

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

ALBENZA® (albendazole) tablets, for oral use
Initial U.S. Approval: 1996

INDICATIONS AND USAGE

ALBENZA is an anthelmintic drug indicated for:

- Treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*. (1.1)
- Treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus*. (1.2)

DOSAGE AND ADMINISTRATION

Patients weighing 60 kg or greater, 400 mg twice daily; less than 60 kg, 15 mg/kg/day in divided doses twice daily (maximum total daily dose 800 mg).

ALBENZA tablets should be taken with food. (2)

- Hydatid disease: 28-day cycle followed by 14-day albendazole-free interval for a total of 3 cycles. (2)
- Neurocysticercosis: 8 to 30 days. (2)

See additional important information in the Full Prescribing Information. (2)

DOSAGE FORMS AND STRENGTHS

- Tablet: 200 mg (3)

CONTRAINDICATIONS

Patients with known hypersensitivity to the benzimidazole class of compounds or any components of ALBENZA. (4)

WARNINGS AND PRECAUTIONS

- Bone Marrow Suppression: Fatalities have been reported due to bone marrow suppression; monitor blood counts in all patients at the beginning of each 28-day cycle of therapy, and every 2 weeks while on therapy. Discontinue ALBENZA if clinically significant changes in blood counts occur. (5.1, 5.4)
- Teratogenic Effects: Obtain pregnancy test in women of reproductive potential prior to therapy and avoid usage in pregnant women except in

clinical circumstances where no alternative management is appropriate. Discontinue therapy if pregnancy occurs and apprise patient of potential hazard to the fetus. (5.2)

- Risk of Neurologic Symptoms: Neurocysticercosis patients may experience cerebral hypertensive episodes, seizures or focal neurologic deficits after initiation of therapy; begin appropriate steroid and anticonvulsant therapy. (5.3)
- Risk of Retinal Damage in Retinal Cysticercosis: Cases of retinal involvement have been reported; examine the patient for the presence of retinal lesions before initiating therapy for neurocysticercosis. (5.4)
- Hepatic Effects. Elevations of liver enzymes may occur. Monitor liver enzymes before the start of each treatment cycle and at least every 2 weeks while on ALBENZA therapy and discontinue if clinically significant elevations occur. (5.5)

ADVERSE REACTIONS

- Adverse reactions 1% or greater in hydatid disease: abnormal liver function tests, abdominal pain, nausea/vomiting, reversible alopecia, headache, dizziness/vertigo, fever. (6.1)
- Adverse reactions 1% or greater in neurocysticercosis: headache, nausea/vomiting, raised intracranial pressure, meningeal signs. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Impax Laboratories, Inc. at 1-877-994-6729 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Dexamethasone: Steady-state trough concentrations of albendazole sulfoxide were about 56% higher when dexamethasone was coadministered with each dose of albendazole. (7.1)
- Praziquantel: In the fed state increased mean maximum plasma concentration and area under the curve of albendazole sulfoxide by about 50% in healthy subjects. (7.2)
- Cimetidine: Increased albendazole sulfoxide concentrations in bile and cystic fluid by about 2-fold in hydatid cyst patients. (7.3)
- Theophylline: Albendazole induces cytochrome P450 1A in human hepatoma cells; therefore, it is recommended that plasma concentrations of theophylline be monitored during and after treatment. (5.5, 7.4)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 05/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

- 1.1 Neurocysticercosis
- 1.2 Hydatid Disease

2 DOSAGE AND ADMINISTRATION

- 2.1 Dosage
- 2.2 Concomitant Medication to Avoid Adverse Reactions
- 2.3 Monitoring for Safety Before and During Treatment

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Bone Marrow Suppression
- 5.2 Teratogenic Effects
- 5.3 Risk of Neurologic Symptoms in Neurocysticercosis
- 5.4 Risk of Retinal Damage in Patients with Retinal Neurocysticercosis
- 5.5 Hepatic Effects
- 5.6 Unmasking of Neurocysticercosis in Hydatid Patients

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

7 DRUG INTERACTIONS

- 7.1 Dexamethasone
- 7.2 Praziquantel
- 7.3 Cimetidine

7.4 Theophylline

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Patients with Impaired Renal Function
- 8.7 Patients with Extra-Hepatic Obstruction

10 OVERDOSE

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

- 16.1 How Supplied
- 16.2 Storage and Handling

17 PATIENT COUNSELING INFORMATION

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Neurocysticercosis

ALBENZA is indicated for the treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*.

