HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LIKMEZ safely and effectively. See full prescribing information for LIKMEZ.

LIKMEZ™ (metronidazole) oral suspension

Initial U.S. Approval: 1963

WARNING: POTENTIAL FOR CARCINOGENICITY

See full prescribing information for complete boxed warning.

Metronidazole has been shown to be carcinogenic in mice and rats (5.1). Avoid unnecessary use of LIKMEZ. Reserve LIKMEZ for use in the following indications: trichomoniasis (1.1), amebiasis (1.2) and anaerobic bacterial infections (1.3).

----------RECENT MAJOR CHANGES----------

Severe Cutaneous Adverse Reactions (5.2) 7/2024

----------INDICATIONS AND USAGE----------

LIKMEZ is a nitroimidazole antimicrobial indicated for

- Trichomoniasis in adults (1.1)
- Amebiasis in adults and pediatric patients (1.2)
- Anaerobic Bacterial Infections in adults (1.3)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of LIKMEZ and other antibacterial drugs, LIKMEZ should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria (1.4).

----------DOSAGE AND ADMINISTRATION----------

Trichomoniasis:

Adult Female and Male Patients:

- One-day treatment: 2 g (20 mL) of LIKMEZ, given either as a single oral dose or in 2 divided oral doses of 1 g (10 mL) each, given on the same day. (2.1)
- Seven-day course of treatment: 250 mg (2.5 mL) of LIKMEZ given three times daily for 7 consecutive days. (2.1)
- Individualize the dosing regimen. (2.1)

Amebiasis:

Adult Patients:

- *For acute intestinal amebiasis (acute amebic dysentery):* 750 mg (7.5 mL) orally three times daily for 5 days to 10 days. (2.2)
- *For amebic liver abscess:* 500 mg (5 mL) or 750 mg (7.5 mL) orally three times daily for 5 days to 10 days. (2.2)

Pediatric Patients: 35 mg/kg/24 hours to 50 mg/kg/24 hours, divided into three doses, to a maximum dose of 2,250 mg/24 hours (maximum dose 750 mg/dose or 7.5 mL/dose),orally for 10 days. (2.2)

Anaerobic Bacterial Infections:

- In the treatment of most serious anaerobic infections, intravenous metronidazole is usually administered initially. (2.3)
- *Adult Patients:* 7.5 mg/kg every six hours (approx. 500 mg (5 mL) for a 70-kg adult) to a maximum dose of 4 g (40 mL) during a 24-hour period, orally for 7 to 10 days. (2.3)
- Infections of the bone and joint, lower respiratory tract, and endocardium may require longer treatment. (2.3)

Patients with Severe Hepatic Impairment (Child-Pugh C)

- Reduce the dose of LIKMEZ by 50%. (2.4)

Patients Undergoing Hemodialysis:

- Consider a supplemental dose of LIKMEZ following the hemodialysis session, depending on the patient's clinical situation. (2.5)

----------DOSAGE FORMS AND STRENGTHS----------

Oral Suspension: 500 mg/5 mL (3)

----------CONTRAINDICATIONS----------

- Prior history of hypersensitivity to metronidazole or other nitroimidazole derivatives (4.1)
- Patients who have used disulfiram within the last two weeks. (4.2, 7.1)
- Patients who consume alcohol or products containing propylene glycol during and for at least three days after LIKMEZ therapy. (4.3, 7.2)
- Patients with Cockayne syndrome (4.4, 6.2)

----------WARNINGS AND PRECAUTIONS----------

- Severe Cutaneous Adverse Reactions: Severe cutaneous adverse reactions (SCARs) including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported with metronidazole. If symptoms or signs of SCARs develop, discontinue LIKMEZ immediately and institute appropriate therapy. (5.2)
- Central and Peripheral Nervous System Effects: Encephalopathy, convulsive seizures, aseptic meningitis and peripheral neuropathy have been reported with metronidazole. Promptly evaluate the benefit/risk of continuation of LIKMEZ if abnormal neurological signs develop. (5.3)
- Blood Dyscrasias: Use LIKMEZ with care in patients with a history of blood dyscrasias. LIKMEZ may cause mild transient leukopenia. (5.5)

----------ADVERSE REACTIONS----------

Common adverse reactions include nausea, headache, anorexia, vomiting, diarrhea, abdominal cramping, epigastric distress, and constipation. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Saptalis Pharmaceuticals, LLC at 1-833-727-8254 or FDA at 1-800-FDA-1088 or http://www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Disulfiram: Psychotic reactions can occur in patients who are using LIKMEZ and disulfiram concurrently. (4.2, 7.1)
- Alcohol or Other Products Containing Propylene Glycol: Abdominal cramps, nausea, vomiting, headaches, and flushing can occur in patients who are using LIKMEZ and alcohol or other products containing propylene glycol concurrently. (4.3, 7.2)
- Warfarin and Other Oral Anticoagulants: LIKMEZ can potentiate the anticoagulant effect. Carefully monitor prothrombin time and International Normalized Ratio (INR). (7.3)
- Lithium: Increased lithium serum concentrations; measure serum lithium and serum creatinine concentrations during therapy. (7.4)
- Busulfan: Increased busulfan serum concentrations; avoid concomitant use, monitor for plasma concentrations and adjust the busulfan dose accordingly. (7.5)
- CYP Inducers and CYP Inhibitors: Prolonged or accelerated half-life of metronidazole or concomitant medications. (7.6, 7.7)
- Drugs with the Potential for Prolonging the QT Interval: QT prolongation when used with LIKMEZ (7.8)
- Interference with Laboratory Tests: Metronidazole may interfere with certain serum chemistry laboratory values (7.9)

----------USE IN SPECIFIC POPULATIONS----------

Lactation: A lactating woman may choose to pump and discard human milk for the duration of LIKMEZ therapy and for 48 hours after the last dose and feed her infant stored human milk or formula. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 07/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: POTENTIAL FOR CARCINOGENICITY

