**ERAXIS**

## Table of Content

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# ERAXIS™ 100 MG FOR INJECTION

## 1. NAME OF THE MEDICINAL PRODUCT

ERAXIS™ 100 MG FOR INJECTION.

## 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: Fructose 102.5 mg per vial.

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Powder for solution for infusion.

Powder: 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 and in paediatric patients one month and older (see sections 4.4 and 5.1).

### 4.2 Posology and method of administration

Treatment with ERAXIS 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 candidaemia (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 4.4).

ERAXIS should be reconstituted with water for injection 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 ERAXIS be administered at a rate of infusion that does not exceed 1.1 mg/minute (equivalent to 1.4 ml/minute or 84 ml/hour when reconstituted and diluted per instructions). Infusion associated reactions are infrequent when the rate of anidulafungin infusion does not exceed 1.1 mg/minute (see sections 4.4, 4.8 and 6.6).

ERAXIS must not be administered as a bolus injection.

For patients with hereditary fructose intolerance (HFI) see section 4.4.

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. ERAXIS can be given without regard to the timing of haemodialysis (see section 5.2).

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 elderly (see section 5.2).

## 4.3 Contraindications

Hypersensitivity to the active substance, or to any of the excipients.

Hypersensitivity to other medicinal products of the echinocandin class (e.g., caspofungin).

## 4.4 Special warnings and precautions for use

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

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

Hepatic effects
Laboratory abnormalities in liver function tests have been seen in healthy subjects and patients treated with anidulafungin. In some patients with serious underlying medical conditions who were receiving multiple concomitant medications 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 who develop abnormal liver function tests during anidulafungin therapy should be monitored

for evidence of worsening hepatic function and evaluated for risk/benefit of continuing anidulafungin therapy.

Paediatric population
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 5.3), 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.

There is no clinical data to support the efficacy and safety of higher doses of anidulafungin than recommended in 4.2.

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 4.8).

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 4.2, 4.8 and 6.6).

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.

Patients with hereditary fructose intolerance
Patients with hereditary problems of fructose intolerance (HFI) should not take 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.

## 4.5 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 5.2).

*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. Of note, *in vitro* studies do not fully exclude possible *in vivo* interactions.

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.

Paediatric population
Interaction studies have only been performed in adults.

## 4.6 Pregnancy and lactation

Animal studies have shown no selective reproductive toxicity (see section 5.3). 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 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.

## 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

Fifteen hundred and 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 ≥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 neutropenics 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 (see section 4.4).

The following table includes, the all-causality adverse reactions (MedDRA terms) from 840 subjects receiving 100 mg anidulafungin with frequency corresponding to very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥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**

| **System Organ Class** | **Very Common ≥1/10** | **Common ≥1/100 to <1/10** | **Uncommon ≥1/1,000 to <1/100** | **Rare ≥1/10,000 to <1/1,000** | **Very Rare <1/10,000** | **Frequency Not Known** |
|---|---|---|---|---|---|---|
| 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 | | | |

**Table 1. Table of Adverse Reactions**

| System Organ Class | Very Common ≥1/10 | Common ≥1/100 to <1/10 | Uncommon ≥1/1,000 to <1/100 | Rare ≥1/10,000 to <1/1,000 | Very Rare <1/10,000 | Frequency Not Known |
|---|---|---|---|---|---|---|
| Hepatobiliary Disorders | | Alanine aminotransferase increased, blood alkaline phosphatase increased, aspartate aminotransferase increased, blood bilirubin increased, cholestasis | Gamma-glutamyl transferase increased | | | |
| Skin and Subcutaneous Tissue Disorders | | Rash, pruritus | Urticaria | | | |
| Renal and Urinary Disorders | | Blood creatinine increased | | | | |
| General Disorders and Administration Site Conditions | | | Infusion site pain | | | |

* See section 4.4.

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 5.1). 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.

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.

## 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. 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 (≤3x Upper Limit of Normal (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.

ERAXIS is not dialysable.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 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 exhibited *in-vitro* activity against *C. albicans, C. glabrata, C. parapsilosis, C. krusei* and *C. tropicalis.* For the clinical relevance of these findings see "Information from clinical studies".

