LOCAL PRODUCT DOCUMENT
PT. PFIZER INDONESIA

Generic Name: Anidulafungin
Trade Name: **ECALTA**
CDS Effective Date: August 06, 2020
Supersedes: March 09, 2020

NAME OF THE MEDICINAL PRODUCT

ECALTA

QUALITATIVE AND QUANTITATIVE COMPOSITION

Vials containing 100 mg anidulafungin powder and solvent for solution for infusion (see section **Special precautions for disposal and other handling**).

The reconstituted solution contains 3.33 mg/mL anidulafungin and the diluted solution contains 0.77 mg/mL anidulafungin.

For a full list of excipients, see section **List of excipients**.

PHARMACEUTICAL FORM

Anidulafungin powder for solution for infusion. Powder: White to off-white lyophilized solid.

CLINICAL PARTICULARS

Therapeutic indications

ECALTA (anidulafungin) is indicated for the treatment of candidemia in adult non-neutropenic patients.

ECALTA is indicated for the treatment of invasive candidiasis in pediatric patients age 1 month and older who has already been treated previously with other systemic anti fungal.

ECALTA has been studied primarily in patients with candidemia and only in a limited number of patients with deep tissue Candida infections or with abscess-forming disease.

Posology and method of administration

Treatment with anidulafungin should be initiated by a physician experienced in the management of invasive fungal infections. Specimens for fungal culture should be obtained prior to therapy. Therapy may be initiated before culture results are known and can be adjusted accordingly once they are available.

Adult patients
A single 200 mg loading dose should be administered on Day 1, followed by 100 mg daily thereafter. Duration of treatment should be based on the patient's clinical response. In general, antifungal therapy should continue for at least 14 days after the last positive culture.

Paediatric patients (one month and older)
The recommended dose is 3.0 mg/kg (not to exceed 200 mg) loading dose of anidulafungin on Day 1, followed by 1.5 mg/kg (not to exceed 100 mg) daily dose thereafter. In general, antifungal therapy should continue for at least 14 days after the last negative culture (defined as the second of two consecutive negative cultures, separated by at least 24 hours, following the last positive culture) and improvement of clinical signs and symptoms of invasive candidiasis including candidemia (ICC). Switch to an oral antifungal may occur after a minimum of 10 days on anidulafungin intravenous therapy.

The efficacy and safety of anidulafungin has not been established in neonates (less than 1 month) (see section **Special warnings and precautions for use**).

Anidulafungin should be reconstituted with the solvent to a concentration of 3.33 mg/mL and subsequently diluted to a concentration of 0.77 mg/mL before use according to the instructions given in section **Special precautions for disposal and other handling.**

It is recommended that ECALTA be administered at a rate of infusion that does not exceed 1.1 mg/minute (equivalent to 1.4 mL/minute). Infusion associated reactions are infrequent when the rate of anidulafungin infusion does not exceed 1.1 mg/minute.

ECALTA should not be administered as a bolus injection.

For patients with hereditary fructose intolerance (HFI) and all patients under 2 years of age see section **Special warnings and precautions for use**.

Renal and hepatic impairment
No dosing adjustments are required for patients with mild, moderate, or severe hepatic impairment. No dosing adjustments are required for patients with any degree of renal insufficiency, including those on dialysis. ECALTA can be given without regard to the timing of haemodialysis (see section **Pharmacokinetic properties**).

Duration of treatment
There are insufficient data to support the 100 mg dose for longer than 35 days of treatment.

Other special populations
No dosing adjustments are required for adult patients based on gender, weight, ethnicity, HIV positivity, or geriatric status (see section **Pharmacokinetic properties**).

Contraindications
Hypersensitivity to the active substance, or to any of the excipients.
Hypersensitivity to other medicinal products of the echinocandin class (e.g. caspofungin).

Special warnings and precautions for use
Anaphylactic reactions
Anaphylactic reactions, including shock, were reported with the use of anidulafungin. If these reactions occur, anidulafungin should be discontinued and appropriate treatment administered (see section **Undesirable effects**).

The efficacy of anidulafungin in neutropenic patients with candidaemia and in patients with deep tissue Candida infections or intra-abdominal abscess and peritonitis has not been established.

Clinical efficacy has been evaluated primarily in non-neutropenic patients with *C. Albicans* infections and in a smaller number of patients infected with *non-albicans*, mainly *C. Glabrata*, *C. Parapsilosis* and *C. Tropicalis*. Patients with candida endocarditis, osteomyelitis or meningitis and known *C. Krusei* infection have not been studied.

Hepatic effects
Increased levels of hepatic enzymes have been seen in healthy subjects and patients treated with anidulafungin. In some patients with serious underlying medical conditions who were receiving multiple concomitant medicines along with anidulafungin, clinically significant hepatic abnormalities have occurred. Isolated cases of significant hepatic dysfunction, hepatitis, or hepatic failure have been reported in patients; a causal relationship to anidulafungin has not been established. Patients with increased hepatic enzymes during anidulafungin therapy should be monitored for evidence of worsening hepatic function and evaluated for risk/benefit of continuing anidulafungin therapy.

Patients with hereditary fructose intolerance
Patients with hereditary fructose intolerance (HFI) should not be given this medicine unless strictly necessary.

A detailed history with regard to HFI symptoms should be taken of each patient prior to being given this medicinal product.

Infants and children below 2 years of age may not yet be diagnosed with HFI. Medicines containing fructose given intravenously may be life-threatening and should not be administered in this population unless there is an overwhelming clinical need and no alternatives are available.

Paediatric patients
Treatment with anidulafungin in neonates (less than 1 month old) is not recommended. Treating neonates requires consideration for coverage of disseminated candidiasis including Central Nervous System (CNS); nonclinical infection models indicate that higher doses of anidulafungin are needed to achieve adequate CNS penetration (see section **Preclinical safety data**), resulting in higher doses of polysorbate 80, a formulation excipient. High doses of polysorbates have been associated with potentially life-threatening toxicities in neonates as reported in the literature.

Infusion-related reactions
Infusion-related adverse events have been reported with anidulafungin, including rash, urticaria, flushing, pruritus, dyspnea, bronchospasm and hypotension. Infusion-related adverse events are infrequent when the rate of anidulafungin infusion does not exceed 1.1 mg/minute (see sections **Posology and method of administration**, **Undesirable effects** and **Special precautions for disposal and other handling**).

Exacerbation of infusion-related reactions by co-administration of anaesthetics has been seen in a nonclinical (rat) study (see section **Preclinical safety data**). The clinical relevance of this is unknown. Nevertheless, care should be taken when co-administering anidulafungin and anaesthetic agents.

