ERAXIS- anidulafungin injection, powder, lyophilized, for solution
Roerig

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ERAXIS safely and effectively. See full prescribing information for ERAXIS.

ERAXIS™ (anidulafungin)
For injection, for intravenous use
Initial U.S. Approval: 2006

RECENT MAJOR CHANGES

Warnings and Precautions, Hypersensitivity (5.2) 07/2012

INDICATIONS AND USAGE

Anidulafungin is an echinocandin antifungal drug indicated in adults for the treatment of:

- Candidemia and other forms of *Candida* infections (intra-abdominal abscess and peritonitis) (1.1)
- Esophageal candidiasis (1.2)

Limitations of use: has not been studied in endocarditis, osteomyelitis and meningitis due to *Candida* or in sufficient numbers of neutropenic patients (1.3)

DOSAGE AND ADMINISTRATION

- Candidemia and other forms of *Candida* infections: 200 mg loading dose on Day 1, followed by 100 mg daily dose thereafter for at least 14 days after the last positive culture (2.1)
- Esophageal candidiasis: 100 mg loading dose on Day 1, followed by 50 mg daily dose thereafter for a minimum of 14 days and for at least 7 days following resolution of symptoms (2.1)
- 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] (2.3, 5.2)

DOSAGE FORMS AND STRENGTHS

- Lyophilized powder for injection: 50 mg per vial (3)
- Lyophilized powder for injection: 100 mg per vial (3)

CONTRAINDICATIONS

- Known hypersensitivity to anidulafungin, any component of ERAXIS, or other echinocandins (4)

WARNINGS AND PRECAUTIONS

- Hepatic Effects: Risk of abnormal liver function tests, hepatitis, hepatic failure; monitor hepatic function during therapy (5.1)
- Hypersensitivity: Anaphylaxis, including shock has been reported. Risk of infusion-related adverse reactions, possibly histamine-mediated, including rash, urticaria, flushing, pruritus, bronchospasm, dyspnea, and hypotension; to reduce occurrence, do not exceed a rate of infusion of 1.1 mg/minute (2.3,5.2)

ADVERSE REACTIONS

- Candidemia and other forms of *Candida* infections: Most common adverse reactions (≥15%) are hypokalemia, nausea, diarrhea, vomiting, pyrexia, insomnia (6.2)
- Esophageal candidiasis: Most common adverse reactions (≥5%) are diarrhea, pyrexia, anemia, headache, vomiting, nausea and dyspepsia (6.3)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc at 1-800-438-1985 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm (8.1)
- Nursing Mothers: Caution should be exercised when administered to a nursing woman (8.3)
- Pediatrics: The safety and effectiveness in patients ≤16 years has not been established (8.4)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 7/2012

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ERAXIS is indicated for use in adults for the treatment of the following fungal infections listed below. Specimens for fungal culture and other relevant laboratory studies (including histopathology) should be obtained prior to therapy to isolate and identify causative organism(s). Therapy may be instituted before the results of the cultures and other laboratory studies known. However, once these results become available, antifungal therapy should be adjusted accordingly.

1.1 Candidemia and Other Forms of *Candida* Infections (Intra-abdominal Abscess and Peritonitis)

ERAXIS is indicated for the treatment of candidemia and the following *Candida* infections: intra-abdominal abscess and peritonitis [*see Clinical Studies(14.1)* and *Clinical Pharmacology, Microbiology (12.4)*].

1.2 Esophageal Candidiasis

ERAXIS is indicated for the treatment of esophageal candidiasis [*see Clinical Studies (14.2), Table 10 for higher relapse rates off ERAXIS therapy*].

1.3 Limitation of Use

ERAXIS has not been studied in endocarditis, osteomyelitis, and meningitis due to *Candida*, and has not been studied in sufficient numbers of neutropenic patients to determine efficacy in this group.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

Candidemia and other *Candida* infections (intra-abdominal abscess, and peritonitis)

The recommended dose is a single 200 mg loading dose of ERAXIS on Day 1, followed by 100 mg daily dose 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.

Esophageal Candidiasis

The recommended dose is a single 100 mg loading dose of ERAXIS on Day 1, followed by 50 mg daily dose thereafter. Patients should be treated for a minimum of 14 days and for at least 7 days following resolution of symptoms. Duration of treatment should be based on the patient's clinical response. Because of the risk of relapse of esophageal candidiasis in patients with HIV infections, suppressive antifungal therapy may be considered after a course of treatment.

2.2 Preparation for Administration

ERAXIS for Injection must be reconstituted with sterile Water for Injection and subsequently diluted only with 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline). The compatibility of reconstituted ERAXIS with intravenous substances, additives, or medications other than

5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline) has not been established.

Reconstitution 50 mg/vial

Aseptically reconstitute each 50 mg vial with 15 mL of sterile Water for Injection to provide a concentration of 3.33 mg/mL. The reconstituted solution can be stored for up to 24 hours at temperatures up to 25°C (77°F) prior to dilution into the infusion solution.

Reconstitution 100 mg/vial

Aseptically reconstitute each 100 mg vial with 30 mL of sterile Water for Injection to provide a concentration of 3.33 mg/mL. The reconstituted solution can be stored for up to 24 hours at temperatures up to 25°C (77°F) prior to dilution into the infusion solution.

2.3 Dilution and Infusion

Aseptically transfer the contents of the reconstituted vial(s) into the appropriately sized IV bag (or bottle) containing either 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline). See Table 1 for the dilution and infusion instructions for each dose.

Table 1: Dilution Requirements for ERAXIS Administration

Dose	Number of Vials Required	Total Reconstituted Volume Required	Infusion Volume *	Total Infusion Volume †	Rate of Infusion	Minimum Duration of Infusion
50 mg	1–50 mg	15 mL	50 mL	65 mL	1.4 mL/min or 84 mL/ hour)	45 min
100 mg	2–50 mg or 1–100 mg	30 mL	100 mL	130 mL	1.4 mL/min or 84 mL/ hour)	90 min
200 mg	4–50 mg or 2–100 mg	60 mL	200 mL	260 mL	1.4 mL/min or 84 mL/ hour)	180 min

* Either 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline)

† Infusion solution concentration is 0.77 mg/mL

Caution: 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 Warnings and Precautions (5.2)*].

The infusion solution may be stored for up to 48 hours at temperatures up to 25°C (77°F), or stored frozen for at least 72 hours prior to administration.

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

3 DOSAGE FORMS AND STRENGTHS

Lyophilized powder for injection: 50 mg per vial

Lyophilized powder for injection: 100 mg per vial

4 CONTRAINDICATIONS

ERAXIS is contraindicated in persons with known hypersensitivity to anidulafungin, any component of ERAXIS, or other echinocandins.

5 WARNINGS AND PRECAUTIONS

5.1 Hepatic Effects

Laboratory abnormalities in liver function tests have been seen in healthy volunteers and patients treated with ERAXIS. In some patients with serious underlying medical conditions who were receiving multiple concomitant medications along with ERAXIS, 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 ERAXIS has not been established. Patients who develop abnormal liver function tests during ERAXIS therapy should be monitored for evidence of worsening hepatic function and evaluated for risk/benefit of continuing ERAXIS therapy.

