CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

050814Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

CAYSTON® (aztreonam for inhalation solution)
Initial U.S. Approval: 1986

To reduce the development of drug-resistant bacteria and maintain the effectiveness of CAYSTON and other antibacterial drugs, CAYSTON should be used only to treat patients with cystic fibrosis (CF) known to have *Pseudomonas aeruginosa* in the lungs.

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

CAYSTON is a monobactam antibacterial indicated to improve respiratory symptoms in cystic fibrosis (CF) patients with *Pseudomonas aeruginosa*. Safety and effectiveness have not been established in pediatric patients below the age of 7 years, patients with FEV_1 <25% or >75% predicted, or patients colonized with *Burkholderia cepacia*. (1)

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

• Administer one dose (one single use vial and one ampule of diluent) 3 times a day for 28 days. (2.1)
• Use dose immediately after reconstitution. (2.2)
• Administer only with the Altera® Nebulizer System. Do not administer with any other type of nebulizer. (2.3)

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

• Lyophilized aztreonam (75 mg/vial) (3)
• Diluent (0.17% sodium chloride): 1 mL/ampule (3)

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

• Do not administer to patients with a known allergy to aztreonam. (4)

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

• Allergic reaction to CAYSTON was seen in clinical trials. Stop treatment if an allergic reaction occurs. Use caution when CAYSTON is administered to patients with a known allergic reaction to beta-lactams. (5.1)
• Bronchospasm has been reported with CAYSTON. Stop treatment if chest tightness develops during nebulizer use. (5.2)

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

• Common adverse reactions (more than 5%) occurring more frequently in CAYSTON patients are cough, nasal congestion, wheezing, pharyngolaryngeal pain, pyrexia, chest discomfort, abdominal pain and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Gilead Sciences, Inc. at 1-800-GILEAD5, option 3 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-Approved Patient Labeling

Revised: February 2010

FULL PRESCRIBING INFORMATION: CONTENTS*

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

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1 INDICATIONS AND USAGE

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To reduce the development of drug-resistant bacteria and maintain the effectiveness of CAYSTON and other antibacterial drugs, CAYSTON should be used only to treat patients with CF known to have *Pseudomonas aeruginosa* in the lungs.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The recommended dose of CAYSTON for both adults and pediatric patients 7 years of age and older is one single-use vial (75 mg of aztreonam) reconstituted with 1 mL of sterile diluent administered 3 times a day for a 28-day course (followed by 28 days off CAYSTON therapy). Dosage is not based on weight or adjusted for age. Doses should be taken at least 4 hours apart.

CAYSTON is administered by inhalation using an Altera® Nebulizer System. Patients should use a bronchodilator before administration of CAYSTON.

2.2 Instructions for CAYSTON Reconstitution

CAYSTON should be administered immediately after reconstitution. Do not reconstitute CAYSTON until ready to administer a dose.

Take one amber glass vial containing CAYSTON and one diluent ampule from the carton. To open the glass vial, carefully remove the metal ring by pulling the tab and remove the gray rubber stopper. Twist the tip off the diluent ampule and squeeze the liquid into the glass vial. Replace the rubber stopper, then gently swirl the vial until contents have completely dissolved.

The empty vial, stopper, and diluent ampule should be disposed of properly upon completion of dosing.

2.3 Instructions for CAYSTON Administration

CAYSTON is administered by inhalation using an Altera Nebulizer System. CAYSTON should not be administered with any other nebulizer. CAYSTON should not be mixed with any other drugs in the Altera Nebulizer Handset.

CAYSTON is not for intravenous or intramuscular administration.

Patients should use a bronchodilator before administration of CAYSTON. Short-acting bronchodilators can be taken between 15 minutes and 4 hours prior to each dose of CAYSTON. Alternatively, long-acting bronchodilators can be taken between 30 minutes and 12 hours prior to administration of CAYSTON. For patients taking multiple inhaled therapies, the recommended order of administration is as follows: bronchodilator, mucolytics, and lastly, CAYSTON.

To administer CAYSTON, pour the reconstituted solution into the handset of the nebulizer system. Turn the unit on. Place the mouthpiece of the handset in your mouth and breathe normally only through your mouth. Administration typically takes between 2 and 3 minutes. Further patient instructions on how to administer CAYSTON are provided in the FDA-approved patient labeling. Instructions on testing nebulizer functionality and cleaning the handset are provided in the Instructions for Use included with the nebulizer system.