Interaction with other medicinal products and other forms of interaction
Preclinical *in vitro* and *in vivo* studies and clinical studies have demonstrated that anidulafungin is not a clinically relevant substrate, inducer, or inhibitor of cytochrome P450 isoenzymes. Interaction studies have only been performed in adults. Anidulafungin has negligible renal clearance (<1%). Minimal interactions are expected with the concomitant medications (see section **Pharmacokinetic properties**).

In vitro studies showed that anidulafungin is not metabolized by human cytochrome P450 or by isolated human hepatocytes, and anidulafungin does not significantly inhibit the activities of human CYP isoforms (1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 3A) at clinically relevant concentrations.

No clinically relevant drug-drug interactions were observed with the following drugs likely to be co-administered with anidulafungin.

Cyclosporin (CYP3A4 substrate): In a study of 12 healthy adult subjects who received 100 mg/day anidulafungin following a 200 mg loading dose alone and in combination with 1.25 mg/kg oral cyclosporin twice daily, the steady-state plasma peak concentration (C_{max}) of anidulafungin was not significantly altered by cyclosporin; however the steady state area under the concentration-time curve (AUC) was increased by 22%. An *in vitro* study has shown that anidulafungin has no effect on the metabolism of cyclosporine. Adverse events observed in this study were consistent with those observed in other studies where anidulafungin only was administered. No dosage adjustment of either drug is required when they are co-administered.

Voriconazole (CYP2C19, CYP2C9, CYP3A4 inhibitor and substrate): In a study of 17 healthy subjects who received 100 mg/day anidulafungin alone following a 200 mg loading dose, 200 mg twice daily oral voriconazole alone following 400 mg twice on the first day as loading doses, and both in combination, the steady-state C_{max} and AUC of anidulafungin and voriconazole were not significantly altered by co-administration. No dosage adjustment of either drug is required when co-administered.

Tacrolimus (CYP3A4 substrate): In a study of 35 healthy subjects who received a single oral dose of 5 mg tacrolimus alone, 100 mg/day anidulafungin alone following a 200 mg loading dose and both in combination, the steady-state C_{max} and AUC of anidulafungin and tacrolimus were not significantly altered by co-administration. No dosage adjustment of either drug is required when co-administered.

Liposomal amphotericin B: The pharmacokinetics of anidulafungin were examined in 27 patients (100 mg/day anidulafungin) who were co-administered with liposomal amphotericin B (doses up to 5 mg/kg/day). The population pharmacokinetic analysis showed that, the pharmacokinetics of anidulafungin were not significantly altered by co-administration with amphotericin B when compared to data from patients who did not receive amphotericin B. No dosage adjustment of anidulafungin is required.

Rifampicin (potent CYP450 inducer): The pharmacokinetics of anidulafungin were examined in 27 patients (50 or 75 mg/day anidulafungin) who were co-administered with rifampicin (doses up to 600 mg/day). The population pharmacokinetic analysis showed that when compared to data from patients that did not receive rifampicin, the pharmacokinetics of anidulafungin were not significantly altered by co-administration with rifampicin. No dosage adjustment of anidulafungin is required.

Pregnancy and lactation

Animal studies have shown no selective reproductive toxicity (see section **Preclinical safety data**). There are no adequate or well-controlled data regarding the use of anidulafungin in pregnant women. Therefore, anidulafungin is not recommended in pregnancy.

Animal studies have shown excretion of anidulafungin in breast milk. It is not known whether anidulafungin is excreted in human breast milk. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with anidulafungin should be made taking into account the benefit of breast-feeding to the child and the benefit of anidulafungin to the mother.

Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed.

Undesirable effects
Nine hundred and twenty-nine (929) patients received intravenous anidulafungin in clinical trials (672 in Phase 2/3 studies and 257 in Phase I studies). Of the 669 Phase 2/3 patients for whom safety data are available, five hundred and five (505) received anidulafungin for ≥14 days.

Three studies (one comparative vs. fluconazole, 2 non-comparative) assessed the efficacy of anidulafungin (100 mg) in patients with candidaemia and other deep tissue *Candida* infections. In these three studies, a total of 204 patients received anidulafungin, 119 for ≥14 days. Adverse events were typically mild to moderate and seldom led to discontinuation. The drug-related adverse events (MedDRA) listed below were reported with frequencies corresponding to Common (≥1/100, ≤1/10); Uncommon (≥1/1000, <1/100). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Infusion-related adverse events have been reported with anidulafungin, including rash, urticaria, flushing, pruritus, dyspnea, bronchospasm and hypotension. These events can be minimized by infusing anidulafungin at a rate that does not exceed 1.1 mg/minute.

Infections and infestations
Uncommon: Fungaemia, Candidiasis, Clostridium colitis, Oral candidiasis

Blood and lymphatic system disorders
Common: Thrombocytopenia, Coagulopathy
Uncommon: Thrombocythaemia

Immune system disorders
Not known: Anaphylactic shock, Anaphylactic reaction

Metabolism and nutrition disorders
Common: Hyperkalaemia, Hypokalaemia, Hypomagnesaemia
Uncommon: Hyperglycaemia, Hypercalcaemia, Hypernatraemia

Nervous system disorders
Common: Convulsion, Headache

Eye disorders
Uncommon: Eye pain, Visual disturbance, Vision blurred

Cardiac disorders
Uncommon: Atrial fibrillation, Sinus arrhythmia, Ventricular extrasystoles, Bundle branch block right

Vascular disorders
Common: Flushing
Uncommon: Thrombosis, Hypertension, Hot flush

Gastrointestinal disorders
Common: Diarrhoea
Uncommon: Abdominal pain upper, Vomiting, Faecal incontinence, Nausea, Constipation

Hepatobiliary disorders

Common: Gamma-glutamyltransferase increased, Blood alkaline phosphatase increased, Aspartate aminotransferase increased, Alanine aminotransferase increased
Uncommon: Liver function test abnormal, Cholestasis, Hepatic enzyme increased, Transaminases increased

Skin and subcutaneous tissue disorders

Common: Rash, Pruritis
Uncommon: Urticaria, Pruritus generalised

Musculoskeletal and connective tissue disorders
Uncommon: Back pain

General disorders and administration site conditions
Uncommon: Infusion site pain

Investigations
Common: Blood bilirubin increased, Platelet count decreased, Blood creatinine

increased, Electrocardiogram QT prolonged
Uncommon: Blood amylase increased, Blood magnesium decreased, Blood potassium decreased, Electrocardiogram abnormal, Lipase increased, Platelet count increased, Blood urea increased

Respiratory, thoracic and mediastinal disorders
Not known: Bronchospasm

In the safety assessment of the full Phase 2/3 patient population (N = 669), the following additional adverse events, all uncommon (≥1/1000, <1/100), were of note: neutropenia, leukopenia, anaemia, hyperuricaemia, hypocalcaemia, hyponatraemia, hypoalbuminaemia, hypophosphataemia, anxiety, delirium, confusional state, hallucination auditory, dizziness, paraesthesia, central pontine myelinolysis, dysgeusia, Guillain-Barré syndrome, tremor, altered visual depth perception, deafness unilateral, phlebitis, thrombophlebitis superficial, hypotension, lymphangitis, dyspepsia, dry mouth, oesophageal ulcer, hepatic necrosis, angioneurotic edema, hyperhidrosis, myalgia, monoarthritis, renal failure, haematuria, pyrexia, chills, oedema peripheral, injection site reaction, blood creatine phosphokinase increased, blood lactate dehydrogenase increased, lymphocyte count decreased.

