CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

050814Orig1s000

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	January 8, 2010
To:	Wiley Chambers, MD, Acting Director Division of Anti-Infective and Ophthalmology Products
Through:	Todd Bridges, RPh, Team Leader Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Deveonne Hamilton-Stokes, RN, BSN, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Cayston (Aztreonam) for Inhalation Solution 75 mg/vial
Application Type/Number:	NDA # 050814 (IND # 64,402)
Applicant:	Gilead Sciences, Inc.
OSE RCM #:	2009-1742

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CONTENTS

1 INTRODUCTION

This re-assessment of the proprietary name is written in response to a notification that NDA 050814 may be approved within 90 days. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Cayston, acceptable in OSE Review #2007-2440, dated May 12, 2008. The Division of Anti-Infective and Ophthalmology Products did not have any concerns with the proposed name, Cayston, and the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective on April 3, 2008, and November 4, 2009.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review for Cayston. We used the same search criteria that were used in OSE Review #2007-2440 for the proposed proprietary name, Cayston. None of the proposed product characteristics were altered, therefore, we did not re-evaluate previous names of concern. Additionally, DMEPA searches the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

The searches of the databases yielded one new name, (b) (4) thought to look and sound similar to Cayston and represent a potential source of drug name confusion. This name was evaluated using FMEA. The findings of the FMEA indicate that the proposed name, Cayston, is not likely to result in name confusion with (b) (4) for the reasons presented in Appendix A.

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name Cayston, as of January 5, 2010.

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Cayston, is not vulnerable to name confusion that could lead to medication errors nor is the name considered promotional. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Cayston, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Anti-Infective and Ophthalmology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

We are willing to meet with the Division for further discussion, if needed. If you have questions or need clarifications, please contact Brantley Dorch, OSE Project Manager, at 301-796-0150.

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4 REFERENCES

4.1 REVIEW

1. OSE review #2007-2440. Proprietary Name Review of Cayston: Hamilton-Stokes, Deveonne.

4.2 DATABASES

1. ***Drugs@FDA (***http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm***)***
   Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

2. ***USAN Stems (***http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml***)***
   USAN Stems List contains all the recognized USAN stems.

3. ***CDER Proposed Names List***
   Compiled list of proposed proprietary names submitted to the Division of Medication Error and Prevention and Analysis (DMEPA) for review. The list is updated weekly and maintained by DMEPA.

<u>Appendix A</u>: Product with No Overlap in Strength

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Dosage Form/ Strength	Usual Dose (if applicable)
Cayston (Aztreonam)	**N/A**	**Injection: 75 mg**	**75 mg three times a day for a 28 day course to be inhaled through the eFlow Electronic Nebulizer**
(b) (4)			

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Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-50814	ORIG-1	GILEAD SCIENCES INC	CAYSTON(AZTREONAM FOR INHALATION SOL)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

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01/08/2010

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Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date:	May 12, 2008
To:	Wiley Chambers, M.D., Acting Director Division of Anti-Infective and Ophthalmology Products
Through:	Todd Bridges, RPh, Team Leader Denise Toyer, Pharm D, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention
From:	Deveonne Hamilton-Stokes, RN, BSN, Safety Evaluator Division of Medication Error Prevention
Subject:	Proprietary Name Review for Cayston
Drug Name(s):	Cayston (Aztreonam Lysine for Inhalation) 75 mg/vial
Application Type/Number:	NDA # 50-814 (IND # 64,402)
Applicant:	Gilead Sciences, Inc.
OSE RCM #:	2007-2440

*** **Note: This review contains proprietary and confidential information that should not be released to the public.** ***

CONTENTS

EXECUTIVE SUMMARY

Gilead Sciences submitted a rebuttal in response to the Division of Medication Error Prevention's finding that Cayston had orthographic similarity to Capoten. This rebuttal included new information which was unavailable during the initial review. Specifically, the Applicant stated that Cayston will only be available through specialty pharmacies and is used to treat a small, highly specialized patient population. Thus, the Division of Medication Error Prevention conducted a new Proprietary Name Risk Assessment including this new information. The results of the Proprietary Name Risk Assessment found that the proposed name, Cayston, has some similarity to other proprietary and established drug names, but the findings of the FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. This finding reverses our previous recommendation. Therefore, we do not object to the name Cayston.