1 INDICATIONS AND USAGE

1.1 Trichomoniasis

1.2 Amebiasis

1.3 Anaerobic Bacterial Infections

1.4 Usage

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage for Trichomoniasis

2.2 Recommended Dosage for Amebiasis

2.3 Recommended Dosage for Anaerobic Bacterial Infections

2.4 Recommended Dosage in Patients with Severe Hepatic Impairment

2.5 Recommended Dosage in Patients Undergoing Hemodialysis

2.6 Important Administration Instructions

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

Reference ID: 5407000

4.1 Hypersensitivity Reactions
4.2 Psychotic Reactions with Disulfiram
4.3 Interaction with Alcohol
4.4 Cockayne Syndrome
5 WARNINGS AND PRECAUTIONS
5.1 Potential for Carcinogenicity
5.2 Severe Cutaneous Adverse Reactions
5.3 Central and Peripheral Nervous System Effects
5.4 Fungal Superinfections
5.5 Blood Dyscrasias
5.6 Drug-Resistant Bacteria
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Postmarketing Experience
7 DRUG INTERACTIONS
7.1 Disulfiram
7.2 Alcoholic Beverages
7.3 Warfarin and other Oral Anticoagulants
7.4 Lithium
7.5 Busulfan
7.6 Inhibitors of CYP450 Liver Enzymes
7.7 Inducers of CYP450 Liver Enzymes
7.8 Drugs that Prolong the QT Interval
7.9 Drug/Laboratory Test Interactions
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Renal Impairment
8.7 Hepatic Impairment
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.3 Pharmacokinetics
12.4 Microbiology
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: POTENTIAL FOR CARCINOGENICITY

Metronidazole has been shown to be carcinogenic in mice and rats. [see *Warnings and Precautions (5.1)*]. Avoid unnecessary use of LIKMEZ. Reserve LIKMEZ for use in the following indications: trichomoniasis [see *Indications and Usage (1.1)*], amebiasis [see *Indications and Usage (1.2)*] and anaerobic bacterial infections [see *Indications and Usage (1.3)*].

1 INDICATIONS AND USAGE

1.1 Trichomoniasis

LIKMEZ is indicated for the treatment of:

- Symptomatic trichomoniasis caused by *Trichomonas vaginalis* in adult females and males when the diagnosis is confirmed by appropriate laboratory procedures.
- Asymptomatic trichomoniasis caused by *Trichomonas vaginalis* in adult females when the organism is associated with endocervicitis, cervicitis, or cervical erosion.

Because trichomoniasis is a sexually transmitted disease with potentially serious sequelae, treat sexual partners of patients simultaneously to prevent re-infection.

1.2 Amebiasis

LIKMEZ is indicated for the treatment of acute intestinal amebiasis (amoebic dysentery) and amebic liver abscess in adults and pediatric patients. In amebic liver abscess, treatment with LIKMEZ does not obviate the need for aspiration or drainage of pus.

1.3 Anaerobic Bacterial Infections

LIKMEZ is indicated in the treatment of the following serious infections caused by susceptible anaerobic bacteria in adults:

- Intra-abdominal infections, including peritonitis, intra-abdominal abscess, and liver abscess, caused by *Bacteroides* species including the *B. fragilis* group (*B. fragilis, B. ovatus, B. thetaiotaomicron, B. vulgatus*), *Parabacteroides distasonis, Clostridium* species, *Eubacterium* species, *Peptococcus species,* and *Peptostreptococcus* species.
- Skin and skin structure infections caused by *Bacteroides* species including the *B. fragilis* group, *Clostridium* species, *Peptococcus species, Peptostreptococcus* species, and *Fusobacterium* species.
- Gynecologic infections, including endometritis, endomyometritis, tubo-ovarian abscess, and postsurgical vaginal cuff infection, caused by *Bacteroides* species including the *B. fragilis* group, *Clostridium* species, *Peptococcus species, Peptostreptococcus* species, and *Fusobacterium* species.
- Bacterial septicemia caused by *Bacteroides* species including the *B. fragilis* group and *Clostridium* species.
- Bone and joint infections, (as adjunctive therapy), caused by *Bacteroides* species including the *B. fragilis* group.
- Central nervous system (CNS) infections, including meningitis and brain abscess, caused by *Bacteroides* species including the *B. fragilis* group.

Reference ID: 5407000

- Lower respiratory tract infections, including pneumonia, empyema, and lung abscess, caused by *Bacteroides* species including the *B. fragilis* group.
- Endocarditis caused by *Bacteroides* species including the *B. fragilis* group.

Indicated surgical procedures should be performed in conjunction with LIKMEZ therapy. In a mixed aerobic and anaerobic infection, antimicrobials appropriate for the treatment of aerobic infection should be used in addition to LIKMEZ.

1.4 Usage

To reduce the development of drug-resistant bacteria and maintain the effectiveness of LIKMEZ and other antibacterial drugs, LIKMEZ should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage for Trichomoniasis

Adult Female and Male Patients:

- *One-day Treatment* – Administer 2 g (20 mL) of LIKMEZ, either as a single oral dose or in 2 divided oral doses of 1 g (10 mL) each, given on the same day.
- *Seven-day Course of Treatment* – Administer 250 mg (2.5 mL) of LIKMEZ orally 3 times daily for 7 consecutive days.

The dosage regimen should be individualized. Single-dose treatment may help improve compliance, especially if administered under supervision, in those patients who cannot be relied on to continue the seven-day regimen.

A seven-day course of treatment may minimize reinfection by protecting the patient long enough for the sexual contacts to obtain appropriate treatment. There are some data from controlled comparative studies that cure rates as determined by vaginal smears and signs and symptoms, may be higher after a seven-day course of treatment than after a one-day treatment regimen. Further, some patients may tolerate one treatment regimen better than the other.

When repeat courses of LIKMEZ are required, it is recommended that an interval of four to six weeks elapse between courses and that the presence of the trichomonad be reconfirmed by appropriate laboratory measures. Total and differential leukocyte counts should be made before and after re-treatment.

