8.6 Use in Patients with Low CD4 Counts and High Viral Loads

Clinical trials with MYTESI did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

8.7 Use in Pediatric Patients

Studies with MYTESI did not include sufficient numbers of pediatric patients treated with MYTESI (n=22) relative to placebo (n=19).

8.8 Use in Patients with Renal Impairment

Increased bilirubin 7 (3) 3 (1)

8.9 Use in Patients with Liver Impairment

Increased alanine aminotransferase 5 (2) 3 (1)

8.10 Use in Patients with Prolonged QT Interval

Increased aspartate aminotransferase 5 (2) 3 (1)

8.11 Use in Patients with Hepatic Impairment

3.2 Gastrointestinal Effects

3.3 Contraception

3.4 Long-term Use

3.5 Renal and Electrolyte Effects

3.6 Use in the Elderly

3.7 Pediatric Use

3.8 Pregnancy

3.9 Lactation

3.10 Use in Children

3.11 Other Contraindications

3.12 Using Other Medications

3.13 Anticoagulants

3.14 Nelfinavir, Zidovudine, and Lamivudine

3.15 Drugs and Alcohol

3.16 Clinical Pharmacology

3.17 Stability

3.18 Manufacturer

3.19 Package and Store

3.20 How Supplied

3.21 Patient Counseling

3.22 Risks of Treatment in Patients with Inflammatory Bowel Disease

4.1 Indications and Usage

4.2 Dosage and Administration

4.3 Contraindications

4.4 Warnings and Precautions

4.5 Adverse Reactions

4.6 Adverse Reactions

4.7 Adverse Reactions

4.8 Use in Specific Populations

4.9 Pregnancy

4.10 Nursing Mothers

4.11 Lactation

4.12 Children

4.13 Other Contraindications

4.14 Using Other Medications

4.15 Anticoagulants

4.16 Nelfinavir, Zidovudine, and Lamivudine

4.17 Drugs and Alcohol

4.18 Clinical Pharmacology

4.19 Stability

4.20 Manufacturer

4.21 Package and Store

4.22 How Supplied

4.23 Patient Counseling

4.24 Risks of Treatment in Patients with Inflammatory Bowel Disease

5.1 Risks of Treatment in Patients with Infectious Diarrhea

5.2 Warnings and Precautions

5.3 Adverse Reactions

5.4 Clinical Trials Experience

5.5 Use in Specific Populations

5.6 Pediatric Use

5.7 Pregnancy

5.8 Nursing Mothers

5.9 Lactation

5.10 Children

5.11 Other Contraindications

5.12 Using Other Medications

5.13 Anticoagulants

5.14 Nelfinavir, Zidovudine, and Lamivudine

5.15 Drugs and Alcohol

5.16 Clinical Pharmacology

5.17 Stability

5.18 Manufacturer

5.19 Package and Store

5.20 How Supplied

5.21 Patient Counseling

5.22 Risks of Treatment in Patients with Inflammatory Bowel Disease

6.1 Clinical Trials Experience

6.2 Dosage and Administration

6.3 Contraindications

6.4 Warnings and Precautions

6.5 Adverse Reactions

6.6 Use in Specific Populations

6.7 Pediatric Use

6.8 Pregnancy

6.9 Nursing Mothers

6.10 Lactation

6.11 Children

6.12 Other Contraindications

6.13 Using Other Medications

6.14 Anticoagulants

6.15 Nelfinavir, Zidovudine, and Lamivudine

6.16 Drugs and Alcohol

6.17 Clinical Pharmacology

6.18 Stability

6.19 Manufacturer

6.20 Package and Store

6.21 How Supplied

6.22 Patient Counseling

6.23 Risks of Treatment in Patients with Inflammatory Bowel Disease

7.1 Nelfinavir, Zidovudine, and Lamivudine

7.2 Drug/Drug Interactions

7.3 Other Contraindications

7.4 Using Other Medications

7.5 Anticoagulants

7.6 Nelfinavir, Zidovudine, and Lamivudine

7.7 Drugs and Alcohol

7.8 Clinical Pharmacology

7.9 Stability

7.10 Manufacturer

7.11 Package and Store

7.12 How Supplied

7.13 Patient Counseling

7.14 Risks of Treatment in Patients with Inflammatory Bowel Disease

8.1 Pregnancy

8.2 Use in Patients with Low CD4 Counts and High Viral Loads

8.3 Use in Pediatric Patients

8.4 Use in Patients with Renal Impairment

8.5 Use in Patients with Liver Impairment

8.6 Use in Patients with Hepatic Impairment

8.7 Use in Patients with Prolonged QT Interval

8.8 Use in Patients with Liver Impairment

8.9 Use in Patients with Renal Impairment

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8.63 Use in Patients with Renal Impairment

8.64 Use in Patients with Liver Impairment
The primary efficacy endpoint was the proportion of patients with a clinical response, defined as less than or equal to 2 watery bowel movements per week during at least 2 of the 4 weeks of the placebo-controlled period. Patients who received concomitant anti-diarrheal medications or opiates were counted as clinical non-responders.

A significantly larger proportion of patients in the MYTESI 125 mg twice daily group experienced clinical response compared with patients in the placebo group (18% vs. 6%, 1-sided p < 0.01). In the randomized clinical study, examination of duration of diarrhea, baseline number of daily watery bowel movements, use of prostanol inhibitors, CD4 count and age subgroups did not identify differences in the consistency of the crofelemer treatment effect among these subgroups. There were too few female patients and patients with an HIV viral load > 400 copies/mL to adequately assess differences in effects in these populations. Among race subgroups, there were no differences in the consistency of the crofelemer treatment effect except for the subgroup of African-Americans; crofelemer was less effective in African-Americans than non-African-Americans.

Although the CD4 count and HIV viral load did not appear to change over the one month placebo-controlled period, the clinical significance of this finding is unknown because of the short duration of the placebo-controlled period.

Of the 24 clinical responders to MYTESI 125 mg twice daily, 12 entered the placebo-free period; 16 were responding at the end of month 3, and 14 were responding at the end of month 5.

16 HOW SUPPLIED/STORAGE AND HANDLING

MYTESI (crofelemer) 125 mg delayed-release tablets are white, oval tablets printed on one side with 125SLXP. They are available in the following package size:

- Bottles of 60: NDC 70564-802-60
- Store at 20°C-25°C (68°F-77°F); excursions permitted between 15°C-30°C (59°F-86°F). See USP Controlled Room Temperature.

17 PATIENT COUNSELING INFORMATION

- Instruct patients that MYTESI tablets may be taken with or without food.
- Instruct patients to swallow MYTESI tablets whole and not to crush or chew the tablets.

Manufactured by Patheon, Inc.

Napo Pharmaceuticals, Inc., San Francisco, CA 94105

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The botanical drug substance of MYTESI is extracted from Croton lechleri (the botanical raw material) that is harvested from the wild in South America.