Paediatric population
The safety of anidulafungin was investigated in 68 paediatric subjects (1 month to <18 years) with invasive candidiasis, including candidemia (ICC) in a prospective, open-label, non-comparative paediatric study (see section **Pharmacodynamic properties**). The adverse event profile of these 68 paediatric subjects was similar to that observed in adults with ICC but hepatobiliary adverse events, in particular Alanine aminotransferase (ALT) increased and Aspartate aminotransferase (AST) increased appeared at a higher frequency in these paediatric patients than has been observed in adults. Although chance or differences in underlying disease severity may have contributed, it cannot be excluded that hepatobiliary adverse reactions occur more frequently in paediatric patients compared to adults.

Overdose
As with any overdose, general supportive measures should be utilized as necessary.

During clinical trials a single 400 mg dose of anidulafungin was inadvertently administered as a loading dose. No clinical adverse events were reported. In a study of 10 healthy subjects administered a loading dose of 260 mg followed by 130 mg daily, anidulafungin was well tolerated with no dose limiting toxicity; 3 of the 10 subjects experienced transient, asymptomatic transaminase elevations (3 x ULN).

During a paediatric clinical trial, one subject received two doses of anidulafungin that were 143% of the expected dose. No clinical adverse reactions were reported.

Anidulafungin is not dialysable.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

General properties

Pharmacotherapeutic group: Antimycotics for systemic use, other antimycotics
ATC code: JO2 AX 06

Mode of Action

Anidulafungin is a semi-synthetic echinocandin, a lipopeptide synthesised from a fermentation product of *Aspergillus nidulans*.

Anidulafungin selectively inhibits 1,3-β-D glucan synthase, an enzyme present in fungal, but not mammalian cells. This results in inhibition of the formation of 1,3-β-D-glucan, an essential component of the fungal cell wall. Anidulafungin has shown fungicidal activity against *Candida* species and activity against regions of active cell growth of the hyphae of *Aspergillus fumigatus*.

Activity in vitro

Anidulafungin is active *in vitro* against *Candida* spp. including *C. albicans*, *C. glabrata, C. krusei, C. parapsilosis, C. tropicalis, C. dubliniensis, C. lusitaniae, and C. guilliermondii* and *Aspergillus* species including *A. fumigatus, A. flavus, A. niger*, and *A. terreus.* Its activity is not affected by resistance to other classes of antifungal agents.

MICs were determined according to the Clinical and Laboratory Standard Institute (CLSI) approved standard reference method M27 for yeasts. The relationship between clinical response and *in vitro* activity remains to be elucidated.

Activity in vivo

Parenterally administered anidulafungin was effective against *Candida* spp. in immunocompetent and immunocompromised mouse and rabbit models. Anidulafungin treatment prolonged survival and also reduced the organ burden of *Candida* spp.

Experimental infections included disseminated *C. albicans* infection in neutropenic rabbits, esophageal/oropharyngeal infection of neutropenic rabbits with fluconazole-resistant *C. albicans* and disseminated infection of neutropaenic mice with fluconazole-resistant *C. glabrata*. Anidulafungin has also demonstrated activity against *Aspergillus fumigatus* in mouse and rabbit infection models.

In combination with other antifungal agents

In vitro studies of anidulafungin in combination with fluconazole, itraconazole and

amphotericin B suggest no antagonism of antifungal activity against *Candida* species. The clinical significance of these results is unknown. *In vitro* studies have evaluated the activity of anidulafungin in combination with itraconazole, voriconazole, and amphotericin B against *Aspergillus* spp. The combination of anidulafungin and amphotericin B showed indifference for 16 of 26 isolates, while anidulafungin in combination with either itraconazole or voriconazole showed synergy against 18 of 26 isolates. The clinical significance of these results is unknown.

Mechanism of Resistance

As breakpoints have not been established for any echinocandin, potential resistance may be assumed if there is a significant rise in MICs for an isolate. No increase in anidulafungin MICs was seen in isolates from clinical trials. In addition, resistance was not seen in either *in vitro* or animal studies. Among a number of isolates with elevated echinocandin MICs, only one isolate having a mutation in the gene encoding the target enzyme 1,3-beta-D glucan synthase was reported to have an increased anidulafungin MIC, suggesting the lack of complete cross resistance among echinocandins.

Information from Clinical Studies

Candidemia and other forms of Invasive Candidiasis

The safety and efficacy of anidulafungin were evaluated in a pivotal, Phase 3, randomised, double-blind, multicentre, multinational study of patients with candidemia and/or other forms of invasive candidiasis, associated with clinical signs of infection. Patients were randomised to receive once daily i.v. anidulafungin (200 mg loading dose followed by 100 mg maintenance dose) or i.v. fluconazole (800 mg loading dose followed by 400 mg maintenance dose). Patients were stratified by APACHE II score (≤20 and >20) and the presence or absence of neutropenia. Patients with *Candida* endocarditis, osteomyelitis or meningitis, or those with infection due to *C. krusei*, were excluded from the study. Treatment was administered for at least 14 and not more than 42 days. Patients in both study arms were permitted to switch to oral fluconazole after at least 10 days of intravenous therapy, provided that they were able to tolerate oral medication, were afebrile for at least 24 hours, and the most recent blood cultures were negative for *Candida* species.

Patients who received at least one dose of study medication and who had a positive culture for *Candida* species from a normally sterile site before entry into the study (modified intent-to-treat [MITT] population) were included in the primary analysis of global response at the end of i.v. therapy. A successful global response required clinical improvement and microbiological eradication. Patients were followed for six weeks beyond the end of all therapy.

