Candida*.
IVECAS has also not been studied as initial therapy for invasive aspergillosis in paediatric patients.

4.2 Posology and method of administration
Posology
General recommendations in adult patients
Empirical therapy
A single 70 mg loading dose should be administered on day 1, followed by 50 mg daily thereafter.
Duration of treatment should be based on the patient's clinical response. Empirical therapy should be continued until resolution of neutropenia. Patients found to have a fungal infection should be treated for a minimum of 14 days; treatment should continue for at least 7 days after both neutropenia and clinical symptoms are resolved. If the 50 mg is well tolerated but does not provide an adequate clinical response, the daily dose can be increased to 70 mg. Although an increase in efficacy with 70 mg daily has not been demonstrated, safety data suggest that an increase in dose to 70 mg daily is well tolerated.

Invasive candidiasis
A single 70 mg loading dose should be administered on day 1, followed by 50 mg daily thereafter.
Duration of treatment of invasive candidiasis should be dictated by the patient's clinical and microbiological response. In general, antifungal therapy should continue for at least 14 days after the last positive culture. Patients who remain persistently neutropenic may warrant a longer course of therapy pending resolution of the neutropenia.

Oesophageal and oropharyngeal candidiasis
Fifty (50) mg should be administered daily.

Invasive aspergillosis
A single 70 mg loading dose should be administered on day 1, followed by 50 mg daily thereafter.
Duration of treatment should be based upon the severity of the patient's underlying disease, recovery from immunosuppression, and clinical response. The efficacy of doses above 70 mg is not known. Safety data suggests that an increase in dose to 70 mg daily is well tolerated. The efficacy of doses above 70 mg has not been adequately studied in patients with invasive aspergillosis.

Special populations
No dosage adjustment is necessary for elderly patients (65 years of age or more).
No dosage adjustment is necessary based on gender or renal impairment.
When co-administering IVECAS in adult patients with the metabolic inducers efavirenz, nevirapine, rifampicin, dexamethasone, phenytoin, or carbamazepine, use of a daily dose of 70 mg of IVECAS, should be considered (see section 4.5).

Patients with hepatic insufficiency
Adult patients with mild hepatic insufficiency (Child-Pugh score 5 - 6):
No dose adjustment is required.

Adult patients with moderate hepatic impairment (Child-Pugh score 7 - 9):
35 mg IVECAS per day is recommended. However, where recommended, a 70 mg loading dose should still be administered on day 1.

Severe hepatic impairment:
There is no clinical experience in adult patients with severe hepatic insufficiency (Child-Pugh score > 9) (see section 4.3) and in paediatric patients with any degree of hepatic insufficiency.

Paediatric population
IVECAS should be administered in children and adolescents by slow IV infusion over approximately 1 hour.
Dosing in children and adolescents (3 months to 17 years of age) should be based on the patient's body surface area (see section 6.1 "Instructions for use in paediatric patients", Mosteller[1] formula).
For all indications a single 70 mg/m² loading dose (not to exceed an actual dose of 70 mg) should be administered on day 1, followed by 50 mg/m² daily thereafter (not to exceed an actual dose of 70 mg daily). Duration of treatment should be individualised to the indication, as described for each indication in adults (see "General recommendation in adult patients" above).
[1]Mosteller RD: Simplified Calculation of Body Surface Area. N Engl J Med 1987 Oct 22;317(17): 1098 (letter)

If the 50 mg/m² daily dose is well tolerated but does not provide an adequate clinical response, the daily dose can be increased to 70 mg/m² daily (not to exceed an actual daily dose of 70 mg). Although an increase in efficacy with 70 mg/m² has not been demonstrated, limited safety data suggest that an increase in dose to 70 mg/m² daily is well tolerated.
When co-administering caspofungin, as in IVECAS, to paediatric patients with metabolic inducers such as efavirenz, nevirapine, rifampicin, dexamethasone, phenytoin, or carbamazepine, use of a daily dose of 70 mg/m² of IVECAS (not to exceed an actual daily dose of 70 mg), should be considered (see section 4.5).

Method of administration
IVECAS SOLUTION should be administered in by slow intravenous infusion over approximately 1 hour.
For instructions for reconstitution and further dilution, see section 6.6.
IVECAS should be given as a single infusion.

4.3 Contraindications
- hypersensitivity to caspofungin or to any of the ingredients of IVECAS, listed in section 6.1
- severe hepatic insufficiency, as caspofungin as in IVECAS has not been studied in these patients.

4.4 Special warnings and precautions for use
Limited data suggest that less common non-*Candida* yeasts and non-*Aspergillus* moulds are not covered by caspofungin (contained in IVECAS). The efficacy of caspofungin against these fungal pathogens has not been established.

Hypersensitivity reactions
Anaphylaxis has been reported during administration of caspofungin, as in IVECAS. If this occurs, IVECAS should be discontinued and appropriate treatment administered.
Possible histamine-mediated adverse reactions, including rash, facial swelling, angioedema, pruritus, sensation of warmth, or bronchospasm have been reported and may require discontinuation and/or administration of appropriate treatment (see section 4.8).
Cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported after post marketing use of caspofungin (as in IVECAS). Caution should apply in patients with history of allergic skin reactions (see section 4.8).

Concomitant use with ciclosporin
Transient increases in alanine transaminase (ALT) and aspartate transaminase (AST) of less than or equal to 3-fold the upper limit of normal (ULN) may occur when caspofungin, as in IVECAS, is given concomitantly with ciclosporin. These increases can be resolved with discontinuation of these medicines (see section 4.5).
There is an increase of approximately 35 % in the area under the curve (AUC) of caspofungin when IVECAS and ciclosporin are co-administered; blood levels of ciclosporin remain unchanged. IVECAS should only be used in patients receiving ciclosporin when the potential benefit outweighs the potential risk. Close monitoring of liver enzymes should be considered if IVECAS and ciclosporin are used concomitantly.

Hepatic impairment
In adult patients with mild and moderate hepatic impairment, the AUC can be increased by about 20 % and 75 %, respectively (see sections 5.2 and 4.2).
A reduction of the daily dose to 35 mg is recommended for adults with moderate hepatic impairment (see section 4.2).
There is no clinical experience in adults with severe hepatic impairment or in paediatric patients with any degree of hepatic impairment. A higher exposure than in moderate hepatic impairment is expected and IVECAS should not be used in these patients (see section 4.3).
Laboratory abnormalities in liver function tests have been seen in healthy volunteers and adult and paediatric patients treated with caspofungin (as in IVECAS). In some adult and paediatric patients with serious underlying conditions who were also receiving multiple concomitant medicines, cases of clinically significant hepatic dysfunction, hepatitis and hepatic failure have been reported; a causal relationship to caspofungin (as in IVECAS) has not been established. Patients who develop abnormal liver function tests during treatment with IVECAS should be monitored for evidence of worsening hepatic function and the risk/benefit of continuing therapy should be re-evaluated.

Information on excipients of IVECAS
IVECAS contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not receive IVECAS.

IVECAS contains less than 1 mmol (0,023 mg) sodium per 10 mL, that is to say essentially 'sodium free'.

4.5 Interaction with other medicines and other forms of interaction
In vitro, caspofungin is not an inhibitor of any enzyme in the cytochrome P450 (CYP) system and does not induce the CYP3A4 metabolism of other medicines. Caspofungin is not a substrate for P-glycoprotein and is a poor substrate for cytochrome P450 enzymes. However, caspofungin did interact with other medicines in pharmacological and clinical studies (see below).
Limited data from population pharmacokinetics show that concomitant use of IVECAS with the inducers efavirenz, nevirapine, dexamethasone, phenytoin, or carbamazepine may result in a decrease in caspofungin AUC. When co-administering inducers of metabolic enzymes, an increase in the daily dose of caspofungin to 70 mg following the 70 mg loading dose, should be considered in adult patients (see section 4.2).

