

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

ECALTA 100 mg powder for concentrate for solution for infusion

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 100 mg anidulafungin.

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

Excipient with known effect: Fructose 102.5 mg per vial

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Powder for concentrate for solution for infusion.

White to off-white lyophilised solid.

The reconstituted solution has a pH of 3.5 to 5.5.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Treatment of invasive candidiasis in adult patients (see sections 4.4 and 5.1).

### 4.2 Posology and method of administration

Treatment with ECALTA 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.

#### Posology

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.

#### *Duration of treatment*

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

#### *Patients with 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 5.2).

#### *Other special populations*

No dosing adjustments are required for adult patients based on gender, weight, ethnicity, HIV positivity, or elderly (see section 5.2).

### *Paediatric population*

The safety and efficacy of ECALTA in children below 18 years have not been established. Currently available data are described in section 5.2 but no recommendation on a posology can be made.

### Method of administration

For intravenous use only.

ECALTA should be reconstituted with water for injections to a concentration of 3.33 mg/mL and subsequently diluted to a concentration of 0.77 mg/mL. For instructions on reconstitution of the medicinal product before administration, see section 6.6.

It is recommended that ECALTA be administered at a rate of infusion that does not exceed 1.1 mg/min (equivalent to 1.4 mL/min when reconstituted and diluted per instructions). Infusion associated reactions are infrequent when the rate of anidulafungin infusion does not exceed 1.1 mg/min (see section 4.4).

ECALTA must not be administered as a bolus injection.

## **4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.  
Hypersensitivity to other medicinal products of the echinocandin class.

## **4.4 Special warnings and precautions for use**

ECALTA has not been studied in patients with *Candida endocarditis*, osteomyelitis or meningitis.

The efficacy of ECALTA has only been evaluated in a limited number of neutropenic patients (see section 5.1)

### 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. Cases of significant hepatic dysfunction, hepatitis, and hepatic failure were uncommon in clinical trials. 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.

### 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.

### 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/min.

Exacerbation of infusion-related reactions by co-administration of anaesthetics has been seen in a non-clinical (rat) study (see section 5.3). The clinical relevance of this is unknown. Nevertheless, care should be taken when co-administering anidulafungin and anaesthetic agents.

### Fructose content

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

## **4.5 Interaction with other medicinal products and other forms of interaction**

Anidulafungin is not a clinically relevant substrate, inducer, or inhibitor of cytochrome P450 isoenzymes (1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 3A). Of note, *in vitro* studies do not fully exclude possible *in vivo* interactions.

Drug interaction studies were performed with anidulafungin and other medicinal products likely to be co-administered. No dosage adjustment of either medicinal product is recommended when anidulafungin is co-administered with ciclosporin, voriconazole or tacrolimus, and no dosage adjustment for anidulafungin is recommended when co-administered with amphotericin B or rifampicin.

#### Paediatric population

Interaction studies have only been performed in adults.

### **4.6 Fertility, pregnancy and lactation**

#### Pregnancy

There are no data regarding the use of anidulafungin in pregnant women. Slight developmental effects have been observed in rabbits administered anidulafungin during pregnancy, in the presence of maternal toxicity (see section 5.3). The potential risk for humans is unknown. Therefore anidulafungin is not recommended in pregnancy.

#### Breast-feeding

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 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.

#### Fertility

For anidulafungin, there were no effects on fertility in studies conducted in male and female rats (see section 5.3).

### **4.7 Effects on ability to drive and use machines**

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

### **4.8 Undesirable effects**

#### Summary of the safety profile

Fifteen hundred sixty five (1565) subjects received single or multiple doses of intravenous anidulafungin in clinical trials: 1308 in Phase 2/3 trials (923 patients with candidaemia/invasive candidiasis, 355 patients with oral/oesophageal candidiasis, 30 patients with invasive aspergillosis), and 257 in Phase I studies.

The safety profile of anidulafungin is based on 840 patients with candidaemia/invasive candidiasis receiving the recommended daily dose of 100 mg in 9 studies. Originally, in 3 studies (one comparative vs fluconazole, two non-comparative) 204 patients were studied; the mean duration of intravenous treatment in these patients was 13.5 days (range, 1 to 38 days) and 119 patients received  $\geq$  14 days of anidulafungin. In 6 additional studies (two comparative vs. caspofungin and four non-comparative), 636 patients including 53 neutropenic patients and 131 patients with deep tissue infection were studied; the mean durations of intravenous treatment in neutropenic patients and patients with deep tissue infection in these studies were 10.0 (range, 1 to 42 days) and 14.0 (range, 1 to 42 days) days, respectively. Adverse reactions were typically mild to moderate and seldom led to discontinuation.

Infusion-related adverse reactions have been reported with anidulafungin in clinical studies, including flushing, hot flush, pruritus, rash, and urticaria, summarized in Table 1.