However; if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a November 27, 2007, request from the Division of Anti-Infective and Ophthalmology Products to reconsider the acceptability of the proposed proprietary name, Cayston. The Applicant submitted a rebuttal in response to our previous objection to the name. Since the initial review of the proposed name was in 2005, we also reassessed Cayston regarding its potential confusion with other proprietary or established drug names.

1.2 REGULATORY HISTORY

The Division of Medication Error Prevention found the proprietary name, Cayston, unacceptable in OSE review # 05-0108, dated August 19, 2005, based on the potential for orthographic similarity to the name Capoten.

1.3 PRODUCT INFORMATION

Cayston (Aztreonam Lysinate) is (b) (4) Cayston is specifically formulated to be administered by inhalation. The usual adult and pediatric dosage is 75 mg by aerosolization with the *eFlow® electronic nebulizer* three times daily for twenty-eight consecutive days. Cayston is available as a sterile, unit-of-use vial containing 75 mg of aztreonam as the lysine salt, which must be reconstituted before use. The product will be packaged as part of a kit with a 1 mL ampule of diluent containing 0.17% NaCl. The Cayston kit will contain a 28-day supply, which will include 84 Cayston vials and 88 diluent ampules. The four additional diluent ampules are provided in case of spillage. The vials and ampules will be packed in two side-by-side removable carton inserts each containing a 14-day supply of Cayston and diluent.

2 METHODS AND MATERIALS

This section describes the methods and materials used by the Division of Medication Error Prevention staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment). The primary focus of the assessment is to identify and remedy potential sources of medication error prior to drug approval. The Division of Medication Error Prevention defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [1]

2.1 PROPRIETARY NAME RISK ASSESSMENT

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Cayston, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency.

For the proprietary name, Cayston, the staff of the Division of Medication Error Prevention searches a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). The Division of Medication Error Prevention also conducts internal CDER prescription analysis studies (see 2.1.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.3). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.[2] FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently leads to medication errors in the clinical setting. The Division of Medication Error Prevention uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the Staff considers the product characteristics associated with the proposed drug

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[1] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors html. Last accessed 10/11/2007.

[2] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

throughout the risk assessment, since the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, the Division of Medication Error Prevention considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[3]

2.1.1 Search Criteria

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'C' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[4][5]

To identify drug names that may look similar to Cayston, the Staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (two, capital letter 'C', and lower case 't'), downstokes (one, lower case 'y'), cross-strokes (one, lower case 't'), and dotted letters (none). Additionally, several letters in Cayston may be vulnerable to ambiguity when scripted, including the letter 'C' may appear as 'A', 'L'or 'O'; lower case 'a' may appear as lower case 'c' or 'o'; lower case 'y' may appear as lower case 'g', 'p', 'q', 'j', or 'z'; lower case 's' may appear as lower case 'n'; lower case 't' may appear as lower case 'l', 'i', or 'x'; lower case 'o' may appear as lower case 'a' or 'e'; and lower case 'n' may appear as lower case 'r', 's', or 'm'. As such, the Staff also considers these alternate appearances when identifying drug names that may look similar to Cayston.

