In the treatment of bacterial conjunctivitis

DEMONSTRATED EFFICACY.

SIMPLE DOSING REGIMEN.

Helps resolve bacterial conjunctivitis

AzaSite® is indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following microorganisms: CDC coryneform group G*, Haemophilus influenzae, Staphylococcus aureus, Streptococcus mitis group, Streptococcus pneumoniae.

*Efficacy for this organism was studied in fewer than 10 infections.

The only azithromycin-based eyedrop available.1

Recommended dosing

9 DROPS. 7 DAYS.

AzaSite is dosed as a viscous drop in the affected eye.

Unrestricted access to 90% of patients on managed care5, a

SELECT IMPORTANT SAFETY INFORMATION

AzaSite® is contraindicated in patients with hypersensitivity to any component of this product.

AzaSite® is NOT FOR INJECTION. AzaSite is for topical ophthalmic use only and should not be administered systemically, injected subconjunctivally, or introduced directly into the anterior chamber of the eye. In patients receiving systemically administered azithromycin, serious allergic reactions, including angioedema, anaphylaxis, and dermatologic reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported rarely. Although rare, fatalities have been reported. As with other anti-infectives, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If super-infection occurs, discontinue use and institute alternative therapy.

The most frequently reported ocular adverse reaction reported in clinical trials was eye irritation, which occurred in 1% to 2% of patients.

Please refer to full Prescribing Information for complete safety information and the use of AzaSite®.
In the treatment of bacterial conjunctivitis caused by susceptible isolates of certain microorganisms

DEMONSTRATED RESOLUTION AND ERADICATION¹

In a clinical study of 279 participants with bacterial conjunctivitis¹

**CLINICAL RESOLUTION**

Primary endpoint

**BACTERIAL ERADICATION**

Secondary endpoint

Microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

Study Design: A prospective, randomized, vehicle-controlled, parallel-group, double-masked, multicenter clinical study in 279 participants aged 1 to 96 evaluated the efficacy of azithromycin ophthalmic solution 1% compared to vehicle in a 5-day course of treatment for bacterial conjunctivitis. Subjects received study medication (azithromycin or vehicle) in study eye twice daily on days 1 and 2 and once daily on days 3 through 5. Signs of bacterial conjunctivitis (palpebral conjunctival injection, bulbar conjunctival injection, and ocular discharge) were measured at visit 1 (day 1 [study entry]), visit 2 (day 3 or 4), and visit 3 (day 6 or 7). Both follow-up visits occurred at least 12 hours after the previous dose of study medication. The primary efficacy endpoint was resolution of clinical signs on visit 3 (day 6 or 7). The secondary efficacy endpoint was eradication of causative bacteria on visit 3 (day 6 or 7). Clinical resolution was defined as the absence of the 3 clinical signs (palpebral conjunctival injection, bulbar conjunctival injection, and ocular discharge). Bacterial eradication was defined as the absence of bacterial growth.¹

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In patients receiving systemically administered azithromycin, serious allergic reactions, including angioedema, anaphylaxis, and dermatologic reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported rarely. Although rare, fatalities have been reported.

As with other anti-infectives, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. If super-infection occurs, discontinue use and institute alternative therapy.

Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis.

The most frequently reported ocular adverse reaction reported in clinical trials was eye irritation, which occurred in 1% to 2% of patients. Other adverse reactions associated with the use of AzaSite® were reported in less than 1% of patients and included ocular reactions (blurred vision, burning, stinging and irritation upon instillation, contact dermatitis, corneal erosion, dry eye, eye pain, itching, ocular discharge, punctate keratitis, visual acuity reduction) and nonocular reactions (dysgeusia, facial swelling, hives, nasal congestion, periocular swelling, rash, sinusitis, urticaria).

Please refer to full Prescribing Information for complete safety information and the use of AzaSite®.
AzaSite® helps simplify dosing with the fewest drops approved to treat bacterial conjunctivitis\(^2\)\(^-\)\(^4\).