Tabulated list of adverse reactions

The following table includes, the all-causality adverse reactions (MedDRA terms) from 840 subjects receiving 100 mg anidulafungin with frequency corresponding to very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  to  $< 1/1,000$ ), very rare ( $< 1/10,000$ ) and from spontaneous reports with frequency not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

**Table 1. Table of Adverse Reactions**

<b>System Organ Class</b>	<b>Very Common <math>\geq 1/10</math></b>	<b>Common <math>\geq 1/100</math> to <math>&lt; 1/10</math></b>	<b>Uncommon <math>\geq 1/1000</math> to <math>&lt; 1/100</math></b>	<b>Rare <math>\geq 1/10,000</math> to <math>&lt; 1/1,000</math></b>	<b>Very Rare <math>&lt; 1/10,000</math></b>	<b>Not Known</b>
Blood and Lymphatic System Disorders			Coagulopathy			
Immune System Disorders						Anaphylactic shock, anaphylactic reaction*
Metabolism and Nutrition Disorders	Hypokalaemia	Hyperglycaemia				
Nervous System Disorders		Convulsion, headache				
Vascular Disorders		Hypotension, hypertension	Flushing, hot flush			
Respiratory, Thoracic and Mediastinal Disorders		Bronchospasm, Dyspnoea				
Gastrointestinal Disorders	Diarrhoea, nausea	Vomiting	Abdominal pain upper			
Hepatobiliary Disorders		Alanine aminotransferase increased, blood alkaline phosphatase increased, aspartate aminotransferase increased, blood bilirubin increased, cholestasis	Gamma-glutamyltransferase increased			
Skin and Subcutaneous Tissue Disorders		Rash, pruritus	Urticaria			

**Table 1. Table of Adverse Reactions**

System Organ Class	Very Common ≥ 1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Rare ≥ 1/10,000 to < 1/1,000	Very Rare < 1/10,000	Not Known
Renal and Urinary Disorders		Blood creatinine increased				
General Disorders and Administration Site Conditions			Infusion site pain			

\* See section 4.4.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

## 4.9 Overdose

As with any overdose, general supportive measures should be utilised as necessary. In case of overdose, adverse reactions may occur as mentioned in section 4.8.

During clinical trials, a single 400 mg dose of anidulafungin was inadvertently administered as a loading dose. No clinical adverse reactions were reported. No dose limiting toxicity was observed in a study of 10 healthy subjects administered a loading dose of 260 mg followed by 130 mg daily; 3 of the 10 subjects experienced transient, asymptomatic transaminase elevations ( $\leq 3 \times$  Upper Limit of Normal (ULN)).

ECALTA is not dialysable.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: – Antimycotics for systemic use, other antimycotics for systemic use. ATC code: JO2AX06

#### Mechanism of action

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

Anidulafungin selectively inhibits 1,3- $\beta$ -D glucan synthase, an enzyme present in fungal, but not mammalian cells. This results in inhibition of the formation of 1,3- $\beta$ -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 exhibited *in-vitro* activity against *C. albicans*, *C. glabrata*, *C. parapsilosis*, *C. krusei* and *C. tropicalis*. For the clinical relevance of these findings see “Clinical efficacy and safety.”

Isolates with mutations in the hot spot regions of the target gene have been associated with clinical failures or breakthrough infections. Most clinical cases involve caspofungin treatment. However, in animal experiments these mutations confer cross resistance to all three echinocandins and therefore such isolates are classified as echinocandin resistant until further clinical experience are obtained concerning anidulafungin.

The *in vitro* activity of anidulafungin against *Candida* species is not uniform. Specifically, for *C. parapsilosis*, the MICs of anidulafungin are higher than are those of other *Candida* species. A standardized technique for testing the susceptibility of *Candida* species to anidulafungin as well as the respective interpretative breakpoints has been established by European Committee on Antimicrobial Susceptibility Testing (EUCAST).

**Table 2. EUCAST Breakpoints**

<u>Candida Species</u>	<u>MIC breakpoint (mg/L)</u>	
	<u>≤S (Susceptible)</u>	<u>&gt;R (Resistant)</u>
<i>Candida albicans</i>	0.03	0.03
<i>Candida glabrata</i>	0.06	0.06
<i>Candida tropicalis</i>	0.06	0.06
<i>Candida krusei</i>	0.06	0.06
<i>Candida parapsilosis</i> <sup>1</sup>	0.002	4
<i>Other Candida spp.</i> <sup>2</sup>	Insufficient evidence	

<sup>1</sup>*C. parapsilosis* harbours an intrinsic alteration in the target gene, which is the likely mechanism for the higher MICs than with other *Candida* species. In the clinical trials the outcome for anidulafungin with *C. parapsilosis* was not statistically different from other species however, the use of echinocandins in candidaemia due to *C. parapsilosis* may not be regarded as therapy of first choice

<sup>2</sup> EUCAST has not determined non-species related breakpoints for anidulafungin

#### Activity *in vivo*

Parenterally administered anidulafungin was effective against *Candida* species in immunocompetent and immunocompromised mouse and rabbit models. Anidulafungin treatment prolonged survival and also reduced the organ burden of *Candida* species, when determined at intervals from 24 to 96 hours after the last treatment.