Two hundred and fifty-six patients (aged 16 to 91 years) were randomised to treatment and received at least one dose of study medication. Two hundred and forty-five patients (127 anidulafungin, 118 fluconazole) met the criteria for inclusion in the MITT population. Of these, 219 patients (116 anidulafungin (91.3%), 103 fluconazole (87.3%)) had candidemia only; 5.5% patients in the anidulafungin arm and 9.3% patients in the fluconazole arm had infections at other normally sterile sites; finally 3.1% patients in the anidulafungin arm and 3.4% patients in the fluconazole arm had both (candidemia and infections at other normally sterile sites). The most frequent species isolated at baseline were *C. albicans* (63.8% anidulafungin, 59.3% fluconazole), followed by *C. glabrata* (15.7%, 25.4%), *C. parapsilosis* (10.2%, 13.6%) and *C. tropicalis* (11.8%, 9.3%). The majority (97%) of patients were non-neutropenic (ANC >500) and 81% had APACHE II scores less than or equal to 20.

At the end of i.v. therapy, anidulafungin was superior to fluconazole in the treatment of patients with candidemia and/or other forms of invasive candidiasis. In the anidulafungin arm, 96 patients (75.6%) had global success versus 71 patients (60.2%) in the fluconazole arm. The between group difference in global success rate (anidulafungin global success rate minus fluconazole global success rate) was 15.4% (95% CI: 3.9, 27.0).

Paediatric population

A prospective, open-label, non-comparative, multi-national study assessed the safety and efficacy of anidulafungin in 68 paediatric patients aged 1 month to <18 years with invasive candidiasis including candidaemia (ICC). Patients were stratified by age (1 month to <2 years, 2 to <5 years, and 5 to <18 years) and received once daily intravenous anidulafungin (3.0 mg/kg loading dose on Day 1, and 1.5 mg/kg daily maintenance dose thereafter) for up to 35 days followed by an optional switch to oral fluconazole (6-12 mg/kg/day, maximum 800 mg/day). Patients were followed at 2 and 6 weeks after EOT.

Among 68 patients who received anidulafungin, 64 had microbiologically confirmed *Candida* infection and were evaluated for efficacy in the modified intent-to-treat (MITT) population. Overall, 61 patients (92.2%) had *Candida* isolated from blood only. The most commonly isolated pathogens were *Candida albicans* (25 [39.1%] patients), followed by *Candida parapsilosis* (17 [26.6%] patients), and *Candida tropicalis* (9 [14.1%] patients). A successful global response was defined as having both a clinical response of success (cure or improvement) and a microbiological response of success (eradication or presumed eradication). The overall rates of successful global response in the MITT population are presented in Table 1.

Table 1: Summary of Successful Global Response by Age Group, MITT Population					
		Successful Global Response, n (%)			
Timepoint	**Global Response**	**1 month to <2 years (N=16) n (n/N, %)**	**2 to <5 years (N=18) n (n/N, %)**	**5 to <18 years (N=30) n (n/N, %)**	**Overall (N=64) n (n/N, %)**
EOIVT	Success	11 (68.8)	14 (77.8)	20 (66.7)	45 (70.3)
	95% CI	(41.3, 89.0)	(52.4, 93.6)	(47.2, 82.7)	(57.6, 81.1)
EOT	Success	11 (68.8)	14 (77.8)	21 (70.0)	46 (71.9)
	95% CI	(41.3, 89.0)	(52.4, 93.6)	(50.6, 85.3)	(59.2, 82.4)
2-week FU	Success	11 (68.8)	13 (72.2)	22 (73.3)	46 (71.9)
	95% CI	(41.3, 89.0)	(46.5, 90.3)	(54.1, 87.7)	(59.2, 82.4)
6-week FU	Success	11 (68.8)	12 (66.7)	20 (66.7)	43 (67.2)
	95% CI	(41.3, 89.0)	(41.0, 86.7)	(47.2, 82.7)	(54.3, 78.4)

95% CI = exact 95% confidence interval for binomial proportions using Clopper-Pearson method; EOIVT = End of Intravenous Treatment; EOT = End of All Treatment; FU = follow-up; MITT = modified intent-to-treat; N = number of subjects in the population; n = number of subjects with responses

Pharmacokinetic properties

General Pharmacokinetic Characteristics

The pharmacokinetics of anidulafungin have been characterized in healthy subjects, special populations and patients. A low intersubject variability in systemic exposure (coefficient of variation of approximately 25%) was observed. The steady-state was achieved on the first day after a loading dose (twice the daily maintenance dose).

Distribution

The pharmacokinetics of anidulafungin are characterized by a rapid distribution half-life (0.5-1 hour) and a volume of distribution of 30-50 L that is similar to total body fluid volume. Anidulafungin is extensively bound (>99%) to human plasma proteins.

Biotransformation

Hepatic metabolism of anidulafungin has not been observed. Anidulafungin is not a clinically relevant substrate, inducer, or inhibitor of cytochrome P450 isoenzymes. It is unlikely that anidulafungin will have clinically relevant effects on the metabolism of drugs metabolized by cytochrome P450 isoenzymes.

Anidulafungin undergoes slow chemical degradation at physiologic temperature and pH to a ring-opened peptide that lacks antifungal activity. The *in vitro* degradation half-life of anidulafungin under physiologic conditions is approximately 24 hours. *In vivo*, the ring-opened product is subsequently converted to peptidic degradants and eliminated mainly through biliary excretion.

Elimination

The clearance of anidulafungin is about 1 L/h. Anidulafungin has a predominant elimination half-life of approximately 24 hours that characterizes the majority of the plasma concentration-time profile and a terminal half-life of 40-50 hours that

characterizes the terminal elimination phase of the profile.

In a single-dose clinical study, radiolabeled (^{14}C) anidulafungin (~88 mg) was administered to healthy subjects. Approximately 30% of the administered radioactive dose was eliminated in the faeces over 9 days, of which less than 10% was intact drug. Less than 1% of the administered radioactive dose was excreted in the urine. Anidulafungin concentrations fell below the lower limits of quantitation 6 days post-dose. Negligible amounts of drug-derived radioactivity were recovered in blood, urine, and faeces 8 weeks post-dose.

Linearity
Anidulafungin displays linear pharmacokinetics across a wide range of once daily doses (15-130 mg).

Special Populations
Patients with fungal infections
The pharmacokinetics of anidulafungin in patients with fungal infections are similar to those observed in healthy subjects based on population pharmacokinetic analyses. With the 200/100 mg daily dose regimen at an infusion rate of 1 mg/min, the steady-state C_{max} and trough concentrations C_{min} could reach approximately 7 and 3 mg/L, respectively, with an average steady-state AUC of approximately 110 mg h/L.