3 DOSAGE FORMS AND STRENGTHS

A dose of CAYSTON consists of a single-use vial of sterile, lyophilized aztreonam (75 mg) reconstituted with a 1 mL ampule of sterile diluent (0.17% sodium chloride). Reconstituted CAYSTON is administered by inhalation.

4 CONTRAINDICATIONS

CAYSTON is contraindicated in patients with a known allergy to aztreonam.

5 WARNINGS AND PRECAUTIONS

5.1 Allergic Reactions

Severe allergic reactions have been reported following administration of aztreonam for injection to patients with no known history of exposure to aztreonam. In addition, allergic reaction with facial rash, facial swelling, and throat tightness was

reported with CAYSTON in clinical trials. If an allergic reaction to CAYSTON occurs, stop administration of CAYSTON and initiate treatment as appropriate.

Caution is advised when administering CAYSTON to patients if they have a history of beta-lactam allergy, although patients with a known beta-lactam allergy have received CAYSTON in clinical trials and no severe allergic reactions were reported. A history of allergy to beta-lactam antibiotics, such as penicillins, cephalosporins, and/or carbapenems, may be a risk factor, since cross-reactivity may occur.

5.2 Bronchospasm

Bronchospasm is a complication associated with nebulized therapies, including CAYSTON. Reduction of 15% or more in forced expiratory volume in 1 second (FEV_1) immediately following administration of study medication after pretreatment with a bronchodilator was observed in 3% of patients treated with CAYSTON.

5.3 Decreases in FEV_1 After 28-Day Treatment Cycle

In clinical trials, patients with increases in FEV_1 during a 28-day course of CAYSTON were sometimes treated for pulmonary exacerbations when FEV_1 declined after the treatment period. Healthcare providers should consider a patient's baseline FEV_1 measured prior to CAYSTON therapy and the presence of other symptoms when evaluating whether post-treatment changes in FEV_1 are caused by a pulmonary exacerbation.

5.4 Development of Drug-Resistant Bacteria

Prescribing CAYSTON in the absence of known *Pseudomonas aeruginosa* infection in patients with CF is unlikely to provide benefit and increases the risk of development of drug-resistant bacteria.

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 drugs cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of CAYSTON was evaluated in 344 patients from two placebo-controlled trials and one open-label follow-on trial. In controlled trials, 146 patients with CF received 75 mg CAYSTON 3 times a day for 28 days.

Table 1 displays adverse reactions reported in more than 5% of patients treated with CAYSTON 3 times a day in placebo-controlled trials. The listed adverse reactions occurred more frequently in CAYSTON-treated patients than in placebo-treated patients.

Table 1. Adverse Reactions Reported in more than 5% of Patients Treated with CAYSTON in the Placebo-Controlled Trials

Event (Preferred Term)	Placebo (N = 160) n (%)	CAYSTON 75 mg 3 times a day (N = 146) n (%)
Cough	82 (51%)	79 (54%)
Nasal congestion	19 (12%)	23 (16%)
Wheezing	16 (10%)	23 (16%)
Pharyngolaryngeal pain	17 (11%)	18 (12%)
Pyrexia	9 (6%)	19 (13%)
Chest discomfort	10 (6%)	11 (8%)
Abdominal Pain	8 (5%)	10 (7%)
Vomiting	7 (4%)	9 (6%)

Adverse reactions that occurred in less than 5% of patients treated with CAYSTON were bronchospasm (3%) [*see Warnings and Precautions (5.2)*] and rash (2%).

7 DRUG INTERACTIONS

No formal clinical studies of drug interactions with CAYSTON have been conducted.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B

No reproductive toxicology studies have been conducted with CAYSTON. However, studies were conducted with aztreonam for injection. Aztreonam has been shown to cross the placenta and enter fetal circulation. No evidence of embryo or fetotoxicity or

teratogenicity has been shown in studies with pregnant rats and rabbits. In rats receiving aztreonam for injection during late gestation and lactation, no drug induced changes in maternal, fetal or neonatal parameters were observed. These animal reproduction and developmental toxicity studies used parenteral routes of administration that would provide systemic exposures far in excess of the average peak plasma levels measured in humans following CAYSTON therapy.

No adequate and well-controlled studies of aztreonam for injection or CAYSTON in pregnant women have been conducted. Because animal reproduction studies are not always predictive of human response, CAYSTON should be used during pregnancy only if clearly needed.

8.3 Nursing Mothers

Following administration of aztreonam for injection, aztreonam is excreted in human milk at concentrations that are less than one percent of those determined in simultaneously obtained maternal serum. Peak plasma concentrations of aztreonam following administration of CAYSTON (75 mg) are approximately 1% of peak concentrations observed following IV aztreonam (500 mg). Therefore, use of CAYSTON during breastfeeding is unlikely to pose a risk to infants.