Experimental infections included disseminated *C. albicans* infection in neutropenic rabbits, oesophageal/oropharyngeal infection of neutropenic rabbits with fluconazole-resistant *C. albicans* and disseminated infection of neutropenic mice with fluconazole-resistant *C. glabrata*.

#### Clinical efficacy and safety

##### *Candidaemia 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 primarily non-neutropenic patients with candidaemia and a limited number of patients with deep tissue *Candida* infections or with abscess-forming disease. Patients with *Candida* endocarditis, osteomyelitis or meningitis, or those with infection due to *C. krusei*, were specifically excluded from the study. Patients were randomised to receive either anidulafungin (200 mg intravenous loading dose followed by 100 mg intravenous daily) or fluconazole (800 mg intravenous loading dose followed by 400 mg intravenous daily), and were stratified by APACHE II score (≤20 and >20) and the presence or absence of neutropaenia. 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 and were afebrile for at least 24 hours, and that 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 study entry were included in the modified intent-to-treat (MITT) population. In the primary efficacy analysis, global response in the MITT populations at the end of intravenous therapy, anidulafungin was compared to fluconazole in a pre-specified two-step statistical comparison (non-inferiority followed by superiority). 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, ranging from 16 to 91 years in age, were randomised to treatment and received at least one dose of study medication. 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%) - with 20, 13 and 15 isolates of the last 3 species, respectively, in the anidulafungin group. The majority of patients had Apache II scores  $\leq 20$  and very few were neutropenic.

Efficacy data, both overall and by various subgroups, are presented below in Table 3.

<b>Table 3. Global success in the MITT population: primary and secondary endpoints</b>			
	Anidulafungin	Fluconazole	Between group difference <sup>a</sup> (95% CI)
<b>End of IV Therapy (1<sup>o</sup> endpoint)</b>	<b>96/127 (75.6%)</b>	<b>71/118 (60.2%)</b>	<b>15.42 (3.9, 27.0)</b>
Candidaemia only	88/116 (75.9%)	63/103 (61.2%)	14.7 (2.5, 26.9)
Other sterile sites <sup>b</sup>	8/11 (72.7%)	8/15 (53.3%)	-
Peritoneal fluid/IA <sup>c</sup> abscess	6/8	5/8	
Other	2/3	3/7	
<i>C. albicans</i> <sup>d</sup>	60/74 (81.1%)	38/61 (62.3%)	-
Non- <i>albicans</i> species <sup>d</sup>	32/45 (71.1%)	27/45 (60.0%)	-
Apache II score $\leq 20$	82/101 (81.2%)	60/98 (61.2%)	-
Apache II score $> 20$	14/26 (53.8%)	11/20 (55.0%)	-
Non-neutropenic (ANC, cells/mm <sup>3</sup> $> 500$ )	94/124 (75.8%)	69/114 (60.5%)	-
Neutropenic (ANC, cells/mm <sup>3</sup> $\leq 500$ )	2/3	2/4	-
<b>At Other Endpoints</b>			
End of All Therapy	94/127 (74.0%)	67/118 (56.8%)	17.24 (2.9, 31.6) <sup>e</sup>
2 Week Follow-up	82/127 (64.6%)	58/118 (49.2%)	15.41 (0.4, 30.4) <sup>e</sup>
6 Week Follow-up	71/127 (55.9%)	52/118 (44.1%)	11.84 (-3.4, 27.0) <sup>e</sup>

<sup>a</sup> Calculated as anidulafungin minus fluconazole

<sup>b</sup> With or without concurrent candidaemia

<sup>c</sup> Intra-abdominal

<sup>d</sup> Data presented for patients with a single baseline pathogen.

<sup>e</sup> 98.3% confidence intervals, adjusted post hoc for multiple comparisons of secondary time points.



Mortality rates in both the anidulafungin and fluconazole arms are presented below in Table 4:

<b>Table 4. Mortality</b>		
	Anidulafungin	Fluconazole
<b>Overall study mortality</b>	<b>29/127 (22.8%)</b>	<b>37/118 (31.4%)</b>
Mortality during study therapy	10/127 (7.9%)	17/118 (14.4%)
Mortality attributed to <i>Candida</i> infection	2/127 (1.6%)	5/118 (4.2%)