2.2 Recommended Dosage for Amebiasis

Adult Patients:

- *For acute intestinal amebiasis (acute amebic dysentery):* Administer 750 mg (7.5 mL) of LIKMEZ orally three times daily for 5 days to 10 days.
- *For amebic liver abscess:* Administer 500 mg (5 mL) or 750 mg (7.5 mL) of LIKMEZ orally three times daily for 5 days to 10 days.

Pediatric Patients:

- Administer 35 mg/kg/24 hours to 50 mg/kg/24 hours of LIKMEZ, divided into three doses, to a maximum dose of 2250 mg/24 hours (maximum dose 750 mg/dose or 7.5 mL/dose),

Reference ID: 5407000

orally for 10 days.

2.3 Recommended Dosage for Anaerobic Bacterial Infections

In the treatment of most serious anaerobic infections, intravenous metronidazole is usually administered initially.

Adult Patients: Administer 7.5 mg/kg of LIKMEZ orally every six hours (approx. 500 mg (5 mL) for a 70 kg adult) for 7 days to 10 days. Infections of the bone and joint, lower respiratory tract, and endocardium may require longer treatment.

Do **not** exceed a maximum of 4 g (40 mL) during a 24-hour period.

2.4 Recommended Dosage in Patients with Severe Hepatic Impairment

For patients with severe hepatic impairment (Child-Pugh C), reduce the dose of LIKMEZ by 50% *[*see *Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)]*.

2.5 Recommended Dosage in Patients Undergoing Hemodialysis

Hemodialysis removes significant amounts of metronidazole and its metabolites from systemic circulation. The clearance of metronidazole will depend on the type of dialysis membrane used, the duration of the dialysis session, and other factors. If the administration of LIKMEZ cannot be separated from the hemodialysis session, consider a supplemental dose of LIKMEZ following the hemodialysis session, depending on the patient's clinical situation *[*see *Clinical Pharmacology (12.3)]*.

No adjustment in LIKMEZ dose is needed in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) *[*see *Clinical Pharmacology (12.3)]*.

2.6 Important Administration Instructions

Shake the bottle well before administering the recommended dosage.

Use a calibrated oral dosing device to correctly measure the prescribed dose of medication. Do not use household teaspoons or tablespoons to measure doses. Calibrated oral dosing devices may be obtained from the pharmacy.

3 DOSAGE FORMS AND STRENGTHS

Oral Suspension: 500 mg/5 mL white to slightly brown suspension with a characteristic strawberry peppermint flavor.

4 CONTRAINDICATIONS

4.1 Hypersensitivity Reactions

LIKMEZ is contraindicated in patients with known hypersensitivity to metronidazole or other nitroimidazole derivatives *[*see *Adverse Reactions (6.1)]*.

4.2 Psychotic Reactions with Disulfiram

LIKMEZ is contraindicated in patients who have used disulfiram within the last two weeks. Use of oral metronidazole is associated with psychotic reactions in alcoholic patients who were using disulfiram concurrently *[*see *Drug Interactions (7.1)]*.

4.3 Interaction with Alcohol

LIKMEZ is contraindicated in patients who consume alcohol or products containing propylene glycol during and for at least three days after LIKMEZ therapy. Use of oral metronidazole is

associated with a disulfiram-like reaction to alcohol, including abdominal cramps, nausea, vomiting, headaches, and flushing *[*see *Drug Interactions (7.2)]*.

4.4 Cockayne Syndrome

LIKMEZ is contraindicated in patients with Cockayne syndrome. Severe irreversible hepatotoxicity/acute liver failure with fatal outcomes have been reported after initiation of metronidazole in patients with Cockayne syndrome *[*see *Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Potential for Carcinogenicity

Metronidazole has been shown to be carcinogenic in mice and rats. Tumors affecting the liver, lungs, mammary, and lymphatic tissues have been detected in several studies of metronidazole in rats and mice, but not hamsters *[*see *Nonclinical Toxicology (13.1)]*. Avoid unnecessary use of LIKMEZ. Reserve LIKMEZ for use in the following indications: trichomoniasis *[*see *Indications and Usage (1.1)]*, amebiasis *[*see *Indications and Usage (1.2)]* and anaerobic bacterial infections *[*see *Indications and Usage (1.3)]*.

5.2 Severe Cutaneous Adverse Reactions

Severe cutaneous adverse reactions (SCARs) including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported with the use of metronidazole. Symptoms can be serious and potentially life threatening. If symptoms or signs of SCARs develop, discontinue LIKMEZ immediately and institute appropriate therapy.

5.3 Central and Peripheral Nervous System Effects

Encephalopathy, aseptic meningitis, peripheral neuropathy (including optic neuropathy) and convulsive seizures have been reported with metronidazole. Encephalopathy has been reported in association with cerebellar toxicity characterized by ataxia, dizziness, and dysarthria. CNS lesions seen on MRI have been described in reports of encephalopathy. CNS symptoms are generally reversible within days to weeks upon discontinuation of metronidazole. CNS lesions seen on MRI have also been described as reversible. Peripheral neuropathy, mainly of sensory type has been reported and is characterized by numbness or paresthesia of an extremity. Cases of aseptic meningitis have been reported with metronidazole *[*see *Adverse Reactions (6.1)]*. Symptoms may occur within hours of dose administration and generally resolve after metronidazole therapy is discontinued. The appearance of abnormal neurological signs and symptoms demands the prompt evaluation of the benefit/risk ratio of the continuation of therapy.

5.4 Fungal Superinfections

Known or previously unrecognized candidiasis may present more prominent symptoms during therapy with LIKMEZ and requires treatment with an antifungal agent.

5.5 Blood Dyscrasias

LIKMEZ is a nitroimidazole and should be used with care in patients with evidence of or history of blood dyscrasia. A mild leukopenia has been observed during metronidazole administration; however, no persistent hematologic abnormalities attributable to metronidazole have been observed in clinical studies. Total and differential leukocyte counts are recommended before and after therapy *[*see *Adverse Reactions (6.1)]*.