8.4 Pediatric Use

Patients 7 years and older were included in clinical trials with CAYSTON. Fifty-five patients under 18 years of age received CAYSTON in placebo-controlled trials. No dose adjustments were made for pediatric patients. Pyrexia was more commonly reported in pediatric patients than in adult patients. Safety and effectiveness in pediatric patients below the age of 7 years have not been established.

8.5 Geriatric Use

Clinical trials of CAYSTON did not include CAYSTON-treated patients aged 65 years of age and older to determine whether they respond differently from younger patients.

8.6 Use in Patients with Renal Impairment

Aztreonam is known to be excreted by the kidney. Placebo-controlled clinical trials with CAYSTON excluded patients with abnormal baseline renal function (defined as serum creatinine greater than 2 times the upper limit of normal range). Given the low systemic

exposure of aztreonam following administration of CAYSTON, clinically relevant accumulation of aztreonam is unlikely to occur in patients with renal impairment. Therefore, CAYSTON may be administered to patients with mild, moderate and severe renal impairment with no dosage adjustment.

10 OVERDOSAGE

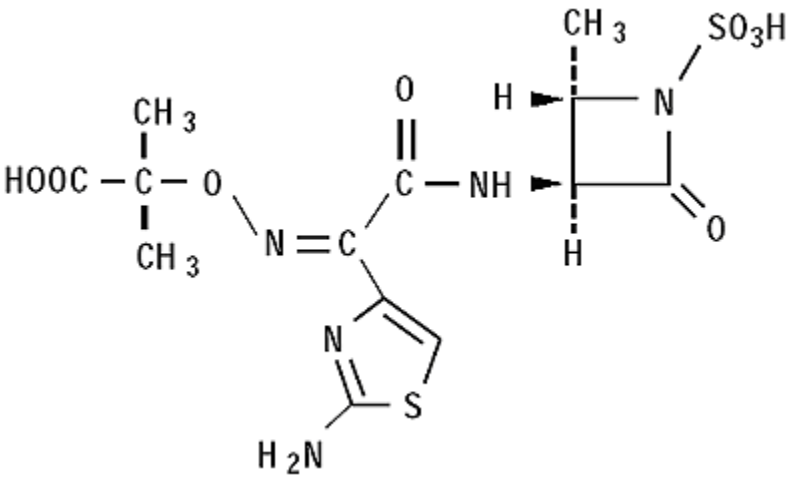
No overdoses have been reported with CAYSTON in clinical trials to date. In clinical trials, 225 mg doses of CAYSTON via inhalation were associated with higher rates of drug-related respiratory adverse reactions, particularly cough. Since the peak plasma concentration of aztreonam following administration of CAYSTON (75 mg) is approximately 0.6 mcg/mL, compared to a serum concentration of 54 mcg/mL following administration of aztreonam for injection (500 mg), no systemic safety issues associated with CAYSTON overdose are anticipated.

11 DESCRIPTION

A dose of CAYSTON consists of a 2 mL amber glass vial containing lyophilized aztreonam (75 mg) and lysine (46.7 mg), and a low-density polyethylene ampule containing 1 mL sterile diluent (0.17% sodium chloride). The reconstituted solution is for inhalation. The formulation contains no preservatives or arginine.

The active ingredient in CAYSTON is aztreonam, a monobactam antibacterial. The monobactams are structurally different from beta-lactam antibiotics (e.g., penicillins, cephalosporins, carbapenems) due to a monocyclic nucleus. This nucleus contains several side chains; sulfonic acid in the 1-position activates the nucleus, an aminothiazolyl oxime side chain in the 3-position confers specificity for aerobic Gram-negative bacteria including *Pseudomonas spp*., and a methyl group in the 4-position enhances beta-lactamase stability.

Aztreonam is designated chemically as (*Z*)-2-[[[(2-amino-4-thiazolyl)[[(2*S*,3*S*)-2-methyl-4-oxo-1-sulfo-3-azetidinyl]carbamoyl]methylene]amino]oxy]-2-methylpropionic acid. The structural formula is presented below:



CAYSTON is a white to off-white powder. CAYSTON is sterile, hygroscopic, and light sensitive. Once reconstituted with the supplied diluent, the pH range is 4.5 to 6.0.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Aztreonam is an antibacterial drug [*see Clinical Pharmacology (12.4)*].