1.2 Hydatid Disease

ALBENZA is indicated for the treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus*.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

Dosing of ALBENZA will vary depending upon the indication. ALBENZA tablets may be crushed or chewed and swallowed with a drink of water. ALBENZA tablets should be taken with food [see *Clinical Pharmacology* (12.3)].

Table 1: ALBENZA Dosage

Indication	Patient Weight	Dose	Duration
Hydatid Disease	60 kg or greater	400 mg twice daily, with meals	28-day cycle followed by a 14-day albendazole-free interval, for a total of 3 cycles
	Less than 60 kg	15 mg/kg/day given in divided doses twice daily with meals (maximum total daily dose 800 mg)	
Neurocysticercosis	60 kg or greater	400 mg twice daily, with meals	8 to 30 days
	Less than 60 kg	15 mg/kg/day given in divided doses twice daily with meals (maximum total daily dose 800 mg)	

2.2 Concomitant Medication to Avoid Adverse Reactions

Patients being treated for neurocysticercosis should receive appropriate steroid and anticonvulsant therapy as required. Oral or intravenous corticosteroids should be considered to prevent cerebral hypertensive episodes during the first week of treatment [see *Warnings and Precautions* (5.3)].

2.3 Monitoring for Safety Before and During Treatment

- Monitor blood counts at the beginning of each 28-day cycle of therapy, and every 2 weeks while on therapy with ALBENZA in all patients [see *Warnings and Precautions (5.1)*].
- Monitor liver enzymes (transaminases) at the beginning of each 28-day cycle of therapy, and at least every 2 weeks during treatment with ALBENZA in all patients [see *Warnings and Precautions (5.5)*].
- Obtain a pregnancy test in women of reproductive potential prior to therapy [see *Warnings and Precautions (5.2)*].

3 DOSAGE FORMS AND STRENGTHS

- Tablet: 200 mg

4 CONTRAINDICATIONS

ALBENZA is contraindicated in patients with known hypersensitivity to the benzimidazole class of compounds or any components of ALBENZA.

5 WARNINGS AND PRECAUTIONS

5.1 Bone Marrow Suppression

Fatalities associated with the use of ALBENZA have been reported due to granulocytopenia or pancytopenia. ALBENZA may cause bone marrow suppression, aplastic anemia, and agranulocytosis. Monitor blood counts at the beginning of each 28-day cycle of therapy, and every 2 weeks while on therapy with ALBENZA in all patients. Patients with liver disease and patients with hepatic echinococcosis are at increased risk for bone marrow suppression and warrant more frequent monitoring of blood counts. Discontinue ALBENZA if clinically significant decreases in blood cell counts occur.

5.2 Teratogenic Effects

ALBENZA may cause fetal harm and should not be used in pregnant women except in clinical circumstances where no alternative management is appropriate. Obtain pregnancy test prior to prescribing ALBENZA to women of reproductive potential. Advise women of reproductive potential to use effective birth control for the duration of ALBENZA therapy and for one month after end of therapy. Immediately discontinue ALBENZA if a patient becomes pregnant and apprise the patient of the potential hazard to the fetus [see *Use in Specific Populations (8.1)*].

5.3 Risk of Neurologic Symptoms in Neurocysticercosis

Patients being treated for neurocysticercosis should receive steroid and anticonvulsant therapy to prevent neurological symptoms (e.g. seizures, increased intracranial pressure and focal signs) as a result of an inflammatory reaction caused by death of the parasite within the brain.

5.4 Risk of Retinal Damage in Patients with Retinal Neurocysticercosis

Cysticercosis may involve the retina. Before initiating therapy for neurocysticercosis, examine the patient for the presence of retinal lesions. If such lesions are visualized, weigh the need for anticycsticercal therapy against the possibility of retinal damage resulting from inflammatory damage caused by ALBENZA-induced death of the parasite.

5.5 Hepatic Effects

In clinical trials, treatment with ALBENZA has been associated with mild to moderate elevations of hepatic enzymes in approximately 16% of patients. These elevations have generally returned to normal upon discontinuation of therapy. There have also been case reports of acute liver failure of uncertain causality and hepatitis [*see Adverse Reactions (6)*].

Monitor liver enzymes (transaminases) before the start of each treatment cycle and at least every 2 weeks during treatment. If hepatic enzymes exceed twice the upper limit of normal, consideration should be given to discontinuing ALBENZA therapy based on individual patient circumstances. Restarting ALBENZA treatment in patients whose hepatic enzymes have normalized off treatment is an individual decision that should take into account the risk/benefit of further ALBENZA usage. Perform laboratory tests frequently if ALBENZA treatment is restarted.