#### **Additional Data in Neutropenic Patients**

The efficacy of anidulafungin (200 mg intravenous loading dose followed by 100 mg intravenous daily) in adult neutropenic patients (defined as absolute neutrophil count  $\leq 500$  cells/mm<sup>3</sup>, WBC  $\leq 500$  cells/mm<sup>3</sup> or classified by the investigator as neutropenic at baseline) with microbiologically confirmed invasive candidiasis was assessed in an analysis of pooled data from 5 prospective studies (1 comparative versus caspofungin and 4 open-label, non-comparative). Patients were treated for at least 14 days. In clinically stable patients, a switch to oral azole therapy was permitted after at least 5 to 10 days of treatment with anidulafungin. A total of 46 patients were included in the analysis. The majority of patients had candidemia only (84.8%; 39/46). The most common pathogens isolated at baseline were *C. tropicalis* (34.8%; 16/46), *C. krusei* (19.6%; 9/46), *C. parapsilosis* (17.4%; 8/46), *C. albicans* (15.2%; 7/46), and *C. glabrata* (15.2%; 7/46). The successful global response rate at End of Intravenous Treatment (primary endpoint) was 26/46 (56.5%) and End of All Treatment was 24/46 (52.2%). All-cause mortality up to the end of the study (6 Week Follow-up Visit) was 21/46 (45.7%).

The efficacy of anidulafungin in adult neutropenic patients (defined as absolute neutrophil count  $\leq 500$  cells/mm<sup>3</sup> at baseline) with invasive candidiasis was assessed in a prospective, double-blind, randomized, controlled trial. Eligible patients received either anidulafungin (200 mg intravenous loading dose followed by 100 mg intravenous daily) or caspofungin (70 mg intravenous loading dose followed by 50 mg intravenous daily) (2:1 randomization). Patients were treated for at least 14 days. In clinically stable patients, a switch to oral azole therapy was permitted after at least 10 days of study treatment. A total of 14 neutropenic patients with microbiologically confirmed invasive candidiasis (MITT population) were enrolled in the study (11 anidulafungin; 3 caspofungin). The majority of patients had candidemia only. The most common pathogens isolated at baseline were *C. tropicalis* (4 anidulafungin, 0 caspofungin), *C. parapsilosis* (2 anidulafungin, 1 caspofungin), *C. krusei* (2 anidulafungin, 1 caspofungin), and *C. ciferrii* (2 anidulafungin, 0 caspofungin). The successful global response rate at the End of Intravenous Treatment (primary endpoint) was 8/11 (72.7%) for anidulafungin and 3/3 (100.0%) for caspofungin (difference -27.3, 95% CI -80.9, 40.3); the successful global response rate at the End of All Treatment was 8/11 (72.7%) for anidulafungin and 3/3 (100.0%) for caspofungin (difference -27.3, 95% CI -80.9, 40.3). All-cause mortality up to the 6 Week Follow-Up visit for anidulafungin (MITT population) was 4/11 (36.4%) and 2/3 (66.7%) for caspofungin.

Patients with microbiologically confirmed invasive candidiasis (MITT population) and neutropenia were identified in an analysis of pooled data from 4 similarly designed prospective, open-label, non-comparative studies. The efficacy of anidulafungin (200 mg intravenous loading dose followed by 100 mg intravenous daily) was assessed in 35 adult neutropenic patients defined as absolute neutrophil count  $\leq 500$  cells/mm<sup>3</sup> or WBC  $\leq 500$  cells/mm<sup>3</sup> in 22 patients or classified by the investigator as neutropenic at baseline in 13 patients. All patients were treated for at least 14 days. In clinically stable patients, a switch to oral azole therapy was permitted after at least 5 to 10 days of treatment with anidulafungin. The majority of patients had candidemia only (85.7%). The most common pathogens isolated at baseline were *C. tropicalis* (12 patients), *C. albicans* (7 patients), *C. glabrata* (7 patients), *C. krusei* (7 patients), and *C. parapsilosis* (6 patients). The successful global response rate at the End of Intravenous Treatment (primary endpoint) was 18/35 (51.4%) and 16/35 (45.7%) at the End of All Treatment. All-cause mortality by Day 28 was 10/35 (28.6%). The successful global response rate at End of Intravenous Treatment and End of All Treatment were both 7/13 (53.8%) in the 13 patients with neutropenia assessed by investigators at baseline.

## Additional Data in Patients with Deep Tissue Infections

The efficacy of anidulafungin (200 mg intravenous loading dose followed by 100 mg intravenous daily) in adult patients with microbiologically confirmed deep tissue candidiasis was assessed in an analysis of pooled data from 5 prospective studies (1 comparative and 4 open-label). Patients were treated for at least 14 days. In the 4 open-label studies, a switch to oral azole therapy was permitted after at least 5 to 10 days of treatment with anidulafungin. A total of 129 patients were included in the analysis. Twenty one (16.3%) had concomitant candidemia. The mean APACHE II score was 14.9 (range, 2 – 44). The most common sites of infection included the peritoneal cavity (54.3%; 70 of 129), hepatobiliary tract (7.0%; 9 of 129), pleural cavity (5.4%; 7 of 129) and kidney (3.1%; 4 of 129). The most common pathogens isolated from a deep tissue site at baseline were *C. albicans* (64.3%; 83 of 129), *C. glabrata* (31.0%; 40 of 129), *C. tropicalis* (11.6%; 15 of 129), and *C. krusei* (5.4%; 7 of 129). The successful global response rate at the end of intravenous treatment (primary endpoint) and end of all treatment and all-cause mortality up to the 6 week follow-up visit is shown in Table 5.