Reference ID: 5407000

5.6 Drug-Resistant Bacteria

Prescribing LIKMEZ in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Severe Cutaneous Adverse Reactions *[*see *Warnings and Precautions (5.2)]*
- Central and Peripheral Nervous System Effects *[*see *Warnings and Precautions (5.3)]*
- Blood Dyscrasias *[*see *Warnings and Precautions (5.5)]*

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 following reactions have been reported during treatment with metronidazole:

Central and Peripheral Nervous System: The most serious adverse reactions reported in patients treated with metronidazole have been convulsive seizures, encephalopathy, aseptic meningitis, optic and peripheral neuropathy, the latter characterized mainly by numbness or paresthesia of an extremity. Persistent peripheral neuropathy has been reported in some patients receiving prolonged administration of metronidazole. In addition, headache, syncope, dizziness, vertigo, incoordination, ataxia, confusion, dysarthria, irritability, depression, weakness, and insomnia have been reported.

Gastrointestinal: The most common adverse reactions reported have been referable to the gastrointestinal tract, particularly nausea, sometimes accompanied by headache, anorexia, and occasionally vomiting; diarrhea; epigastric distress; and abdominal cramping and constipation.

Mouth: A sharp, unpleasant metallic taste is not unusual. Furry tongue, glossitis, and stomatitis have occurred; these may be associated with a sudden overgrowth of *Candida* which may occur during therapy.

Dermatologic: Erythematous rash and pruritus.

Hematopoietic: Reversible neutropenia (leukopenia); reversible thrombocytopenia.

Cardiovascular: QT prolongation has been reported, particularly when metronidazole was administered with drugs with the potential for prolonging the QT interval. Flattening of the T-wave may be seen in electrocardiographic tracings.

Hypersensitivity: Urticaria, erythematous rash, Stevens-Johnson Syndrome, toxic epidermal necrolysis, flushing, nasal congestion, dryness of the mouth (or vagina or vulva), and fever.

Renal: Dysuria, cystitis, polyuria, incontinence, and a sense of pelvic pressure. Instances of darkened urine have been reported by approximately one patient in 100,000. Although the pigment which is probably responsible for this phenomenon has not been positively identified, it is almost certainly a metabolite of metronidazole and seems to have no clinical significance.

Other: Proliferation of *Candida* in the vagina, dyspareunia, decrease of libido, proctitis, and fleeting joint pains sometimes resembling “serum sickness.” Cases of pancreatitis, which generally abated on withdrawal of the drug, have been reported.

Patients with Crohn's disease are known to have an increased incidence of gastrointestinal and certain extraintestinal cancers. There have been some reports in the medical literature of breast and colon cancer in Crohn's disease patients who have been treated with metronidazole at high doses for extended periods of time. A cause-and-effect relationship has not been established. Crohn's disease is not an approved indication for LIKMEZ.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of metronidazole. 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.

The cases of severe irreversible hepatotoxicity/acute liver failure, including cases with fatal outcomes with very rapid onset after initiation of systemic use of metronidazole have been reported in patients with Cockayne syndrome (latency from drug start to signs of liver failure as short as 2 days) *[*see *Contraindications (4.4)]*.

Central and Peripheral Nervous System: Tinnitus, hearing impairment, and hearing loss.

Hypersensitivity: Drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP) *[*see *Warnings and Precautions (5.2)]*.

7 DRUG INTERACTIONS

7.1 Disulfiram

Psychotic reactions have been reported in alcoholic patients who are using metronidazole and disulfiram concurrently. LIKMEZ is contraindicated in patients who have taken disulfiram within the last two weeks *[*see *Contraindications (4.2)]*.

7.2 Alcoholic Beverages

LIKMEZ is contraindicated in patients who consume alcohol or products containing propylene glycol during and for at least 3 days after therapy with LIKMEZ. Use of LIKMEZ with alcohol or other products containing propylene glycol is associated with a disulfiram-like reaction (abdominal cramps, nausea, vomiting, headaches, and flushing) *[*see *Contraindications (4.3)]*.

7.3 Warfarin and other Oral Anticoagulants

Metronidazole has been reported to potentiate the anticoagulant effect of warfarin and other oral coumarin anticoagulants, resulting in a prolongation of prothrombin time. When LIKMEZ is prescribed for patients on this type of anticoagulant therapy, prothrombin time and INR should be carefully monitored.

7.4 Lithium

In patients stabilized on relatively high doses of lithium, short-term use of LIKMEZ has been associated with elevation of serum lithium concentrations and signs of lithium toxicity due to the interaction between metronidazole and lithium. Monitor serum lithium and serum creatinine concentrations for several days after beginning treatment with LIKMEZ to detect any increase that may precede clinical symptoms of lithium toxicity.

7.5 Busulfan

Metronidazole has been reported to increase plasma concentrations of busulfan, which can result in an increased risk for serious busulfan toxicity. Do not administer LIKMEZ concomitantly with busulfan unless the benefit outweighs the risk. If no therapeutic alternatives

Reference ID: 5407000

to LIKMEZ are available, and concomitant administration with busulfan is medically needed, monitor for busulfan plasma concentrations and adjust the busulfan dose accordingly.

7.6 Inhibitors of CYP450 Liver Enzymes

The simultaneous administration of LIKMEZ and drugs that decrease microsomal liver enzymes, such as cimetidine, may prolong the half-life and decrease plasma clearance of metronidazole.

7.7 Inducers of CYP450 Liver Enzymes

The simultaneous administration of LIKMEZ and drugs that induce microsomal liver enzymes, such as phenytoin or phenobarbital, may accelerate the elimination of metronidazole, resulting in reduced plasma concentrations of metronidazole. Impaired clearance of phenytoin has also been reported.

7.8 Drugs that Prolong the QT Interval

QT prolongation has been reported, particularly when metronidazole was administered with drugs with the potential for prolonging the QT interval.