5.2 Hypersensitivity

Anaphylactic reactions, including shock were reported with the use of ERAXIS. If these reactions occur, ERAXIS should be discontinued and appropriate treatment administered [*see Adverse Reactions (6.5)*].

Infusion-related adverse reactions, possibly histamine-mediated, have been reported with ERAXIS, including rash, urticaria, flushing, pruritus, bronchospasm, dyspnea, and hypotension [*see Adverse Reactions (6)*]. To reduce occurrence of these reactions, do not exceed a rate of ERAXIS infusion of 1.1 mg/minute [*see Dosage and Administration (2.3)*].

6 ADVERSE REACTIONS

The most serious adverse reactions reported with ERAXIS are:

- Hepatic effects [*see Warnings and Precautions (5.1)*]
- Hypersensitivity [*see Warnings and Precautions (5.2)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of ERAXIS for Injection was assessed in 929 individuals, including 257 healthy subjects and 672 patients in clinical trials of candidemia, other forms of *Candida* infections, and esophageal candidiasis. A total of 633 patients received ERAXIS at daily doses of either 50 mg or 100 mg. A total of 481 patients received ERAXIS for ≥14 days.

6.2 Candidemia/other *Candida* Infections

Three studies (one comparative vs. fluconazole, two non-comparative) assessed the efficacy and safety of ERAXIS (100 mg) in patients with candidemia and other *Candida* infections.

The data described below reflect exposure to ERAXIS and fluconazole in 127 and 118 patients, respectively, with candidemia and other forms of invasive candidiasis, in the randomized, comparative trial of the efficacy and safety of ERAXIS to that of fluconazole. In ERAXIS-treated patients, the age range was 16–89 years, the gender distribution was 51% male and 49% female, and the race distribution was 72% White, 18% Black/African American, 9% other races. Patients were randomized to receive once daily IV ERAXIS (200 mg loading dose followed by 100 mg maintenance dose) or IV fluconazole (800 mg loading dose followed by 400 mg maintenance dose). Treatment was administered for at least 14 and not more than 42 days.

The number of patients with adverse reactions leading to discontinuation of study medication was 11.5% in the ERAXIS arm and 21.6% in the fluconazole arm. The most common adverse reactions leading to study drug discontinuation were multi-organ failure and systemic *Candida* infection in the ERAXIS arm.

Table 2 presents adverse reactions that were reported in ≥5% of subjects receiving ERAXIS or fluconazole therapy in this trial.

Table 2: Adverse Reactions Reported in ≥5% of Subjects Receiving ERAXIS or Fluconazole Therapy for Candidemia/other Candida Infections*, †

	ERAXIS 100 mg N=131	**Fluconazole 400 mg N=125**
	N (%)	**N (%)**
Subjects with a least one adverse reaction	**130 (99)**	**122 (98)**
Infections and infestations	**82 (63)**	**80 (64)**
Bacteremia	23 (18)	23 (18)
Urinary tract infection	19 (15)	22 (18)
Sepsis	9 (7)	11 (9)
Pneumonia	8 (6)	19 (15)
Gastrointestinal disorders	**81 (62)**	**72 (58)**
Nausea	32 (24)	15 (12)
Diarrhea	24 (18)	23 (18)
Vomiting	23 (18)	12 (10)
Constipation	11 (8)	14 (11)
Abdominal pain	8 (6)	16 (13)
General disorders and administration site conditions	**70 (53)**	**76 (61)**
Pyrexia	23 (18)	23 (18)
Edema peripheral	14 (11)	16 (13)
Chest pain	7 (5)	6 (5)
Respiratory, thoracic, and mediastinal disorders	**67 (51)**	**55 (44)**
Dyspnea	15 (12)	4 (3)
Pleural effusion	13 (10)	11 (9)
Cough	9 (7)	7 (6)
Respiratory distress	8 (6)	2 (2)
Investigations	**66 (50)**	**46 (37)**
Blood alkaline phosphatase increased	15 (12)	14 (11)
White blood cell increased	11 (8)	3 (2)
Hepatic enzyme increased	7 (5)	14 (11)
Blood creatinine increased	7 (5)	1 (1)
Metabolism and nutrition disorders	**61 (47)**	**61 (49)**
Hypokalemia	33 (25)	24 (19)
Hypomagnesemia	15 (12)	14 (11)
Hypoglycemia	9 (7)	10 (8)
Hyperkalemia	8 (6)	14 (11)
Hyperglycemia	8 (6)	8 (6)
Dehydration	8 (6)	2 (2)
Vascular disorders	**50 (38)**	**41 (33)**
Hypotension	19 (15)	18 (14)
Hypertension	15 (12)	5 (4)
Deep vein thrombosis	13 (10)	9 (7)

Psychiatric disorders	**48(37)**	**45 (36)**
Insomnia	20 (15)	12 (10)
Confusional state	10 (8)	10 (8)
Depression	8 (6)	5 (4)
Blood and lymphatic system disorders	**34 (26)**	**36 (29)**
Anemia	12 (9)	20 (16)
Thrombocythemia	8 (6)	1 (1)
Leukocytosis	7 (5)	6 (5)
Skin and subcutaneous tissue disorders	**30 (23)**	**32 (26)**
Decubitus ulcer	7 (5)	10 (8)
Nervous system disorders	**27 (21)**	**31 (25)**
Headache	11 (8)	10 (8)
Musculoskeletal and connective tissue disorders	**27 (21)**	**25 (20)**
Back pain	7 (5)	13 (10)

* A patient who experienced multiple reactions with a System Organ Class (SOC) or preferred term was counted one time for that class, one time for the preferred term and one time for "subjects with at least one adverse reaction"

† This trial was not designed to support comparative claims for ERAXIS for the adverse reactions reported in this table.

6.3 Esophageal Candidiasis

The data described below reflect exposure to ERAXIS and fluconazole in 300 and 301 patients, respectively, with esophageal candidiasis in a randomized trial comparing the efficacy and safety of ERAXIS to that of oral fluconazole. In ERAXIS-treated patients, the age range was 18–68 years, the gender distribution was 42% male and 58% female and the race distribution was 15% White, 49% Black/African American, 15% Asian, 0.3 % Hispanic, 21% other races. Patients were randomized to receive IV ERAXIS (100 mg on day 1, followed by 50 mg per day) or oral fluconazole (200 mg on day 1, followed by 100 mg per day) for 7 days beyond resolution of symptoms (range, 14–21 days).

Twenty eight (9%) patients in the ERAXIS arm and 36 (12%) patients in the fluconazole arm had adverse reactions leading to discontinuation of study medication. The most common adverse reactions leading to study drug discontinuation were maculopapular rash for the ERAXIS arm. The most common adverse reactions leading to discontinuation were rash and increased AST for the fluconazole arm.

Table 3 presents adverse reactions that were reported in ≥5% of subjects receiving ERAXIS therapy.