Patients with elevated liver enzyme test results are at increased risk for hepatotoxicity and bone marrow suppression [*see Warnings and Precautions (5.1)*]. Discontinue therapy if liver enzymes are significantly increased or if clinically significant decreases in blood cell counts occur.

5.6 Unmasking of Neurocysticercosis in Hydatid Patients

Undiagnosed neurocysticercosis may be uncovered in patients treated with ALBENZA for other conditions. Patients with epidemiologic factors who are at risk for neurocysticercosis should be evaluated prior to initiation of therapy.

6 ADVERSE REACTIONS

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 adverse reaction profile of ALBENZA differs between hydatid disease and neurocysticercosis. Adverse reactions occurring with a frequency of 1% or greater in either disease are described in [Table 2](#) below.

These symptoms were usually mild and resolved without treatment. Treatment discontinuations were predominantly due to leukopenia (0.7%) or hepatic abnormalities (3.8% in hydatid disease). The following incidence reflects adverse reactions that were reported to be at least possibly or probably related to ALBENZA.

Table 2: Adverse Reaction Incidence 1% or Greater in Hydatid Disease and Neurocysticercosis

Adverse Reaction	Hydatid Disease	Neurocysticercosis
Gastrointestinal		
Abdominal Pain	6	0
Nausea	4	6
Vomiting	4	6
General disorders and administration site conditions		
Fever	1	0
Investigations		
Elevated Hepatic Enzymes	16	less than 1
Nervous system disorders		
Dizziness	1	less than 1
Headache	1	11
Meningeal Signs	0	1
Raised Intracranial Pressure	0	2
Vertigo	1	less than 1
Skin and subcutaneous tissue disorders		
Reversible Alopecia	2	less than 1

The following adverse events were observed at an incidence of less than 1%:

Blood and Lymphatic System Disorders: There have been reports of leukopenia, granulocytopenia, pancytopenia, agranulocytosis, or thrombocytopenia [*see Warnings and Precautions (5.1)*].

Immune System Disorders: Hypersensitivity reactions, including rash and urticaria.

6.2 Postmarketing Experience

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

Blood and Lymphatic System Disorders: Aplastic anemia, bone marrow suppression, neutropenia.

Eye Disorders: Vision blurred.

Gastrointestinal Disorders: Diarrhea.

General System Disorders: Asthenia.

Hepatobiliary Disorders: Elevations of hepatic enzymes, hepatitis, acute liver failure.

Musculoskeletal and Connective Tissue Disorders: Rhabdomyolysis.

Nervous System Disorders: Somnolence, convulsion.

Renal and Urinary Disorders: Acute renal failure.

Skin and Subcutaneous Tissue Disorders: Erythema multiforme, Stevens-Johnson syndrome.

7 DRUG INTERACTIONS

7.1 Dexamethasone

Steady-state trough concentrations of albendazole sulfoxide were about 56% higher when 8 mg dexamethasone was co-administered with each dose of albendazole (15 mg/kg/day) in 8 neurocysticercosis patients.

7.2 Praziquantel

In the fed state, praziquantel (40 mg/kg) increased mean maximum plasma concentration and area under the curve of albendazole sulfoxide by about 50% in healthy subjects (n = 10) compared with a separate group of subjects (n = 6) given albendazole alone. Mean T_{max} and mean plasma elimination half-life of albendazole sulfoxide were unchanged. The pharmacokinetics of praziquantel were unchanged following co-administration with albendazole (400 mg).

7.3 Cimetidine

Albendazole sulfoxide concentrations in bile and cystic fluid were increased (about 2-fold) in hydatid cyst patients treated with cimetidine (10 mg/kg/day) (n = 7) compared with albendazole (20 mg/kg/day) alone (n = 12). Albendazole sulfoxide plasma concentrations were unchanged 4 hours after dosing.

7.4 Theophylline

Following a single dose of albendazole (400 mg), the pharmacokinetics of theophylline_ (aminophylline 5.8 mg/kg infused over 20 minutes) were unchanged. Albendazole induces cytochrome P450 1A in human hepatoma cells; therefore, it is recommended that plasma concentrations of theophylline be monitored during and after treatment.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C.