7.9 Drug/Laboratory Test Interactions

Metronidazole may interfere with certain types of determinations of serum chemistry values, such as aspartate aminotransferase (AST, SGOT), alanine aminotransferase (ALT, SGPT), lactate dehydrogenase (LDH), triglycerides, and glucose hexokinase. Values of zero may be observed. All of the assays in which interference has been reported involve enzymatic coupling of the assay to oxidation-reduction of nicotinamide adenine dinucleotide ($NAD^+ \rightleftharpoons$ NADH). Interference is due to the similarity in absorbance peaks of NADH (340 nm) and metronidazole (322 nm) at pH 7.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

While available studies cannot definitively establish the absence of risk, published data from case-control studies, cohort studies and meta-analyses have not established an association with metronidazole use during pregnancy and major birth defects, miscarriage or other adverse maternal or fetal outcomes *(see Data).*

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Human Data

There are published data from case-control studies, cohort studies, and 2 meta-analyses that include more than 5,000 pregnant women who used metronidazole during pregnancy. Many studies included first trimester exposures. One study showed an increased risk of cleft lip, with or without cleft palate, in infants exposed to metronidazole *in-utero*; however, these findings were not confirmed. In addition, more than ten randomized, placebo-controlled clinical trials enrolled more than 5,000 pregnant women to assess the use of antibiotic treatment (including

Reference ID: 5407000

metronidazole) for bacterial vaginosis on the incidence of preterm delivery. Most studies did not show an increased risk for congenital anomalies or other adverse fetal outcomes following metronidazole exposure during pregnancy. Three studies conducted to assess the risk of infant cancer following metronidazole exposure during pregnancy did not show an increased risk; however, the ability of these studies to detect such a signal was limited.

Animal Data

Metronidazole crosses the placental barrier. Reproduction studies have been performed in rats, rabbits, and mice at doses similar to the maximum recommended human dose based on body surface area comparisons. There was no evidence of harm to the fetus due to metronidazole.

8.2 Lactation

Risk Summary

Metronidazole is present in human milk at concentrations similar to maternal serum levels, and infant serum levels can be close to or comparable to infant therapeutic levels. There are no data on the effects of metronidazole on milk production. Animal studies have shown the potential for tumorigenicity after oral metronidazole was administered chronically to rats and mice *[*see *Nonclinical Toxicology (13.1)]*. This drug is not intended to be administered chronically; therefore, the clinical relevance of the findings of the animal studies is unclear.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for LIKMEZ and any potential adverse effects on the breastfed infant from LIKMEZ or from the underlying maternal condition. Alternatively, a lactating woman may choose to pump and discard human milk for the duration of LIKMEZ therapy, and for 48 hours after the last dose and feed her infant stored human milk or formula.

8.4 Pediatric Use

The safety and effectiveness of LIKMEZ for the treatment of amebiasis have been established in pediatric patients.

The safety and effectiveness of LIKMEZ for the treatment of trichomoniasis and anaerobic bacterial infections have not been established in pediatric patients.

8.5 Geriatric Use

In elderly geriatric patients, monitoring for LIKMEZ associated adverse reactions is recommended *[*see *Clinical Pharmacology (12.3)]*. Decreased liver function in geriatric patients can result in increased concentrations of metronidazole that may necessitate adjustment of metronidazole dosage *[*see *Dosage and Administration (2.4)]*.

8.6 Renal Impairment

Patients with end-stage renal disease may excrete metronidazole and metabolites slowly in the urine, resulting in significant accumulation of metronidazole metabolites. Monitor for LIKMEZ associated adverse reactions *[*see *Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment

Patients with hepatic impairment metabolize metronidazole slowly, with resultant accumulation of metronidazole in the plasma. For patients with severe hepatic impairment (Child-Pugh C), reduce the dose of LIKMEZ by 50%. For patients with mild to moderate hepatic impairment, no dosage adjustment is needed but these patients should be monitored for LIKMEZ associated adverse reactions *[*see *Clinical Pharmacology (12.3)* and *Dosage and Administration (2.4)]*.

10 OVERDOSAGE

General

Single oral doses of metronidazole, up to 15 g (7.5 times the maximum recommended single dose), have been reported in suicide attempts and accidental overdoses. Symptoms reported include nausea, vomiting, and ataxia. Metronidazole is dialyzable.

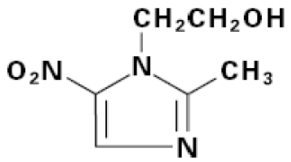
Neurotoxic effects, including seizures and peripheral neuropathy, have been reported after 5 days to 7 days of doses of 6 g to 10.4 g every other day (3 times to 5.2 times the maximum recommended single dose).

Treatment of Overdosage

There is no specific antidote for metronidazole overdose; therefore, management of the patient should consist of symptomatic and supportive therapy.

11 DESCRIPTION

LIKMEZ (metronidazole) oral suspension is a nitroimidazole antimicrobial. The chemical name of metronidazole is 2-methyl-5-nitro-1H-imidazole-1-ethanol. The structural formula is shown as:



Metronidazole is a white to pale yellow crystalline powder with a molecular formula of $C_6H_9N_3O_3$ and a molecular weight of 171.2 g/mole. The pKa of metronidazole is 14.44 ± 0.10. The pH of a 1% aqueous solution of metronidazole is 5.5-7.5. It is slightly soluble in water, acetone, alcohol, and methylene chloride.

LIKMEZ is an oral suspension containing 500 mg of metronidazole per 5 mL, and the following inactive ingredients: Glycerin, magnesium aluminum silicate, methylparaben, microcrystalline cellulose, natural peppermint flavor, natural strawberry flavor, propylparaben, purified water, sodium phosphate dibasic, sodium phosphate monobasic, sucralose, and sucrose.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Metronidazole is a nitroimidazole antimicrobial drug *[*see *Microbiology (12.4)]*.

12.3 Pharmacokinetics

Metronidazole pharmacokinetics are similar for both oral and intravenous dosage forms. The C_{max} is dose proportional between 250 mg, 500 mg, and 2,000 mg for metronidazole oral tablets, producing peak plasma concentrations of 6 mcg/mL, 12 mcg/mL, and 40 mcg/mL, respectively.