12.3 Pharmacokinetics

Sputum Concentrations
Sputum aztreonam concentrations exhibited considerable variability between patients receiving CAYSTON (75 mg) in clinical trials. The mean sputum concentration 10 minutes following the first dose of CAYSTON (n = 195 patients with CF) was 726 mcg/g. Mean sputum concentrations of aztreonam in patients receiving CAYSTON 3 times a day for 28 days were 984 mcg/g, 793 mcg/g, and 715 mcg/g 10 minutes after dose administration on Days 0, 14, and 28, respectively, indicating no accumulation of aztreonam in sputum.

Plasma Concentrations
Plasma aztreonam concentrations exhibited considerable variability between patients receiving CAYSTON (75 mg) in the clinical trials. The mean plasma concentration one hour following the first dose of CAYSTON (at approximately the peak plasma concentration) was 0.59 mcg/mL. Mean peak plasma concentrations in patients receiving CAYSTON 3 times a day for 28 days were 0.55 mcg/mL, 0.67 mcg/mL, and 0.65 mcg/mL on Days 0, 14, and 28, respectively,

indicating no systemic accumulation of aztreonam. In contrast, the serum concentration of aztreonam following administration of aztreonam for injection (500 mg) is approximately 54 mcg/mL.

Absorption

Evaluation of plasma and urine aztreonam concentrations following administration of CAYSTON indicates low systemic absorption of aztreonam. Approximately 10% of the total CAYSTON dose is excreted in the urine as unchanged drug, as compared to 60–65% following intravenous administration of aztreonam for injection.

Distribution

The protein binding of aztreonam in serum is approximately 56% and is independent of dose.

Metabolism

Following intramuscular administration of aztreonam for injection 500 mg every 8 hours for 7 days, approximately 6% of the dose was excreted as a microbiologically inactive open β-lactam ring hydrolysis product in an 8-hour urine collection on the last day of multiple dosing.

Excretion

The elimination half-life of aztreonam from plasma is approximately 2.1 hours following administration of CAYSTON to adult patients with CF, similar to what has been reported for aztreonam for injection. Approximately 10% of the total CAYSTON dose is excreted in the urine as unchanged drug. Systemically absorbed aztreonam is eliminated about equally by active tubular secretion and glomerular filtration. Following administration of a single intravenous dose of radiolabeled aztreonam for injection, about 12% of the dose was recovered in the feces.

12.4 Microbiology

Mechanism of Action

Aztreonam exhibits activity *in vitro* against Gram-negative aerobic pathogens including *P. aeruginosa*. Aztreonam binds to penicillin-binding proteins of susceptible bacteria, which leads to inhibition of bacterial cell wall synthesis and death of the cell. Aztreonam activity is not decreased in the presence of CF lung secretions.

Susceptibility Testing

A single sputum sample from a patient with CF may contain multiple morphotypes of *P. aeruginosa* and each morphotype may have a different level of *in vitro* susceptibility to aztreonam. There are no *in vitro* susceptibility test interpretive criteria for isolates of *P. aeruginosa* obtained from the sputum of CF patients.[1]

Development of Resistance

No changes in the susceptibility of *P. aeruginosa* to aztreonam were observed following a 28-day course of CAYSTON in the placebo-controlled trials.

Cross-Resistance

No cross-resistance to other classes of antibiotics, including aminoglycosides, quinolones, and beta-lactams, was observed following a 28-day course of CAYSTON in the Phase 3 placebo-controlled trials or in an open-label follow-on trial of up to nine 28-day courses of 75 mg CAYSTON 3 times a day.

Other

No trends in the treatment-emergent isolation of other bacterial respiratory pathogens (*Burkholderia cepacia*, *Stenotrophomonas maltophilia*, *Achromobacter xylosoxidans*, and *Staphylococcus aureus*) were observed in clinical trials. There was a slight increase in the isolation of *Candida spp*. following up to nine 28-day courses of CAYSTON therapy.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

A 104-week rat inhalation toxicology study to assess the carcinogenic potential of aztreonam demonstrated no drug-related increase in the incidence of tumors. Rats were exposed to aztreonam for up to 4 hours per day. Peak plasma levels of aztreonam averaging approximately 6.8 mcg/mL were measured in rats at the highest dose level. This is approximately 12-fold higher than the average peak plasma level measured in humans following CAYSTON therapy.

Genetic toxicology studies performed *in vitro* demonstrated that aztreonam did not induce structural chromosome aberrations in CHO cells and did not induce mutations at the TK locus in mouse lymphoma L5178Y $TK^{+/-}$ cells. Likewise, genetic toxicology

studies performed *in vivo* did not reveal evidence of mutagenic potential.