There are no adequate and well-controlled studies of ALBENZA administration in pregnant women. ALBENZA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

ALBENZA should not be used in pregnant women except in clinical circumstances where no alternative management is appropriate. Obtain pregnancy test prior to prescribing ALBENZA to women of reproductive potential. Advise women of reproductive potential to use effective birth control for the duration of ALBENZA therapy and for one month after end of therapy. If a patient becomes pregnant while taking this drug, ALBENZA should be discontinued immediately. If pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

ALBENZA has been shown to be teratogenic (to cause embryotoxicity and skeletal malformations) in pregnant rats and rabbits. The teratogenic response in the rat was shown at oral doses of 10 and 30 mg/kg/day (0.10 times and 0.32 times the recommended human dose based on body surface area in mg/m^2 , respectively) during gestation days 6 to 15 and in pregnant rabbits at oral doses of 30 mg/kg/day (0.60 times the recommended human dose based on body surface area in mg/m^2) administered during gestation days 7 to 19. In the rabbit study, maternal toxicity (33% mortality) was noted at 30 mg/kg/day. In mice, no teratogenic effects were observed at oral doses up to 30 mg/kg/day (0.16 times the recommended human dose based on body surface area in mg/m^2), administered during gestation days 6 to 15.

8.3 Nursing Mothers

ALBENZA is excreted in animal milk. It is not known whether it is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ALBENZA is administered to a nursing woman.

8.4 Pediatric Use

Hydatid disease is uncommon in infants and young children. In neurocysticercosis, the efficacy of ALBENZA in children appears to be similar to that in adults.

8.5 Geriatric Use

In patients aged 65 and older with either hydatid disease or neurocysticercosis, there was insufficient data to determine whether the safety and effectiveness of ALBENZA is different from that of younger patients.

8.6 Patients with Impaired Renal Function

The pharmacokinetics of ALBENZA in patients with impaired renal function has not been studied.

8.7 Patients with Extra-Hepatic Obstruction

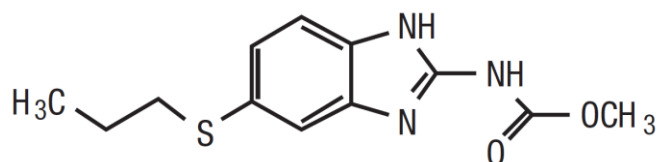
In patients with evidence of extrahepatic obstruction (n = 5), the systemic availability of albendazole sulfoxide was increased, as indicated by a 2-fold increase in maximum serum concentration and a 7-fold increase in area under the curve. The rate of absorption/conversion and elimination of albendazole sulfoxide appeared to be prolonged with mean T_{max} and serum elimination half-life values of 10 hours and 31.7 hours, respectively. Plasma concentrations of parent ALBENZA were measurable in only 1 of 5 patients.

10 OVERDOSAGE

In case of overdosage, symptomatic therapy and general supportive measures are recommended.

11 DESCRIPTION

ALBENZA (albendazole) is an orally administered anthelmintic drug. Chemically, it is methyl 5-(propylthio)-2-benzimidazolecarbamate. Its molecular formula is C₁₂H₁₅N₃O₂S. Its molecular weight is 265.34. It has the following chemical structure:



Albendazole is a white to yellowish powder. It is freely soluble in anhydrous formic acid and very slightly soluble in ether and in methylene chloride. Albendazole is practically insoluble in alcohol and in water.

Each white to off-white, circular, biconvex, bevel-edged film coated, TILTAB tablet is debossed with “ap” and “550” and contains 200 mg of albendazole.

Inactive ingredients consist of: carnauba wax, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone, sodium lauryl sulfate, sodium saccharin, sodium starch glycolate, and starch.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ALBENZA (albendazole) is a synthetic, antihelminthic drug of the class benzimidazole [*see Clinical Pharmacology (12.4)*].

12.3 Pharmacokinetics

Absorption

Albendazole is poorly absorbed from the gastrointestinal tract due to its low aqueous solubility. Albendazole concentrations are negligible or undetectable in plasma as it is rapidly converted to the sulfoxide metabolite prior to reaching the systemic circulation. The systemic anthelmintic activity has been attributed to the primary metabolite, albendazole sulfoxide. Oral bioavailability appears to be enhanced when albendazole is coadministered with a fatty meal (estimated fat content 40 grams) as evidenced by higher (up to 5-fold on average) plasma concentrations of albendazole sulfoxide as compared to the fasted state.

Maximal plasma concentrations of albendazole sulfoxide were achieved 2 hours to 5 hours after dosing and were on average 1310 ng/mL (range 460 ng/mL to 1580 ng/mL) following oral doses of albendazole (400 mg) in 6 hydatid disease patients, when administered with a fatty meal. Plasma concentrations of albendazole sulfoxide increased in a dose-proportional manner over the therapeutic dose range following ingestion of a high-fat meal (fat content 43.1 grams). The mean apparent terminal elimination half-life of albendazole sulfoxide ranged from 8 hours to 12 hours in 25 healthy subjects, as well as in 14 hydatid and 8 neurocysticercosis patients.