When searching to identify potential names that may sound similar to Cayston, the Medication Error Staff search for names with similar number of syllables (two), stresses (CAY-ston or cay-STON), and the placement of vowel and consonant sounds. In addition, several letters in Cayston may be subject to interpretation when spoken, including the letter 'C' may be interpreted as 'K' or 'S'; the letters 'ay' may be interpreted as 'a' or 'ai'; the letter 't' may be interpreted as 'd'; and the letters 'on' may be interpreted as 'en' or 'in' . As such, the staff also considers the alternate pronunciations when identifying drug names that may sound similar to Cayston. The

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[3] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

[4] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

[5] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artifical Inteligence in Medicine (2005)

Applicant's intended pronunciation of the proprietary name, cay-ston, was taken into consideration.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting For this review, the Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary name (Cayston), the established name (Aztreonam lysine for inhalation), proposed indication (to improve respiratory symptoms and pulmonary function in cystic fibrosis patients with Pseudomonas aeruginosa), strength (75 mg), dose (75 mg), frequency of administration (three times a day for a 28-day course), route (oral inhalation via nebulizer), and dosage form of the product (lyophilized powder for inhalation). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff general take into consideration.

Lastly, the Medication Error Staff also consider the potential for the proposed name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.1.1 Data base and information sources

The proposed proprietary name, Cayston, was provided to the medication error staff of the Division of Medication Error Prevention to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Cayston using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the Medication Error Staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the Medication Error Staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.1.2 CDER Expert Panel Discussion

An Expert Panel Discussion is held by the Division of Medication Error Prevention to gather CDER professional opinions on the safety of the product and the proprietary name, Cayston. Potential concerns regarding drug marketing and promotion related to the proposed names are also discussed. This group is composed of Division of Medication Error Prevention staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of the medication error staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to

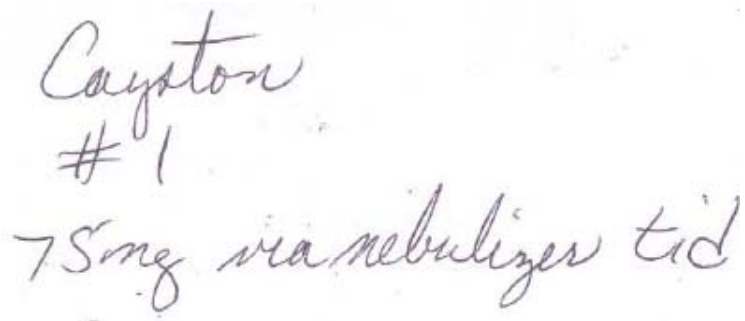
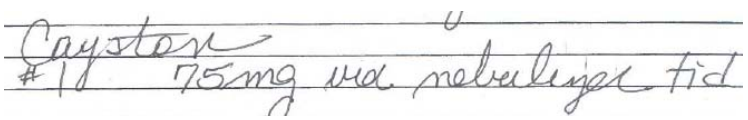
supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.1.2 CDER Prescription analysis studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Cayston with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ a total of 123 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterepreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of Cayston in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These prescriptions are optically scanned and one prescription is delivered to a random sample of 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to the medication error staff.

Figure 1 Cayston Study (conducted on April 23, 2008)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Outpatient Prescription: 	"Cayston #1 75 mg via nebullizer tid"
Inpatient Medication Order : 	

2.1.3 Applicant Rebuttal Assessment

For this product, the Applicant submitted a rebuttal to our objection of the proposed proprietary name (See Appendix I). The Division of Medication Error Prevention conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the rebuttal.

After the Safety Evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of their overall risk assessment with the findings of the rebuttal submitted by the Applicant. The Safety Evaluator then determines whether the Division of Medication Error Prevention's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention provides a detailed explanation of these differences.

2.1.4 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[6] When applying FMEA to assess the risk of a proposed proprietary name, the Division of Medication Error Prevention seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective then remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking: "Is the name Cayston convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?" An affirmative answer indicates a failure mode and represents a potential for Cayston to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking "Could the confusion of the

[6] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

drug names conceivably result in medication errors in the usual practice setting?" The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

The Division of Medication Error Prevention will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. We identify that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug another drug product.