Aztreonam did not impair the fertility of rats when administered at doses that would provide systemic exposures far in excess of peak plasma levels measured in humans following CAYSTON therapy.

14 CLINICAL STUDIES

CAYSTON was evaluated over a period of 28 days of treatment in a randomized, double-blind, placebo-controlled, multicenter trial that enrolled patients with CF and *P. aeruginosa*. This trial was designed to evaluate improvement in respiratory symptoms. Patients 7 years of age and older and with FEV_1 of 25% to 75% predicted were enrolled. All patients received CAYSTON or placebo on an outpatient basis administered with the Altera Nebulizer System. All patients were required to take a dose of an inhaled bronchodilator (beta-agonist) prior to taking a dose of CAYSTON or placebo. Patients were receiving standard care for CF, including drugs for obstructive airway diseases.

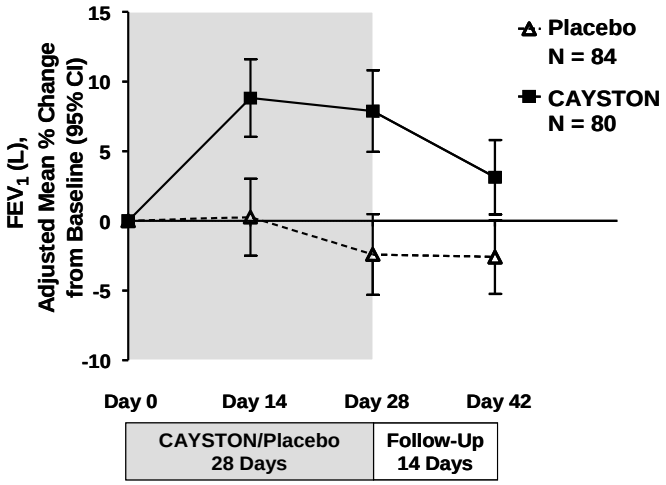
The trial enrolled 164 patients with CF and *P. aeruginosa*. The mean age was 30 years, and the mean baseline FEV_1 % predicted was 55%; 43% were females and 96% were Caucasian. These patients were randomized in a 1:1 ratio to receive either CAYSTON (75 mg) or volume-matched placebo administered by inhalation 3 times a day for 28 days. Patients were required to have been off antibiotics for at least 28 days before treatment with study drug. The primary efficacy endpoint was improvement in respiratory symptoms on the last day of treatment with CAYSTON or placebo. Respiratory symptoms were also assessed two weeks after the completion of treatment with CAYSTON or placebo. Changes in respiratory symptoms were assessed using a questionnaire that asks patients to report on symptoms like cough, wheezing, and sputum production.

Improvement in respiratory symptoms was noted for CAYSTON-treated patients relative to placebo-treated patients on the last day of drug treatment. Statistically significant improvements were seen in both adult and pediatric patients, but were substantially smaller in adult patients. Two weeks after completion of treatment, a difference in respiratory symptoms between treatment groups was still present, though the difference was smaller.

Pulmonary function, as measured by FEV_1 (L), increased from baseline in patients treated with CAYSTON (see Figure 1). The treatment difference at Day 28 between CAYSTON-treated and

placebo-treated patients for percent change in FEV_1 (L) was statistically significant at 10% (95% CI: 6%, 14%). Improvements in FEV_1 were comparable between adult and pediatric patients. Two weeks after completion of drug treatment, the difference in FEV_1 between CAYSTON and placebo groups had decreased to 6% (95% CI: 2%, 9%).

Figure 1. Adjusted Mean Percent Change in FEV_1 from Baseline to Study End (Days 0-42).



15 REFERENCES

1. Clinical and Laboratory Standards Institute (CLSI). Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically—Eighth Edition; Approved Standard. CLSI Document M7-A8. CLSI, Wayne, PA 19087. January, 2009.

16 HOW SUPPLIED/STORAGE AND HANDLING

Each kit for a 28-day course of CAYSTON contains 84 sterile vials of CAYSTON and 88 ampules of sterile diluent packed in 2 cartons, each carton containing a 14-day supply. The four additional diluent ampules are provided in case of spillage.

Package Configuration	Dosage Strength	NDC No.
28-Day Kit	75 mg	61958-0901-1

CAYSTON vials and diluent ampules should be stored in the refrigerator at 2 °C to 8 °C (36 °F to 46 °F) until needed. Once removed from the refrigerator, CAYSTON and diluent may be stored at room temperature (up to 25 °C/77 °F) for up to 28 days. Do not separate the CAYSTON vials from the diluent ampules. CAYSTON should be protected from light.