Table 3 Adverse Reactions Reported in ≥5% of Subjects Receiving ERAXIS or Fluconazole Therapy for Esophageal Candidiasis*, †

	ERAXIS 50 mg N=300	**Fluconazole 100 mg N=301**
	N (%)	**N (%)**
Subjects with a least one adverse reactions	**239 (80)**	**227 (75)**
Infections and infestations	**115 (38)**	**99 (33)**
Oral candidiasis	15 (5)	10 (3)
Gastrointestinal disorders	**106 (35)**	**113 (38)**
Diarrhea	27(9)	26(9)
Vomiting	27(7)	30(10)
Nausea	20(7)	23(8)

Dyspepsia	20(7)	21(7)
Blood and lymphatic system disorders	**55 (18)**	**50 (17)**
Anemia	25 (8)	22 (7)
Metabolism and nutrition disorders	**50 (17)**	**46 (15)**
Hypokalemia	14 (5)	17 (6)
General disorders and administration site condition	**49 (16)**	**54 (18)**
Pyrexia	27(9)	28(9)
Nervous system disorders	**39 (13)**	**36 (12)**
Headache	25 (8)	20 (7)

* A patient who experienced multiple reactions with a System Organ Class (SOC) or preferred term was counted one time for that class, one time for the preferred term and one time for "subjects with at least one adverse reaction"

† This trial was not designed to support comparative claims for ERAXIS for the adverse reactions reported in this table.

6.4 Less Common Adverse Reactions

The following selected adverse reactions occurred in <2% of patients:

Blood and Lymphatic: coagulopathy, thrombocytopenia

Cardiac: atrial fibrillation, bundle branch block (right), sinus arrhythmia, ventricular extrasystoles

Eye: eye pain, vision blurred, visual disturbance

General and Administration Site: infusion related reaction, peripheral edema, rigors

Hepatobiliary: abnormal liver function tests, cholestasis, hepatic necrosis

Infections: clostridial infection

Investigations: amylase increased, bilirubin increased, CPK increased, electrocardiogram QT prolonged, gamma-glutamyl transferase increased, lipase increased, potassium decreased, prothrombin time prolonged, urea increased

Nervous System: convulsion, dizziness

Respiratory, Thoracic and Mediastinal: cough

Skin and Subcutaneous Tissue: angioneurotic edema, erythema, pruritus, sweating increased, urticaria

Vascular: flushing, hot flushes, thrombophlebitis superficial

6.5 Post-marketing Experience

The following adverse reactions have been identified during post approval use of anidulafungin. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune: Anaphylactic shock, anaphylactic reaction, bronchospasm [*see Warnings and Precautions (5.2)*].

7 DRUG INTERACTIONS

7.1 Cyclosporine

Administration of multiple doses of anidulafungin and cyclosporine to healthy subjects resulted in no significant alteration in the steady state pharmacokinetics of either drug. No dosage adjustment of cyclosporine or anidulafungin is needed when the two drugs are co-administered [*see Clinical Pharmacology (12.4)*].

7.2 Voriconazole

Administration of multiple doses of anidulafungin and voriconazole to healthy subjects resulted in no significant alteration in the steady state pharmacokinetics of either drug. No dosage adjustment of voriconazole or anidulafungin is needed when the two drugs are co-administered [*see Clinical Pharmacology (12.4)*].

7.3 Tacrolimus

Administration of multiple doses of anidulafungin and a single dose of tacrolimus to healthy subjects resulted in no significant alteration in the steady state pharmacokinetics of either drug. No dosage adjustment of tacrolimus or anidulafungin is needed when the two drugs are co-administered [*see Clinical Pharmacology (12.4)*].

7.4 Rifampin

Administration of multiple doses of anidulafungin and rifampin to patients resulted in no significant alteration in the steady state pharmacokinetics of anidulafungin. No dosage adjustment of anidulafungin is needed when it is co-administered with rifampin [*see Clinical Pharmacology (12.4)*].

7.5 Amphotericin B Liposome for Injection

Administration of multiple doses of anidulafungin and liposomal amphotericin B to patients resulted in no significant alteration in the steady state pharmacokinetics of anidulafungin. No dosage adjustment of anidulafungin is needed when it is co-administered with liposomal amphotericin B [*see Clinical Pharmacology (12.4)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B

Embryo-fetal development studies were conducted with doses up to 20 mg/kg/day in rats and rabbits (equivalent to 2 and 4 times, respectively, the proposed therapeutic maintenance dose of 100 mg/day on the basis of relative body surface area). In rats, anidulafungin crossed the placental barrier, was detected in fetal plasma, and was associated with incomplete ossification of several bones. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, ERAXIS should be used during pregnancy only if clearly needed.

8.3 Nursing Mothers

Anidulafungin was found in the milk of lactating rats. It is not known whether anidulafungin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ERAXIS is administered to a nursing woman.

8.4 Pediatric Use

The safety and effectiveness of ERAXIS in patients ≤16 years old has not been established [*see Clinical Pharmacology (12.4)*].

8.5 Geriatric Use

Dosage adjustments are not required for geriatric patients [*see Clinical Pharmacology (12.4)*].

Of the total number of subjects (N = 197) in the pivotal clinical studies of anidulafungin, 35% were 65 years and over, while 18% were 75 years and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has

not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Hepatic Insufficiency

No dosing adjustments are required for patients with any degree of hepatic insufficiency. Anidulafungin is not hepatically metabolized. 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. Though a slight decrease in AUC was observed in patients with Child-Pugh C hepatic insufficiency, it was within the range of population estimates noted for healthy subjects [*see Clinical Pharmacology (12.4)*].

8.7 Renal Insufficiency

Dosage adjustments are not required for patients with any degree of renal insufficiency including those on hemodialysis. Anidulafungin has negligible (<1%) renal clearance. In a clinical study of subjects with mild, moderate, severe or end stage (dialysis-dependent) renal insufficiency, anidulafungin pharmacokinetics were similar to those observed in subjects with normal renal function. Anidulafungin is not dialyzable and may be administered without regard to the timing of hemodialysis [*see Clinical Pharmacology (12.4)*].

10 OVERDOSAGE

During clinical trials a single 400 mg dose of ERAXIS was inadvertently administered as a loading dose. No clinical adverse events were reported. In a study of 10 healthy subjects administered a loading dose of 260 mg followed by 130 mg daily, ERAXIS was generally well tolerated; 3 of the 10 subjects experienced transient, asymptomatic transaminase elevations (≤3 x ULN) [*see Warnings and Precautions (5.1)*].

Anidulafungin is not dialyzable.

The maximum non-lethal dose of anidulafungin in rats was 50 mg/kg, a dose which is equivalent to 10 times the recommended daily dose for esophageal candidiasis (50 mg/day) or equivalent to 5 times the recommended daily dose for candidemia and other *Candida* infections (100 mg/day), based on relative body surface area comparisons.

11 DESCRIPTION

ERAXIS for Injection is a sterile, lyophilized product for intravenous (IV) infusion that contains anidulafungin. ERAXIS (anidulafungin) is a semi-synthetic lipopeptide synthesized from a fermentation product of *Aspergillus nidulans*. Anidulafungin is an echinocandin, a class of antifungal drugs that inhibits the synthesis of 1,3-β-D-glucan, an essential component of fungal cell walls.