**Table 5. Rate of Successful Global Response<sup>a</sup> and All-Cause Mortality in Patients with Deep Tissue Candidiasis – Pooled Analysis**

	MITT Population n/N (%)
<b>Global Response of Success at EOIVT<sup>b</sup></b>	
Overall	102/129 (79.1)
Peritoneal cavity	51/70 (72.9)
Hepatobiliary tract	7/9 (77.8)
Pleural cavity	6/7 (85.7)
Kidney	3/4 (75.0)
<b>Global Response of Success at EOT<sup>b</sup></b>	94/129 (72.9)
<b>All-Cause Mortality</b>	40/129 (31.0)

<sup>a</sup> A successful global response was defined as both clinical and microbiologic success  
<sup>b</sup> EOIVT, End of Intravenous Treatment; EOT, End of All Treatment

## 5.2 Pharmacokinetic properties

### General pharmacokinetic characteristics

The pharmacokinetics of anidulafungin have been characterised in healthy subjects, special populations and patients. A low intersubject variability in systemic exposure (coefficient of variation ~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 characterised by a rapid distribution half-life (0.5-1 hour) and a volume of distribution, 30-50 l, which is similar to total body fluid volume. Anidulafungin is extensively bound (>99%) to human plasma proteins. No specific tissue distribution studies of anidulafungin have been done in humans. Therefore, no information is available about the penetration of anidulafungin into the cerebrospinal fluid (CSF) and/or across the blood-brain barrier.

### 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 metabolised 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 characterises the terminal elimination phase of the profile.

In a single-dose clinical study, radiolabeled (<sup>14</sup>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, indicating negligible renal clearance. 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 1.1 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*

Although 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 Caucasians, 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 dialysable and may be administered without regard to the timing of hemodialysis.

### *Paediatric*

The pharmacokinetics of anidulafungin after at least 5 daily doses were investigated in 24 immunocompromised paediatric (2 to 11 years old) and adolescent (12 to 17 years old) patients with neutropenia. Steady state was achieved on the first day after a loading dose (twice the maintenance dose), and steady state  $C_{max}$  and  $AUC_{ss}$  increase in a dose-proportional manner. Systemic exposure following daily maintenance dose of 0.75 and 1.5 mg/kg/day in this population were comparable to those observed in adults following 50 and 100 mg/day, respectively. Both regimens were well-tolerated by these patients.

## **5.3 Preclinical safety data**

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 foetal plasma.

Embryo-foetal development studies were conducted with doses between 0.2- and 2-fold (rats) and between 1- and 4-fold (rabbits) the proposed therapeutic maintenance dose of 100 mg/day. Anidulafungin did not produce any drug-related developmental toxicity in rats at the highest dose tested. Developmental effects observed in rabbits (slightly reduced foetal weights) occurred only at the highest dose tested, a dose that also produced maternal toxicity.

The concentration of anidulafungin in the brain was low (brain to plasma ratio of approximately 0.2) in uninfected adult and neonatal rats after a single dose. However, brain concentrations increased in uninfected neonatal rats after five daily doses (brain to plasma ratio of approximately 0.7). In multiple dose studies in rabbits with disseminated candidiasis and in mice with CNS candida infection, anidulafungin has been shown to reduce fungal burden in the brain.

Rats were dosed with anidulafungin at three dose levels and anaesthetised within one hour using a combination of ketamine and xylazine. Rats in the high dose group experienced infusion-related reactions that were exacerbated by anaesthesia. Some rats in the mid dose group experienced similar reactions but only after administration of anaesthesia. There were no adverse reactions in the low-dose animals in the presence or absence of anaesthesia, and no infusion-related reactions in the mid-dose group in the absence of anaesthesia.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Fructose  
Mannitol  
Polysorbate 80  
Tartaric acid  
Sodium hydroxide (for pH-adjustment)  
Hydrochloric acid (for pH-adjustment)

### **6.2 Incompatibilities**

This medicinal product must not be mixed with other medicinal products or electrolytes except those mentioned in section 6.6.

### **6.3 Shelf life**

3 years

Excursions for 96 hours up to 25°C are permitted, and the powder can be returned to refrigerated storage.

#### Reconstituted solution:

The reconstituted solution may be stored at up to 25°C for up to 24 hours.

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:

The infusion solution may be stored at 25°C for 48 hours or stored frozen for at least 72 hours.

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.

### **6.4 Special precautions for storage**

Store in a refrigerator (2°C – 8°C).

For storage conditions after reconstitution and dilution of the medicinal product, see section 6.3.

