**TABLE 3**

<table>
<thead>
<tr>
<th>Dose</th>
<th>AUC 1/2 (hr)</th>
<th>Bioavailability of Posaconazole</th>
<th>CV (%)</th>
<th>Recalculation Required</th>
<th>Readministration Necessary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200 mg TID</td>
<td>2.7 (2.3-3.1)</td>
<td>95%</td>
<td>14.6%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>400 mg</td>
<td>5.4 (4.2-6.5)</td>
<td>97%</td>
<td>11.4%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Intranasal</td>
<td>3.5 (3.0-4.1)</td>
<td>94%</td>
<td>15.5%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Intravenous</td>
<td>3.0 (2.6-3.6)</td>
<td>98%</td>
<td>11.2%</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

**TABLE 4**

<table>
<thead>
<tr>
<th>Dose</th>
<th>AUC 1/2 (hr)</th>
<th>Bioavailability of Posaconazole</th>
<th>CV (%)</th>
<th>Recalculation Required</th>
<th>Readministration Necessary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200 mg TID</td>
<td>2.7 (2.3-3.1)</td>
<td>95%</td>
<td>14.6%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>400 mg</td>
<td>5.4 (4.2-6.5)</td>
<td>97%</td>
<td>11.4%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Intranasal</td>
<td>3.5 (3.0-4.1)</td>
<td>94%</td>
<td>15.5%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Intravenous</td>
<td>3.0 (2.6-3.6)</td>
<td>98%</td>
<td>11.2%</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

**TABLE 1**

<table>
<thead>
<tr>
<th>Dose</th>
<th>AUC 1/2 (hr)</th>
<th>Bioavailability of Posaconazole</th>
<th>CV (%)</th>
<th>Recalculation Required</th>
<th>Readministration Necessary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200 mg TID</td>
<td>2.7 (2.3-3.1)</td>
<td>95%</td>
<td>14.6%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>400 mg</td>
<td>5.4 (4.2-6.5)</td>
<td>97%</td>
<td>11.4%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Intranasal</td>
<td>3.5 (3.0-4.1)</td>
<td>94%</td>
<td>15.5%</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Intravenous</td>
<td>3.0 (2.6-3.6)</td>
<td>98%</td>
<td>11.2%</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
There is no information regarding cross-sensitivity between NOXAFIL® and other azole antifungal agents.

Liver function tests should be evaluated at the start of and during the course of posaconazole administration with glipizide does not require a dose adjustment in either drug; however, glucose concentrations should be monitored in accordance with the current standard of care for patients with diabetes when posaconazole is co-administered with glipizide.

As a triazole antifungal agent, posaconazole blocks the synthesis of ergostear, a key component of the fungal cell membrane, by inhibiting the synthesis of the enzyme lanosterol 14-demethylase and accumulation of methylated sterol precursors.

In summary, two clinical studies of prophylaxis were conducted. As seen in the accompanying tables (TABLES 5 and 8), clinical failure represented a composite endpoint of breakthrough IFI, mortality and use of systemic antifungal therapy. In Study 1 (TABLE 5), the clinical failure rate of posaconazole (33%) was similar to fluconazole (37%) (95% CI for the difference posaconazole-comparator -10.3% to 7.9%). In Study 2 (TABLE 8), clinical failure was lower for patients treated with posaconazole (21%) compared to patients treated with fluconazole (42%). (99% CI for the difference posaconazole-comparator -22.9% to -7.8%). All cause mortality was lower at 100 days for posaconazole-treated patients in Study 2 (70-day PFS 50/151 (19%)) vs. fluconazole 62/298 (21%). Both studies demonstrated substantial improvement in Aspergillus species in patients receiving posaconazole prophylaxis when compared to patients receiving fluconazole or itraconazole.

Myelocytic response rates were assessed after 14 days of treatment and 4 weeks after the end of treatment. In Study 2, the myelocytic response rates did not differ significantly between the treatment arms (Table 7). The myelocytic response rates were also similar in the two treatment groups at day 28, week 4, and week 12.

CLINICAL STUDIES

Treatment of Oropharyngeal Candidiasis (OPC)

Patients were treated with posaconazole or fluconazole oral suspension (both posaconazole and fluconazole were given as 300 mg every 12 hours during the first 100 mg every 24 hours) for 30 days as mycologic relapse rates (4 weeks after the end of therapy) were similar between the two treatment arms (Table 7). Cumulative incidence of relapse (4 weeks after the end of treatment) was also similar in the two treatment arms (Table 7).