In the event that the Division of Medication Error Prevention objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, we will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while the Division of Medication Error Prevention will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then the Division of Medication Error Prevention will not object to the use of the proprietary name. If any of these conditions are met, then the Division of Medication Error Prevention will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Applicant; however, the

safety concerns set forth in criteria 1 through 5 are supported either by Food and Drug Administration Regulation or by external healthcare authorities, including The Institute of Medicine, The World Health Organization, The Joint Commission, and The Institute for Safe Medication Practices, who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, the Division of Medication Error Prevention contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Applicant, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Applicant's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, the Division of Medication Error Prevention believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If we object to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. The Division of Medication Error Prevention is likely to recommend that the Applicant select an alternative proprietary name and submit the alternate name to the Agency for us to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so we may be able to provide the Applicant with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and information sources

The Division of Medication Error Prevention conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to Cayston to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, 21 names were identified as having some similarity to the name Cayston.

Sixteen of the twenty-one names were thought to look like Cayston, which include: Capitrol, Capoten, Celestone, Cysteine, Lipitor, Lipofen, Cystagon, Ceftin, Cortan, Avastin, Copaxone, (b) (4) Calvisin, Capilon, Causalin tab, and Aygestin. Three names (Capsin, Caesium and Casein peptides) were thought to sound similar to Cayston and two additional names (Clistin and Catron) were thought to look and sound similar to Cayston. We note that five of the twenty-one names (Capsin, Capitrol, Capoten, Cystagon and (b) (4)) were previously reviewed in OSE Review #05-0108.

In addition, a search of the USAN Stem List identified no USAN Stems within the proposed name, Cayston.

3.1.2 Expert panel discussion

The Expert Panel reviewed the pool of names identified by the Division of Medication Error Prevention staff (see section 3.1.1. above), and noted no additional names thought to have orthographic or phonetic similarity to Cayston. The Expert Panel also noted that despite phonetic similarity of the letter 'C' with the letter 'K', no names beginning with this letter was included in the pool. The Expert Panel recommended that independent searches consider the potential for confusion with drug names beginning with this letter.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.1.3 CDER Prescription analysis studies

A total of 30 practitioners responded, none of the responses overlapped with any existing or proposed drug names. About three-fourths (n=23) of the participants interpreted the name correctly as "Cayston," with correct interpretation occurring more frequently in the written studies. The remainder of the responses (n=7) misinterpreted the drug name. The majority of misinterpretations occurred in the verbal prescription studies with all respondents (n=4) misinterpreting the drug name. The letter 'C' was misinterpreted as 'K' and the second syllable 'ston' misinterpreted as 'sein', 'ssin' or 'sin'. In the written prescription studies, the letter 'o' was misinterpreted as 'e' by two respondents and the letter 'n' was misinterpreted as an 'r' by one respondent. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Applicant Rebuttal

The Division of Medication Error Prevention concurs with the Applicants statements in points 1 (first statement), 2, 4, and 5 of their rebuttal (See Appendix I). However, we note that we had no phonetic concerns with Cayston and Capoten. Moreover, the Applicant did not provide data to support their assertion that Capoten is generally referred to by pharmacists as Captopril and that cardiovascular disease is rare in cystic fibrosis patients (points 1 {second statement} and 6).

Additionally, the Applicant stated there is little safety concern should confusion occur (point 7). We concur that in tablet form, Capoten cannot be aerosolized in the nebulizer and conversely, aztreonam is not orally bioavailable. However, we disagree that there is little safety concern should confusion occur between these two products. Adverse events associated with administration of the wrong drug could result if an order for either drug is misinterpreted as the other.

The Applicant submitted new information which was not provided to the Division of Medication Error Prevention during our initial review. The Applicant stated that Cayston would only be dispensed through specialty pharmacies (point 3).