Absorption

Following oral administration, LIKMEZ is well absorbed, with peak plasma concentrations occurring between 0.25 and 6 hours after administration.

Two pharmacokinetic studies (Study 1 and Study 2) performed in healthy adult volunteers

Reference ID: 5407000

evaluated the bioavailability of LIKMEZ under fasting and fed conditions.

Effect of Food

Food delays T_{max} and lowers C_{max} when compared to fasted conditions, but systemic exposure (AUC) is similar in fed and fasted state (see Table 1).

Table 1: Mean (± S.D.) Pharmacokinetic Parameters Following Single Oral Doses of 500 mg LIKMEZ in Healthy Adults Under Fed and Fasting Conditions

Formulation	C_{max} (mcg/mL)	$AUC_{0-\infty}$ (mcg.h/mL)	T_{max}* (h)
Study 1- Fasting state (n = 44)			
LIKMEZ	13 ± 3	146 ± 36	0.75 (0.25 to 6)
Study 2- Fed State[1] (n = 46)			
LIKMEZ	10 ± 1	144 ± 30	2.33 (0.25 to 4)

*Median (min – max)

[1]Fed study administered LIKMEZ following a high-fat, high-calorie breakfast (approximately 1,000 calories, 26.5% carbohydrates, 16.5% protein, and 57% fat).

Distribution

Metronidazole is the major component appearing in the plasma, with lesser quantities of metabolites also being present. Less than 20% of the circulating metronidazole is bound to plasma proteins. Metronidazole appears in cerebrospinal fluid, saliva, and breast milk in concentrations similar to those found in plasma. Bactericidal concentrations of metronidazole have also been detected in pus from hepatic abscesses.

Elimination

Metabolism

The metabolites of metronidazole that appear in the urine result primarily from side-chain oxidation [1-(β-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole and 2-methyl-5-nitroimidazole-1-ylacetic acid] and glucuronide conjugation, with unchanged metronidazole accounting for approximately 20% of the total. Both the parent compound and the hydroxyl metabolite possess *in vitro* antimicrobial activity.

Excretion

The major route of elimination of metronidazole and its metabolites is via the urine (60% to 80% of the dose), with fecal excretion accounting for 6% to 15% of the dose.

Renal clearance of metronidazole is approximately 10 mL/min/1.73 m^2. The average elimination half-life of LIKMEZ in healthy adult subjects is nine hours.

Specific Populations

Geriatric Patients

Following a single 500 mg oral or IV dose of metronidazole, subjects >70 years old with no apparent renal or hepatic dysfunction had a 40% to 80% higher mean AUC of hydroxy-metronidazole (active metabolite), with no apparent increase in the mean AUC of

Reference ID: 5407000

metronidazole (parent compound), compared to young healthy controls <40 years old *[*see *Use in Specific Populations (8.5)]*.

Pediatric Patients

In one study, newborn infants appeared to demonstrate diminished capacity to eliminate metronidazole. The elimination half-life, measured during the first 3 days of life, was inversely related to gestational age. In infants whose gestational ages were between 28 weeks and 40 weeks, the corresponding elimination half-lives ranged from 109 hours to 22.5 hours.

Male and Female Patients

Studies reveal no significant bioavailability differences between males and females; however, because of weight differences, the resulting plasma levels in males are generally lower.

Patients with Renal Impairment

Decreased renal function does not alter the single-dose pharmacokinetics of metronidazole.

Subjects with end-stage renal disease (ESRD; CL_{CR}= 8.1±9.1 mL/min) and who received a single intravenous infusion of metronidazole 500 mg had no significant change in metronidazole pharmacokinetics but had 2-fold higher C_{max} of hydroxy-metronidazole and 5-fold higher C_{max} of metronidazole acetate, compared to healthy subjects with normal renal function (CL_{CR} = 126±16 mL/min). Thus, on account of the potential accumulation of metronidazole metabolites in ESRD patients, monitoring for metronidazole associated adverse reactions are recommended *[*see *Use in Specific Populations (8.6)]*.

Following a single intravenous infusion or oral dose of metronidazole 500 mg, the clearance of metronidazole was investigated in ESRD subjects undergoing hemodialysis or continuous ambulatory peritoneal dialysis (CAPD). A hemodialysis session lasting for 4 hours to 8 hours removed 40% to 65% of the administered metronidazole dose, depending on the type of dialyzer membrane used and the duration of the dialysis session. If the administration of metronidazole cannot be separated from the dialysis session, supplementation of metronidazole dose following hemodialysis should be considered *[*see *Dosage and Administration (2.5)]*. A peritoneal dialysis session lasting for 7.5 hours removed approximately 10% of the administered metronidazole dose. No adjustment in metronidazole dose is needed in ESRD patients undergoing CAPD.

Patients with Hepatic Impairment

Following a single intravenous infusion of 500 mg metronidazole, the mean AUC_{24} of metronidazole was higher by 114% in patients with severe (Child-Pugh C) hepatic impairment, and by 54% and 53% in patients with mild (Child-Pugh A) and moderate (Child-Pugh B) hepatic impairment, respectively, compared to healthy control subjects. There were no significant changes in the AUC_{24} of hydroxyl-metronidazole in these hepatically impaired patients. A reduction in metronidazole dosage by 50% is recommended in patients with severe (Child-Pugh C) hepatic impairment. No dosage adjustment is needed for patients with mild to moderate hepatic impairment. Patients with mild to moderate hepatic impairment should be monitored for metronidazole associated adverse reactions *[*see *Use in Specific Populations (8.7)* and *Dosage and Administration (2.4)]*.

12.4 Microbiology

Mechanism of Action

Metronidazole, a nitroimidazole, exerts antibacterial effects in an anaerobic environment against most obligate anaerobes. Once metronidazole enters the organism by passive diffusion

Reference ID: 5407000

and activated in the cytoplasm of susceptible anaerobic bacteria, it is reduced; this process includes intracellular electron transport proteins such as ferredoxin, transfer of an electron to the nitro group of the metronidazole, and formation of a short-lived nitroso free radical. Because of this alteration of the metronidazole molecule, a concentration gradient is created and maintained which promotes the drug's intracellular transport. The reduced form of metronidazole and free radicals can interact with DNA leading to inhibition of DNA synthesis and DNA degradation leading to death of the bacteria. The precise mechanism of action of metronidazole is unclear.