**RECOMMENDED DOSING SCHEDULE**

<table>
<thead>
<tr>
<th>9 DROPS. 7 DAYS.</th>
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<tr>
<td>AzaSite is dosed as a viscous drop in the affected eye.</td>
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</table>

**AzaSite® is dosed as a viscous drop in the affected eye**

- AzaSite® is a 1% sterile aqueous topical ophthalmic solution of azithromycin formulated in DuraSite® (polycarbophil, edetate disodium, sodium chloride).

**Storage and handling**

- Store unopened bottle under refrigeration at 2°C to 8°C (36°F to 46°F).
- Once the bottle is opened, store at 2°C to 25°C (36°F to 77°F) for up to 14 days. Discard after the 14 days.

**SELECT IMPORTANT SAFETY INFORMATION**

There are no adequate and well-controlled studies in pregnant women. Azithromycin should be used during pregnancy only if clearly needed.

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

Safety and effectiveness of AzaSite® solution in pediatric patients below 1 year of age have not been established.

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

Please refer to full Prescribing Information for complete safety information and the use of AzaSite®.
HELPs TO RESOLVE BACTERIAL CONJUNCTIVITIS

AzaSite® helps resolve bacterial conjunctivitis

AzaSite® is indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following microorganisms: CDC coryneform group G*, Haemophilus influenzae, Staphylococcus aureus, Streptococcus mitis group, and Streptococcus pneumoniae.

*Efficacy for this organism was studied in fewer than 10 infections.

AzaSite® is simple dosing regimen with the fewest drops approved to treat bacterial conjunctivitis

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Unrestricted access to 90% of patients on managed care


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The most frequently reported ocular adverse reaction reported in clinical trials was eye irritation, which occurred in 1% to 2% of patients.

Please refer to full Prescribing Information for complete safety information and the use of AzaSite®


AZASITE is a registered trademark of Insite Vision Incorporated and is used under license. All other trademarks are the property of their respective owners.
**HIGHLIGHTS OF PRESCRIBING INFORMATION**

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

AzaSite® (azithromycin ophthalmic solution) 1%
Sterile topical ophthalmic drops

Initial U.S. Approval: 2007

**RECENT MAJOR CHANGES**

Contraindications (4) 07/2012

**INDICATIONS AND USAGE**

AzaSite is a macrolide antibiotic indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following microorganisms: CDC coryneform group G, Haemophilus influenzae, Staphylococcus aureus, Streptococcus mitis group, and Streptococcus pneumoniae. (1)

**DOSEAGE AND ADMINISTRATION**

Instill 1 drop in the affected eye(s) twice daily, eight to twelve hours apart for the first two days and then instill 1 drop in the affected eye(s) once daily for the next five days. (2)

**FULL PRESCRIBING INFORMATION: CONTENTS**

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2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
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5.2 Anaphylaxis and Hypersensitivity with Systemic Use of Azithromycin
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**DOSEAGE FORMS AND STRENGTHS**

2.5 mL of 1% sterile topical ophthalmic solution. (3)

**CONTRAINDICATIONS**

5.2 Anaphylaxis and Hypersensitivity with Systemic Use of Azithromycin

**WARNINGS AND PRECAUTIONS**

5.1 Topical Ophthalmic Use Only

- For topical ophthalmic use only. (5.1)
- Anaphylaxis and hypersensitivity have been reported with systemic use of azithromycin. (5.2)
- Growth of resistant organisms may occur with prolonged use. (5.3)
- Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis. (5.4)

**ADVERSE REACTIONS**

Most common adverse reaction reported in patients was eye irritation (1-2% of patients). (6)

To report SUSPECTED ADVERSE REACTIONS, contact Akorn, Inc. at 1-800-932-5676 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