3.1.5 Safety evaluator risk assessment

Independent searches by the primary Safety Evaluator identified two additional names thought to look similar to Cayston and represent a potential source of drug name confusion. The names are Cogentin and Cenestin. Careful evaluation was afforded to drug names beginning with the letter 'K' in accordance with the Expert Panel's recommendations, but no drug names beginning with this letter were thought to have the potential for confusion with Cayston. As such, a total of 23 names were analyzed to determine if the drug names could be confused with Cayston and if the drug name confusion would likely result in a medication error. Although five of the twenty-three names were analyzed in our previous consult, we are reassessing the names against the new Cayston product characteristics to determine if these names pose a risk of confusion with Cayston.

All of the identified names were determined to have some orthographic and/or phonetic similarity to Cayston, and thus determined to present some risk for confusion. Failure modes and effects analysis was then applied to determine if the proposed name, Cayston, could potentially be confused with any of the twenty-three names and lead to medication error.

Our analysis determined that the name similarity between Cayston and the identified names was unlikely to result in medication error for all of the 23 product names. One name (Calvisin) lacked convincing orthographic similarity with Cayston. Three names (Catron, Capilon and Causalin tab) were withdrawn by the FDA Commissioner (see Appendix D). One name (b) (4) was not considered further because it was found unacceptable by the Division of Medication Error Prevention and the product was subsequently approved without a name. For fourteen of the names identified, FMEA determined that medication errors were unlikely because the products do no overlap in strength or dosage with Cayston and have minimal orthographic and/or phonetic similarity to Cayston (see Appendix F). For three of the names, the strength or dose of Cayston can be achieved; however, it would be unlikely because of patient population or number of tablets required per dose (see Appendix G).

The remaining name (Capoten) has some orthographic similarities to Cayston and overlapped with Cayston in an attainable strength of 75 mg and attainable usual dose of 75 mg three times a day (see Appendix H). However, analysis of the failure mode did not determine the effect of this similarity to result in medication errors in the usual practice setting because Cayston will only be distributed by specialty pharmacies thereby decreasing the likelihood that the drug would be dispensed for Capoten. Additionally, Cayston was designated an orphan drug in 2002 and thus we do not anticipate that this product will be frequently prescribed or widely known as it will be used to treat a small, highly specialized patient population. Therefore, our previous concerns with orthographic similarity and overlapping product characteristics between Cayston and Capoten have been addressed by the Applicant.

4 DISCUSSION

The results of the Proprietary Name Risk Assessment found that the proposed name, Cayston, has some similarity to other proprietary and established drug names, but the findings of the FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. This finding was consistent with and supported by a rebuttal submitted by the Applicant. Therefore we are reversing our previous objection to the name because of additional information provided by the Applicant.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, the Division of Medication Error Prevention believes that these limitations are sufficiently minimized by the use of an Expert Panel and, in this case, the data submitted by the Applicant from an independent proprietary name risk assessment firm, which included the responses of frontline practitioners.

However, our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, the Division of Medication Error Prevention recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Cayston, does not appear to be vulnerable to name confusion that could lead to medication errors. This finding was consistent with and supported by a rebuttal submitted by the Applicant. As such, the Division of Medication Error Prevention does not object to the use of the proprietary name, Cayston, for this product.

5.1 COMMENTS TO THE DIVISION

After reviewing the Applicant's Rebuttal, which stated Cayston will only be available through specialty pharmacies, the Division of Medication Error Prevention is reversing our previous recommendation based on this new information provided. Additionally, Cayston was designated an orphan drug in 2002 and thus we do not anticipate that this product will be frequently prescribed or widely known as it will be used to treat a small, highly specialized patient population.

The Division of Medication Error Prevention has no objections to the use of the proprietary name Cayston for this product. If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

We would appreciate feedback of the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention on any communication to the sponsor with regard to this review. If you have further questions or need clarifications, please contact Cherye Milburn, project manager, at 301-796-2084.