Weight
Though weight was identified as a source of variability in clearance in the population pharmacokinetic analysis, weight has little clinical relevance on the pharmacokinetics of anidulafungin.

Gender
Plasma concentrations of anidulafungin in healthy men and women were similar. In multiple-dose patient studies, drug clearance was slightly faster (approximately 22%) in men.

Elderly
The population pharmacokinetic analysis showed that median clearance differed slightly between the elderly group (patients ≥65, median CL = 1.07 L/h) and the non-elderly group (patients <65, median CL = 1.22 L/h), however, the range of clearance was similar.

Ethnicity
Anidulafungin pharmacokinetics were similar among Caucasian, Blacks, Asians, and Hispanics.

HIV Positivity

Dosage adjustments are not required based on HIV positivity, irrespective of concomitant anti-retroviral therapy.

Hepatic Insufficiency
Anidulafungin is not hepatically metabolised. Anidulafungin pharmacokinetics were examined in subjects with Child-Pugh class A, B or C hepatic insufficiency. Anidulafungin concentrations were not increased in subjects with any degree of hepatic insufficiency. Although a slight decrease in AUC was observed in patients with Child-Pugh C hepatic insufficiency, the decrease was within the range of population estimates noted for healthy subjects.

Renal Insufficiency
Anidulafungin has negligible renal clearance (<1%). In a clinical study of subjects with mild, moderate, severe or end stage (dialysis-dependent) renal insufficiency, anidulafungin pharmacokinetics were similar to those observed in subjects with normal renal function. Anidulafungin is not dialyzable and may be administered without regard to the timing of hemodialysis.

Paediatric
The pharmacokinetics of anidulafungin after daily doses were investigated in 24 immunocompromised paediatric (2 to 11 years old) and adolescent (12 to 17 years old) patients with neutropenia. The steady-state was achieved on the first day after a loading dose (twice the maintenance dose), and the steady-state C_{max} and AUC_{ss} increase in a dose-proportional manner. The systemic exposures following the daily maintenance doses, 0.75 and 1.5 mg/kg/day in patients aged 2 to 17 years old were comparable to those observed in adults following 50 and 100 mg/day, respectively.

The pharmacokinetics of anidulafungin was investigated in 66 paediatric patients (1 month to <18 years) with ICC in a prospective, open-label, non-comparative paediatric study following administration of 3.0 mg/kg loading dose and 1.5 mg/kg/day maintenance dose (see section **Pharmacodynamic properties**). Based on population pharmacokinetic analysis of combined data from adult and paediatric patients with ICC, the mean exposure parameters ($AUC_{0-24,ss}$ and $C_{min,ss}$) at steady state in the overall paediatric patients across age groups (1 month to <2 years, 2 to <5 years, and 5 to <18 years) were comparable to those in adults receiving 200 mg loading dose and 100 mg/day maintenance dose. Body weight adjusted CL (L/h/kg) and volume of distribution at steady state (L/kg) were similar across the age groups.

Preclinical safety data

Non-clinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, acute toxicity, repeated dose toxicity, and toxicity to reproduction. In 3-month studies, evidence of liver toxicity, including elevated enzymes and morphologic alterations, was observed in both rats and monkeys at doses 4- to 6-fold higher than the anticipated clinical therapeutic exposure. *In vitro* and *in vivo* genotoxicity studies with anidulafungin provided no evidence of genotoxic potential. Long-term studies in animals have not been conducted to evaluate the carcinogenic potential of anidulafungin.

Administration of anidulafungin to rats did not indicate any effects on reproduction, including male and female fertility.

Anidulafungin crossed the placental barrier in rats and was detected in fetal plasma. The potential risk to the human fetus is unknown.

Anidulafungin was found in the milk of lactating rats. It is not known whether anidulafungin is excreted in human milk.

Anidulafungin did not produce any drug-related developmental toxicity in rats at the highest dose of 20 mg/kg/day, a dose equivalent to 2 times the proposed therapeutic maintenance dose of 100 mg on the basis of relative body surface area. Developmental effects observed in rabbits (slightly reduced fetal weights) occurred in the high dose group, a dose that also produced maternal toxicity.

Results of pharmacokinetic-pharmacodynamic studies in rabbit models of disseminated candidiasis and hematogenous *Candida* meningoencephalitis indicated that higher doses of anidulafungin were needed to optimally treat infections of CNS tissues relative to non-CNS tissues.

Studies conducted in juvenile rats did not indicate a greater susceptibility to anidulafungin hepatotoxicity compared to adult animals.

PHARMACEUTICAL PARTICULARS

List of excipients

Powder*:*
Fructose
Mannitol (E421)
Polysorbate 80 (E433)
Tartaric acid (E334)
Sodium hydroxide (for pH-adjustment)
Hydrochloric acid (for pH-adjustment)

Incompatibilities

This medicinal product must not be mixed or co-administered with other medicinal

products or electrolytes except those mentioned in section **Special precautions for disposal and other handling**.

Shelf life
3 years

Reconstituted Solution:
Chemical and physical in-use stability of the reconstituted solution has been demonstrated for 24 hours at 25°C.

From a microbiological point of view, following good aseptic practices, the reconstituted solution can be utilized for up to 24 hours when stored at 25°C.

Infusion Solution:

Do not freeze.

Chemical and physical in-use stability of the infusion solution has been demonstrated for 48 hours at 25°C.

From a microbiological point of view, following good aseptic practices, the infusion solution can be utilized for up to 48 hours from preparation when stored at 25°C.

Special precautions for storage
The unreconstituted vials should be stored at 2°C - 8°C. Excursions for up to 96 hours for temperatures up to 25°C are permitted, and the vial can be returned to the refrigerated storage (2°C – 8°C).

Special precautions for disposal and other handling
Anidulafungin must be reconstituted with water for injection and subsequently diluted with ONLY 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion. The compatibility of reconstituted anidulafungin with intravenous substances, additives, or medications other than 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion has not been established. The infusion must not be frozen.

Reconstitution
Aseptically reconstitute each vial with 30 mL water for injection to provide a concentration of 3.33 mg/mL. The reconstituted solution should be clear and free from visible particulates. The reconstituted solution should be further diluted within an hour.

Dilution and Infusion

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If particulate matter or discoloration are identified, discard the solution.

Adult Patients

Aseptically transfer the contents of the reconstituted vial(s) into an IV bag (or bottle) containing either 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion to obtain the appropriate anidulafungin concentration. The table below provides the dilution to a concentration of 0.77 mg/mL for the final infusion solution and infusion instructions for each dose.