Revised: 11/2013

**FULL PRESCRIBING INFORMATION**

1 INDICATIONS AND USAGE
AzaSite® is indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following microorganisms:

CDC coryneform group G
Haemophilus influenzae
Staphylococcus aureus
Streptococcus mitis group
Streptococcus pneumoniae

1.1 Description

Azithromycin is a macrolide antibiotic with a 15-membered ring, its chemical name is (2R,3S,4R,5R,8R,10R,11S,13R,14R)-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-D-ribohexitopyranosyl)oxy]-2-ethyl-3,4,10,11-tetrahydro-3,5,6,8,10,12,14-heptamethyl-11-[(3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl)oxy]-1-oxa-6-aza-cyclopentadecan-15-one, and the structural formula is:

![Structural formula of azithromycin](image)

Azithromycin has a molecular weight of 749, and its empirical formula is C_{38}H_{72}N_{2}O_{12}.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Azithromycin is a macrolide antibiotic [see Clinical Pharmacology (12.1)].

12.3 Pharmacokinetics

The plasma concentration of azithromycin following ocular administration of AzaSite (azithromycin ophthalmic solution) in humans is unknown. Based on the proposed dose of one drop to each eye (total dose of 100 mcL or 1 mg) and exposure information from systemic administration, the systemic concentration of azithromycin following ocular administration is estimated to be below quantifiable limits (≤10 ng/mL) at steady-state in humans, assuming 100% systemic availability.

12.4 Microbiology
Azithromycin acts by binding to the 50S ribosomal subunit of susceptible microorganisms and interfering with bacterial protein synthesis.

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

- CDC coryneform group G
- Haemophilus influenzae
- Staphylococcus aureus
- Streptococcus mitis group
- Streptococcus pneumoniae

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy

- Pregnancy Category B. Reproduction studies have been performed in rats and mice at doses up to 200 mg/kg/day.
- The highest dose was associated with moderate maternal toxicity. These doses are estimated to be approximately 5,000 times the maximum human ocular daily dose of 2 mg.

In the animal studies, no evidence of harm to the fetus due to azithromycin was found. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, azithromycin should be used during pregnancy only if clearly needed.

8.3 Nursing Mothers

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

8.4 Pediatric Use

The safety and effectiveness of AzaSite solution in pediatric patients below 1 year of age have not been established. The efficacy of AzaSite in treating bacterial conjunctivitis in pediatric patients one year or older has been demonstrated in controlled clinical trials [see Clinical Studies (14)].

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

11 DESCRIPTION

AzaSite (azithromycin ophthalmic solution) is a 1% sterile aqueous topical ophthalmic solution of azithromycin formulated in DuraSite® (polycarbophil, edetate disodium, sodium chloride). AzaSite is an off-white, viscous liquid with an osmolality of approximately 290 mOsm/kg.

Preservative: 0.003% benzalkonium chloride. Inactives: mannitol, citric acid, sodium citrate, poloxamer 407, polycarbophil, edetate disodium (EDTA), sodium chloride, water for injection, and sodium hydroxide to adjust pH to 6.3.