5.2 COMMENTS TO THE APPLICANT

The Division of Medication Error Prevention is reversing our previous objection to the name Cayston. Cayston will only be distributed by specialty pharmacies thereby decreasing the likelihood that the drug would be dispensed for Capoten. Therefore, we have no objections to the use of the proprietary name Cayston for this product. If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, the Division of Medication Error Prevention rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

6 REFERENCES

1. Micromedex Integrated Index (http://weblern/)

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. Phonetic and Orthographic Computer Analysis (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for the Division of Medication Error Prevention, FDA.

3. Drug Facts and Comparisons, online version, St. Louis, MO (http://weblern/)

Drug Facts and Comparisons is a compendium organized by therapeutic Course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in review divisions.

5. Division of Medication Error Prevention proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention from the Access database/tracking system.

6. Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and "Chemical Type 6" approvals.

7. Electronic online version of the FDA Orange Book (http://www.fda.gov/cder/ob/default.htm)

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. WWW location http://www.uspto.gov.

Provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (http://weblern/)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

10. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. Natural Medicines Comprehensive Databases (http://weblern/)

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. Stat!Ref (http://weblern/)

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

13. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. Lexi-Comp (www.pharmacist.com)

A web-based searchable version of the Drug Information Handbook.

16. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

7 APPENDICES

Appendix A:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. The Division of Medication Error Prevention also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The Medication Error Staff also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. "T" may look like "F," lower case 'a' looks like a lower case 'u,' etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, we will consider the Applicant's intended pronunciation of the proprietary name. However, because the Applicant has little control over how the name will be spoken in practice, we also consider a variety of pronunciations that could occur in the English language.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstokes Downstrokes Cross-stokes	• Names may look similar when scripted, and lead to drug name confusion in written communication

		Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B:

CDER Prescription Study Responses

Outpatient Prescription	Voice Prescription	Inpatient Medication Order
Cayston	Casein	Caysten
Cayston	Kaystin	Cayston
Cayston	Kassin	Cayston
Cayston	Kasin	Cayston
Cayston		Cayston
Cayston		Cayston
Cayston		Cayston
Cayston		Cayston
Cayston		Cayston
		Cayston
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		Cayston

		Caysten
		Cayston
		Cayston
		Caystor
		Cayston

Appendix C: Names identified in previous Division of Medication Error Prevention review as having some similarity to Cayston

Proprietary Name	Similarity to Cayston
Capsin	Sound
Capitrol	Look
Capoten	Look
Cystagon	Look
(b) (4)	Look

Appendix D: Proprietary names Withdrawn by the Commissioner

Proprietary Name	Similarity to Steatavan	Date in DSS
(b) (4)		
(b) (4)		
(b) (4)		

Appendix E: Proprietary name found unacceptable by Agency

Proprietary Name	Similarity to Steatavan	Division
(b) (4)		Division of Medication Errors and Technical Support objection (OSE # 04-0141)

Appendix F: Products with no numerical overlap in strength and dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Cayston (Aztreonam Lysinate for Inhalation)		**75 mg**	**75 mg three times a day for a 28 day course to be inhaled through the eFlow Electronic Nebulizer**
Celestone (Betamethasone)	Look	0.6 mg/5 mL oral solution	0.6 mg to 7.2 mg per day depending on the specific disease entity being treated
Cysteine Hydrochloride (Cysteine Hydrochloride)	Look	0.5 gram (50 mg/mL) Injection	For use only after dilution as an additive to Aminosyn (a crystalline amino acid solution) to meet the IV amino acid nutritional requirements of infants receiving total parenteral nutrition. Cysteine Hydrochloride Injection, USP 0.5 gram is intended for use only after dilution in Aminosyn (a crystalline amino acid solution). Each 10 mL of Cysteine Hydrochloride Injection, USP 0.5 gram should be combined aseptically with 12.5 grams of amino acids, such as that present in 250 mL of Aminosyn 5%. The admixture is then diluted with 250 mL of dextrose 50% or such lesser volume as indicated. Equal volumes of Aminosyn 5% and dextrose 50% produce a final solution which contains Aminosyn 2.5% in dextrose 25%, which is suitable for administration by central venous infusion.
Cystagon (Cysteamine Bitartrate)	Look	50 mg, 150 mg capsules	Patients over age 12 and over 100 pounds: 2 grams per day, in four divided doses
Cortan (Prednisone)	Look	20 mg	5 mg to 60 mg depending on disease being treated
Avastin (Bevacizumab)	Look	100 mg, 400 mg vials	5 mg/kg, 10 mg/kg, or 15 mg/kg every 14 days to 21 days depending on disease being treated
Copaxone (Glatiramer Acetate)	Look	20 mg/vial	20 mg/day injected subcutaneously
Caesium	Sound	Not available	6 gram to 9 grams in 3 divided doses