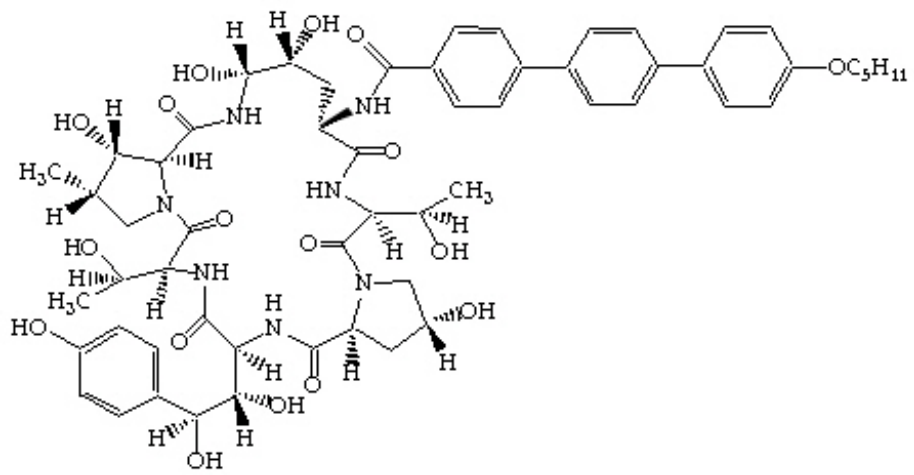
ERAXIS (anidulafungin) is 1-[(4R,5R)-4,5-dihydroxy-N_2-[[4"-(pentyloxy)[1,1':4',1"-terphenyl]-4-yl]carbonyl]-L-ornithine]echinocandin B. Anidulafungin is a white to off-white powder that is practically insoluble in water and slightly soluble in ethanol. In addition to the active ingredient, anidulafungin, ERAXIS for Injection contains the following inactive ingredients:

50 mg/vial - fructose (50 mg), mannitol (250 mg), polysorbate 80 (125 mg), tartaric acid (5.6 mg), and sodium hydroxide and/or hydrochloric acid for pH adjustment.

100 mg/vial - fructose (100 mg), mannitol (500 mg), polysorbate 80 (250 mg), tartaric acid (11.2 mg), and sodium hydroxide and/or hydrochloric acid for pH adjustment.

The empirical formula of anidulafungin is $C_{58}H_{73}N_7O_{17}$ and the formula weight is 1140.3.

The structural formula is:



Prior to administration, ERAXIS for Injection requires reconstitution with sterile Water for Injection and subsequent dilution with either 5% Dextrose Injection, USP or 0.9% Sodium Chloride Injection, USP (normal saline).

DO NOT dilute with other solutions or co-infuse with other medications or electrolytes [*see Dosage and Administration (2)*].

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Anidulafungin is an anti-fungal drug [*see Microbiology (12.4)*].

12.3 Pharmacokinetics

General Pharmacokinetic Characteristics

The pharmacokinetics of anidulafungin following intravenous (IV) administration have been characterized in healthy subjects, special populations and patients. Systemic exposures of anidulafungin are dose-proportional and have low intersubject variability (coefficient of variation <25%) as shown in Table 4. The steady state was achieved on the first day after a loading dose (twice the daily maintenance dose) and the estimated plasma accumulation factor at steady state is approximately 2.

Table 4: Mean (%CV) Steady State Pharmacokinetic Parameters of Anidulafungin Following IV Administration of Anidulafungin Once Daily for 10 Days in Healthy Adult Subjects

PK Parameter*	Anidulafungin IV Dosing Regimen (LD/MD, mg)†		
	70/35‡,§ (N=6)	200/100 (N=10)	260/130§,¶ (N=10)
$C_{max, ss}$ [mg/L]	3.55 (13.2)	8.6 (16.2)	10.9 (11.7)
AUC_{ss} [mg·h/L]	42.3 (14.5)	111.8 (24.9)	168.9 (10.8)
CL [L/h]	0.84 (13.5)	0.94 (24.0)	0.78 (11.3)
$t_{1/2}$ [h]	43.2 (17.7)	52.0 (11.7)	50.3 (9.7)

$C_{max, ss}$ = the steady state peak concentration

AUC_{ss} = the steady state area under concentration vs. time curve

CL = clearance

$t_{1/2}$ = the terminal elimination half-life

* Parameters were obtained from separate studies

† LD/MD: loading dose/maintenance dose once daily

‡ Data were collected on Day 7

§ Safety and efficacy of these doses has not been established
¶ See OVERDOSAGE

The clearance of anidulafungin is about 1 L/h and anidulafungin has a terminal elimination half-life of 40–50 hours.

Distribution

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

Metabolism

Hepatic metabolism of anidulafungin has not been observed. Anidulafungin is not a clinically relevant substrate, inducer, or inhibitor of cytochrome P450 (CYP450) isoenzymes. It is unlikely that anidulafungin will have clinically relevant effects on the metabolism of drugs metabolized by CYP450 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 about 24 hours. *In vivo*, the ring-opened product is subsequently converted to peptidic degradants and eliminated.

Excretion

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

Specific Populations

Patients with fungal infections

Population pharmacokinetic analyses from four clinical trials including 107 male and 118 female patients with fungal infections showed that the pharmacokinetic parameters of anidulafungin are not affected by age, race, or the presence of concomitant medications which are known metabolic substrates, inhibitors or inducers.

The pharmacokinetics of anidulafungin in patients with fungal infections are similar to those observed in healthy subjects. The pharmacokinetic parameters of anidulafungin estimated using population pharmacokinetic modeling following IV administration of a maintenance dose of 50 mg/day or 100 mg/day (following a loading dose) are presented in Table 5.

Table 5: Mean (%CV) Steady State Pharmacokinetic Parameters of Anidulafungin Following IV Administration of Anidulafungin in Patients with Fungal Infections Estimated Using Population Pharmacokinetic Modeling

PK Parameter*	Anidulafungin IV Dosing Regimen (LD/MD, mg)†	
	100/50	200/100
$C_{max, ss}$ [mg/L]	4.2 (22.4)	7.2 (23.3)
$C_{min, ss}$ [mg/L]	1.6 (42.1)	3.3 (41.8)
AUC_{ss} [mg·h/L]	55.2 (32.5)	110.3 (32.5)
CL [L/h]	1.0 (33.5)	
$t_{1/2, \beta}$ [h]‡	26.5 (28.5)	

* All the parameters were estimated by population modeling using a two-compartment model with first order elimination; AUC_{ss}, $C_{max,ss}$ and $C_{min,ss}$ (steady state trough plasma concentration) were estimated using individual PK parameters and infusion rate of 1 mg/min to administer recommended doses of 50 and 100 mg/day.

† LD/MD: loading dose/daily maintenance dose

‡ $t_{1/2,\beta}$ is the predominant elimination half-life that characterizes the majority of the concentration-time profile.

Gender

Dosage adjustments are not required based on 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.

Geriatric

Dosage adjustments are not required for geriatric patients. 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) and the range of clearance was similar.