In vitro and *in vivo* studies of caspofungin in combination with amphotericin B, does not result in antagonism of antifungal activity against either *A. fumigatus* or *C. albicans*. Results from *in vitro* studies suggest that there was some evidence of additive/indifferent or synergistic activity against *A. fumigatus* and additive/indifferent activity against *C. albicans*. The clinical significance of these results is unknown.

Ciclosporin
Ciclosporin A increases the AUC of caspofungin (as in IVECAS) by approximately 35 %. The increase in AUC is probably due to reduced uptake of caspofungin by the liver. Caspofungin does not increase the plasma levels of ciclosporin. There are transient increases in liver ALT and AST of less than or equal to 3-fold the ULN when IVECAS and ciclosporin are co-administered, which should resolve with discontinuation of both these medicines (see section 4.4).
Close monitoring of liver enzymes should be considered if the two medicines are used concomitantly.

Tacrolimus
Caspofungin, as in IVECAS, reduces the trough concentration of tacrolimus by 26 % in healthy subjects. For patients receiving both therapies, standard monitoring of tacrolimus blood concentrations and appropriate tacrolimus dosage adjustments are essential.

Rifampicin
IVECAS does not influence the pharmacokinetics of rifampicin, however rifampicin may cause a 60 % increase in AUC and 170 % increase in trough concentration of caspofungin on the first day of co-administration when both medicines are initiated together. Caspofungin trough levels gradually decrease upon repeated administration. After two weeks' administration rifampicin has limited effect on AUC, but trough levels are 30 % lower than in adult patients who receive IVECAS alone. The mechanism of interaction may possibly be due to an initial inhibition and subsequent induction of transport proteins. A similar effect could be expected for other medicines that induce metabolic enzymes.
Data suggest that the inducible medicine clearance mechanism involved in caspofungin disposition is likely an uptake transport process, rather than metabolism. Therefore, when IVECAS is co-administered to adult patients with inducers of medicine clearance, such as efavirenz, nevirapine, rifampicin, dexamethasone, phenytoin or carbamazepine, use of a daily dose of 70 mg of IVECAS should be considered (see section 4.2)

Clinical studies in adult healthy volunteers show that medicines such as itraconazole, amphotericin B, mycophenolate, nelfinavir or tacrolimus do not alter the pharmacokinetics of caspofungin. IVECAS has no effect on the pharmacokinetics of itraconazole, amphotericin B, rifampicin, or the active metabolite of mycophenolate.

All adult drug-drug interaction studies were conducted at a 50 or 70 mg daily caspofungin dose. The interaction of higher doses of caspofungin with other medicines has not been formally studied.

Paediatric population
In paediatric patients, co-administration of dexamethasone with caspofungin, as in IVECAS, may result in clinically meaningful reductions in caspofungin trough concentrations. Paediatric patients may possibly have similar reductions with inducers as seen in adults.
When caspofungin as in IVECAS is co-administered to paediatric patients (12 months to 17 years of age) with inducers of medicine clearance, such as rifampicin, efavirenz, nevirapine, phenytoin, dexamethasone, or carbamazepine, an IVECAS dose of 70 mg/m² daily (not to exceed an actual daily dose of 70 mg) should be considered.

4.6 Fertility, pregnancy and lactation
Pregnancy
IVECAS should not be used during pregnancy as there is no clinical experience involving pregnant women.
Animal studies have shown developmental toxicity. Caspofungin has been shown to cross the placental barrier in animal studies.

Breastfeeding
It is not known whether caspofungin as in IVECAS is excreted in human milk; therefore, women receiving IVECAS should not breastfeed their babies.
Available pharmacodynamic/toxicological data in animals have shown excretion of caspofungin in milk.

Fertility
There are no clinical data for caspofungin, as in IVECAS, to assess its impact on fertility.

4.7 Effects on ability to drive and use machines
IVECAS may cause dizziness, somnolence and blurred vision. Patients should be advised not to drive or operate machinery or tools until they know how treatment with IVECAS affects them.

4.8 Undesirable effects
Summary of the safety profile
Hypersensitivity reactions (anaphylaxis and possibly histamine-mediated adverse reactions) have been reported (see section 4.4).
Also reported in patients with invasive aspergillosis were pulmonary oedema, adult respiratory distress syndrome (ARDS), and radiographic infiltrates.

a. Adult patients
Phlebitis was a commonly reported local injection-site adverse reaction in all patient populations. Other local reactions included erythema, pain/tenderness, itching, discharge, and a burning sensation.
Reported clinical and laboratory abnormalities among all adults treated with caspofungin were typically mild and rarely led to discontinuation.

Tabulated list of adverse reactions

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	*Frequent*	Decreased haemoglobin, decreased haematocrit, anaemia, decreased white blood cell count
	Less frequent	Thrombocytopaenia, coagulopathy, leukopaenia, eosinophil count increased, decreased platelet count, increased platelet count, decreased lymphocyte count, increased white blood cell count, decreased neutrophil count
Immune system disorders	*Frequency unknown*	Hypersensitivity reactions (anaphylaxis and possibly histamine-mediated adverse reactions) (see section 4.4)
Metabolism and nutrition disorders	*Frequent*	Hypokalaemia
	Less frequent	Fluid overload, hypomagnesaemia, anorexia, electrolyte imbalance, hyperglycaemia, hypocalcaemia, metabolic acidosis
Psychiatric disorders	*Less frequent*	Anxiety, disorientation, insomnia
Nervous system disorders	*Frequent*	Headache
	Less frequent	Dizziness, dysgeusia, paraesthesia, somnolence, tremor, hypaesthesia
Eye disorders	*Less frequent*	Ocular icterus, vision blurred, eyelid oedema, increased lacrimation
Cardiac disorders	*Less frequent*	palpitations, tachycardia, dysrhythmia, atrial fibrillation, congestive cardiac failure
Vascular disorders	*Frequent*	Phlebitis
	Less frequent	Thrombophlebitis, flushing, hot flush, hypertension, hypotension
	Frequency unknown	Swelling, peripheral oedema
Respiratory, thoracic and mediastinal disorders	*Frequent*	Dyspnoea
	Less frequent	Nasal congestion, pharyngolaryngeal pain, tachypnoea, bronchospasm, cough, dyspnoea paroxysmal nocturnal, hypoxia, rales, wheezing
	Frequency unknown	Pulmonary oedema, adult respiratory distress syndrome (ARDS) and radiographic infiltrates
Gastrointestinal disorders	*Frequent*	Nausea, diarrhoea, vomiting
	Less frequent	Abdominal pain, abdominal pain upper, dry mouth, dyspepsia, stomach discomfort, abdominal distension, ascites, constipation, dysphagia, flatulence
Hepatobiliary disorders	*Frequent*	Elevated liver values (alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood alkaline phosphatase, conjugated bilirubin, blood bilirubin)
	Less frequent	Cholestasis, hepatomegaly, hyperbilirubinaemia, jaundice, abnormal hepatic function, hepatotoxicity, liver disorder, increased gamma-glutamyl transferase (GGT)
	Frequency unknown	Hepatic dysfunction
Skin and subcutaneous tissue disorders	*Frequent*	Rash, pruritus, erythema, hyperhidrosis
	Less frequent	Erythema multiforme, macular rash, maculopapular rash, pruritic rash, urticaria, allergic dermatitis, generalised pruritus, erythematous rash, generalised rash, morbilliform rash, skin lesion
	Frequency unknown	Toxic epidermal necrolysis and Stevens-Johnson syndrome (see section 4.4)
Musculoskeletal, connective tissue and bone disorders	*Frequent*	Arthralgia
	Less frequent	Back pain, pain in extremity, bone pain, muscular weakness, myalgia
Renal and urinary disorders	*Less frequent*	Renal failure, acute renal failure
General disorders and administrative site conditions	*Frequent*	Pyrexia, chills, infusion site pruritus
	Less frequent	Pain, catheter site pain, fatigue, feeling cold, feeling hot, infusion site erythema, infusion site induration, infusion site pain, infusion site swelling, injection site phlebitis, oedema peripheral, tenderness, chest discomfort, chest pain, face oedema, feeling of body temperature change, induration, infusion site extravasation, infusion site irritation, infusion site phlebitis, infusion site rash, infusion site urticaria, injection site erythema, injection site oedema, injection site pain, injection site swelling, malaise, oedema
Investigations	*Frequent*	Decreased blood potassium, decreased blood albumin
	Less frequent	Increased blood creatinine, positive red blood cells urine, decreased total protein, protein urine present, prolonged prothrombin time, shortened prothrombin time, decreased blood sodium, increased blood sodium, increased blood calcium, decreased blood chloride, decreased blood phosphorus, increased blood phosphorus, increased blood urea, prolonged activated partial thromboplastin time, decreased blood bicarbonate, increased blood chloride, increased blood potassium, decreased blood uric acid, blood urine present, abnormal breath sounds, decreased carbon dioxide, increased immunosuppressant medicine level, international normalised ratio increased, urinary casts, positive white blood cells urine, and increased pH urine.