Dilution Requirements for Anidulafungin Administration

Dose	Number of Vials Required	Total Reconstituted Volume Required	Infusion Volume [A]	Total Infusion Volume [B]	Rate of Infusion	Minimum Duration of Infusion
100 mg	1	30 mL	100 mL	130 mL	1.4 mL/min or 84 mL/hour	90 min
200 mg	2	60 mL	200 mL	260 mL	1.4 mL/min or 84 mL/hour	180 min

[A] Either 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion.
[B] Infusion solution concentration is 0.77 mg/mL.

The rate of infusion should not exceed 1.1 mg/minute (see section CLINICAL PARTICULARS-sections Special warnings and precautions for use and **Undesirable effects).** The rate of infusion is equivalent to 1.4 mL/min or 84 mL/hour for the 100 mg and 200 mg doses.

Paediatric Patients

For paediatric patients aged 1 month to <18 years, the volume of infusion solution required to deliver the dose will vary depending on the weight of the patient. The reconstituted solution must be further diluted to a concentration of 0.77 mg/mL for the final infusion solution. A programmable syringe or infusion pump is recommended. **The rate of infusion should not exceed 1.1 mg/minute (equivalent to 1.4 mL/minute or 84 mL/hour when reconstituted and diluted per instructions)** (see sections **Posology and method of administration** and **Special warnings and precautions for use**).

1. Calculate patient dose and reconstitute vial(s) required according to

reconstitution instructions to provide a concentration of 3.33 mg/mL (see sections **QUALITATIVE AND QUANTITATIVE COMPOSITION** and **Posology and method of administration**)

2. Calculate the volume (mL) of reconstituted anidulafungin required:

• Volume of anidulafungin (mL) = Dose of anidulafungin (mg) ÷ 3.33 mg/mL

3. Calculate the total volume of dosing solution (mL) required to provide a final concentration of 0.77 mg/mL:

• Total volume of dosing solution (mL) = Dose of anidulafungin (mg) ÷ 0.77 mg/mL

4. Calculate the volume of diluent [5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline)] required to prepare the dosing solution:

• Volume of diluent (mL) = Total volume of dosing solution (mL) – Volume of anidulafungin (mL)

5. Aseptically transfer the required volumes (mL) of anidulafungin and 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline) into an infusion syringe or IV infusion bag needed for administration.

For single use only. Waste materials should be disposed of in accordance with local requirements.

Supply
ECALTA 100 mg: Box, vial 100 mg; No. Reg. DKI1272100880A1

HARUS DENGAN RESEP DOKTER

Manufactured by:
Pharmacia & Upjohn Company LLC, Kalamazoo, USA

Imported by:
PT. Pfizer Indonesia
Jakarta, Indonesia

Nama Generik: Anidulafungin
Nama Dagang: ECALTA
Tanggal Berlaku CDS: 6 Agustus 2020
Menggantikan: Tidak Ada
Disetujui oleh BPOM:

Leaflet kemasan: Informasi bagi pengguna

ECALTA 100 mg serbuk untuk konsentrat larutan infus
Anidulafungin

Baca isi leaflet ini dengan saksama sebelum Anda mulai menggunakan obat ini karena berisi informasi penting bagi Anda.
- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan berikan kepada orang lain. Obat ini dapat membahayakan mereka, sekali pun tanda-tanda penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter, apoteker, atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 12.

Apa isi leaflet ini?

1. Nama obat
ECALTA

2. Bentuk sediaan
Serbuk untuk larutan infus.

3. Deskripsi obat
Serbuk: padatan terliofilisasi berwarna putih hingga hamper putih. ECALTA termasuk dalam kelompok obat-obatan yang disebut ekinokandin. Obat-obatan ini digunakan untuk mengobati infeksi jamur parah.

4. Apa kandungan obat ini?
Vial yang berisi serbuk anidulafungin 100 mg dan pelarut untuk larutan infus.

Daftar eksipien
Serbuk:
Fruktosa; Manitol (E421); Polisorbat 80 (E433); Asam tartrat (E334); Natrium hidroksida (untuk pengaturan pH); Asam hidroklorida (untuk pengaturan pH)

5. Kekuatan obat
100 mg

6. Apa kegunaan obat ini?
ECALTA (anidulafungin) diindikasikan untuk pengobatan kandidemia pada pasien dewasa tanpa kondisi sel darah putih neutrophil kadar rendah dan untuk pengobatan invasif kandidiasis pada pasien pediatrik berusia satu bulan atau lebih yang telah mendapatkan pengobatan sebelumnya dengan anti jamur lain.

7. Berapa banyak dan seberapa sering Anda seharusnya menggunakan obat ini? Apa yang harus dilakukan jika ada dosis terlewat?
ECALTA akan selalu disiapkan dan diberikan kepada Anda oleh dokter atau petugas kesehatan (terdapat informasi selengkapnya mengenai metode penyiapan di akhir leaflet ini pada bagian untuk tenaga medis dan petugas kesehatan saja).

Untuk penggunaan pada orang dewasa, perawatan dimulai dengan 200 mg pada hari pertama (dosis awal). Dosis ini dilanjutkan dengan dosis harian 100 mg (dosis pemeliharaan).

Untuk penggunaan pada anak-anak dan remaja (berusia mulai dari 1 bulan hingga kurang dari 18 tahun), pengobatan dimulai dengan dosis 3,0 mg/kg (tidak lebih dari 200 mg) pada hari pertama (dosis awal). Dosis ini diikuti dengan dosis harian 1,5 mg/kg (tidak lebih dari 100 mg) (dosis pemeliharaan). Dosis yang diberikan bergantung pada berat badan pasien.

ECALTA harus diberikan kepada Anda satu kali sehari, melalui infus lambat (tetes) ke dalam pembuluh darah Anda. Untuk orang dewasa, proses ini memakan waktu setidaknya 1,5 jam untuk dosis pemeliharaan dan 3 jam untuk dosis awal. Untuk anak-anak dan remaja, pemberian infus mungkin memakan waktu yang lebih pendek bergantung pada berat badan pasien.

Dokter akan menentukan durasi perawatan Anda dan jumlah ECALTA yang akan Anda terima setiap hari dan akan memantau respons dan kondisi Anda.

Secara umum, perawatan akan dilanjutkan setidaknya selama 14 hari setelah hari terakhir Kandida ditemukan dalam darah Anda.

ECALTA tidak boleh diberikan dalam bentuk injeksi bolus.

Jika Anda lupa menggunakan ECALTA
Karena Anda akan menerima obat ini di bawah pengawasan medis yang ketat, kecil kemungkinannya dosis Anda akan terlewat. Akan tetapi beri tahu dokter atau apoteker Anda jika Anda merasa ada dosis yang terlewat.