Myelocytic response rates, using a criterion for success as a post-treatment quantitative culture with ≤20 colony-forming units (CFU)/mL were similar between the two groups (posaconazole 51.3%, fluconazole 68.1%). The clinical significance of this finding is unknown.

On therapy plus 7 days

**Failure due to:**

- Proven/probable IFI (posaconazole-comparator)
- Candida
- Other
- All
- Proven/probable fungal infection prior to death
- SAF* (posaconazole-comparator)

- Proven/probable IFI (posaconazole)
- Candida
- Other
- All
- Proven/probable fungal infection prior to death
- SAF* (posaconazole)

**Proven/probable IFI**

- Proven/probable IFI (posaconazole-comparator)
- Proven/probable IFI (posaconazole)

**Candida**

- Candida (posaconazole-comparator)
- Candida (posaconazole)

**Other**

- Other (posaconazole-comparator)
- Other (posaconazole)

**All**

- All (posaconazole-comparator)
- All (posaconazole)

**Proven/probable fungal infection**

- Proven/probable fungal infection prior to death (posaconazole-comparator)
- Proven/probable fungal infection prior to death (posaconazole)

**SAF**

- SAF* (posaconazole-comparator)
- SAF* (posaconazole)

**Clinical Failure**

- Clinical Failure (posaconazole-comparator)
- Clinical Failure (posaconazole)

**Patients who are lost to follow-up**

- Patients who are lost to follow-up (posaconazole-comparator)
- Patients who are lost to follow-up (posaconazole)

**Patients who are lost to follow-up (not observed for 112 days)**

- Patients who are lost to follow-up (not observed for 112 days) (posaconazole-comparator)
- Patients who are lost to follow-up (not observed for 112 days) (posaconazole)

**Patients who are lost to follow-up (not observed for 100 days)**

- Patients who are lost to follow-up (not observed for 100 days) (posaconazole-comparator)
- Patients who are lost to follow-up (not observed for 100 days) (posaconazole)

**Patients who are lost to follow-up (not observed for 75 days)**

- Patients who are lost to follow-up (not observed for 75 days) (posaconazole-comparator)
- Patients who are lost to follow-up (not observed for 75 days) (posaconazole)

**Patients who are lost to follow-up (not observed for 14 days)**

- Patients who are lost to follow-up (not observed for 14 days) (posaconazole-comparator)
- Patients who are lost to follow-up (not observed for 14 days) (posaconazole)

**Patients who are lost to follow-up (not observed for 7 days)**

- Patients who are lost to follow-up (not observed for 7 days) (posaconazole-comparator)
- Patients who are lost to follow-up (not observed for 7 days) (posaconazole)

**Clinical Success**

- Clinical Success (posaconazole-comparator)
- Clinical Success (posaconazole)

**Myelocytic response rates**

- Myelocytic response rates (posaconazole-comparator)
- Myelocytic response rates (posaconazole)

**Relapse rates**

- Relapse rates (posaconazole-comparator)
- Relapse rates (posaconazole)

**Contraindications**

- Contraindications (posaconazole)
- Contraindications (fluconazole)

**Drug Interactions**

- Drug Interactions (posaconazole)
- Drug Interactions (fluconazole)

**Cyclosporine drug interaction**

- Cyclosporine drug interaction (posaconazole)
- Cyclosporine drug interaction (fluconazole)

Hypersensitivity

There is no information regarding cross-sensitivity between NOXAFIL® and other azole antifungal agents.

Heaptic Toxicity

In clinical trials, there were infrequent cases of hepatic reactions (mg, mild to moderate elevations in ALT, AST, alkaline phosphatase, total bilirubin or total bilirubin and AST, alkaline phosphatase, total bilirubin in the presence of systemic antifungal therapy. The effects of posaconazole on hepatic enzymes are reversible on dose discontinuation of therapy, and in some instances these tests normalized without drug interruption and rarely required drug discontinuation. Rarely, more severe hepatic reactions including cholestasis or hepatic failure including fatalities were reported in patients with underlying moderate or severe hepatic impairment (Child-Pugh score 9-15) during treatment with posaconazole. These severe hepatic events were seen primarily in subjects receiving the 500 mg daily (400 mg BID or 200 mg OD) in another indication. The patient had a history of fulminant hepatic failure due to sepsis that resulted in the death of the patient. In the post-marketing experience, 2/150 patients developed transaminase elevations greater than 5 times the upper limit of normal, and 3/150 patients developed bilirubin elevations greater than 3 times the upper limit of normal.