b. Paediatric patients
The most common medicine related clinical adverse experiences reported in paediatric patients treated with caspofungin (as in IVECAS) were pyrexia, rash and headache.

Tabulated list of adverse reactions

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	*Frequent*	Eosinophil counts increased
Nervous system disorders	*Frequent*	Headache
Cardiac disorders	*Frequent*	Tachycardia
Vascular disorders	*Frequent*	Flushing, hypotension
Hepatobiliary disorders	*Frequent*	Elevated liver enzyme levels (AST, ALT)
Skin and subcutaneous tissue disorders	*Frequent*	Rash, pruritus
General disorders and administration site conditions	*Frequent*	Fever, chills, catheter site pain
Investigations	*Frequent*	Decreased potassium, hypomagnesaemia, increased glucose, decreased phosphorus, and increased phosphorus

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website. An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 Overdose
Signs and symptoms:
In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).
In clinical studies, the highest dose was 210 mg, which was administered as a single dose to 6 adult subjects and was generally well tolerated. In addition, a dose of 150 mg once daily up to 51 days has been administered to 100 adult patients and was generally well tolerated.

Management of overdose:
Caspofungin is not dialysable.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Other antimycotics for systemic use.
ATC code: J02AX04
Pharmacological classification: A 20.2.2 Antimicrobial (chemotherapeutic agents): Fungicides

Mechanism of action
Caspofungin acetate inhibits the synthesis of beta (1,3)-D-glucan, an essential component of the cell wall of many filamentous fungi and yeasts. Beta (1,3)-D-glucan is not present in mammalian cells.
Fungicidal activity with caspofungin has been demonstrated against *Candida* and *Aspergillus species.*

Resistance
Mutants of *Candida* with reduced susceptibility to caspofungin have been identified in some patients during treatment. A caspofungin minimal inhibitory concentration (MIC) of < 2 micrograms/mL using the CLSI (clinical and laboratory standards institute) M27-A3 method indicates that the *Candida* isolate is likely to be inhibited, if caspofungin therapeutic concentrations are achieved; there is insufficient treatment outcome information on isolates with reduced caspofungin susceptibility to define categories other than susceptible. Breakthrough infections with *Candida* isolates requiring caspofungin concentration > 2 micrograms/mL for growth inhibition have developed in a mouse model of *C. albicans* infection and in some patients with *Candida*- infections. Some of these isolates had mutations in the FKS1 gene.
Development of *in vitro* resistance to caspofungin by *Aspergillus* species has been identified. In limited clinical experience, resistance to caspofungin in patients with invasive *aspergillosis* has been observed. The mechanism of resistance has not been established. The incidence of resistance to caspofungin in various clinical isolates of *Candida*- and *Aspergillus* species is unknown. Caspofungin resistance in *Candida* has been observed, but the incidence may differ by species or region.
Less frequently non-*Candida* yeasts and non-*Aspergillus* moulds are not sensitive to caspofungin. The efficacy of caspofungin against these fungal pathogens has not been established.

Cross-resistance
Caspofungin acetate is active against strains of *Candida* with intrinsic or acquired resistance to fluconazole, amphotericin B, or flucytosine, consistent with their different mechanisms of action.

5.2 Pharmacokinetic properties
Distribution:
Plasma concentrations of caspofungin decline in a polyphasic manner following single 1 hour intravenous infusions. A short alpha-phase occurs immediately post-infusion, followed by a beta-phase with a half-life of 9 - 11 hours that characterises much of the profile and exhibits clear log-linear behaviour from 6 - 48 hours post-dose during which the plasma concentration decreases by 10-fold. An additional gamma-phase also occurs (half-life 40 - 50 hours).
Distribution, rather than excretion or biotransformation, is the dominant mechanism influencing plasma clearance.
Caspofungin is extensively bound to albumin (approximately 97 %), and distribution into red blood cells is minimal. There is little excretion or biotransformation of caspofungin during the first 30 hours after administration.

Biotransformation:
Caspofungin is slowly metabolised by hydrolysis and N-acetylation.
Caspofungin also undergoes spontaneous chemical degradation to an open-ring peptide compound. At later time points (> 5 days post-dose), there is a low level of covalent binding, which may be due to two reactive intermediates formed during the chemical degradation of caspofungin. Additional metabolism involves hydrolysis into constitutive amino acids and their derivatives, including dihydroxyhomotyrosine and N-acetyl-dihydroxyhomotyrosine. These two tyrosine derivatives are found only in urine, suggesting rapid clearance of these derivatives by the kidneys.

Elimination:
Two single-dose radio-labelled pharmacokinetic studies were conducted. In one study, plasma, urine and faeces were collected over 27 days, and in the second study plasma was collected over 6 months. Approximately 75 % of the radioactivity was recovered: 41 % in urine and 34 % in faeces.
Plasma concentrations of radioactivity and of caspofungin were similar during the first 24 - 48 hours post-dose; thereafter medicine levels fell more rapidly. In plasma, caspofungin concentrations fall below the limit of quantitation 6 - 8 days post-dose, while radio-label fell below the limit of quantitation at 22,3 weeks post-dose. A small amount of caspofungin is excreted unchanged in urine (approximately 1,4 % of the administered dose).
Renal clearance of the parent substance is low (approximately 0,15 mL/min).

Pharmacokinetics in special patient groups
Paediatric population
Caspofungin has been studied in five prospective studies involving patients under 18 years of age, including three paediatric pharmacokinetic studies (initial study in adolescents [12 - 17 years old] and children [2 - 11 years old] followed by a study in younger patients [3 - 23 months old] and then followed by a study in neonates and infants [< 3 months]).

In adolescents (ages 12 - 17 years) receiving caspofungin at 50 mg/m² daily, the caspofungin plasma AUC_{0-24h} was generally comparable to that seen in adults receiving caspofungin at 50 mg daily.
All adolescents received doses > 50 mg daily, and in fact, 6 of 8 received the maximum dose of 70 mg/day. The caspofungin plasma concentrations in these adolescents were reduced relative to adults receiving 70 mg daily, the dose most often administered to adolescents.