Azithromycin is a macrolide antibiotic with a 15-membered ring. Its chemical name is (2R,3S,4R,5R,8R,10R,11S,13R,14R)·13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-D-ribohexitopyranosyl)oxy]-2-ethyl-3.4,10,11-tetrahydro-3,5,6,8,10,12,14-heptamethyl-11-[(3,4,6-trideoxy-3-(dimethylamino)-β-D-xylo-hexopyranosyl)oxy]-1-oxa-6-aza-cyclopentadecan-15-one, and the structural formula is: C_{38}H_{72}N_{2}O_{12}.
The following in vitro data are also available, but their clinical significance in ophthalmic infections is unknown. The safety and effectiveness of AzaSite in treating ophthalmological infections due to these microorganisms have not been established. The following microorganisms are considered susceptible when evaluated using systemic break points. However, a correlation between the in vitro systemic breakpoint and ophthalmological infection has not been established. This list of microorganisms is provided as an aid only in assessing the potential treatment of conjunctival infections. Azithromycin exhibits in vitro minimal inhibitory concentrations (MICs) of equal or less (systemic susceptible breakpoint) against most (≥80%) of isolates of the following ocular pathogens: Chlamydia pneumoniae, Chlamydia trachomatis, Legionella pneumophila, Moraxella catharralis, Mycoplasma hominis, Mycoplasma pneumoniae, Neisseria gonorrhoeae, Peptostreptococcus species, Streptococci (Groups C, F, G), Streptococcus pyogenes, Streptococcus agalactiae, Ureaplasma urealyticum, Viridans group streptococci.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate carcinogenic potential. Azithromycin has shown no mutagenic potential in standard laboratory tests: mouse lymphoma assay, human lymphocyte clastogenic assay, and mouse bone marrow clastogenic assay. No evidence of impaired fertility due to azithromycin was found in mice or rats that received dosages of up to 200 mg/kg/day.

13.2 Animal Toxicology and/or Pharmacology
Phospholipidosis (intracellular phospholipid accumulation) has been observed in some tissues of mice, rats, and dogs given multiple systemic doses of azithromycin. Cytoplasmic microvacuolation, which is likely a manifestation of phospholipidosis, has been observed in the corneas of rabbits given multiple ocular doses of AzaSite. This effect was reversible upon cessation of AzaSite treatment. The significance of this toxicological finding for animals and for humans is unknown.

14 CLINICAL STUDIES
In a randomized, vehicle-controlled, double-blind, multicenter clinical study in which patients were dosed twice daily for the first two days, then once daily on days 3, 4, and 5. AzaSite solution was superior to vehicle on days 6-7 in patients who had a confirmed clinical diagnosis of bacterial conjunctivitis. Clinical resolution was achieved in 83% (250/302) of patients treated with AzaSite versus 55% (74/145) of patients treated with vehicle. The p-value for the comparison was 0.03 and the 95% confidence interval around the 13% (83%-50%) difference was 2% to 25%. The microbiological success rate for the eradication of the baseline pathogens was approximately 88% compared to 66% of patients treated with vehicle (p<0.001, confidence interval around the 22% difference was 13% to 31%). Microbiological eradication does not always correlate with clinical outcome in anti-infective trials.

16 HOW SUPPLIED/STORAGE AND HANDLING
AzaSite is a sterile aqueous topical ophthalmic formulation of 1% azithromycin.

NDC 17478-307-02: 2.5 mL in 5 mL bottle containing a total of 25 mg of azithromycin in a white, round, low-density polyethylene (LDPE) bottle, with a clear LDPE dropper tip, and a tan colored high density polyethylene (HDPE) eyedropper cap. A white tamper evident over-cap is provided.

NDC 17478-307-04: 2.5 mL in 4 mL bottle containing a total of 25 mg of azithromycin in a white, round, low-density polyethylene (LDPE) bottle, with a clear LDPE dropper tip, and a tan colored high density polyethylene (HDPE) eyedropper cap. A white tamper evident over-cap is provided.

Storage and Handling:
Store unopened bottle under refrigeration at 2°C to 8°C (36°F to 46°F). Once the bottle is opened, store at 2°C to 25°C (36°F to 77°F) for up to 14 days. Discard after the 14 days.

17 PATIENT COUNSELING INFORMATION
See FDA-Approved Patient Labeling (Patient Information). Patients should be advised to avoid contaminating the applicator tip by allowing it to touch the eye, fingers or other sources.

Patients should be directed to discontinue use and contact a physician if any signs of an allergic reaction occur. Patients should be told that although it is common to feel better early in the course of the 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 AzaSite (azithromycin ophthalmic solution) or other antibacterial drugs in the future.

Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis. Patients should be advised to thoroughly wash hands prior to treatment and (2) increase the likelihood that bacteria may not improve from AzaSite or other drugs that treat infections from bacteria.