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**

| **Candida Species** | **MIC breakpoint (mg/L)** | |
|---|---|---|
| | **≤S (Susceptible)** | **>R (Resistant)** |
| *Candida albicans* | 0.03 | 0.03 |
| *Candida glabrata* | 0.06 | 0.06 |
| *Candida tropicalis* | 0.06 | 0.06 |
| *Candida krusei* | 0.06 | 0.06 |
| *Candida parapsilosis*[1] | 0.002 | 4 |
| *Other Candida* spp.[2] | Insufficient evidence | |

[1] *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
[2] 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.*

Information from clinical studies

*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 neutropenia. 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. 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%) - with 20, 13 and 15 isolates of the last 3 species, respectively, in the anidulafungin group. The majority of patients had Apache II scores ≤20 and very few were neutropenic. Efficacy data, both overall and by various subgroups, are presented below in Table 3.

**Table 3. Global success in the MITT population: primary and secondary endpoints**

| | **Anidulafungin** | **Fluconazole** | **Between group difference[a] (95% CI)** |
|---|---|---|---|
| **End of IV Therapy (1º endpoint)** | **96/127 (75.6%)** | **71/118 (60.2%)** | **15.42 (3.9, 27.0)** |
| Candidaemia only | 88/116 (75.9%) | 63/103 (61.2%) | 14.7 (2.5, 26.9) |

| | | | |
|---|---|---|---|
| Other sterile sites[b] | 8/11 (72.7%) | 8/15 (53.3%) | - |
| Peritoneal fluid/IA[c] abscess | 6/8 | 5/8 | |
| Other | 2/3 | 3/7 | |
| | | | |
| *C. albicans*[d] | 60/74 (81.1%) | 38/61 (62.3%) | - |
| Non-*albicans* species[d] | 32/45 (71.1%) | 27/45 (60.0%) | - |
| | | | |
| Apache II score ≤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$^3$ >500)** | 94/124 (75.8%) | 69/114 (60.5%) | - |
| **Neutropenic (ANC, cells/mm$^3$ ⩽500)** | 2/3 | 2/4 | - |
| **At Other Endpoints** | | | |
| End of All Therapy | 94/127 (74.0%) | 67/118 (56.8%) | 17.24 (2.9, 31.6)[e] |
| 2 Week Follow-up | 82/127 (64.6%) | 58/118 (49.2%) | 15.41 (0.4, 30.4)[e] |
| 6 Week Follow-up | 71/127 (55.9%) | 52/118 (44.1%) | 11.84 (-3.4, 27.0)[e] |

[a] Calculated as anidulafungin minus fluconazole.
[b] With or without concurrent candidaemia.
[c] Intra-abdominal.
[d] Data presented for patients with a single baseline pathogen.
[e] 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:

**Table 4. Mortality**

| | **Anidulafungin** | **Fluconazole** |
|---|---|---|
| **Overall study mortality** | **29/127 (22.8%)** | **37/118 (31.4%)** |
| Mortality during study therapy | 10/127 (7.9%) | 17/118 (14.4%) |
| Mortality attributed to *Candida* 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 ≤500 cells/mm$^3$, WBC ≤500 cells/mm$^3$ 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 ≤500 cells/mm$^3$ 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. parapsilosi*s (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 ≤500 cells/$mm^3$ or WBC ≤500 cells/$mm^3$ 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[a] and All-cause Mortality in Patients with Deep Tissue Candidiasis – Pooled Analysis**

| | **MITT Population n/N (%)** |
|---|---|
| **Global Response of Success at EOIVT[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) |
| **Global Response of Success at EOT[b]** | 94/129 (72.9) |
| **All-Cause Mortality** | 40/129 (31.0) |

[a] A successful global response was defined as both clinical and microbiologic success
[b] EOIVT, End of Intravenous Treatment; EOT, End of All Treatment

**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 6.

**Table 6: 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.

## 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 ($^{14}C$) 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, 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 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. The systemic exposure following 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 5.1). 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.

## 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. 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.

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 anesthetised 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.

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.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Powder*:*
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

Powder:
Refer to outer carton.

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.

### 6.4 Special precautions for storage

Powder:

Store this medicinal product in a refrigerator (2°C - 8°C). Excursions for up to 96 hours at temperature up to 25°C are permitted, and the powder can be returned to refrigerated storage.

## 6.5 Nature and contents of container

Powder:
30 ml Type I 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, or alternatively bromobutyl rubber with a lubricant) and aluminium seal with flip-off cap.

ERAXIS will be available as a box containing 1 vial of 100 mg powder.