In children (ages 2 - 11 years) receiving caspofungin at 50 mg/m² daily (maximum 70 mg daily), the caspofungin plasma AUC_{0-24h} after multiple doses was comparable to that seen in adults receiving caspofungin at 50 mg/day.
On the first day of administration, AUC_{0-24hr} was somewhat higher in children than adults for these comparisons (37 % increase for the 50 mg/m²/day to 50 mg/day comparison). However, it should be recognised that the AUC values in these children on day 1 were still less than those seen in adults at steady-state conditions.

In young children and toddlers (ages 3 - 23 months) receiving caspofungin at 50 mg/m² daily (maximum 70 mg daily), the caspofungin plasma AUC_{0-24h} after multiple doses was comparable to that seen in adults receiving caspofungin at 50 mg daily.
As in the older children, these young children who received 50 mg/m² daily had slightly higher AUC_{0-24hr} values on day 1 relative to adults receiving the standard 50 mg daily dose. The caspofungin pharmacokinetic results from the young children (3 - 23 months of age) that received 50 mg/m² caspofungin daily were similar to the pharmacokinetic results from older children (2 - 11 years old) that received the same dosing regimen.

In neonates and infants (< 3 months) receiving caspofungin at 25 mg/m² daily, caspofungin peak concentration (C_{1hr}) and caspofungin trough concentration (C_{24hr}) after multiple doses were comparable to that seen in adults receiving caspofungin at 50 mg daily. On day 1, C_{1hr} was comparable and C_{24hr} modestly elevated (36 %) in these neonates and infants relative to adults. AUC_{0-24hr} measurements were not performed in this study due to the sparse plasma sampling.
The efficacy and safety of caspofungin have not been adequately studied in infants under 3 months of age and IVECAS is therefore not indicated for this age group.

Gender
The plasma concentration of caspofungin is similar in healthy men and women on day 1 following a single 70 mg dose. After 13 daily 50 mg doses, the caspofungin plasma concentration in some women may be elevated approximately 20 % relative to men.

Elderly patients
The plasma concentration of caspofungin in healthy older men and women (aged > 65 years) is increased by approximately 28 % in area under the curve (AUC) compared to young healthy males. In patients who were treated empirically or who had invasive candidiasis, a similar modest effect of age was seen in older patients relative to younger patients. However, no dosage adjustment is necessary for elderly patients.

Hepatic insufficiency
Plasma concentrations of caspofungin after a single 70 mg dose in patients with mild hepatic insufficiency (Child-Pugh score 5 - 6) are increased by approximately 55 % in AUC compared to healthy subjects.
Plasma concentrations in patients with mild hepatic insufficiency are increased modestly (19 - 25 % in AUC) on days 7 and 14 relative to healthy subjects. A reduction of the daily dose to 35 mg in moderate hepatic impairment can provide an AUC similar to that obtained in subjects with normal hepatic function, receiving the standard regimen.
No data are available on patients with severe hepatic insufficiency (see section 4.3).

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Glacial acetic acid
Mannitol
Sodium hydroxide (for pH adjustment)
Sucrose

6.2 Incompatibilities
DO NOT use any diluents containing dextrose (alpha-D-glucose), as IVECAS is not stable in such diluents.
In the absence of compatibility studies, IVECAS must not be mixed with other medicines.

6.3 Shelf life
Storage of the product before reconstitution
24 months

Storage of the reconstituted product in vials
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. Chemical and physical in-use stability has been demonstrated for 24 hours when stored at or below 25 °C or in the refrigerator at 2 °C - 8 °C prior to the preparation of the patient's infusion solution.

Storage of the diluted product for infusion
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. Chemical and physical in-use stability has been demonstrated for 48 hours when stored in the refrigerator at 2 °C - 8 °C in the intravenous bag or bottle.

6.4 Special precautions for storage
Unopened vials: Store in the original packaging in a refrigerator (2 °C - 8 °C).
Do not freeze.
For storage conditions after reconstitution and dilution of the medicine, see section 6.3.

6.5 Nature and contents of container
IVECAS 50 IV and IVECAS 70 IV powder for concentrate for solution for infusion are supplied in clear glass type I, 10mL vials, sealed with a rubber stopper and an aluminium band with a plastic flip-off cap.
Supplied in packs of one 10 mL vial.

6.6 Special precautions for disposal and other handling
Reconstitution
DO NOT use any diluents containing dextrose (alpha-D-glucose), as IVECAS is not stable in such diluents.
DO NOT mix or co-infuse IVECAS with any other medicines. There is no data available on the compatibility of IVECAS with other intravenous substances, additives, or medicines. Visually inspect the infusion solution for particulate matter or discolouration before use.
Any unused medicine or waste material must be disposed of in accordance with local requirements.

INSTRUCTION FOR USE IN ADULTS
1. Reconstitution of vials
To reconstitute the lyophilised powder, bring the refrigerated vial of IVECAS to room temperature and aseptically add 10,5 mL of sterile water for injection. The concentrations of the reconstituted vials will be: 7,2 mg/mL (70 mg vial) or 5,2 mg/mL (50 mg vial).
The white to off-white compact powder will dissolve completely. Mix gently until a clear solution is obtained.
Reconstituted solutions should be visually inspected for particulate matter or discolouration. The reconstituted solution may be stored for up to 24 hours at or below 25 °C.
The reconstituted solution is clear and essentially free from visible particles.

2. Addition of reconstituted IVECAS to patient infusion solution
Diluents for the final solutions for infusion are sodium chloride 0,225 %; 0,45 % or 0,9 % *m/v* for injection, or lactated Ringer's solution.
The standard patient infusion is prepared by aseptically adding the appropriate amount of reconstituted medicines (see "Preparation of the patient infusion solutions") to a 250 mL intravenous bag or bottle. Reduced volume infusions in 100 mL may be used, if necessary, for 50 mg or 35 mg daily doses. Do not use if the solution is cloudy or if any precipitation is detected.

The prepared infusion solution must be used within 24 hours if stored at or below 25 °C or within 48 hours if refrigerated at 2 - 8 °C. IVECAS should be administered by slow intravenous infusion over approximately 1 hour.

Preparation of the patient infusion solutions in adults:

DOSE*	Volume of reconstituted IVECAS for transfer to intravenous bag or bottle	Standard preparation (reconstituted IVECAS added to 250 mL) final concentration	Reduced volume infusion (reconstituted IVECAS added to 100 mL) final concentration
70 mg	10 mL	0,28 mg/mL	Not recommended
70mg (from two 50 mg vials)**	14 mL	0,28 mg/mL	Not recommended
50 mg	10 mL	0,20 mg/mL	0,47 mg/mL
35 mg for moderate hepatic insufficiency (from one 70 mg vial)	5 mL	0,14 mg/mL	0,34 mg/mL
35mg for moderate hepatic insufficiency (from one 50 mg vial)	7 mL	0,14 mg/mL	0,34 mg/mL

* 10,5 mL should be used for reconstitution of all vials
**If a 70 mg vial is not available, the 70 mg dose can be prepared from two 50 mg vials

INSTRUCTIONS FOR USE IN PAEDIATRIC PATIENTS
Calculation of body surface area (BSA) for paediatric dosing
Before preparation of infusion, calculate the BSA of the patient using the following formula (Mosteller formula)[1]:

$$BSA\ (m^2) = \sqrt{\frac{\text{Height (cm) X Weight (kg)}}{3600}}$$

[1]Mosteller RD: Simplified Calculation of Body Surface Area. N Engl J Med 1987 Oct 22;317(17): 1098 (letter)