18 WHAT SHOULD I BE AWARE OF WHILE USING AzaSite?
Do not wear contact lenses if you have signs or symptoms of bacterial conjunctivitis and until you have finished your prescribed course of treatment. The symptoms of bacterial conjunctivitis may include:
- discharge coming from the eye
- eye redness
- eye irritation

Your doctor can tell you if you have bacterial conjunctivitis.

Severe allergic reactions have been reported rarely when azithromycin has been taken by mouth.

- Serious rash or serious allergic reactions may occur. Azithromycin, the active ingredient in AzaSite, may cause a serious rash or a serious allergic reaction. Both of these reactions may need to be treated in a hospital and may be life-threatening.
- Stop taking AzaSite and call your doctor right away or get emergency help if you have any of these symptoms:
  - skin rash, hives, sores in your mouth, or your skin blisters and peels
  - swelling of your face, eyes, lips, tongue, or throat
  - trouble swallowing or breathing

Increased risk of other infections caused by bacteria or fungi.

- Using AzaSite for a long time may cause other bacteria or fungi to grow. If this happens you may get a new infection. Tell your doctor right away if your symptoms do not get better.

What are the possible side effects of AzaSite?
The most common side effect of AzaSite is eye irritation.

Other side effects seen with AzaSite include:
- eye burning, stinging and irritation when the drop hits your eye.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use AzaSite for a condition for which it was not prescribed. Do not give AzaSite to other people, even if they have the same symptoms that you have. It may harm them.

This Patient Information summarizes the most important information about AzaSite. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about AzaSite that is written for health professionals.

For more information, go to www.azasite.com or call 1-800-932-5676.

What are the ingredients in AzaSite?
Active ingredient: azithromycin
Inactive ingredients: 0.003% benzalkonium chloride, mannitol, citric acid, sodium citrate, poloxamer 407, polycarbophil, edetate disodium (EDTA), sodium chloride, water, and sodium hydroxide.

Instructions for Use
AzaSite® (A- zuh-site) (azithromycin ophthalmic solution) 1%
Read this Instructions for Use for AzaSite before you start using it and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your doctor about your medical condition or treatment.

Important:
• AzaSite is for use as an eye drop only.
The checklist below tells you when to use your medicine for each eye that has bacterial conjunctivitis:

|   | Day 1: |   | Day 2: |   | Day 3: |   | Day 4: |   | Day 5: |   | Day 6: |   | Day 7: |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
|   | 1 drop in the morning and 1 drop in the evening | 1 drop in the morning and 1 drop in the evening | 1 drop anytime during the day | 1 drop anytime during the day | 1 drop anytime during the day | 1 drop anytime during the day | 1 drop anytime during the day |

This is a total of 9 drops of AzaSite for each infected eye.
• Avoid letting the applicator tip touch your eye, your fingers, or other objects.
• If a drop misses your eye, try again.
• Follow the steps below to use AzaSite correctly.

Before using a new bottle of AzaSite:

• Turn the white cap clockwise until it comes off. Throw away the white cap. See Figure A
• Hold the bottle straight, turn the tan cap counterclockwise until it comes off. Put the tan cap back on the bottle and close tightly. (This lets out the air.) See Figure B

Wash your hands each time you use AzaSite.

To use AzaSite:
Step 1. Turn the closed bottle upside down. See Figure C
Step 2. Shake your hand firmly. This helps move the medicine into the tip of the bottle. See Figure D
Step 3. Hold the bottle upside down and take off the tan cap. See Figure E
Step 4. Tilt your head back. Hold the bottle over your eye and gently squeeze the bottle to let 1 drop into each eye that has bacterial conjunctivitis. Put the tan cap back on the bottle and close tightly. See Figure F

If a drop does not come out of the bottle, repeat steps one to four.

This Patient Information and Instructions for Use have been approved by the U.S. Food and Drug Administration.

OPZTA0N Rev. 02/15