### **6.5 Nature and contents of container**

30 mL Type 1 glass vial with an elastomeric stopper (butyl rubber with an inert polymer coating on the product contact surface and lubricant on the top surface for easier machinability) and aluminium seal with flip-off cap.

Pack size of 1 vial.

### **6.6 Special precautions for disposal and other handling**

There are no special requirements for disposal.

ECALTA must be reconstituted with water for injections and subsequently diluted with ONLY sodium chloride 9 mg/mL (0.9%) solution for injection or 50 mg/mL (5%) glucose for infusion. The compatibility of reconstituted ECALTA with intravenous substances, additives, or medicines other than 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion has not been established.

#### Reconstitution

Aseptically reconstitute each vial with 30 mL water for injections to provide a concentration of 3.33 mg/mL. The reconstitution time can be up to 5 mins. After subsequent dilution, the solution is to be discarded if particulate matter or discoloration is identified.

**Dilution and infusion**

Aseptically transfer the contents of the reconstituted vial(s) into an intravenous bag (or bottle) containing either 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion obtaining an anidulafungin concentration of 0.77 mg/mL. The table below provides the volumes required for each dose.

**Dilution requirements for ECALTA administration**

<b>Dose</b>	<b>Number of vials of powder</b>	<b>Total reconstituted volume</b>	<b>Infusion volume<sup>A</sup></b>	<b>Total infusion volume<sup>B</sup></b>	<b>Rate of infusion</b>	<b>Minimum duration of infusion</b>
100 mg	1	30 mL	100 mL	130 mL	1.4 mL/min	90 min
200 mg	2	60 mL	200 mL	260 mL	1.4 mL/min	180 min

<sup>A</sup> Either 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion.

<sup>B</sup> Infusion solution concentration is 0.77 mg/mL

The rate of infusion should not exceed 1.1 mg/min (equivalent to 1.4 mL/min when reconstituted and diluted per instructions) (see sections 4.2, 4.4 and 4.8).

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

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

**7.      MARKETING AUTHORISATION HOLDER**

Pfizer Limited  
Ramsgate Road, Sandwich  
Kent, CT13 9NJ, United Kingdom.

**8.      MARKETING AUTHORISATION NUMBER(S)**

EU/1/07/416/002

**9.      DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 20 September 2007  
Date of latest renewal: 23 August 2012

**10.     DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

**ANNEX II**

- A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

**A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer responsible for batch release

Pfizer Manufacturing Belgium NV  
Rijksweg 12  
2870 Puurs  
Belgium

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

• **Periodic Safety Update Reports**

The marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

**D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

• **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.



**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**Outer Carton**

**1. NAME OF THE MEDICINAL PRODUCT**

ECALTA 100 mg powder for concentrate for solution for infusion  
Anidulafungin

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each vial contains 100 mg anidulafungin.  
The reconstituted solution contains 3.33 mg/mL anidulafungin and the diluted solution contains 0.77 mg/mL anidulafungin.

**3. LIST OF EXCIPIENTS**

Excipients: fructose, mannitol, polysorbate 80, tartaric acid and NaOH and/or HCl for pH adjustment.

**4. PHARMACEUTICAL FORM AND CONTENTS**

1 vial

Powder for concentrate for solution for infusion

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Reconstitute the contents with water for injections and dilute before use.

Read the package leaflet before use.

For intravenous use only.

Rate of infusion should not exceed 1.1 mg/min

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

EXP {MONTH – YYYY}

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Pfizer Ltd  
Ramsgate Road  
Sandwich  
KENT  
CT13 9NJ United-Kingdom

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/07/416/002

**13. BATCH NUMBER**

Lot {number}

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription.

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

[Justification for not including Braille accepted.]

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**Vial label**

**1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

ECALTA 100 mg powder for concentrate for solution for infusion  
Anidulafungin  
Intravenous use

**2. METHOD OF ADMINISTRATION**

Read the package leaflet before use

**3. EXPIRY DATE**

EXP {MM/YYYY}

**4. BATCH NUMBER**

Lot {number}

**5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

100 mg

**6. OTHER**

Store in a refrigerator

**B. PACKAGE LEAFLET**

## Package leaflet: Information for the user

### ECALTA 100 mg powder for concentrate for solution for infusion Anidulafungin

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist or nurse.
- If you get any side effects, talk to your doctor, or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet:**

1. What ECALTA is and what it is used for
2. What you need to know before you use ECALTA
3. How to use ECALTA
4. Possible side effects
5. How to store ECALTA
6. Contents of the pack and other information

#### **1. What ECALTA is and what it is used for**

ECALTA contains the active substance anidulafungin and is prescribed in adults to treat a type of fungal infection of the blood or other internal organs called invasive candidiasis. The infection is caused by fungal cells (yeasts) called *Candida*.

ECALTA belongs to a group of medicines called echinocandins. These medicines are used to treat serious fungal infections.