Do not use CAYSTON if it has been stored at room temperature for more than 28 days. Do not use CAYSTON beyond the expiration date stamped on the vial. Do not use diluent beyond the expiration date embossed on the ampule.

CAYSTON should be used immediately upon reconstitution. Do not reconstitute more than one dose at a time.

Do not use diluent or reconstituted CAYSTON if it is cloudy or if there are particles in the solution.

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling

Patients should be advised that CAYSTON is for inhalation use only and that CAYSTON should only be administered using the Altera Nebulizer System. Patients should be instructed only to reconstitute CAYSTON with the provided diluent and not mix other drugs with CAYSTON in the Altera Nebulizer System.

Patients should be advised to complete the full 28-day course of CAYSTON even if they are feeling better. Inform the patient that if they miss a dose, they should take all 3 daily doses as long as the doses are at least 4 hours apart.

Patients should be advised to use a bronchodilator prior to administration of CAYSTON. Patients taking several inhaled medications should be advised to use the medications in the following order of administration: bronchodilator, mucolytics, and lastly, CAYSTON.

Patients should be advised to tell their doctor if they have new or worsening symptoms. Patients who believe they are experiencing an allergic reaction to CAYSTON should be advised to contact their doctor immediately.

Patients should be counseled that antibacterial drugs including CAYSTON should only be used to treat bacterial infections. They do not treat viral infection (e.g., the common cold). When CAYSTON 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 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 CAYSTON or other antibacterial drugs in the future.

Manufactured by: Gilead Sciences, Inc., Foster City, CA 94404

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50-814-DGS-002

FDA-Approved Patient Labeling

Patient Information

CAYSTON® (kay-stun)
(aztreonam for inhalation solution)

Read this Patient Information before you start taking CAYSTON and each time you get a refill. This information does not take the place of talking with your doctor about your medical condition or your treatment.

What is CAYSTON?
CAYSTON is a prescription inhaled antibiotic. CAYSTON is used to improve breathing symptoms in people with cystic fibrosis (CF) who have *Pseudomonas aeruginosa (P. aeruginosa)* in their lungs.

CAYSTON is only for infections caused by bacteria. It is not for infections caused by viruses, such as the common cold.

CAYSTON is used only with the Altera® Nebulizer System.

It is not known if CAYSTON is safe and effective in children under the age of 7.

Who should not take CAYSTON?
Do not take CAYSTON if you are allergic to aztreonam (AZACTAM®).

What should I tell my doctor before taking CAYSTON?
Before taking CAYSTON, tell your doctor if you:

- are allergic to any antibiotics.
- are pregnant or plan to become pregnant.
- are breast-feeding or plan to breast feed. Talk to your doctor about the best way to breast feed your baby if you take CAYSTON.

Tell your doctor about all the medicine you take, including prescription and non-prescription medicines, vitamins and herbal supplements.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I take CAYSTON?

- Take CAYSTON exactly as prescribed by your doctor.

- The dose of CAYSTON for both adults and children 7 years of age and older is one vial of CAYSTON, mixed with one ampule of saline (diluent) 3 times a day.
- Doses of CAYSTON should be taken at least 4 hours apart (for example: morning, after school, and before bed).
- CAYSTON should be taken for 28 days.
- CAYSTON is taken as a breathing treatment (inhalation) with the Altera Nebulizer System. Do not use any other nebulizer for your CAYSTON treatment.
- You should use an inhaled bronchodilator (a type of medicine used to relax and open your airways) before taking a dose of CAYSTON. If you do not have an inhaled bronchodilator, ask your doctor to prescribe one for you.
- If you are taking several medicines or treatments to treat your cystic fibrosis, you should take your medicines or other treatments in this order:
    1) bronchodilator
    2) mucolytics (medicines to help clear mucus from your lungs)
    3) CAYSTON
- You should take CAYSTON as prescribed, in courses of 28 days on CAYSTON, followed by at least 28 days off CAYSTON, as directed by your doctor.
- Do not mix CAYSTON with any other medicines in your Altera Nebulizer System.
- Do not mix CAYSTON with the saline until right before you are ready to use it. Do not mix more than one dose of CAYSTON at a time.
- Each treatment should take about 2 to 3 minutes.
- If you miss a dose of CAYSTON, you can still take all 3 daily doses as long as they are at least 4 hours apart.
- It is important for you to finish taking the full 28-day course of CAYSTON even if you are feeling better. If you skip doses or do not finish the full 28-day course of CAYSTON, your infection may not be fully treated and CAYSTON may not work as well as a treatment for infections in the future.
- See the end of this Patient Information leaflet for the Patient Instructions for Use on how to take CAYSTON the right way.