Casein peptides	Sound	Not available	100 mg to 200 mg twice daily
Capitrol (Chloroxine)	Look	2% topical	Massage thoroughly into wet scalp. Allow later to remain on scalp for 3 minutes; rinse. Repeat application and rinse. Two treatments per week are usually sufficient.
Capsin (Capsaicin Topical) (OTC)	Sound	0.025%, 0.075% lotion 0.025% Cream	Apply a thin film to affected area 3 to 4 times daily
Cogentin (Benztropine Mesylate) (Tablets discontinued, but generics available)	Look	0.5 mg, 1 mg, 2 mg tablets 1 mg/mL injection solution	*Parkinsons:* Usual daily dose is 1 mg to 2 mg given orally or parenterally. *Drug-Induced Extrapyramidal Disorders:* 1 to 4 mg once or twice a day orally or parenterally.
Cenestin (Synthetic conjugated estrogens, A)	Look	0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg and 1.25 mg tablets	*Treatment of moderate to severe symptoms associated with menopause:* Initial daily dose of 0.45 mg daily; titrated to individual patient response. *Treatment of moderate to severe symptoms of vulvar and vaginal atrophy:* 0.3 mg daily
Lipitor (Atorvastatin Calcium)	Look	10 mg, 20 mg, 40 mg, 80 mg tablets	10 mg to 80 mg once daily
Lipofen (Fenofibrate)	Look	50 mg, 100 mg, 150 mg capsules	*Treatment of hypercholesterol or hyperlipidemia:* 150 mg per day *Treatment of hypertriglyceridemia:* 50 to 150 mg per day

Appendix G: Products in which a dose is achievable but unlikely because of patient population, or number of tablets/milliliters required.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength Usual Dose	Rationale
Cayston **(Aztreonam Lysinate for Inhalation)**		**75 mg tablets** **75 mg three times a day for a 28 day course to be inhaled through the eFlow Electronic Nebulizer**	
Aygestin (Norethindrone acetate)	Look	5 mg tablets *Secondary amenorrhea/abnormal uterine bleeding:* 2.5 mg to 10 mg given daily for 5 to 10 days during the second half of the menstrual cycle *Endometriosis:* Initial daily dosage of 5 mg for two weeks. Dosage should be increased by 2.5 mg per day every two weeks until 15 mg per day is reached	Although a 75 mg dose is attainable with Aygestin, this dose would require 15 tablets which would alert practitioners.
Ceftin (Cefuroxime axetil)	Look	250 mg, 500 mg tablets 125 mg/5 mL, 250 mg/5 mL oral suspension Tablets: 250 mg, 500 mg bid for 5 days-20 days depending on disease being treated; 1000 mg once as a single treatment dose Oral Suspension: 20 mg/kg/day to 30 mg/kg/day divided twice a day depending on disease being treated	The 75 mg dose is achievable with suspension. However, the dose would be for a 3.75 kg infant, who would not likely receive an antibiotic orally, but rather intravenously.
Clistin (Carbinoxamine Maleate)	Look and Sound	4 mg tablet 4 mg/5 mL oral elixir 4 mg three or four times daily	The 75 mg dose is achievable with suspension. However, the equivalent Clistin dose would be 93 mL which would alert practitioners.