Race

Dosage adjustments are not required based on race. Anidulafungin pharmacokinetics were similar among Whites, Blacks, Asians, and Hispanics.

HIV Status

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

Hepatic Insufficiency

Dosage adjustments are not required on the basis of mild, moderate or severe hepatic insufficiency. Anidulafungin is not hepatically metabolized. 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. Though a slight decrease in AUC was observed in patients with Child-Pugh C hepatic insufficiency, it was within the range of population estimates noted for healthy subjects.

Renal Insufficiency

Dosage adjustments are not required for patients with any degree of renal insufficiency including those on hemodialysis. Anidulafungin has negligible renal clearance. In a clinical study of subjects with mild, moderate, severe or end stage (dialysis-dependent) renal insufficiency, anidulafungin pharmacokinetics were similar to those observed in subjects with normal renal function. Anidulafungin is not dialyzable and may be administered without regard to the timing of hemodialysis.

Pediatric

The pharmacokinetics of anidulafungin after daily doses were investigated in immunocompromised pediatric (2 through 11 years) and adolescent (12 through 17 years) patients with neutropenia. The steady state was achieved on the first day after administration of the loading dose (twice the maintenance dose), and the C_{max} and AUC_{ss} increased in a dose-proportional manner. Concentrations and exposures following administration of maintenance doses of 0.75 and 1.5 mg/kg/day in this population were similar to those observed in adults following maintenance doses of 50 and 100 mg/day, respectively (as shown in Table 6).

Table 6: Mean (%CV) Steady State Pharmacokinetic Parameters of Anidulafungin Following IV Administration of Anidulafungin Once Daily in Pediatric Subjects

	Anidulafungin IV Dosing Regimen

PK Parameter*	(LD/MD, mg/kg)†			
	1.5/0.75		3.0/1.5	
Age Group ‡	2–11 years (N = 6)	12–17 years (N = 6)	2–11 years (N = 6)	12–17 years (N = 6)
$C_{max, ss}$ [mg/L]	3.32 (50.0)	4.35 (22.5)	7.57 (34.2)	6.88 (24.3)
AUC_{ss} [mg·h/L]	41.1 (38.4)	56.2 (27.8)	96.1 (39.5)	102.9 (28.2)

* Data were collected on Day 5

† LD/MD: loading dose/daily maintenance dose

‡ Safety and effectiveness has not been established in pediatric patients ≤16 years of age

Drug Interactions

In vitro studies showed that anidulafungin is not metabolized by human cytochrome P450 or by isolated human hepatocytes, and does not significantly inhibit the activities of human CYP isoforms (1A2, 2B6, 2C8, 2C9, 2C19, 2D6 and 3A) in clinically relevant concentrations. No clinically relevant drug-drug interactions were observed with drugs likely to be co-administered with anidulafungin.

Cyclosporine (CYP3A4 substrate)

In a study in which 12 healthy adult subjects received 100 mg/day maintenance dose of anidulafungin following a 200 mg loading dose (on Days 1 to 8) and in combination with 1.25 mg/kg oral cyclosporine twice daily (on Days 5 to 8), the steady state C_{max} of anidulafungin was not significantly altered by cyclosporine; the steady state AUC of anidulafungin was increased by 22%. A separate *in vitro* study showed that anidulafungin has no effect on the metabolism of cyclosporine. No dosage adjustment of either drug is warranted when co-administered [*see Drug Interactions (7.1)*].

Voriconazole (CYP2C19, CYP2C9, CYP3A4 inhibitor and substrate)

In a study in which 17 healthy subjects received 100 mg/day maintenance dose of anidulafungin following a 200 mg loading dose, 200 mg twice daily oral voriconazole (following two 400 mg 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 warranted when co-administered [*see Drug Interactions (7.2)*].

Tacrolimus (CYP3A4 substrate)

In a study in which 35 healthy subjects received a single oral dose of 5 mg tacrolimus (on Day 1), 100 mg/day maintenance dose of anidulafungin following a 200 mg loading dose (on Days 4 to 12) and both in combination (on Day 13), 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 warranted when co-administered [*see Drug Interactions (7.3)*].

Rifampin (potent CYP450 inducer)

The pharmacokinetics of anidulafungin were examined in 27 patients that were co-administered anidulafungin and rifampin. The population pharmacokinetic analysis showed that when compared to data from patients that did not receive rifampin, the pharmacokinetics of anidulafungin were not significantly altered by co-administration with rifampin. No dosage adjustment of anidulafungin is warranted [*see Drug Interactions (7.4)*].

Amphotericin B liposome for injection

The pharmacokinetics of anidulafungin were examined in 27 patients that were co-administered liposomal amphotericin B. The population pharmacokinetic analysis showed that when compared to data from patients that did not receive amphotericin B, the pharmacokinetics of anidulafungin were not significantly altered by co-administration with amphotericin B. No dosage adjustment of anidulafungin is warranted [*see Drug Interactions (7.5)*].

12.4 Microbiology

Mechanism of Action

Anidulafungin is a semi-synthetic echinocandin with antifungal activity. Anidulafungin inhibits 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.

Activity *in vitro*

Anidulafungin has been shown to be active against *Candida albicans*, *C. glabrata*, *C. parapsilosis*, and *C. tropicalis* both in vitro and in clinical infections as described in INDICATIONS AND USAGE and CLINICAL STUDIES. Because of the potential for reduced susceptibility to anidulafungin, it is recommended that susceptibility be determined by a standardized method.

Anidulafungin minimal inhibitory concentrations (MICs) were determined for isolates of *Candida* spp. obtained during clinical studies using a standardized method. However, no correlation between *in vitro* activity as determined by this method and clinical outcome was established.

Drug Resistance

Echinocandin resistance is due to point mutations within the genes (FKS1 and FKS2) encoding for subunits in the glucan synthase enzyme complex. There have been reports of *Candida* isolates with reduced susceptibility to anidulafungin, suggesting a potential for development of drug resistance. The clinical significance of this observation is not fully understood.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal carcinogenicity studies of anidulafungin have not been conducted.

Anidulafungin was not genotoxic in the following *in vitro* studies: bacterial reverse mutation assays, a chromosome aberration assay with Chinese hamster ovary cells, and a forward gene mutation assay with mouse lymphoma cells. Anidulafungin was not genotoxic in mice using the *in vivo* micronucleus assay.

Anidulafungin produced no adverse effects on fertility in male or female rats at intravenous doses of 20 mg/kg/day (equivalent to 2 times the proposed therapeutic maintenance dose of 100 mg/day on the basis of relative body surface area).

13.2 Animal Toxicology and/or Pharmacology

In 3 month studies, liver toxicity, including single cell hepatocellular necrosis, hepatocellular hypertrophy and increased liver weights were observed in monkeys and rats at doses equivalent to 5–6 times human exposure. For both species, hepatocellular hypertrophy was still noted one month after the end of dosing.