ECALTA prevents normal development of fungal cell walls. In the presence of ECALTA, fungal cells have incomplete or defective cell walls, making them fragile or unable to grow.

#### **2. What you need to know before you use ECALTA**

##### **Do not use ECALTA**

- if you are allergic to anidulafungin, other echinocandins (e.g. CANCIDAS), or any of the other ingredients of this medicine (listed in section 6).

##### **Warnings and precautions**

Talk to your doctor or pharmacist or nurse before using ECALTA.

Your doctor may decide to monitor

- your liver function more closely if you develop liver problems during your treatment.
- if you are given anaesthetics during your treatment with ECALTA.

##### **Children**

ECALTA should not be given to patients under 18 years of age.

### **Other medicines and ECALTA**

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not start or stop any other medicines without your doctor's or pharmacist's approval.

### **Pregnancy and breast-feeding**

The effect of ECALTA in pregnant women is not known. Therefore ECALTA is not recommended during pregnancy. Effective contraception should be used in women of childbearing age. Contact your doctor immediately if you become pregnant while taking ECALTA.

The effect of ECALTA in breast-feeding women is not known. Ask your doctor or pharmacist for advice before taking ECALTA while breast-feeding.

Ask your doctor or pharmacist for advice before taking any medicines.

### **ECALTA contains fructose**

This medicine contains fructose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

## **3. How to use ECALTA**

ECALTA will always be prepared and given to you by a doctor or a healthcare professional (there is more information about the method of preparation at the end of the leaflet in the section for medical and healthcare professionals only).

The treatment starts with 200 mg on the first day (loading dose). This will be followed by a daily dose of 100 mg (maintenance dose).

ECALTA should be given to you once a day, by slow infusion (a drip) into your vein. This will take at least 1.5 hours for the maintenance dose and 3 hours for the loading dose.

Your doctor will determine the duration of your treatment and how much ECALTA you will receive each day and will monitor your response and condition.

In general, your treatment should continue for at least 14 days after the last day *Candida* was found in your blood.

### **If you receive more ECALTA than you should**

If you are concerned that you may have been given too much ECALTA, tell your doctor or another healthcare professional immediately.

### **If you forgot to use ECALTA**

As you will be given this medicine under close medical supervision, it is unlikely that a dose would be missed. However tell your doctor or pharmacist if you think that a dose has been forgotten.

You should not be given a double dose by doctor.

### **If you stop using ECALTA**

You should not experience any effects from ECALTA if your doctor stops ECALTA treatment.



Your doctor may prescribe another medicine following your treatment with ECALTA to continue treating your fungal infection or prevent it from returning.

If your original symptoms come back, tell your doctor or another healthcare professional immediately.

If you have any further questions on the use of this medicine, ask your doctor, or pharmacist or nurse.

#### **4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them. Some of these side effects will be noted by your doctor while monitoring your response and condition.

Life-threatening allergic reactions that might include difficulty breathing with wheezing or worsening of an existing rash have been rarely reported during administration of ECALTA.

**Serious side effects – tell your doctor or another healthcare professional immediately should any of the following occur:**

- Convulsion (seizure)
- Flushing
- Rash, pruritis (itching)
- Hot flush
- Hives
- Sudden contraction of the muscles around the airways resulting in wheezing or coughing
- Difficulty of breathing

#### **Other side effects**

**Very common side effects (may affect more than 1 in 10 people) are:**

- Low blood potassium (hypokalaemia)
- Diarrhoea
- Nausea

**Common side effects (may affect up to 1 in 10 people) are:**

- Convulsion (seizure)
- Headache
- Vomiting
- Changes in blood tests of liver function
- Rash, pruritis (itching)
- Changes in blood tests of kidney function
- Abnormal flow of bile from the gallbladder into the intestine (cholestasis)
- High blood sugar
- High blood pressure
- Low blood pressure
- Sudden contraction of the muscles around the airways resulting in wheezing or coughing
- Difficulty of breathing

**Uncommon side effects (may affect up to 1 in 100 people) are:**

- Disorder of blood clotting system
- Flushing
- Hot flush
- Stomach pain
- Hives
- Pain at injection site

**Not known (frequency cannot be estimated from the available data) are:**

- Life-threatening allergic reactions

**Reporting of side effects**

If you get any side effects, talk to your doctor or, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via **the national reporting system listed in Appendix V**. By reporting side effects you can help provide more information on the safety of this medicine.

**5. How to store ECALTA**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label. The expiry data refers to the last day of that month.

Store in a refrigerator (2°C – 8°C).

The reconstituted solution may be stored up to 25°C for up to 24 hours. The infusion solution may be stored at 25°C (room temperature) for 48 hours or stored frozen for at least 72 hours, and should be administered at 25°C (room temperature) within 48 hours.

Do not throw away any medicines via wastewater or household waste.