Cyclosporine drug interaction

Cases of elevated cyclosporine levels resulting in rare serious adverse events, including nephrotoxicity and leukoencephalopathy, and death were reported in clinical efficacy studies. Dose reduction and more frequent clinical monitoring of cyclosporine, tacrolimus, and sirolimus should be performed when posaconazole therapy is initiated.

**Precautions**

- Precautions (POSANIZOLE)
- Precautions (fluconazole)

**Drug Interactions**

- Drug Interactions (POSANIZOLE)
- Drug Interactions (fluconazole)

Hypersensitivity

There is no information regarding cross-sensitivity between NOXAFIL® and other azole antifungal agents.

Hepatic Toxicity

In clinical trials, there were infrequent cases of hepatic reactions (mg, mild to moderate elevations in ALT, AST, alkaline phosphatase, total bilirubin or total bilirubin and AST, alkaline phosphatase, total bilirubin in the presence of systemic antifungal therapy. The effects of posaconazole on hepatic enzymes are reversible on dose discontinuation of therapy, and in some instances these tests normalized without drug interruption and rarely required drug discontinuation. Rarely, more severe hepatic reactions including cholestasis or hepatic failure including fatalities were reported in patients with underlying moderate or severe hepatic impairment (Child-Pugh score 9-15) during treatment with posaconazole. These severe hepatic events were seen primarily in subjects receiving the 500 mg daily (400 mg BID or 200 mg OD) in another indication. The patient had a history of fulminant hepatic failure due to sepsis that resulted in the death of the patient. In the post-marketing experience, 2/150 patients developed transaminase elevations greater than 5 times the upper limit of normal, and 3/150 patients developed bilirubin elevations greater than 3 times the upper limit of normal.

Cyclosporine drug interaction

Cases of elevated cyclosporine levels resulting in rare serious adverse events, including nephrotoxicity and leukoencephalopathy, and death were reported in clinical efficacy studies. Dose reduction and more frequent clinical monitoring of cyclosporine, tacrolimus, and sirolimus should be performed when posaconazole therapy is initiated.

**Precautions**

- Precautions (POSANIZOLE)
- Precautions (fluconazole)

**Drug Interactions**

- Drug Interactions (POSANIZOLE)
- Drug Interactions (fluconazole)

Hypersensitivity

There is no information regarding cross-sensitivity between NOXAFIL® and other azole antifungal agents.
Pregnancy

Pregnancy Category C. Posaconazole has been shown to cause skeletal malformations (cranial malformations and missing ribs) in rats when given in doses ≥72 mg/kg (≤ 14 times the 400 mg BID regimen based on steady-state plasma concentrations of drug in healthy volunteers). Co-administration with posaconazole and ergot alkaloids is contraindicated. (See CONTRAINDICATIONS.)

Breastfeeding

Lactation studies in rats and a dog have shown that posaconazole and its metabolites are excreted in milk. Because many drugs are excreted in human milk, caution should be exercised when posaconazole is administered to a nursing mother, especially during the first 24 hours following delivery. (See CLINICAL PHARMACOLOGY, Drug Interactions, and WARNINGS.)

ADVERSE REACTIONS

The safety of posaconazole therapy has been assessed in 1,844 patients. This includes 605 patients in the prophylaxis studies, 796 in OPCOPC studies, and over 400 patients treated for other indications.

The most common adverse events associated with posaconazole therapy were gastrointestinal disorders, allergic reactions, and hematological disorders. The most common laboratory abnormalities were elevation of hepatic enzymes (SGOT, SGPT), elevated gamma-glutamyl transpeptidase (GGT), elevated bilirubin, and hypokalemia.

Although not specifically studied, adverse events observed in mice were similar to those observed in clinical trials. The incidence of adverse events was generally lower in the mouse studies than in the clinical trials. In general, the toxicities observed in mice were not associated with clinical adverse events in humans.

The incidence of adverse events was similar between posaconazole and placebo in the prophylaxis studies. However, the incidence of allergic reactions was higher in the posaconazole group than in the placebo group. The incidence of laboratory abnormalities was also higher in the posaconazole group than in the placebo group.

The incidence of adverse events was similar between posaconazole and fluconazole in the prophylaxis studies. However, the incidence of allergic reactions was higher in the posaconazole group than in the fluconazole group. The incidence of laboratory abnormalities was also higher in the posaconazole group than in the fluconazole group.

The safety of posaconazole therapy has been assessed in 1,844 patients. This includes 605 patients in the prophylaxis studies, 796 in OPCOPC studies, and over 400 patients treated for other indications.