14 CLINICAL STUDIES

14.1 Candidemia and Other *Candida* Infections (Intra-abdominal Abscess and Peritonitis)

The safety and efficacy of ERAXIS were evaluated in a Phase 3, randomized, double-blind study of patients with candidemia and/or other forms of invasive candidiasis. Patients were randomized to receive once daily IV ERAXIS (200 mg loading dose followed by 100 mg maintenance dose) or IV fluconazole (800 mg loading dose followed by 400 mg maintenance dose). Patients were stratified by APACHE II score (≤20 and >20) and the presence or absence of neutropenia. Patients with *Candida* endocarditis, osteomyelitis or meningitis, or those with infection due to *C. krusei*, were excluded from the study. Treatment was administered for at least 14 and not more than 42 days. Patients in both study arms were permitted to switch to oral fluconazole after at least 10 days of intravenous therapy, provided

that they were able to tolerate oral medication, were afebrile for at least 24 hours, and the last blood cultures were negative for *Candida* species.

Patients who received at least one dose of study medication and who had a positive culture for *Candida* species from a normally sterile site before entry into the study (modified intent-to-treat [MITT] population) were included in the analysis of global response at the end of IV therapy. A successful global response required clinical cure or improvement (significant, but incomplete resolution of signs and symptoms of the *Candida* infection and no additional antifungal treatment), and documented or presumed microbiological eradication. Patients with an indeterminate outcome were analyzed as failures in this population.

Two hundred and fifty-six patients in the intent-to-treat (ITT) population were randomized and received at least one dose of study medication. In ERAXIS-treated patients, the age range was 16–89 years, the gender distribution was 50% male and 50% female, and the race distribution was 71% White, 20% Black/African American, 7% Hispanic, 2% other races. The median duration of IV therapy was 14 and 11 days in the ERAXIS and fluconazole arms, respectively. For those who received oral fluconazole, the median duration of oral therapy was 7 days for the ERAXIS arm and 5 days for the fluconazole arm.

Patient disposition is presented in Table 7.

Table 7: Patient Disposition and Reasons for Discontinuation in Candidemia and other Candida Infections Study

	ERAXIS	**Fluconazole**
	n (%)	**n (%)**
Treated patients	131	125
Patients completing study through 6 week follow-up	94 (72)	80 (64)
DISCONTINUATIONS FROM STUDY MEDICATION		
Total discontinued from study medication	34 (26)	48 (38)
Discontinued due to adverse events	12 (9)	21 (17)
Discontinued due to lack of efficacy	11 (8)	16 (13)

Two hundred and forty-five patients (127 ERAXIS, 118 fluconazole) met the criteria for inclusion in the MITT population. Of these, 219 patients (116 ERAXIS, 103 fluconazole) had candidemia only. Risk factors for candidemia among patients in both treatment arms in this study were: presence of a central venous catheter (78%), receipt of broad-spectrum antibiotics (69%), recent surgery (42%), recent hyperalimentation (25%), and underlying malignancy (22%). The most frequent species isolated at baseline was *C. albicans* (62%), followed by *C. glabrata* (20%), *C. parapsilosis* (12%) and *C. tropicalis* (11%). The majority (97%) of patients were non-neutropenic (ANC >500) and 81% had APACHE II scores less than or equal to 20.

Global success rates in patients with candidemia and other *Candida* infections are summarized in Table 8.

Table 8: Efficacy Analysis: Global Success in patients with Candidemia and other Candida Infections (MITT Population)

Time-point	**ERAXIS (N=127) n (%)**	**Fluconazole (N=118) n (%)**	**Treatment Difference*, % (95% C.I.)**
End of IV Therapy	96 (75.6)	71 (60.2)	15.4 (3.9, 27.0)
End of All Therapy†	94 (74.0)	67 (56.8)	17.2 (2.9, 31.6)‡
			15.4

2 Week Follow-up	82 (64.6)	58 (49.2)	15.4 (0.4, 30.4)‡
6 Week Follow-up	71 (55.9)	52 (44.1)	11.8 (-3.4, 27.0)‡

* Calculated as ERAXIS minus fluconazole

† 33 patients in each study arm (26% ERAXIS and 29% fluconazole-treated) switched to oral fluconazole after the end of IV therapy.

‡ 98.3% confidence intervals, adjusted post hoc for multiple comparisons of secondary time points

Table 9 presents global response by patients with candidemia or multiple sites of *Candida* infection and mortality data for the MITT population.

Table 9: Global Response and Mortality in Candidemia and other Candida Infections

	ERAXIS	**Fluconazole**	**Between group difference * (95% CI)**
No. of MITT patients	127	118	
Global Success (MITT) At End Of IV Therapy			
Candidemia	88/116 (75.9%)	63/103 (61.2%)	14.7 (2.5, 26.9)
Neutropenic	1/2	2/4	-
Non neutropenic	87/114 (76.3%)	61/99 (61.6%)	-
Multiple sites			
Peritoneal fluid/ intra-abdominal abscess	4/6	5/6	-
Blood/ peritoneum (intra-abdominal abscess)	2/2	0/2	-
Blood /bile	-	1/1	-
Blood/renal	-	1/1	-
Pancreas	-	0/3	-
Pelvic abscess	-	1/2	-
Pleural fluid	1/1	-	-
Blood/ pleural fluid	0/1	-	-
Blood/left thigh lesion biopsy	1/1	-	-
Total	8/11 (72.7%)	8/15 (53.3%)	-
Mortality			
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*	2/127 (1.6%)	5/118 (4.2%)	-

* Calculated as ERAXIS minus fluconazole

14.2 Esophageal Candidiasis

ERAXIS was evaluated in a double-blind, double-dummy, randomized Phase 3 study. Three hundred patients received ERAXIS (100 mg loading dose IV on Day 1 followed by 50 mg/day IV) and 301 received oral fluconazole (200 mg loading dose on Day 1 followed by 100 mg/day). Treatment duration was 7 days beyond resolution of symptoms for a minimum of 14 and a maximum of 21 days.

Of the 442 patients with culture confirmed esophageal candidiasis, most patients (91%) had *C. albicans* isolated at the baseline.

Treatment groups were similar in demographic and other baseline characteristics. In ERAXIS-treated patients, the age range was 16–69 years, the gender distribution was 42% male and 58% female, and the

race distribution was 15% White, 49% Black/African American, 15% Asian, 0.3 % Hispanic, 21% other races.

In this study, of 280 patients tested, 237 (84.6%) tested HIV positive. In both groups the median time to resolution of symptoms was 5 days and the median duration of therapy was 14 days.

Efficacy was assessed by endoscopic outcome at end of therapy (EOT). Patients were considered clinically evaluable if they received at least 10 days of therapy, had an EOT assessment with a clinical outcome other than 'indeterminate', had an endoscopy at EOT, and did not have any protocol violations prior to the EOT visit that would affect an assessment of efficacy.

An endoscopic success, defined as cure (endoscopic grade of 0 on a 4-point severity scale) or improvement (decrease of one or more grades from baseline), was seen in 225/231 (97.4%) ERAXIS-treated patients and 233/236 (98.7%) fluconazole-treated patients (Table 10). The majority of these patients were endoscopic cures (grade=0). Two weeks after completing therapy, the ERAXIS group had significantly more endoscopically-documented relapses than the fluconazole group, 120/225 (53.3%) vs. 45/233 (19.3%), respectively (Table 10).