What are the possible side effects of CAYSTON?

CAYSTON can cause serious side effects, including:

- **Severe allergic reactions. Stop your treatment with CAYSTON and call your doctor right away if you have any symptoms of an allergic reaction, including:**
    - Rash or swelling of your face
    - Throat tightness

- **Trouble breathing right after treatment with CAYSTON (bronchospasm).** To decrease the chance of this happening, be sure to use your inhaled bronchodilator medicine before each treatment with CAYSTON. See "How should I take CAYSTON?"

Common side effects of CAYSTON include:

- Cough
- Nasal congestion
- Wheezing
- Sore throat
- Fever. Fever may be more common in children than in adults.
- Chest discomfort
- Stomach area (abdominal) pain
- Vomiting

Tell your doctor if you have any new or worsening symptoms while taking CAYSTON. Tell your doctor about any side effect that bothers you or that does not go away.

These are not all the possible side effects of CAYSTON. For more information, ask your doctor or pharmacist.

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 CAYSTON?

- Each CAYSTON kit contains enough vials of CAYSTON and ampules of saline for 28 days of treatment. There are 4 extra saline ampules in case some saline spills.
- Always keep your CAYSTON and saline together.
- Store CAYSTON and saline in the refrigerator at 36 °F to 46 °F (2 °C to 8 °C) until needed.
- When you remove CAYSTON and saline from the refrigerator, they may be stored at room temperature (less than 77 °F) for up to 28 days. Do not use any CAYSTON that has been stored at room temperature for more than 28 days.
- Keep CAYSTON away from light.
- Do not use CAYSTON after the expiration date on the vial. Do not use the saline after the expiration date on the ampule.

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

General information about CAYSTON

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use CAYSTON for a condition for which it was not prescribed. Do not give CAYSTON to other people, even if they have the same symptoms that you have. It may harm them.

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

For more information, call 1-877-7CAYSTON (1-877-722-9786).

What are the ingredients in CAYSTON?
Active ingredient: aztreonam
Inactive ingredient: sodium chloride (diluent)

Patient Instructions for Use

CAYSTON®
(aztreonam for inhalation solution)

Be sure that you read, understand and follow the Patient Instructions for Use below for the right way to take CAYSTON. If you have any questions, ask your doctor or pharmacist.

You will need the following supplies (Figure 1):

- 1 amber colored CAYSTON vial
- 1 ampule of saline (diluent)
- Altera Nebulizer System

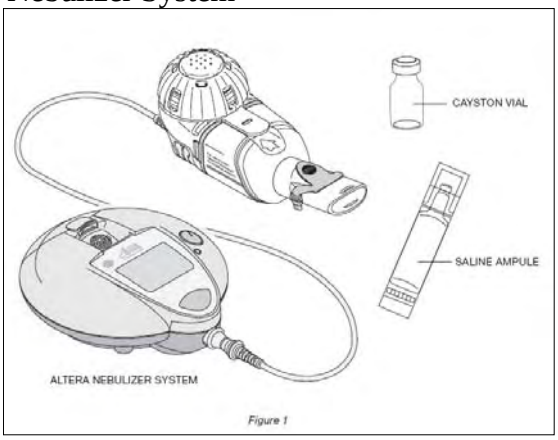

Figure 1

Check to make sure that your Altera Nebulizer System works properly before starting your treatment with CAYSTON. See the manufacturer's instructions for use that comes with your Altera Nebulizer System. This should have complete information about how to put together (assemble), prepare, use, and care for your Altera Nebulizer System.

Step 1 Preparing your CAYSTON for inhalation

1. Mix (reconstitute) CAYSTON with the saline only when ready to take a dose. Take one amber vial of CAYSTON and one ampule of saline from the carton. Separate the saline ampules by gently pulling apart.

2. Look at the ampule of saline. If it looks cloudy do not use it. Throw away this ampule and get another ampule of saline.

3. Gently tap the vial so that the powder settles to the bottom of the vial. This helps you get the proper dose of medicine. Open the amber drug vial by lifting up the metal flap on the top (Figure 2) and pulling down (Figure 3) to carefully remove the entire metal ring from the vial (Figure 4). Safely dispose of the ring in household garbage. Carefully remove the rubber stopper.