Appendix H: Potential confusing name with numerical overlap in strength or dose

Cayston (Aztreonam Lysine)	**75 mg/vial**	**75 mg three times a day for a 28 day course to be inhaled through the eFlow Electronic Nebulizer**
Failure Mode: Name confusion	**Causes (could be multiple)**	**Effects**
Capoten (Captopril)	12.5 mg, 25 mg, 50 mg, 100 mg tablets Orthographic similarity both begin with the letter 'Ca', 'p' may look like 'y' when scripted, and 'ten' may look like 'ton' when scripted. Numerical overlap in usual attainable dose. Capoten usual dose of 25 mg to 150 mg twice a day or three times a day can overlap with Cayston usual dose of 75 mg three times a day. Numerically similar strength of 25 mg and 75 mg if the '2' is not prominently scripted or the tail is trailed off	Differentiating product characteristics such as the limited distribution of Cayston only through specialty pharmacies and since it will only be used to treat a small, highly specialized patient population (orphan status) minimize the likelihood of medication error in the usual practice setting. *Rationale:* The risk for medication error is minimized by differentiating product characteristics. Although both medications are orthographically similar, the restricted distribution of Cayston through specialty pharmacies will limit the availability of the medication. Cayston has been given Orphan Drug Designation, as such this drug is being developed to treat a rare disease or condition and we do not anticipate a large number of prescriptions. Cayston is administered via nebulizer; therefore, an order for Cayston would typically be accompanied with "via nebulizer" on the initial order. Cayston will primarily be prescribed by Cystic Fibrosis healthcare practitioners and Pulmonologists, whereas Capoten will be prescribed by General practitioners. Additionally, the products have different patient population since Cystic Fibrosis is usually seen in children and hypertension/heart failure is generally seen in adults. Cayston will need to be refrigerated and Capoten is stored at room temperature.

Appendix I: Applicant Rebuttal

1. Gilead does not believe there is a significant potential for verbal confusion based on the results from a trademark analysis report (submitted in Serial No. 56 and appended here) which found that only one professional pharmacist out of 123 mentioned similarity to Capoten unaided and that 121 out of 123 professional pharmacists did not cite "similarity to a proprietary drug name" in their overall assessment rationale.

The trade name Capoten is rarely used as the product is now generic and generally referred to as captopril by pharmacists. Also, please note that the names differ in number of syllables.

2. There is no overlap in indication, mechanism of action, formulation, route of administration, dosage strength, or packing. Please see the table below for a direct comparison of the products.

	Cayston (aztreonam lysine for inhalation)	**Capoten (captopril)**
Indication	CF patients with P.aeruginosa in their lungs	Diabetic Nephropathy, Heart Failure, Hypertension
Mechanism of Action	Anti-Infective	ACE inhibitor
Formulation/Appearance	Lyophilized powder reconstituted and used with a nebulizer	Tablet
Dosage	75 mg	12.5, 25, 50 and 100 mg
Administration	Inhaled	Oral
Packaging	Carton containing 84 vials of active drug in glass vials packaged with 84 blow filled ampoules containing 1 mL of saline diluent	Pharmacy Bottle

3. The prescription and distribution of both products will be different. Cayston will be prescribed by CF caregivers and only dispensed through specialty pharmacies by individual order. There will be a further control on the prescription as it must be matched with a second prescription on the first course for CF patients for the accompanying nebulizer.

4. AI will likely require pre-approval due to reimbursement requirements. The cost of the products will differ significantly.

5. Capoten has a black box warning label; it is unlikely that AI will.

6. Capoten is not a product routinely used in CF patients, as cardiovascular disease is rare in CF patients.

7. *There is little safety concern should confusion occur. In tablet form, Capoten cannot be aerosolized in the nebulizer and conversely, aztreonam is not orally bioavailable.*

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