Resistance

A potential for development of resistance exists against metronidazole.

Resistance may be due to multiple mechanisms that include decreased uptake of the drug, altered reduction efficiency, overexpression of the efflux pumps, inactivation of the drug, and/or increased DNA damage repair.

Metronidazole does not possess any clinically relevant activity against facultative anaerobes or obligate aerobes.

Antimicrobial Activity

Metronidazole has been shown to be active against most isolates of the following microorganisms, both *in vitro* and in clinical infections *[*see *Indications and Usage (1)]*.

Gram-positive anaerobes

Clostridium species *Eubacterium* species

Peptococcus species

Peptostreptococcus species

Gram-negative anaerobes

Bacteroides fragilis group *(B. fragilis, B. ovatus, B. thetaiotaomicron, B. vulgatus)*

Parabacteroides distasonis

Fusobacterium species

Protozoal parasites

Entamoeba histolytica

Trichomonas vaginalis

The following *in vitro* data are available, but their clinical significance is unknown. At least 90 percent of the following bacteria exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for metronidazole against isolates of similar genus or organism group. However, the efficacy of metronidazole in treating clinical infections caused by these bacteria has not been established in adequate and well-controlled clinical trials.

Gram-negative anaerobes

Bacteroides fragilis group *(B. caccae, B. uniformis)*

Prevotella species *(P. bivia, P. buccae, P. disiens)*

Susceptibility Testing

For specific information regarding susceptibility test interpretive criteria and associated test methods and quality control standards recognized by FDA for this drug, please see: https://www.fda.gov/STIC.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Tumors affecting the liver, lungs, mammary, and lymphatic tissues have been detected in several studies of metronidazole in rats and mice, but not hamsters. Pulmonary tumors have been observed in all six reported studies in the mouse, including one study in which the animals were dosed on an intermittent schedule (administration during every fourth week only). Malignant liver tumors were increased in male mice treated at approximately 1,500 mg/m^2 (similar to the maximum recommended daily dose, based on body surface area comparisons). Malignant lymphomas and pulmonary neoplasms were also increased with lifetime feeding of the drug to mice. Mammary and hepatic tumors were increased among female rats administered oral metronidazole compared to concurrent controls. Two lifetime tumorigenicity studies in hamsters have been performed and reported to be negative.

Mutagenesis

Metronidazole has shown mutagenic activity in *in vitro* assay systems including the Ames test. Studies in mammals *in vivo* have failed to demonstrate a potential for genetic damage.

Impairment of Fertility

Metronidazole failed to produce any adverse effects on fertility or testicular function in male rats at doses up at 400 mg/kg/day (similar to the maximum recommended clinical dose, based on body surface area comparisons) for 28 days. However, rats treated at the same dose for 6 weeks or longer were infertile and showed severe degeneration of the seminiferous epithelium in the testes as well as marked decreases in testicular spermatid counts and epididymal sperm counts. Fertility was restored in most rats after an eight-week, drug-free recovery period.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

LIKMEZ 500 mg/5 mL is a white to slightly brown suspension with characteristic strawberry peppermint flavor packed in white HDPE round bottles with a child-resistant cap and supplied as follows:

NDC 71656-066-75	Bottles of 75 mL
NDC 71656-066-20	Bottles of 200 mL

Storage

Store between 20°C to 25°C (68°F to 77°F). Brief exposure to 15°C to 30°C (59°F to 86°F) permitted [See USP Controlled Room Temperature]. *Do not freeze*.

Dispense in a tight container as defined in USP. Discard 60 days after opening container.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Administration Instructions

Instruct the patients and caregivers to:

- Ensure the prescribed dose of LIKMEZ oral suspension is taken as directed *[*see *Dosage and Administration (2)]*.
- Use a calibrated oral dosing device to correctly measure the prescribed dose of medication. Do not use a household teaspoon or tablespoon to measure doses. Calibrated oral dosing devices may be obtained from the pharmacy.
- Shake LIKMEZ oral suspension well before use each time.

Severe Cutaneous Adverse Reactions

Advise patients that LIKMEZ may increase the risk of serious and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and drug reaction with eosinophilia and systemic symptoms (DRESS). Instruct the patient to be alert for skin rash, blisters, fever or other signs and symptoms of these hypersensitivity reactions. Advise patients to stop LIKMEZ immediately if they develop any type of rash and seek medical attention *[*see *Warnings and Precautions (5.2)]*.

Alcohol or Products Containing Propylene Glycol

Advise patients to avoid consumption of alcoholic beverages and preparations containing ethanol or propylene glycol during LIKMEZ therapy and for 3 days afterward because abdominal cramps, nausea, vomiting, headaches, and flushing may occur *[*see *Contraindications (4.3)* and *Drug Interactions (7.2)]*.

Lactation

Advise lactating women that they may choose to pump and discard human milk for the duration of LIKMEZ therapy and for 48 hours after the last dose and feed her infant stored human milk or formula *[*see *Use in Specific Populations (8.2)]*.

Central and Peripheral Nervous System Effects

Inform patients of the risk of central and peripheral nervous system effects while taking LIKMEZ. Advise patients to stop taking LIKMEZ and report immediately to their healthcare provider if any neurological symptoms occur *[*see *Warnings and Precautions (5.3)]*.

Drug Interactions

Advise patients to report the use of any other medications while taking LIKMEZ. The administration of any of the following drugs with LIKMEZ may result in clinically significant adverse reactions or reduced effectiveness of the drug *[*see *Contraindications (4.2)* and *Drug Interactions (7.1 to 7.7)]*:

- Disulfiram
- Warfarin and other oral Anticoagulants
- Lithium
- Busulfan
- Cimetidine

- Phenytoin and Phenobarbital

Antibacterial Resistance

Patients should be counseled that antibacterial drugs including LIKMEZ should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When LIKMEZ is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by LIKMEZ or other antibacterial drugs in the future.