Preparation of the 70 mg/m² infusion for paediatric patients >3 months of age (using a 70 mg vial)
1. Determine the actual loading dose to be used in the paediatric patient by using the patient's BSA (as calculated above) and the following equation:
   BSA (m²) X 70 mg/m² = Loading Dose
   The maximum loading dose on day 1 should not exceed 70 mg regardless of the patient's calculated dose.
2. Equilibrate the refrigerated vial of IVECAS to room temperature.
3. Aseptically add 10,5 mL of water for injection.[a] This reconstituted solution may be stored for up to 24 hours at or below 25°C.[b] This will give a final caspofungin concentration in the vial of 7,2 mg/mL (if using a 70 mg vial).
4. Remove the volume of medicinal product equal to the calculated loading dose (Step 1) from the vial. Aseptically transfer this volume (mL)[c] of reconstituted IVECAS to an IV bag (or bottle) containing 250 mL of 0,9 %, 0,45 % or 0,225 % sodium chloride injection, or lactated Ringer's injection. Alternatively, the volume (mL)[c] of reconstituted IVECAS can be added to a reduced volume of 0,9 %, 0,45 % or 0,225 % sodium chloride injection or lactated Ringers injection, not to exceed a final concentration of 0,5 mg/mL. This infusion solution must be used within 24 hours if stored at or below 25 °C or within 48 hours if stored refrigerated at 2 - 8°C.
5. If the calculated dose is less than 50 mg, then the dose may be prepared from the 50 mg vial (follow steps 2 - 4 from ***"Preparation of the 50 mg/m² infusion for paediatric patients > 3 months of age (using a 50 mg vial)"***). The final caspofungin concentration in the 50 mg vial after reconstitution is 5,2 mg/mL.

Preparation of the 50 mg/m² infusion for paediatric patients >3 months of age (using a 50 mg vial)
1. Determine the actual daily maintenance dose to be used in the paediatric patient by using the patient's BSA (as calculated above) and the following equation:
   BSA (m²) X 50 mg/m² = Daily Maintenance Dose
   The daily maintenance dose should not exceed 70 mg regardless of the patient's calculated dose.
2. Equilibrate the refrigerated vial of IVECAS to room temperature.
3. Aseptically add 10,5 mL of water for injection.[a] This reconstituted solution may be stored for up to 24 hours at or below 25°C.[b] This will give a final caspofungin concentration in the vial of 5,2 mg/mL (using a 50 mg vial).
4. Remove the volume of medicine equal to the calculated daily maintenance dose (Step 1) from the vial. Aseptically transfer this volume (mL)[c] of reconstituted IVECAS to an IV bag (or bottle) containing 250 mL of 0,9 %, 0,45 % or 0,225 % sodium chloride injection, or lactated Ringers injection. Alternatively, the volume (mL)[c] of reconstituted IVECAS can be added to a reduced volume of 0,9 %, 0,45 % or 0,225 % sodium chloride injection or lactated Ringers injection, not to exceed a final concentration of 0,5 mg/mL. This infusion solution must be used within 24 hours if stored at or below 25 °C or within 48 hours if stored refrigerated at 2 - 8 °C.
5. If the actual daily maintenance dose is > 50 mg, then the dose may be prepared from the 70 mg vial (follow steps 2 - 4 from **"Preparation of the 70 mg/m² infusion for paediatric patients > 3 months of age (using a 70 mg vial)"**). The final caspofungin concentration in the 70 mg vial after reconstitution is 7,2 mg/mL.

Notes:
a. The white to off-white cake will dissolve completely. Mix gently until a clear solution is obtained.
b. Visually inspect the reconstituted solution for particulate matter or discolouration during reconstitution and prior to infusion. Do not use if the solution is cloudy or has precipitated.
c. IVECAS is formulated to provide the full labelled vial dose (50 mg or 70 mg) when 10 mL is withdrawn from the vial.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION
Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, 7945
Cape Town, South Africa
Tel: +27 21 707 7000
or 0860-PHARMA (742 762)

8. REGISTRATION NUMBERS
IVECAS 50 IV: A50/20.2.2/1014
IVECAS 70 IV: A50/20.2.2/1015

9. DATE OF FIRST AUTHORISATION
18 May 2021

10. DATE OF REVISION OF THE TEXT
26 February 2025

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

IVECAS 50 IV powder for solution for infusion
IVECAS 70 IV powder for solution for infusion
Caspofungin
Contains sugar (sucrose and the sugar alcohol, mannitol)
Each 50 mg vial contains sucrose 35,7 mg and mannitol 23,8 mg
Each 70 mg vial contains sucrose 50,0 mg and mannitol 33,3 mg

Read all of this leaflet carefully before you or your child are given IVECAS
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- IVECAS has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What IVECAS is and what it is used for
IVECAS is an antifungal medicine containing caspofungin that interferes with the production of a component (glucan polysaccharide) of the fungal cell wall that is necessary if the fungus is to continue living and growing. Fungal cells exposed to IVECAS have incomplete or defective cell walls, making them fragile and unable to grow.

IVECAS is used to treat certain types of fungal infections in adults and children 3 months to 17 years of age.

2. What you need to know before you are administered IVECAS
IVECAS should not be administered to you
Tell your doctor or healthcare professional before being given the injection if:
- if you are hypersensitive (allergic) to caspofungin or any of the other ingredients of IVECAS (see section 6)
- if you have very poor liver function.

You should not be administered IVECAS if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before IVECAS is administered to you.

Warnings and precautions
Tell your doctor or healthcare professional before being given the injection:
- if you are allergic to any other medicines
- if you are already taking ciclosporin (used to help prevent organ transplant rejection or to suppress your immune system), as your doctor may need to run extra blood tests during your treatment
- if you have ever had liver problems, as your doctor may want to change your dose of IVECAS
- if you have any other medical problem.

IVECAS may also cause serious skin reactions such as Stevens-Johnson syndrome (SJS) (painful skin condition that causes painful blister and sores of the skin and mucous membranes, especially in the mouth) and toxic epidermal necrolysis (TEN) (serious illness with blistering of the skin).

Children and adolescents
No information is available on the use of IVECAS in infants under 3 months of age and it should therefore not be administered to them.

Other medicines and IVECAS
Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)
- ciclosporin or tacrolimus (used to help prevent organ transplant rejection or to suppress your immune system) as your doctor may need to run extra blood tests during your treatment due to possible higher levels of certain liver enzymes and lower levels of tacrolimus in your blood
- rifampicin (an antibiotic used for tuberculosis (TB) or other infections) as the effect of IVECAS can be increased
- the following medicines as it may lower the caspofungin levels in your blood:
  - ◆ some human immunodeficiency virus (HIV) medicines such as efavirenz or nevirapine
  - ◆ phenytoin or carbamazepine (used for the treatment of seizures)
  - ◆ dexamethasone (a steroid - used for inflammation).

If you are not sure, talk to your doctor or healthcare provider before you are given IVECAS.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before IVECAS is administered to you.
IVECAS has not been studied in pregnant women. You should not use IVECAS when you are pregnant.
It is not known if IVECAS is excreted in human breastmilk. You should not breastfeed your baby whilst on treatment with IVECAS.

Driving and using machines
IVECAS may make you feel dizzy or sleepy and may cause blurry vision. You should not drive or use machines until you know how treatment with IVECAS affects you.
It is not always possible to predict to what extent IVECAS may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which IVECAS affects them.

IVECAS contains sugar
IVECAS contains sucrose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, talk to your doctor, nurse or pharmacist before you are given IVECAS.

IVECAS contains sodium
IVECAS contains less than 1 mmol (0,023 mg) sodium per 10 mL, that is to say essentially 'sodium free'.

3. How to use IVECAS
Do not share medicines prescribed for you or your child with any other person.
You will not be expected to give IVECAS to yourself. It will be given to you by a person who is qualified to do so.
IVECAS will be given once daily and will be slowly dripped into a vein (intravenous infusion), over about an hour.
Your doctor will decide on your dose. It will depend on the type of infection, your weight and your liver function.