**6. Contents of the pack and other information**

**What ECALTA contains**

- The active substance is anidulafungin. Each vial of powder contains 100 mg anidulafungin.
- The other ingredients are: fructose, mannitol, polysorbate 80, tartaric acid, sodium hydroxide (for pH-adjustment), hydrochloric acid (for pH-adjustment)

**What ECALTA looks like and contents of the pack**

ECALTA is supplied as a box containing 1 vial of 100 mg powder for concentrate for solution for infusion.

The powder is white to off-white.

**Marketing Authorisation Holder and Manufacturer**

The marketing authorisation for ECALTA is held by:  
Pfizer Limited, Ramsgate Rd, Sandwich, Kent, CT13 9NJ, United Kingdom

**Manufacturer**

Pfizer Manufacturing Belgium NV, Rijksweg 12, 2870 Puurs, Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

**België /Belgique/Belgien**

Pfizer S.A./N.V.

Tél/Tel: +32 (0)2 554 62 11

**България**

Пфайзер Люксембург САРЛ, Клон България

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Pfizer ApS

Tlf: +45 44 20 11 00

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Pfizer Pharma PFE GmbH

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**Eesti**

Pfizer Luxembourg SARL Eesti filiaal

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Τηλ.: +30 210 6785 800

**España**

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**France**

Pfizer PFE France

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Pfizer Healthcare Ireland

Tel: 1800 633 363 (toll free)

Tel: +44 (0)1304 616161

**Ísland**

Icepharma hf.,

Sími: + 354 540 8000

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Pfizer Italia S.r.l.

Tel: +39 06 33 18 21

**Lietuva**

Pfizer Luxembourg SARL

filialas Lietuvoje

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Pfizer S.A.

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Pfizer Kft.

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**Malta**

V.J. Salomone Pharma Ltd.

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**Nederland**

Pfizer bv

Tel: +31 (0)10 406 43 01

**Norge**

Pfizer AS

Tlf: +47 67 52 61 00

**Österreich**

Pfizer Corporation Austria Ges.m.b.H.

Tel: +43 (0)1 521 15-0

**Polska**

Pfizer Polska Sp. z o.o.,

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**Portugal**

Laboratórios Pfizer, Lda.

Tel: + 351 214 235 500

**România**

Pfizer România S.R.L

Tel: +40 (0)21 207 28 00

**Slovenija**

Pfizer Luxembourg SARL

Pfizer, podružnica za svetovanje s področja farmaceutске dejavnosti, Ljubljana

Tel: + 386 (0)152 11 400

**Slovenská republika**

Pfizer Luxembourg SARL, organizačná zložka

Tel: +421-2-3355 5500

**Suomi/Finland**

Pfizer Oy

Puh/Tel: +358(0)9 43 00 40

**Κύπρος**

Pfizer Ελλάς Α.Ε. (Cyprus Branch)  
Τηλ: +357 22 817690

**Sverige**

Pfizer AB  
Tel: +46 (0)8 5505 2000

**Latvija**

Pfizer Luxembourg SARL  
Filiāle Latvijā  
Tel: +371 670 35 775

**United Kingdom**

Pfizer Limited  
Tel: +44 (0)1304 616161

**This leaflet was last revised in {MM/YYYY}.**

Detailed information on this medicine is available on the European Medicines Agency web site:

<http://www.ema.europa.eu>.

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The following information is intended for medical or healthcare professionals only and applies only to the single vial ECALTA 100 mg powder for concentrate for solution for infusion presentation:

The contents of the vial must be reconstituted with water for injections 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 ECALTA with intravenous substances, additives, or medicines other than 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion has not been established.

*Reconstitution*

Aseptically reconstitute each vial with 30 mL water for injections to provide a concentration of 3.33 mg/mL. The reconstitution time can be up to 5 minutes. After subsequent dilution, the solution is to be discarded if particulate matter or discoloration is identified.

The reconstituted solution may be stored up to 25°C for up to 24 hours prior to further dilution.

*Dilution and infusion*

Aseptically transfer the contents of the reconstituted vial(s) into an intravenous bag (or bottle) containing either 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion obtaining an anidulafungin concentration of 0.77 mg/mL. The table below provides the volumes required for each dose.

**Dilution requirements for ECALTA administration**

Dose	Number of vials of powder	Total reconstituted volume	Infusion volume <sup>A</sup>	Total infusion volume <sup>B</sup>	Rate of infusion	Minimum duration of infusion
100 mg	1	30 mL	100 mL	130 mL	1.4 mL/min	90 min
200 mg	2	60 mL	200 mL	260 mL	1.4 mL/min	180 min

<sup>A</sup> Either 9 mg/mL (0.9%) sodium chloride for infusion or 50 mg/mL (5%) glucose for infusion.

<sup>B</sup> Infusion solution concentration is 0.77 mg/mL

The rate of infusion should not exceed 1.1 mg/min (equivalent to 1.4 mL/min when reconstituted and diluted per instructions).

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

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