Jika Anda memiliki pertanyaan lebih lanjut mengenai penggunaan obat ini, tanyakan kepada dokter, apoteker, atau perawat.

8. Kapan seharusnya Anda tidak menggunakan obat ini?

Jika Anda alergi terhadap anidulafungin, obat-obatan ekinokandin lainnya (misalnya kaspofungin asetat), atau bahan apa pun lainnya dalam obat ini (dicantumkan di bagian 4).

9. Apa yang perlu dipertimbangkan saat menggunakan obat ini?

Konsultasikan dengan dokter, apoteker atau perawat sebelum menggunakan ECALTA.

Dokter mungkin memutuskan untuk memantau Anda
- dengan lebih ketat perihal fungsi hati jika Anda mengalami gangguan hati selama menjalani perawatan.
- jika Anda diberi zat anestesi selama pengobatan dengan ECALTA untuk mengamati tanda-tanda reaksi alergi seperti gatal, mengi, kulit kemerahan
- untuk melihat tanda-tanda reaksi terkait infus yang mencakup ruam, kaligata, gatal-gatal, kemerahan,
- untuk sesak napas/kesulitan bernapas, pusing, atau kepala terasa melayang

Pasien anak-anak dan remaja
ECALTA tidak boleh diberikan kepada pasien berusia di bawah 1 bulan.

ECALTA mengandung fruktosa
Obat ini mengandung fruktosa (sejenis gula). Jika Anda telah diberi tahu oleh dokter bahwa Anda memiliki intoleransi terhadap beberapa jenis gula, hubungi dokter Anda sebelum menggunakan produk obat ini.

Jika Anda (atau anak Anda) menderita intoleransi fruktosa (HFI) bawaan, yaitu suatu gangguan genetik yang langka, maka Anda (atau anak Anda) tidak boleh menerima obat ini. Pasien yang menderita HFI tidak dapat menguraikan fruktosa dalam obat ini, sehingga dapat menimbulkan efek samping yang serius.

Anda harus memberi tahu dokter Anda sebelum menerima obat ini jika Anda (atau anak Anda) menderita HFI atau jika anak Anda tidak lagi dapat mengonsumsi makanan atau minuman manis karena mereka merasa mual, muntah, atau mengalami efek yang tidak menyenangkan seperti kembung, kram perut, atau diare.

10. Apa saja obat lain atau makanan yang harus dihindari selama menggunakan obat ini?

Beri tahu dokter atau apoteker Anda jika Anda sedang, belum lama ini, atau akan menggunakan obat lain.

11. Apakah obat ini aman untuk perempuan hamil dan menyusui?

Efek ECALTA pada ibu hamil belum diketahui. Oleh karena itu, ECALTA tidak disarankan untuk diberikan selama kehamilan. Kontrasepsi yang efektif harus digunakan pada wanita yang berpotensi mengandung. Segera hubungi dokter jika Anda kemudian mengandung selama menggunakan ECALTA.

Efek ECALTA pada ibu menyusui belum diketahui. Mintalah saran dari dokter atau apoteker Anda sebelum menggunakan ECALTA selama menyusui.

Mintalah saran dari dokter atau apoteker Anda sebelum menggunakan obat-obatan apa pun,

12. Apa potensi efek yang tidak diinginkan jika menggunakan obat ini?

Seperti semua obat-obatan yang ada, obat ini bisa menimbulkan efek samping, meskipun tidak semua orang mengalaminya. Beberapa efek samping akan dicatat oleh dokter selama memantau respons dan kondisi Anda.

Reaksi alergi yang mengancam jiwa di antaranya kesulitan bernapas disertai mengi atau ruam yang bertambah parah jarang dilaporkan terjadi selama pemberian ECALTA.

Efek samping serius – segera beri tahu dokter Anda atau petugas kesehatan lainnya jika gejala mana pun berikut ini terjadi:

- Konvulsi (kejang)
- Pipi memerah
- Ruam, pruritis (gatal)
- Semburan panas
- Urtikaria
- Kesulitan bernapas

Efek samping lainnya

Efek samping yang umum (dapat dialami hingga 1 di antara 10 orang) adalah:

- Konvulsi (kejang)
- Sakit kepala
- Perubahan fungsi hati dalam tes darah
- Ruam, pruritis (gatal)

- Perubahan fungsi ginjal dalam tes darah
- Wajah memerah
- Kadar kalium darah rendah (hipokalemia)
- Kenaikan kadar kalium darah
- Kadar magnesium darah rendah
- Diare
- Hitungan trombosit darah rendah
- Gangguan sistem pembekuan darah
- QT elektrokardiogram memanjang

Efek samping yang tidak umum (dapat dialami hingga 1 di antara 100 orang) adalah:

- Muntah
- Merembesnya feses karena sulit mengendalikan buang air besar
- Konstipasi
- Semburan panas
- Sakit perut
- Urtikaria
- Nyeri punggung
- Nyeri pada tempat injeksi
- Mual
- Aliran cairan empedu abnormal dari kantung empedu ke dalam usus halus (kolestasis)
- Peningkatan jumlah trombosit
- Tekanan darah tinggi
- Bekuan darah
- Kadar gula darah tinggi
- Kadar kalsium darah tinggi
- Kadar natrium darah tinggi
- Peningkatan kadar amilase darah
- Penurunan kadar kalium darah
- Peningkatan lipase
- Peningkatan hitungan trombosit
- Peningkatan kadar urea darah
- Nyeri mata
- Gangguan penglihatan
- Penglihatan kabur
- Denyut jantung tidak teratur dan seringkali cepat
- Tertundanya atau penyumbatan di sepanjang jalur yang dilewati impuls listrik untuk membuat jantung berdenyut
- Elektrokardiogram abnormal

Tidak diketahui (frekuensi tidak dapat diestimasi dari data yang tersedia):

- Reaksi alergi yang mengancam jiwa
- Kesulitan bernapas

Melaporkan efek samping
Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter, apoteker, atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Dengan melaporkan efek samping, Anda dapat membantu memberikan lebih banyak informasi perihal keamanan obat ini.

13. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?
Jika Anda khawatir terlalu banyak menerima ECALTA, segera beri tahu dokter Anda atau petugas kesehatan lainnya.

14. Bagaimana cara menyimpan obat ini?
Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan gunakan obat ini setelah melewati tanggal kedaluwarsa yang tertera pada labelnya. Tanggal kedaluwarsa mengacu pada hari terakhir bulan yang dimaksud.

Umur simpan: 3 tahun

Simpan di dalam lemari pendingin (2 °C – 8 °C).