Your doctor will work out the dose for your child, based on his/her height and weight.
The dose for children and adolescents may differ from the adult dose.

Your doctor will tell you how long your treatment with IVECAS will last.
If you have the impression that the effect of IVECAS is too strong or too weak, tell your doctor or pharmacist.

If you use more IVECAS than you should
Since a healthcare professional will administer IVECAS, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdose.

If you forget to use IVECAS
Since a healthcare professional will administer IVECAS, it is unlikely that the dose will be missed.

If you stop using IVECAS
Do not stop receiving treatment before your doctor agrees; the fungus (mould) causing the disease may become resistant to IVECAS.

4. Possible side effects
IVECAS can have side effects.
Not all side effects reported for IVECAS are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using IVECAS, please consult your doctor, pharmacist or other healthcare professional for advice.

If any of the following happens, stop using IVECAS and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash that gets worse or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to IVECAS. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- cough, serious breathing difficulties - if you are an adult and have invasive aspergillosis (infection, usually of the lungs) you may be experiencing a serious respiratory problem that could result in respiratory failure
- rash, skin peeling, mucous membrane sores, hives, large areas of peeling skin
- decreased flow of bile, enlarged liver, yellowing of the skin and/or whites of the eyes (jaundice), liver injury, liver disorder
- if your child or adolescent is having a faster heartbeat than normal.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- decreased haemoglobin (decreased oxygen carrying substance in the blood) and red blood cell count – you may feel weak, dizzy and have a headache
- feeling tired and getting infections easily (low white blood cell count)
- decreased blood albumin (a type of protein) in your blood, decreased potassium or low potassium levels in the blood
- headache
- inflammation of the vein (red and tender skin)
- shortness of breath
- nausea (feeling sick), vomiting (being sick), diarrhoea (loose bowels)
- changes in some laboratory tests (including increased values of some liver tests)
- skin rashes, itching, redness, sweating more than usual
- joint pains
- fever, chills
- itching at the site of the injection
- catheter site pain, flushing, low blood pressure.

Less frequent side effects:
- changes in some laboratory blood tests (including diseases of blood clotting, platelets and white blood cells)
- bruising or bleeding more easily and feeling tired. This could be because of various blood problems. Your blood will be tested in hospital
- loss of appetite
- swelling (increase in amount of body fluid), imbalance of salts/electrolytes in the body, high sugar level in the blood, low calcium level in the blood, increase calcium level in the blood, low magnesium level in the blood
- confusion, feeling tired, having tremors (metabolic acidosis; this occurs when your body produces too much acid)
- low blood pressure (you may feel dizzy when getting up)
- disorientation, feeling nervous, being unable to sleep
- feeling dizzy, decreased feeling or sensitivity (especially in the skin), shaking, feeling sleepy, change in the way things taste, tingling or numbness
- blurred vision, increase in tears, swollen eyelid, yellowing of the whites of the eyes
- sensation of fast or irregular heartbeats, palpitations (feeling your heartbeat), abnormal heart rhythm, heart failure
- flushing, hot flush, high blood pressure, low blood pressure, redness along a vein which is extremely tender when touched
- tightening of the bands of muscle around the airways resulting in wheezing or coughing, fast breathing rate, shortness of breath that wakes you up, shortage of oxygen in the blood, abnormal breath sounds, crackling sounds in the lungs, wheezing, stuffy nose, cough, throat pain
- belly pain, upper belly pain, bloating, constipation, difficulty swallowing, dry mouth, indigestion, passing gas, stomach discomfort, swelling due to build-up of fluid around the belly
- abnormal skin tissue, generalised itching, hives, rash of varying appearance, abnormal skin, red often itchy spots on your arms and legs and sometimes on the face and the rest of the body
- back pain, pain in an arm or leg, bone pain, muscle pain, muscle weakness
- loss of kidney function, sudden loss of kidney function
- injection/infusion site complaints (redness, hard lump, pain, swelling, irritation, rash, hives, leaking of fluid from the catheter into the tissue), inflammation of vein at injection site, feeling hot, feeling cold
- alterations in some laboratory blood and urine tests (including kidney electrolyte and clotting tests), increased levels of the medicines you are taking that weaken the immune system
- chest discomfort, chest pain, feeling of body temperature change, generally feeling unwell, general pain, swelling of the face, tenderness, feeling tired.

The following side effects have been reported but the frequency for them to occur is not known:
- Stevens-Johnson syndrome (SJS) (painful skin condition that causes painful blister and sores of the skin and mucous membranes, especially in the mouth) and toxic epidermal necrolysis (TEN) (serious illness with blistering of the skin).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website. By reporting side effects, you can help provide more information on the safety of IVECAS. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

5. How to store IVECAS
Store all medicines out of reach of children.
Store in the original outer packaging in a refrigerator at or between 2 - 8 °C.
Do not freeze.
Reconstituted concentrate should be used immediately. Chemically and physically stable for 24 hours at or below 25 °C or in the refrigerator at 2 - 8 °C prior to the preparation of the infusion solution.

Your healthcare provider will check that IVECAS is not past its expiry date stated on the label and carton before giving you the injection.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What IVECAS contains:
The active substance is caspofungin.
- each 10 mL vial of IVECAS 50 IV contains caspofungin acetate equivalent to caspofungin 50 mg
- each 10 mL vial of IVECAS 70 IV contains caspofungin acetate equivalent to caspofungin 70 mg.

The other ingredients are glacial acetic acid, mannitol, sodium hydroxide (for pH adjustment) and sucrose.

What IVECAS looks like and contents of the pack
Unopened vials
Each vial of IVECAS contains white to off-white lyophilised powder.

Reconstituted product in vials
Clear solution essentially free from visible particles.

Diluted product for infusion
Clear solution essentially free from visible particles.
IVECAS 50 IV and 70 IV lyophilised powder for solution for infusion are supplied in clear glass type I, 10 mL vials, sealed with a rubber stopper and an aluminium band with a plastic flip-off cap.

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This leaflet was last revised in
26 February 2025

Registration numbers
IVECAS 50 IV: A50/20.2.2/1014
IVECAS 70 IV: A50/20.2.2/1015

pharma dynamics

PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS: S4

IVECAS 50 IV poeier vir oplossing vir infusie
IVECAS 70 IV poeier vir oplossing vir infusie
Kaspofungien
Bevat suiker (sukrose en die suikeralkohol, mannitol)
Elke 50 mg flessie bevat sukrose 35,7 mg en mannitol 23,8 mg
Elke 70 mg flessie bevat sukrose 50,0 mg en mannitol 33,3 mg

Lees hierdie hele inligtingsblad deeglik deur, voordat u, of u kind, IVECAS toegedien word
- Hou hierdie inligtingsblad. Dit mag nodig wees vir u om dit weer te lees.
- Indien u verdere vrae het, vra asseblief u dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer.
- IVECAS is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander mense deel nie. Dit mag skadelik wees vir hulle, selfs al is hulle simptome dieselfde as u eie.

Inhoud van hierdie inligtingsblad

1. Wat IVECAS is en waarvoor dit gebruik word
IVECAS is 'n swamwerende medisyne, wat kaspofungien bevat, en inmeng met die produksie van 'n komponent van die swamselwand (glukanpolisakkaried). Hierdie komponent word benodig vir die swam se voortbestaan en groei. Swamselle wat aan IVECAS blootgestel word, het onvolledige, of defektiewe selwande, wat hul broos maak en nie in staat stel om te groei nie.