Manufactured by:
Saptalis Pharmaceuticals LLC
Hauppauge, NY 11788

Made in USA

PATIENT INFORMATION
LIKMEZ™ (lik mez)
(metronidazole)
oral suspension

What is LIKMEZ?
LIKMEZ is an antibiotic medicine used to treat:
- trichomoniasis (a sexually transmitted infection) in adults
- amebiasis (an infection caused by a parasite) in adults and children
- anaerobic bacterial infections (infections caused by bacteria that do not need oxygen to survive) in adults

It is not known if LIKMEZ is safe and effective in children, except for the treatment of amebiasis.

Do not take LIKMEZ if you:
- are allergic to metronidazole or other nitroimidazole medicines.
- have taken disulfiram (medicine used to help people stop drinking alcohol) in the last 2 weeks. Taking LIKMEZ with disulfiram can cause psychotic symptoms (seeing or hearing things that are not really there) in people who drink alcohol.
- drink alcohol or use products with propylene glycol during treatment with LIKMEZ and for at least 3 days after you stop taking LIKMEZ, because this can cause side effects including abdominal cramps, nausea, vomiting, headaches, and flushing.
- have Cockayne Syndrome (a rare genetic disorder that affects growth and development).

Before taking LIKMEZ, tell your healthcare provider about all of your medical conditions, including if you:
- have liver problems.
- have kidney problems.
- have medical problems that affect the brain.
- have a yeast infection.
- have a history of blood problems.
- are breastfeeding or plan to breastfeed. LIKMEZ can pass into your breastmilk. Talk to your healthcare provider about the best way to feed your baby while taking LIKMEZ. If you are breastfeeding, you may consider pumping and throwing away your breast milk during treatment with LIKMEZ and for 48 hours after your last dose of LIKMEZ and feeding your infant stored human milk or formula.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. LIKMEZ and other medicines can affect each other causing side effects.

Especially tell your healthcare provider if you take:
- warfarin or other blood thinners (anticoagulants)
- lithium
- busulfan
- cimetidine
- phenytoin and phenobarbital

You can ask your pharmacist for a list of medicines that interact with LIKMEZ.
Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take LIKMEZ?
- Take LIKMEZ exactly as your healthcare provider tells you to.
- Shake LIKMEZ oral suspension well before each use.
- Always use an accurate measuring device to measure the correct amount of LIKMEZ. **Do not** use a household teaspoon or tablespoon to measure your medicine. You can ask your pharmacist for the measuring device you should use and how to measure the correct dose.
- Do not skip any doses of LIKMEZ or stop taking it, even if you begin to feel better, until you have finished your prescribed treatment. Taking all of your LIKMEZ doses will help make sure that all of the bacteria are killed. Taking all of your LIKMEZ doses will help lower the chance that the bacteria will become resistant to LIKMEZ. If you become resistant to LIKMEZ, LIKMEZ and other antibacterial medicines may not work for you in the future.
- If you take too much LIKMEZ, call your healthcare provider or go to the nearest emergency room right away.

Reference ID: 5407000

What are the possible side effects of LIKMEZ?
LIKMEZ may cause serious side effects including:

- **Severe skin reactions**. Serious skin reactions that may affect any part of the body and can lead to death, including toxic epidermal necrolysis (TEN), Stevens-Johnson Syndrome (SJS), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP), have happened in some people taking metronidazole (the active ingredient in LIKMEZ). These severe skin reactions may be life threatening and you may need to be treated in a hospital. Stop taking LIKMEZ right away and call your healthcare provider or get emergency help if you have any of the following symptoms:
  - skin rash or acne
  - dry skin
  - itching
  - blisters on your skin
  - redness or swelling of your face, hands, or soles of your feet
  - blisters or sores in your mouth
  - peeling of your skin
  - fever
  - muscle or joint aches
  - swollen glands
- **Nervous system problems**, including brain disorder (encephalopathy), inflammation of the brain and spinal cord membranes (aseptic meningitis), numbness or tingling in the hands or feet (peripheral neuropathy) and seizures (convulsions). Tell your healthcare provider right away if you have any nervous system problems while taking LIKMEZ.
- **Worsening yeast infection (candidiasis) symptoms** in people with a known yeast infection or a yeast infection they were not aware of.
- **Low white blood cell count (leukopenia) in people with a history of blood problems**. This can affect how well the body fights infection.

The most common side effects of LIKMEZ include: nausea, headache, anorexia, vomiting, diarrhea, pain in the upper abdomen, abdominal cramping, and constipation.

Other side effects of LIKMEZ include:

- allergic reactions: such as itching, hives (urticaria), flushing of the skin, red skin rash that can be widespread, blisters and separation of skin layers, nasal congestion, dryness of the mouth and vagina, and fever
- abnormal heart rhythm (QT prolongation)

These are not all the possible side effects of LIKMEZ. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store LIKMEZ?

- Store LIKMEZ oral suspension at room temperature between 68°F to 77°F (20°C to 25°C).
- Do not freeze.
- Throw away (discard) any unused LIKMEZ 60 days after opening the container.

Keep LIKMEZ and all medicines out of the reach of children.

General information about the safe and effective use of LIKMEZ.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use LIKMEZ for a condition for which it was not prescribed. Do not give LIKMEZ to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about LIKMEZ that is written for health professionals.

What are the ingredients in LIKMEZ?
Active ingredient: metronidazole
Inactive ingredients: glycerin, magnesium aluminum silicate, methylparaben, microcrystalline cellulose, natural peppermint flavor, natural strawberry flavor, propylparaben, purified water, sodium phosphate dibasic, sodium phosphate monobasic, sucralose, and sucrose.

Manufactured by:
Saptalis Pharmaceuticals LLC
Hauppauge, NY 11788
Made in USA
For more information, call 1-833-727-8254.

This Patient Information has been approved by the U.S. Food and Drug Administration. Issued: 7/2024