Jangan buang obat melalui saluran pembuangan air atau bersama sampah rumah tangga.

15. Berapa lama umur simpan obat setelah wadahnya dibuka untuk pertama kali?
Larutan yang direkonstitusi dapat disimpan hingga suhu 25 °C maksimal selama 24 jam. Larutan infus dapat disimpan pada suhu 25 °C (suhu ruangan) selama 48 jam (jangan dibekukan) dan harus diberikan pada suhu 25 °C (suhu ruangan) dalam waktu 48 jam.

16. Bagaimana cara melarutkan obat ini?
Isi vial harus direkonstitusi dengan air untuk injeksi dan kemudian diencerkan HANYA dengan larutan infus natrium klorida 9 mg/ml (0,9%) atau larutan infus glukosa 50 mg/ml (5%).

17. Nomor izin pemasaran
ECALTA 100 mg: Dus, vial 100 mg; No. Reg. DKI1272100880A1

18. Nama dan alamat pemohon dan/atau pemilik obat sesuai dengan ketentuan yang berlaku
Diproduksi oleh:
Pharmacia & Upjohn Company LLC, Kalamazoo, USA

Diimpor oleh:
PT. Pfizer Indonesia
Jakarta, Indonesia

19. Tanggal revisi PIL
10/2021

20. Peringatan khusus
HARUS DENGAN RESEP DOKTER

Informasi berikut ini ditujukan bagi tenaga medis atau petugas kesehatan saja dan berlaku hanya untuk penyiapan satu vial ECALTA 100 mg, serbuk untuk konsentrat larutan infus:

Isi vial harus direkonstitusi dengan air untuk injeksi dan kemudian diencerkan HANYA dengan larutan infus natrium klorida 9 mg/ml (0,9%) atau larutan infus glukosa 50 mg/ml (5%). Kompatibilitas ECALTA hasil rekonstitusi dengan zat intravena, aditif, atau obat-obatan selain larutan infus natrium klorida 9 mg/ml (0,9%) atau larutan infus glukosa 50 mg/ml (5%) masih belum ditetapkan. Larutan infus tidak boleh dibekukan.

Rekonstitusi
Rekonstitusi secara aseptik setiap vial dengan 30 ml air untuk injeksi untuk menghasilkan konsentrasi 3,33 mg/ml. Rekonstitusi dapat memakan waktu hingga 5 menit. Setelah pengenceran berikutnya, larutan harus dibuang jika tampak adanya bahan partikulat atau perubahan warna.

Larutan yang direkonstitusi dapat disimpan hingga suhu 25 °C selama maksimal 24 jam sebelum pengenceran lebih lanjut.

Pengenceran dan infus

Produk obat parenteral harus diperiksa secara visual untuk melihat adanya bahan partikulat dan perubahan warna sebelum pemberian, jika larutan dan wadahnya memungkinkan. Jika ditemukan adanya bahan partikulat atau perubahan warna, buang larutan tersebut.

Pasien Dewasa
Secara aseptik pindahkan isi vial rekonstitusi ke dalam kantong (atau botol) intravena yang berisi larutan infus natrium klorida 9 mg/ml (0,9%) atau larutan infus glukosa 50 mg/ml (5%) sehingga diperoleh konsentrasi anidulafungin sebesar 0,77 mg/ml. Tabel di bawah ini menampilkan pengenceran hingga konsentrasi 0,77 mg/ml untuk larutan infus final dan petunjuk infus untuk masing-masing dosis.

Persyaratan pengenceran untuk pemberian ECALTA

Dosis	Jumlah Vial yang Diperlukan	Total Volume Direkonstitusi yang Diperlukan	Volume Infus[A]	Total Volume Infus[B]	Laju Infus	Durasi Infus Minimum
100 mg	1	30 ml	100 ml	130 ml	1,4 ml/menit atau 84 ml/jam	90 menit
200 mg	2	60 ml	200 ml	260 ml	1,4 ml/menit atau 84 ml/jam	180 menit

[A] Larutan infus natrium klorida 9 mg/ml (0,9%) atau larutan infus glukosa 50 mg/ml (5%).
[B] Konsentrasi larutan infus adalah 0,77 mg/ml.

Laju infus tidak boleh melebihi 1,1 mg/menit (setara dengan 1,4 ml/menit atau 84 ml/jam jika direkonstitusi dan diencerkan sesuai petunjuk).

Pasien Pediatrik

Untuk pasien pediatrik berusia 1 bulan hingga < 18 tahun, volume larutan infus yang diperlukan untuk menghantarkan dosis bervariasi bergantung pada berat badan pasien. Larutan yang direkonstitusi harus diencerkan lebih lanjut hingga mencapai konsentrasi 0,77 mg/ml untuk larutan infus final. Disarankan untuk menggunakan alat suntik atau pompa infus yang dapat diprogram. Laju infus tidak boleh lebih dari 1,1 mg/menit (setara dengan 1,4 ml/menit atau 84 ml/jam jika direkonstitusi dan diencerkan sesuai petunjuk) (lihat bagian Posologi dan metode pemberian serta Peringatan khusus dan tindakan pencegahan terkait penggunaan).

1. Hitung dosis pasien dan lakukan rekonstitusi terhadap vial yang dibutuhkan sesuai dengan petunjuk rekonstitusi untuk menghasilkan konsentrasi 3,33 mg/ml (lihat bagian KOMPOSISI KUALITATIF DAN KUANTITATIF serta Posologi dan metode pemberian)

2. Hitung volume (ml) rekonstitusi anidulafungin yang dibutuhkan:

   • Volume anidulafungin (ml) = Dosis anidulafungin (mg) ÷ 3,33 mg/ml

3. Hitung total volume larutan dosis (ml) yang diperlukan untuk menghasilkan konsentrasi akhir 0,77 mg/ml:

   • Total volume larutan dosis (ml) = Dosis anidulafungin (mg) ÷ 0,77 mg/ml

4. Hitung volume pengencer [5% Injeksi Dekstrosa, USP, atau 0,9% Injeksi Natrium Klorida, USP (larutan garam fisiologis)] yang diperlukan untuk menyiapkan larutan dosis:

   • Volume pengencer (ml) = Total volume larutan dosis (ml) – Volume anidulafungin (ml)

5. Pindahkan secara aseptik volume anidulafungin (ml) yang diperlukan dan 5% Injeksi Dekstrosa, USP, atau 0,9% Injeksi Natrium Klorida, USP (larutan garam fisiologis) ke dalam alat suntik infus atau kantong infus intravena yang dibutuhkan untuk pemberian.

Hanya untuk sekali pakai. Bahan limbah harus dibuang sesuai dengan persyaratan setempat.