The most common adverse events associated with posaconazole therapy were gastrointestinal disorders, allergic reactions, and hematological disorders. The most common laboratory abnormalities were elevation of hepatic enzymes (SGOT, SGPT), elevated gamma-glutamyl transpeptidase (GGT), elevated bilirubin, and hypokalemia.

Although not specifically studied, adverse events observed in mice were similar to those observed in clinical trials. The incidence of adverse events was generally lower in the mouse studies than in the clinical trials. In general, the toxicities observed in mice were not associated with clinical adverse events in humans.

The incidence of adverse events was similar between posaconazole and placebo in the prophylaxis studies. However, the incidence of allergic reactions was higher in the posaconazole group than in the placebo group. The incidence of laboratory abnormalities was also higher in the posaconazole group than in the placebo group.

The incidence of adverse events was similar between posaconazole and fluconazole in the prophylaxis studies. However, the incidence of allergic reactions was higher in the posaconazole group than in the fluconazole group. The incidence of laboratory abnormalities was also higher in the posaconazole group than in the fluconazole group.

The safety of posaconazole therapy has been assessed in 1,844 patients. This includes 605 patients in the prophylaxis studies, 796 in OPCOPC studies, and over 400 patients treated for other indications.

The most common adverse events associated with posaconazole therapy were gastrointestinal disorders, allergic reactions, and hematological disorders. The most common laboratory abnormalities were elevation of hepatic enzymes (SGOT, SGPT), elevated gamma-glutamyl transpeptidase (GGT), elevated bilirubin, and hypokalemia.

Although not specifically studied, adverse events observed in mice were similar to those observed in clinical trials. The incidence of adverse events was generally lower in the mouse studies than in the clinical trials. In general, the toxicities observed in mice were not associated with clinical adverse events in humans.

The incidence of adverse events was similar between posaconazole and placebo in the prophylaxis studies. However, the incidence of allergic reactions was higher in the posaconazole group than in the placebo group. The incidence of laboratory abnormalities was also higher in the posaconazole group than in the placebo group.

The incidence of adverse events was similar between posaconazole and fluconazole in the prophylaxis studies. However, the incidence of allergic reactions was higher in the posaconazole group than in the fluconazole group. The incidence of laboratory abnormalities was also higher in the posaconazole group than in the fluconazole group.
Loading dose of 100 mg (2.5 mL) twice a day on the first day, then 100 mg (2.5 mL) once a day. LFT abnormalities were present in some of these patients prior to initiation of the study drug.

The most common treatment-related serious adverse events (1% each) in the combined prophylaxis studies were bilirubinemia, proteinuria, drug-induced liver injury, and vomiting. In the controlled OPC studies, the numbers of patients who reported SAEs were fever (13%) and neutropenia (10%). Treatment-related SAEs were reported for 14% (34/239) of these patients and included neutropenia (5%) and abdominal pain (2%). Posaconazole was discontinued in two patients who developed neutropenia that was considered serious and treatment-related. All other reported treatment-related SAEs occurred in ≤5% of subjects on posaconazole.

In non-OPC/OPC patients, serious adverse events occurred in ≤5% of subjects on posaconazole. These included local superinfections, angioedema, and hypokalemia that were considered to be unrelated to the study drug. Additionally, in another indication, 42% patients were treated with ≥800 mg/day with a similar AE profile.

Clinical Laboratory Values

In healthy volunteers and patients, elevation of liver function test values did not appear to be associated with higher plasma concentrations of posaconazole. The majority of abnormal liver function tests were minor, transient, and did not lead to discontinuation of therapy. For the prophylaxis studies, the number of patients with changes in liver function tests from Common Toxicity Criteria (CTC) Grade 0, 1 or 2, at baseline observation and at least one post-baseline observation.

Posaconazole is not removed by hemodialysis.

OVERDOSAGE

During the clinical trials, some patients received posaconazole up to 1600 mg/day with no adverse events noted that were different from the lower doses. In addition, accidental overdose was noted in one patient who took 1200 mg BID for 3 days. No adverse events were noted by the investigator.

Indication

Dose and Duration of Therapy

Phosphatase of invasive fungal infections

200 mg (5 mL) three times a day. The duration of therapy depends on healing response and clinical improvement.

Prophylaxis of invasive fungal infections

400 mg (10 mL) once a day. Duration of therapy should depend on the patient's underlying disease and clinical response.