Table 10: Endoscopy Results in Patients with Esophageal Candidiasis (Clinically Evaluable Population)

Endoscopic Response at End of Therapy				
Response	**ERAXIS N=231**	**Fluconazole N=236**	**Treatment Difference***	**95% CI**
Endoscopic Success, n (%)	225 (97.4)	233 (98.7)	-1.3%	-3.8%, 1.2%
Cure	204 (88.3)	221 (93.6)		
Improvement	21 (9.1)	12 (5.1)		
Failure, n (%)	6 (2.6)	3 (1.3)		
Endoscopic Relapse Rates at Follow-Up, 2 Weeks Post-Treatment				
	ERAXIS	**Fluconazole**	**Treatment Difference***	**95% CI**
Endoscopic Relapse, n/N (%)	120/225 (53.3%)	45/233 (19.3%)	34.0%	25.8%, 42.3%

* Calculated as ERAXIS minus fluconazole

Clinical success (cure or improvement in clinical symptoms including odynophagia/dysphagia and retrosternal pain) occurred in 229/231 (99.1%) of the ERAXIS-treated patients and 235/236 (99.6%) of the fluconazole-treated patients at the end of therapy. For patients with *C. albicans*, microbiological success occurred in 142/162 (87.7%) of the ERAXIS-treated group and 157/166 (94.6%) of the fluconazole-treated group at the end of therapy. For patients with *Candida* species other than *C. albicans*, success occurred in 10/12 (83.3%) of the ERAXIS-treated group and 14/16 (87.5%) of the fluconazole-treated group.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

ERAXIS (anidulafungin) for Injection is supplied in a single-use vial of sterile, lyophilized, preservative-free, powder. ERAXIS (anidulafungin) is available in the following packaging configuration:

Single-Use Vial of ERAXIS 50 mg

NDC 0049-0114-28 One - 50 mg vial

Single-Use Vial of ERAXIS 100 mg

NDC 0049-0116-28 One - 100 mg vial

16.2 Storage

Unreconstituted vials

ERAXIS unreconstituted vials should be stored in a refrigerator at 2°C – 8°C (36°F – 46°F). Do not freeze.

Excursions for 96 hours up to 25ºC (77ºF) are permitted, and the vial can be returned to storage at 2°C – 8°C (36°F – 46°F).

Reconstituted solution

ERAXIS reconstituted solution can be stored at up to 25°C (77°F) for up to 24 hours.

Chemical and physical in-use stability of the reconstituted solution has been demonstrated for 24 hours at 25ºC (77ºF).

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

Infusion Solution

ERAXIS infusion solution can be stored at temperatures up to 25°C (77°F) for up to 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 25ºC (77ºF) or 72 hours when stored frozen.

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 25ºC.

17 PATIENT COUNSELING INFORMATION

17.1 Hepatic Effects

Inform patients about the risk of developing abnormal liver function tests and/or hepatic dysfunction. Advise the patient that liver function tests may be monitored during treatment.

17.2 Hypersensitivity

Inform the patient that anaphylactic reactions, including shock were reported with ERAXIS. Inform the patient if these reactions occur, ERAXIS may be discontinued and appropriate treatment administered.

Inform the patient that ERAXIS is also known to cause infusion-related adverse reactions, possibly histamine-mediated. Inform the patient to report symptoms including rash, urticaria, flushing, pruritus, dyspnea, and hypotension to their healthcare provider.

17.3 Pregnant Women and Nursing Mothers

Inform patients that ERAXIS has not been studied in pregnant women or nursing mothers so the effects of ERAXIS on pregnant women or nursing infants are not known. Instruct patients to tell their healthcare provider if they are pregnant, become pregnant, or are thinking about becoming pregnant. Instruct patients to tell their healthcare provider if they plan to breast-feed their infant.

LAB-0336-8.0
July 2012

PRINCIPAL DISPLAY PANEL - 50 mg Vial Label

Rx only

1 Sterile Single-use Vial

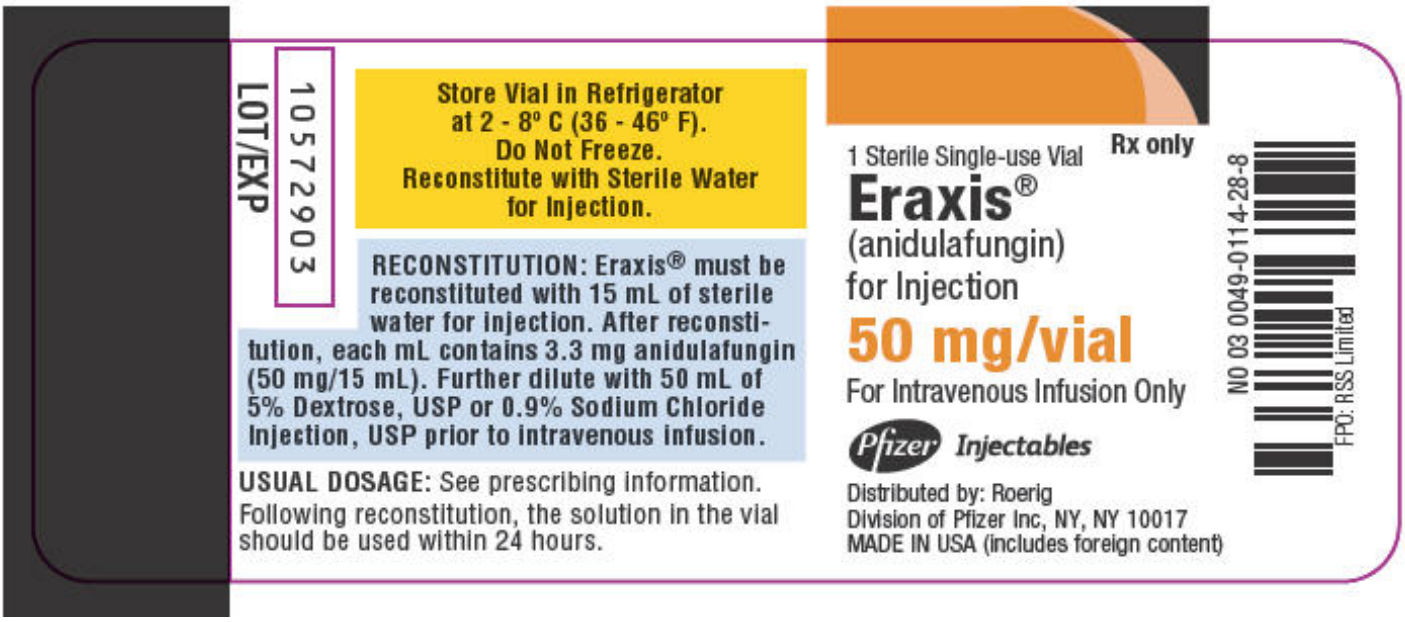
Eraxis®
(anidulafungin)
for Injection

50 mg/vial

For Intravenous Infusion Only

Pfizer Injectables

Distributed by: Roerig
Division of Pfizer Inc, NY, NY 10017
MADE IN USA (includes foreign content)



PRINCIPAL DISPLAY PANEL - 50 mg Vial Carton

NDC 0049-0114-28
Rx only

Unit Pack Contains:
1 Sterile Single-use Vial
Eraxis® 50 mg

Eraxis®
(anidulafungin)
for Injection

50 mg/vial

For Intravenous Infusion Only

Store Vial in Refrigerator

at 2 - 8° C (36 - 46° F).
Do Not Freeze.
Reconstitute with Sterile Water
for Injection.