IVECAS word gebruik om sekere tipes swaminfeksies by volwassenes en kinders (vanaf 3 maande tot 17-jarige ouderdom), te behandel.

2. Wat u nodig het om te weet, voordat IVECAS aan u toegedien word
IVECAS moet nie aan u toegedien word
Vertel u dokter of gesondheidsorgdeskundige, voordat die inspuiting aan u toegedien word, indien:
- u hipersensitief (allergies) is vir kaspofungien, of enige van die ander bestanddele van IVECAS nie (sien afdeling 6)
- indien u 'n baie swak lewerfunksie het nie.

IVECAS moet nie aan u toegedien word, indien enige van bogenoemde op u van toepassing is nie. Indien u onseker is, praat met u dokter of apteker, voordat IVECAS aan u toegedien word.

Waarskuwings en voorsorgmaatreëls
Vertel u dokter of gesondheidsorgdeskundige, voordat die inspuiting aan u toegedien word:
- indien u allergies is vir enige ander medisyne
- indien u alreeds siklosporien neem (gebruik om te voorkom dat 'n orgaanoorplanting verwerp word, of om u immuunstelsel te onderdruk), aangesien dit nodig mag wees vir u dokter om bykomende bloedtoetse tydens u behandeling uit te voer
- indien u ooit lewerkwale gehad het, aangesien u dokter mag besluit om u IVECAS dosis te verander
- indien u enige ander mediese kwaal het.

IVECAS mag ook ernstige velreaksies, soos Stevens-Johnson-sindroom (SJS) (pynlike veltoestand wat seer blase en sere van die vel en slymvliesmembrane, veral in die mond, veroorsaak) en toksiese epidermale nekrolise (TEN) (ernstige siekte, met blaasvorming op die vel), veroorsaak.

Kinders en adolessente
Geen inligting is beskikbaar aangaande die gebruik van IVECAS by babas jonger as 3 maande nie en moet dus nie aan hulle toegedien word nie.

Ander medisyne en IVECAS
Vertel altyd u gesondheidsorgdeskundige indien u enige ander medisyne neem (Hierdie sluit aanvullende of tradisionele medisyne in).
- siklosporien of takrolimus (gebruik om te verhoed dat 'n orgaanoorplanting verwerp word, of om u immuunstelsel te onderdruk), aangesien dit nodig mag wees vir u dokter om bykomende bloedtoetse tydens u behandeling uit te voer, weens die moontlikheid vir hoër vlakke van sekere lewerensieme en laer vlakke van takrolimus in u bloed
- rifampisien, ('n antibiotikum wat gebruik word vir tuberkulose (TB), of ander infeksies), aangesien dit die werking van IVECAS mag versterk
- die volgende medisyne, aangesien dit die kaspofungienvlakke in u bloed mag verlaag:
  - ◆ sekere menslike immuniteitsgebreksvirus (MIV) medisyne, soos efavirens, of nevirapien
  - ◆ fenitoïen, of karbamasepien (gebruik vir die behandeling van aanvalle)
  - ◆ deksametasoon ('n steroïed – gebruik vir inflammasie).

Indien u nie seker is nie, praat met u dokter of gesondheidsorgverskaffer, voordat IVECAS aan u toegedien word.

Swangerskap, borsvoeding en fertiliteit
Indien u swanger is, of u baba borsvoed, vermoed dat u swanger is, of 'n baba beplan, raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgverskaffer vir advies, voordat IVECAS aan u toegedien word.
IVECAS is nie nagevors onder swanger vroue nie. U moet dus nie IVECAS toegedien word tydens swangerskap nie. Dit is onbekend of IVECAS in menslike borsmelk uitgeskei word. U moet dus nie borsvoed terwyl u met IVECAS behandel word nie.

Bestuur en die hantering van masjiene
IVECAS mag u duiselig, of slaperig laat voel en versteurde visie veroorsaak. U moet nie bestuur of masjiene gebruik, totdat u weet hoe die behandeling met IVECAS u beïnvloed nie.
Dit is nie altyd moontlik om te voorspel tot watter mate IVECAS met die daaglikse aktiwiteite van 'n pasiënt inmeng nie. Pasiënte moet verseker dat hulle nie by bogenoemde aktiwiteite betrokke raak, totdat hulle bewus is tot watter mate IVECAS hulle aantas nie.

IVECAS bevat suiker
IVECAS bevat sukrose ('n tipe suiker). Indien u dokter u ingelig het dat u 'n onverdraagsaamheid teenoor sekere suikers toon, praat met u dokter, verpleegkundige of apteker, voordat IVECAS aan u toegedien word.

IVECAS bevat natrium
IVECAS bevat minder as 1 mmol (0,023 mg) natrium per 10 mL, dit wil sê wesenlik 'natriumvry'.

3. Hoe om IVECAS te gebruik
Moet nie medisyne wat vir u, of u kind voorgeskryf is, met enige ander persoon deel nie.
Daar sal nie van u verwag word om IVECAS aan uself toe te dien nie. Dit sal toegedien word, deur 'n gekwalifiseerde persoon.
IVECAS sal een keer daagliks toegedien word en sal stadig-druppend in 'n aar gevoer word (intraveneuse infusie), oor 'n tydperk van ongeveer een uur. U dokter sal u dosis bepaal. Dit sal afhang van die tipe infeksie, u gewig en u lewerfunksie.

U dokter sal die dosis vir u kind, gebaseer op sy/haar lengte en gewig, bepaal.
Die dosis vir kinders en adolessente mag verskil van die volwasse dosis.

U dokter sal u vertel vir hoe lank u behandeling met IVECAS sal duur.
Indien u onder die indruk is, dat die uitwerking van IVECAS té sterk, of té swak is, vertel u dokter of apteker.

Indien u meer IVECAS ontvang as wat u behoort
Aangesien 'n gesondheidsorgdeskundige IVECAS sal toedien, sal hy/sy die dosis beheer. In die geval van 'n oordosering, sal u dokter egter die oordosering hanteer.

Indien u vergeet om IVECAS te gebruik
Aangesien 'n gesondheidsorgdeskundige IVECAS sal toedien, is dit onwaarskynlik dat die dosis oorgeslaan sal word.

Indien u die toediening van IVECAS staak
Moet nie ophou om behandeling te ontvang, voordat u dokter dit bevestig het nie; die swam (gis), wat die siekte veroorsaak, mag weerstandig raak teenoor IVECAS.

4. Moontlike newe-effekte
IVECAS mag newe-effekte hê.
Nie alle newe-effekte wat aangemeld word vir IVECAS, word in hierdie inligtingsblad ingesluit nie. Sou u algemene gesondheid versleg, of indien u enige ongunstige effekte ervaar terwyl u IVECAS ontvang, raadpleeg asseblief u dokter, apteker, of ander gesondheidsorgdeskundige vir advies.

Indien enige van die volgende gebeur, staak die gebruik van IVECAS en vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal:
- swelling van u hande, voete, enkels, gesig, lippe en mond of keel, wat sluk en asemhaling mag bemoeilik,
- veluitslae wat vererger, of 'n gejeuk
- floute.

Hierdie is alles baie ernstige newe-effekte. Indien u dit het, kon u 'n ernstige reaksie teenoor IVECAS ondervind het. U mag dringende mediese aandag of hospitalisasie benodig.

Vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal, indien u enige van die volgende opmerk:
- hoes, ernstige asemhalingsprobleme – indien u 'n volwassene is en indringende aspergilloses (infeksie, gewoonlik van die longe) het, mag u 'n ernstige asemhalingsprobleem ervaar, wat respiratoriese ineenstorting tot gevolg mag hê
- uitslag, velafskilfering, mukusmembraansere, urtikarie, groot oppervlaktes van afskilferende vel
- vermindering in galvloei, vergrote lewer, vergeling van die vel en/of wit gedeelte van die oë (geelsug), lewerskade, lewerkwaal
- indien u kind of adolessent 'n vinniger hartklop as wat normaal is, ondervind.