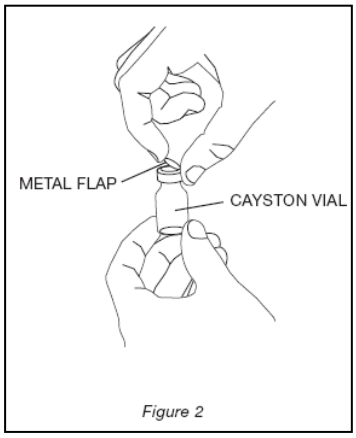

Figure 2

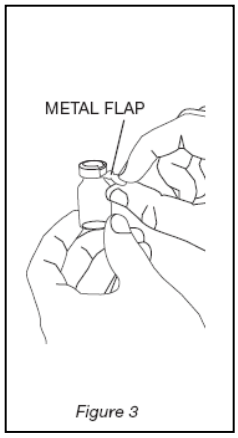

Figure 3

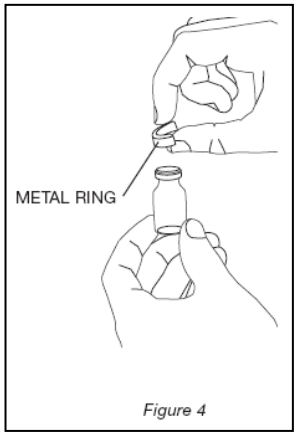

Figure 4

4. Open the ampule of saline by twisting off the tip. Squeeze out the contents completely into the vial (Figure 5). Next, close the vial with the rubber stopper and gently swirl the vial until the powder has completely dissolved and the liquid is clear.

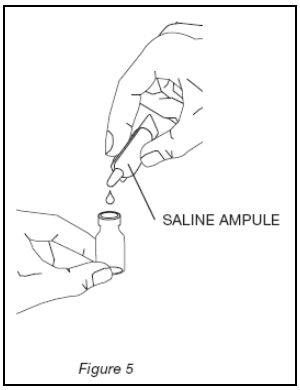

Figure 5

5. After mixing CAYSTON with the saline, check to make sure the diluted medicine is clear. If it is cloudy or has particles in it, do not use this medicine. Throw away this dose of medicine and start over again with a new vial of CAYSTON and a new ampule of saline.

6. Use CAYSTON right away after you mix with the saline.

Step 2 Taking your CAYSTON treatment

See the manufacturer's instructions for use that comes with your Altera Nebulizer System for complete instructions on taking a treatment, and how to clean and disinfect your Altera Nebulizer Handset.

7. Make sure the handset is on a flat, stable surface.

8. Remove the rubber stopper from the vial, then pour all of the mixed CAYSTON and saline into the Medication Reservoir of the handset (Figure 6). Be sure to completely empty the vial, gently tapping the vial against the side of the Medication Reservoir if necessary. Close the Medication Reservoir (Figure 7).

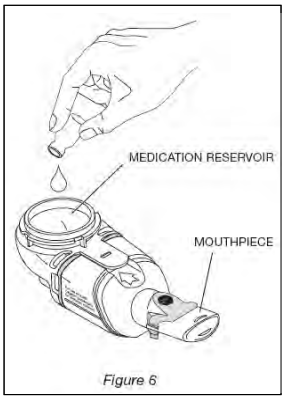

Figure 6

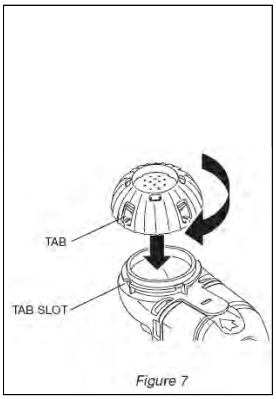

Figure 7

9. Begin your treatment by sitting in a relaxed, upright position. Hold the handset level, and place the Mouthpiece in your mouth. Close your lips around the Mouthpiece (Figure 8).

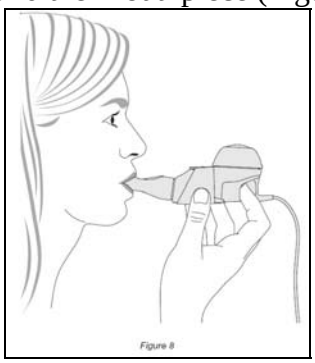

Figure 8

10. Breathe in and out normally (inhale and exhale) through the Mouthpiece. **Avoid breathing through your nose**. Continue to inhale and exhale comfortably until the treatment is finished.

11. The empty vial, stopper and saline ampule should be disposed of in household garbage upon completion of dosing.

Manufactured by: Gilead Sciences, Inc., Foster City, CA 94404

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