Pfizer Injectables

Distributed by: Roerig
Division of Pfizer Inc, NY, NY 10017
MADE IN USA (includes foreign content)

PRINCIPAL DISPLAY PANEL - 100 mg Vial Label

Rx only

1 Sterile Single-use Vial

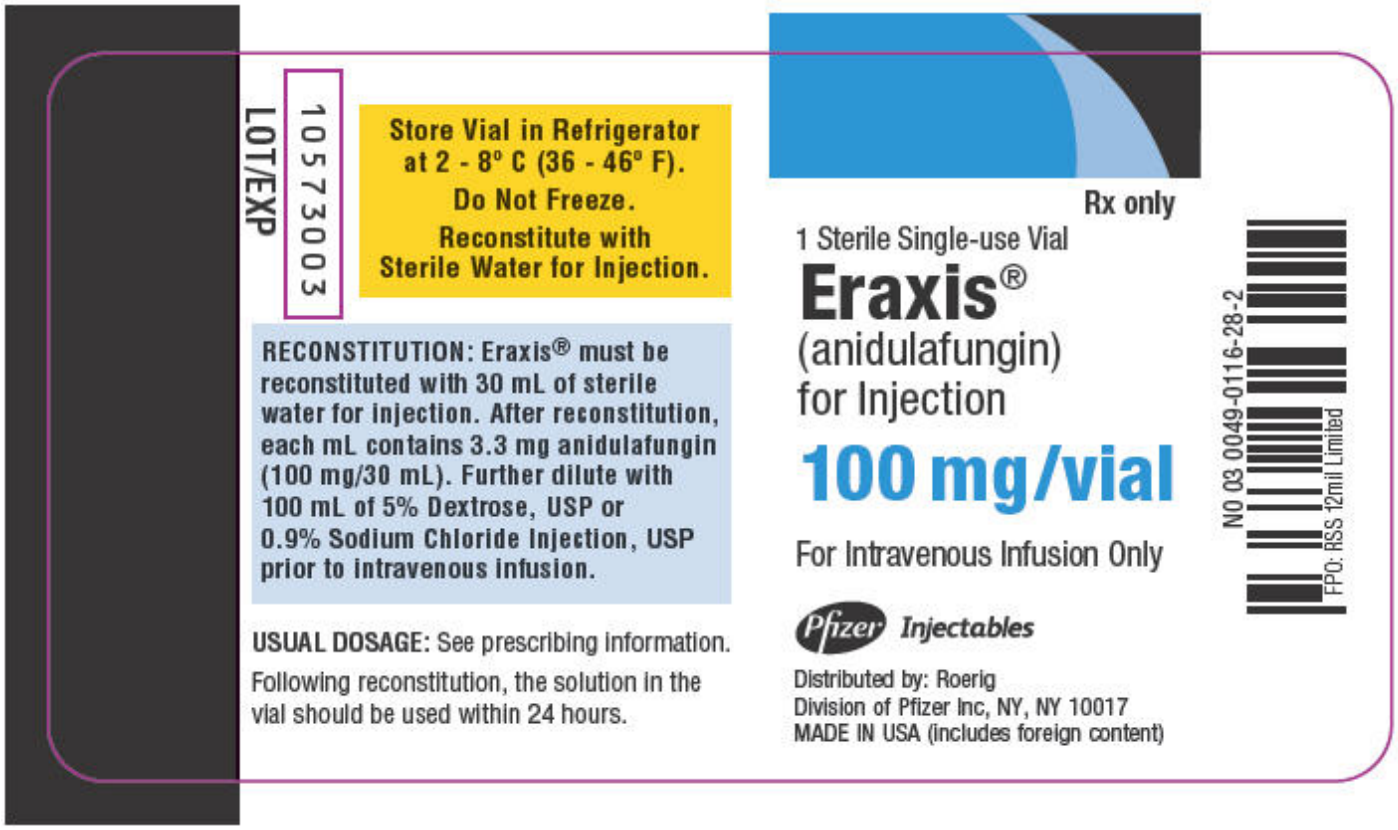
Eraxis®
(anidulafungin)
for Injection

100 mg/vial

For Intravenous Infusion Only

Pfizer Injectables

Distributed by: Roerig
Division of Pfizer Inc, NY, NY 10017
MADE IN USA (includes foreign content)



PRINCIPAL DISPLAY PANEL - 100 mg Vial Carton

NDC 0049-0116-28
Rx only

Unit Pack Contains:
1 Sterile Single-use Vial
Eraxis® 100 mg

Eraxis®
(anidulafungin)
for Injection

100 mg/vial

For Intravenous Infusion Only

Store Vial in Refrigerator
at 2 - 8° C (36 - 46° F).
Do Not Freeze.
Reconstitute with Sterile Water
for Injection.

Pfizer Injectables

Distributed by: Roerig
Division of Pfizer Inc, NY, NY 10017
MADE IN USA (includes foreign content)

ERAXIS

anidulafungin injection, powder, lyophilized, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:0049-0114
Route of Administration	INTRAVENOUS	**DEA Schedule**	

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ANIDULAFUNGIN (ANIDULAFUNGIN)	ANIDULAFUNGIN	50 mg in 15 mL

Inactive Ingredients	
Ingredient Name	**Strength**
FRUCTOSE	50 mg in 15 mL
MANNITOL	250 mg in 15 mL
POLYSORBATE 80	125 mg in 15 mL
TARTARIC ACID	5.6 mg in 15 mL
SODIUM HYDROXIDE	
HYDROCHLORIC ACID	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0049-0114-28	15 mL in 1 VIAL, SINGLE-USE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021632	02/17/2006	

ERAXIS

anidulafungin injection, powder, lyophilized, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:0049-0116
Route of Administration	INTRAVENOUS	**DEA Schedule**	

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ANIDULAFUNGIN (ANIDULAFUNGIN)	ANIDULAFUNGIN	100 mg in 30 mL

Inactive Ingredients

Ingredient Name	Strength
FRUCTOSE	100 mg in 30 mL
MANNITOL	500 mg in 30 mL
POLYSORBATE 80	250 mg in 30 mL
TARTARIC ACID	11.2 mg in 30 mL
SODIUM HYDROXIDE	
HYDROCHLORIC ACID	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0049-0116-28	30 mL in 1 VIAL, SINGLE-USE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA021632	02/17/2006	

Labeler - Roerig (829076996)

Registrant - Pfizer Inc (113480771)

Establishment

Name	Address	ID/FEI	Business Operations
Pharmacia and Upjohn Company LLC		829076566	API MANUFACTURE(0049-0116, 0049-0114), MANUFACTURE(0049-0116, 0049-0114), PACK(0049-0116, 0049-0114)

Revised: 2/2013 Roerig