## 6.6 Special precautions for disposal and other handling

ERAXIS 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 ERAXIS 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. The infusion solution 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 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 at up to 25°C for 24 hours.

*Dilution and infusion*
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 is identified, discard the solution.

Adult Patients
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 dilution to a concentration of 0.77 mg/ml for the final infusion solution and infusion instructions for each dose.

**Dilution requirements for ERAXIS administration**

| Dose | Number of vials of powder | Total reconstituted volume | 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/min (equivalent to 1.4 ml/min or 84 ml/hour when reconstituted and diluted per instructions) (see sections 4.2, 4.4 and 4.8).

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 4.2 and 4.4).

1. Calculate patient dose and reconstitute vial(s) required according to reconstitution instructions to provide a concentration of 3.33 mg/ml (see sections 2 and 4.2)

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

**7. PRODUCT OWNER**

Pfizer Inc.
235 East, 42nd Street
New York, NY 10017
UNITED STATES

ERA-SIN-0920/2
Date of last revision: August 2021

**Package leaflet: Information for the user**

**ERAXIS™ 100 MG FOR INJECTION**
Anidulafungin

**Read all of this leaflet carefully before you or your child 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 or your child 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 ERAXIS is and what it is used for

ERAXIS contains the active substance anidulafungin and is prescribed in adults and in paediatric patients aged 1 month and older 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*.

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

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

## 2. What you need to know before you or your child use ERAXIS

**Do not use ERAXIS**
- if you are allergic to anidulafungin, other echinocandins (e.g., caspofungin), 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 ERAXIS.

Your doctor may decide to monitor you:
- for liver function more closely if you develop liver problems during your treatment.
- if you are given anaesthetics during your treatment with ERAXIS.
- for signs of an allergic reaction such as itching, wheezing, blotchy skin.
- for signs of an infusion-related reaction which could include a rash, hives, itching, redness.
- for shortness of breath/breathing difficulties, dizziness or lightheadedness.

**Children and adolescents**

ERAXIS should not be given to patients under 1 month of age.

**Other medicines and ERAXIS**

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

**Pregnancy and breast-feeding**

The effect of ERAXIS in pregnant women is not known. Therefore, ERAXIS 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 ERAXIS.

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

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

**ERAXIS contains fructose**

This medicine contains 102.5 mg fructose (a type of sugar) in each vial. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

If you (or your child) have hereditary fructose intolerance (HFI), a rare genetic disorder, you (or your child) must not receive this medicine. Patients with HFI cannot break down fructose in this medicine, which may cause serious side effects.

You must tell your doctor before receiving this medicine if you (or your child) have HFI or if your child can no longer take sweet foods or drinks because they feel sick, vomit or get unpleasant effects such as bloating, stomach cramps or diarrhoea.

## 3. How to use ERAXIS

ERAXIS will always be prepared and given to you or your child by a doctor or a healthcare professional.

For use in adults, 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).

For use in children and adolescents (age from 1 month and older), the treatment starts with 3.0 mg/kg (not to exceed 200 mg) on the first day (loading dose). This will be followed by a daily dose of 1.5 mg/kg (not to exceed 100 mg) (maintenance dose). The dose that is given depends on the patient's weight.

ERAXIS should be given to you once a day, by slow infusion (a drip) into your vein. For adults, this will take at least 1.5 hours for the maintenance dose and 3 hours for the loading dose. For children and adolescents, the infusion may take less time depending on the patient's weight.

Your doctor will determine the duration of your treatment and how much ERAXIS 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 ERAXIS than you should**

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

**If you forgot to use ERAXIS**

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 ERAXIS**

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

Your doctor may prescribe another medicine following your treatment with ERAXIS 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 ERAXIS.

**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
- Increase in liver enzymes (gamma-glutamyl transferase)

**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. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store ERAXIS

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 date 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 (do not freeze) 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 ERAXIS contains**

- The active substance is anidulafungin. Each vial of powder contains 100 mg anidulafungin.
- The other ingredients are: fructose (see section 2 “ERAXIS contains fructose”), mannitol, polysorbate 80, tartaric acid, sodium hydroxide (for pH-adjustment), hydrochloric acid (for pH-adjustment).

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

ERAXIS is supplied as a box containing 1 vial of 100 mg powder.

The powder is white to off-white.

ERA-SIN-0222/PIL/0
Date of last revision: February 2022