Following 4 weeks of treatment with albendazole (200 mg three times daily), 12 patients' plasma concentrations of albendazole sulfoxide were approximately 20% lower than those observed during the first half of the treatment period, suggesting that albendazole may induce its own metabolism.

Distribution

Albendazole sulfoxide is 70% bound to plasma protein and is widely distributed throughout the body; it has been detected in urine, bile, liver, cyst wall, cyst fluid, and cerebrospinal fluid (CSF). Concentrations in plasma were 3-fold to 10-fold and 2-fold to 4-fold higher than those simultaneously determined in cyst fluid and CSF, respectively.

Metabolism and Excretion

Albendazole is rapidly converted in the liver to the primary metabolite, albendazole sulfoxide, which is further metabolized to albendazole sulfone and other primary oxidative metabolites that have been identified in human urine. Following oral administration, albendazole has not been detected in human urine. Urinary excretion of albendazole sulfoxide is a minor elimination pathway with less than 1% of the dose recovered in the urine. Biliary elimination presumably accounts for a portion of the elimination as evidenced by biliary concentrations of albendazole sulfoxide similar to those achieved in plasma.

Specific Populations

Pediatrics

Following single-dose administration of 200 mg to 300 mg (approximately 10 mg/kg) ALBENZA to 3 fasted and 2 fed pediatric patients with hydatid cyst disease (age range 6 to 13 years), albendazole sulfoxide pharmacokinetics were similar to those observed in fed adults.

Geriatrics

Although no studies have investigated the effect of age on albendazole sulfoxide pharmacokinetics, data in 26 hydatid cyst patients (up to 79 years) suggest pharmacokinetics similar to those in young healthy subjects.

12.4 Microbiology

Mechanism of Action

ALBENZA binds to the colchicine-sensitive site of β -tubulin inhibiting their polymerization into microtubules. The decrease in microtubules in the intestinal cells of the parasites decreases their absorptive function, especially the uptake of glucose by the adult and larval forms of the parasites, and also depletes glycogen storage. Insufficient glucose results in insufficient energy for the production of adenosine triphosphate (ATP) and the parasite eventually dies.

Mechanism of Resistance

Parasitic resistance to albendazole is caused by changes in amino acids that result in changes in the β -tubulin protein. This causes reduced binding of the drug to β -tubulin.

In the specified treatment indications albendazole appears to be active against the larval forms of the following organisms:

Echinococcus granulosus

Taenia solium

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies were conducted in mice and rats.

No evidence of increased incidence of tumors was found in the mice or rats at up to 400 mg/kg/day or 20 mg/kg/day respectively (2 times and 0.2 times the recommended human dose on a body surface area basis).

In genotoxicity tests, albendazole was found negative in an Ames Salmonella/Microsome Plate mutation assay, Chinese Hamster Ovary chromosomal aberration test, and *in vivo* mouse micronucleus test. In the *in vitro* BALB/3T3 cells transformation assay, albendazole produced weak activity in the presence of metabolic activation while no activity was found in the absence of metabolic activation.

Albendazole did not adversely affect male or female fertility in the rat at an oral dose of 30 mg/kg/day (0.32 times the recommended human dose based on body surface area in mg/m²).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Each white to off-white, circular, biconvex, bevel-edged film coated, TILTAB tablet is debossed with “ap” and “550” and contains 200 mg of albendazole.

Bottles of 2 Tablets NDC 64896-693-49

16.2 Storage and Handling

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Patients should be advised that:

- Some people, particularly children, may experience difficulties swallowing the ALBENZA tablets whole.
- Take ALBENZA with food.
- ALBENZA may cause fetal harm, therefore, obtain a pregnancy test in women of reproductive potential prior to initiating therapy.
- Advise women of reproductive potential to use effective birth control while on ALBENZA and for one month after completing treatment.
- During ALBENZA therapy, monitor blood counts and liver enzymes every 2 weeks because of the possibility of harm to the liver or bone marrow.

ALBENZA and TILTAB are registered trademarks of GlaxoSmithKline, used with permission.

Dist. by:
Impax Specialty Pharma
Hayward, CA 94544

1908-02
Rev. 05/2018



David
Lewis

Digitally signed by David Lewis
Date: 10/31/2018 09:32:59AM
GUID: 508da72000029f287fa31e664741b577