Hierdie is alles baie ernstige newe-effekte. U mag dringende mediese aandag benodig.

Vertel u dokter indien u enige van die volgende opmerk:
Algemene newe-effekte:
- afname in hemoglobien (afname in suurstofdraende substans in die bloed) en rooibloedseltelling – u mag swak en duiselig voel en 'n hoofpyn ervaar
- voel moeg en doen maklik infeksies op (lae witbloedseltelling)
- afname in bloedalbumien ('n tipe proteïen) in u bloed, afname in kalium, of lae kaliumvlakke in die bloed
- hoofpyn
- inflammasie van die aar (rooi en gevoelige vel)
- asemnood
- naarheid (voel naar), braking (gooi op), diarree (los stoelgang)
- veranderinge in sommige laboratoriumtoetse (insluitend verhoogde vlakke van sommige lewertoetse)
- veluitslae, gejeuk, rooiheid, sweet meer as wat normaal is
- gewrigspyne
- koors, koue rillings
- gejeuk by die inspuitingsplek
- pyn in die omgewing van die kateter, blosvorming, lae bloeddruk.

Minder algemene newe-effekte:
- veranderinge in sommige laboratoriumbloedtoetse (insluitend bloedstollings-, plaatjie- en witbloedselsiektes)
- kneusing of bloei makliker en voel moeg. Dit kan voorkom weens 'n verskeidenheid van bloedprobleme. U bloed sal in die hospitaal getoets word
- aptytverlies
- swelling (toename in die hoeveelheid liggaamsvloeistof), wanbalans van soute/elektroliete in die liggaam, hoë bloedsuikervlakke, lae kalsiumvlakke in die bloed, verhoogde kalsiumvlak in die bloed, lae magnesiumvlak in die bloed
- verwarring, voel moeg, bewing (metaboliese asidose; dit kom voor wanneer u liggaam te veel suur vervaardig)
- lae bloeddruk (u mag duiselig voel wanneer u opstaan)
- disoriëntasie, voel senuweeagtig, nie in staat om te slaap nie
- voel duiselig, afname in gevoel, of sensitiwiteit (veral die vel), bewing, voel slaperig, smaaksteurnis, tinteling, of gevoelloosheid
- sigsteurnis, meer trane, geswelde ooglid, vergeling van die wit gedeeltes van die oë
- sensasie van 'n vinnige, of onreëlmatige hartklop, palpitasies (voel u hartklop) abnormale hartritme, hartversaking
- blosvorming, warm gloed, hoë bloeddruk, lae bloeddruk, rooiheid langs 'n aar, wat uiters gevoelig is vir aanraking
- vernouing van die spierbande rondom die lugweë, wat lei tot gehyg, of hoes, vinnige asemhaling, asemnood wat u wakker maak, tekort aan suurstof in die bloed, abnormale asemhalingsgeluide, krakende geluid in die longe, gehyg, toe neus, hoes, keelpyn
- buikpyn, boonste buikpyn, opgeblaasdheid, hardlywigheid, sluk moeilik, droë mond, indigestie, winderigheid, maagongemak, swelling weens die opbou van vloeistof in die buikomgewing
- abnormale velweefsel, algemene gejeuk, urtikarie, uitslag met 'n verskeidenheid van voorkoms, abnormale vel, rooi, dikwels jeukerige kolle op u arms en bene en somtyds in die gesig en op die res van die liggaam
- rugpyn, pyn in 'n arm of been, beenpyn, spierpyn, spierswakheid
- verlies van nierfunksie, skielike verlies van nierfunksie
- inspuitings/infusieplek klagtes (rooiheid, harde knop, pyn, swelling, irritasie, uitslag, urtikarie, lekkasie van vloeistof vanuit die kateter in die weefsel), inflammasie van 'n aar by die inspuitingtoedieningsarea, voel warm, voel koud
- veranderinge in sommige laboratorium bloed- en urientoetse (insluitend nier-elektroliet en stollingstoetse), verhoogde vlakke van die medisyne wat u neem, wat die immuunstelsel verswak
- borsongemak, borspyn, gevoel van liggaamstemperatuur wat verander, algemene gevoel van ongesteldheid, algemene pyn, swelling van die gesig, gevoeligheid, voel moeg.

Die volgende newe-effekte is aangemeld, maar die frekwensie van voorkoms is onbekend:
- Stevens-Johnson-sindroom (SJS) (pynlike veltoestand, wat seer blase en sere op die vel en slymvliesmembrane, veral in die mond, veroorsaak) en toksiese epidermale nekrolise (TEN) (ernstige siekte met blaasvorming op die vel).

Indien u enige newe-effekte opmerk, wat nie in hierdie inligtingsblad genoem word nie, lig asseblief u dokter of apteker in.

Aanmelding van newe-effekte
Indien u newe-effekte ervaar, praat met u dokter, apteker of verpleegkundige. U kan ook newe-effekte aanmeld by SAHPRA via die Med Safety toepassing (Medsafety X SAHPRA) en eReporting platform (who-umc.org), wat op SAHPRA se webtuiste gevind kan word. Deur die aanmelding van newe-effekte, kan u help om meer inligting aangaande die veiligheid van IVECAS in te win. U kan ook 'n epos direk aan die maatskappy stuur, pharmacovigilance@pharmadynamics.co.za, om die veiligheid van die produk te verseker.

5. Hoe om IVECAS te bewaar
Bewaar alle medisyne buite die bereik van kinders.
Bewaar in die oorspronklike buitenste verpakking, in 'n yskas, teen of tussen 2 - 8 °C.
Moet nie vries nie.
Hersaamgestelde konsentraat, moet onmiddellik gebruik word. Chemies en fisies stabiel vir 24 uur, teen of benede 25 °C, of in die yskas teen 2 - 8 °C voor die voorbereiding van die infusie-oplossing.

U gesondheidsorgverskaffer sal seker maak dat IVECAS se vervaldatum wat op die etiket en kartonhouer aangedui word, nie oorskry is, voordat die inspuiting aan u toegedien word nie.
Neem alle ongebruikte medisyne na u apteker terug.
Moet nie ongebruikte medisyne in afvoerpype of rioolstelsels (bv. toilette), weggooi nie.

6. Verpakkingsinhoud en die ander inligting
Wat IVECAS bevat:
Die aktiewe bestanddeel is kaspofungien.
- elke 10 mL flessie IVECAS 50 IV bevat kaspofungienasetaat gelykstaande aan kaspofungien 50 mg
- elke 10 mL flessie IVECAS 70 IV bevat kaspofungienasetaat gelykstaande aan kaspofungien 70 mg.

Die ander bestanddele is mannitol, natriumhidroksied (vir pH aanpassing), sukrose en ysasynsuur.

Hoe IVECAS lyk en die verpakkingsinhoud
Geslote flessies
Elke flessie IVECAS bevat wit, tot naaswit geliofiliseerde poeier.

Hersaamgestelde produkflessies
Helder oplossing, feitlik vry van sigbare deeltjies.

Verdunde produk vir infusie
Helder oplossing, feitlik vry van sigbare deeltjies.
IVECAS 50 IV en 70 IV geliofiliseerde poeier vir oplossing vir infusie word voorsien in helder glas tipe I, 10 mL flessies, geseël met 'n rubberstopper en 'n aluminiumring met 'n plastiese opskietdoppie.

Eienaar van die Registrasiesertifikaat
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Registrasienommers
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IVECAS 70 IV: A50/20.2.2/1015

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