Each dose of NOXARIL should be administered with a full meal or with a liquid nutritional supplement in patients who cannot eat a full meal. (See CLINICAL PHARMACOLOGY). To enhance the oral absorption of posaconazole and optimize plasma concentrations:

- Each dose of NOXARIL Oral Suspension should be administered with a full meal or liquid nutritional supplement. For patients who cannot eat a full meal or tolerate an oral nutritional supplement, alternative antifungal therapy should be considered or patients should be monitored closely for breakthrough fungal infections.
- Patients who have severe diarrhea or vomiting should be monitored closely for breakthrough fungal infections.
- Co-administration of drugs that can decrease the plasma concentrations of posaconazole should generally be avoided unless the benefit outweighs the risk. If such drugs are necessary, patients should be monitored closely for breakthrough fungal infections. (See CLINICAL PHARMACOLOGY, Drug Interactions.)

TABLE 14. Treatment-Emergent Adverse Events of Clinical Significance in OPC studies

<table>
<thead>
<tr>
<th>Body System/Preferred Term</th>
<th>Controlled OPC Pool</th>
<th>Fluconazole (n=262)</th>
<th>Fluconazole Itraconazole (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Event</td>
<td>Number (%) of Patients</td>
<td>Number (%) of Patients</td>
<td>Number (%) of Patients</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Body as a Whole - General Disorders</td>
<td>Headache</td>
<td>15 (3)</td>
<td>10 (4)</td>
</tr>
<tr>
<td></td>
<td>Abdominal Pain</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Dyspnea</td>
<td>4 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
<td>4 (1)</td>
<td>3 (1)</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>2 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Musculoskeletal NOS</td>
<td>7 (2)</td>
<td>5 (2)</td>
</tr>
<tr>
<td></td>
<td>Myalgia</td>
<td>1 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>22 (7)</td>
<td>15 (6)</td>
</tr>
<tr>
<td></td>
<td>Neutropenia</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Rash</td>
<td>2 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Respiratory System Disorders</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Somnolence</td>
<td>2 (&lt;1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td></td>
<td>Swelling Increased</td>
<td>13 (2)</td>
<td>5 (2)</td>
</tr>
<tr>
<td></td>
<td>Thrombocytopenia</td>
<td>3 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>15 (5)</td>
<td>12 (5)</td>
</tr>
<tr>
<td></td>
<td>WBC Decrease</td>
<td>3 (1)</td>
<td>1 (1)</td>
</tr>
</tbody>
</table>

POC-By-pass prophylaxis candidates: SGPT=serum glutamic pyruvic transaminase; SGOT=serum glutamic oxaloacetic transaminase; SGPT=serum glutamic pyruvic transaminase.

The most common treatment-related serious adverse events (1% each) in the combined prophylaxis studies were bilirubinemia, increased hepatic enzymes, hypokalemia, liver dysfunction, nausea, and vomiting.

TABLE 15. Treatment-Related Adverse Events (Any Grade) ≥2% in

<table>
<thead>
<tr>
<th>Indication</th>
<th>Controlled OPC Pool</th>
<th>Fluconazole (n=262)</th>
<th>Fluconazole Itraconazole (n=58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication</td>
<td>Number (%) of Patients</td>
<td>Number (%) of Patients</td>
<td>Number (%) of Patients</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>Body as a Whole - General Disorders</td>
<td>Headache</td>
<td>16 (3)</td>
<td>10 (4)</td>
</tr>
<tr>
<td></td>
<td>Anorexia</td>
<td>6 (1)</td>
<td>4 (2)</td>
</tr>
<tr>
<td></td>
<td>Asthenia</td>
<td>4 (1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>9 (2)</td>
<td>3 (1)</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
<td>6 (1)</td>
<td>3 (1)</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>10 (2)</td>
<td>1 (&lt;1)</td>
</tr>
</tbody>
</table>
It is recommended that the spoon is rinsed with water after each administration and before storage.

Renal Insufficiency
No dose adjustment is recommended for patients with renal dysfunction. However, the range of the posaconazole AUC estimates was highly variable (CV=96%) in subjects with severe renal insufficiency as compared to that in the other renal impairment groups (CV<40%). Due to the variability in exposure, patients with severe renal impairment should be monitored closely for breakthrough IFIs. (See CLINICAL PHARMACOLOGY.)

Hepatic Insufficiency
The pharmacokinetic data in subjects with hepatic impairment was not sufficient to determine if dose adjustment is necessary in patients with hepatic dysfunction. It is recommended that posaconazole be used with caution in patients with hepatic impairment. (See CLINICAL PHARMACOLOGY and WARNINGS.)