CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-703

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO 22, STOP: 4447)

DATE RECEIVED: November 7, 2005 **DATE OF DOCUMENT:** September 27, 2005	**DESIRED COMPLETION DATE:** February 6, 2006 **PDUFA DATE:** July 28, 2006	**OSE REVIEW #:** 05-0254

TO: Norman Stockbridge, MD
Director, Division of Cardiovascular and Renal Products
HFD-110

THROUGH: Linda Kim-Jung, PharmD., Team Leader
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FROM: Linda Wisniewski, RN, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME: **Prismasol**
(Replacement Solution [redacted] for Continuous Renal Replacement Therapy)
BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, and BK0/0

NDA#: **21-703**

NDA SPONSOR: **Gambro Renal Products**

RECOMMENDATIONS:

1. DMETS does not recommend use of the proprietary name, PrismaSol.

2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to in order minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name PrismaSol acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-796-0538.

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
HFD: 420, WO 22, Mailstop: 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: November 30, 2005

NDA#: 21-703

NAME OF DRUG: PrismaSol
(Replacement Solution ———————
Continuous Renal Replacement Therapy)
BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5
BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0,

NDA HOLDER: Gambro Renal Products

I. INTRODUCTION:

This consult was written in response to a request from the Division of Cardiovascular and Renal Products (HFD-110), for assessment of the proprietary name, "PrismaSol", regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were provided for review and comment.

This product was previously approved for use as a terminally sterilized device under the name, Prismasate, by the Division of Reproductive, Abdominal, and Radiological Devices of the Center for Devices and Radiological Health on January 15, 2002 for use as a dialysate in Continuous Renal Replacement Therapy.

The firm is now proposing to market the same product as a sterile drug product for use as a replacement solution in hemofiltration and hemodialfiltration ———————in hemodialysis and hemodialfiltration. The sponsor proposes that the product PrismaSol will use the same packaging configuration (two compartment bag) and will be marketed concurrently with Prismasate. According to the microbiologist, there are no physical, chemical, or pharmacological differences with these products.

PRODUCT INFORMATION

PrismaSol solution is a sterile solution free of bacterial endotoxins. This solution is used in Continuous Renal Replacement Therapies either as a replacement solution in hemofiltration and hemodiafiltration ——— ——— in hemodialysis and hemodialfiltration. PrismaSol solution may also be used in case of drug poisoning when CRRT is used to remove ——— filterable substances. It contains no bacteriostatic or antimicrobial agents. PrismaSol solution is packaged in a two compartment bag. The small compartment A has a volume of 250 mL and contains the electrolyte solution. The large compartment B has a volume of 4750 mL and contains the buffer solution. The final reconstituted solution (5000) is obtained after breaking the red frangible pin between compartments A and B and mixing both solutions. The mode of therapy, solute formulation, flow rates, and length of therapy is

based on the patient's conditions, as well as the patient's fluid, electrolyte, acid-base and glucose balance. Commonly used flow rates for _____ replacement fluid in hemofiltration, hemodiafiltration and hemodialysis are: (1) adults and adolescents: 500-2,500 mL/hour and (2) children: 15-35 mL/kg/hour. When used as a replacement solution, PrismaSol can be administered into the extra-corporeal circuit before (pre-dilution) and/or after the hemofilter or hemodiafilter (post-dilution). PrismaSol is supplied in nine strengths: BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, and BK0/0. The numbers in the strengths refer to the amount of potassium and calcium in the fluid, (e.g. 0/2.5 = 0 mmol/L or mEq/L potassium and 2.5 mmol/L or mEq/L Calcium, 0/0 = 0 mmol/L or mEq/L potassium and 0 mmol/L or mEq/L calcium, etc.).

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3,4] for existing drug names which sound-alike or look-alike to PrismaSol to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[5]. The Saegis[6] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two pharmacy requisition orders and one verbal requisition study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name PrismaSol. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proposed proprietary name, PrismaSol, acceptable from a promotional perspective.

2. The Expert Panel identified six proprietary names that were thought to have the potential for confusion with PrismaSol. These products are listed in table 1 (see page 4), along with the dosage forms available and usual dosage.

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[1] MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, and the electronic online version of the FDA Orange Book.
[4] Phonetic and Orthographic Computer Analysis (POCA)
[5] WWW location http://www.uspto.gov/tmdb/index.html.
[6] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
PrismaSol	Replacement solution [redacted] for Continuous Renal Replacement Therapy BGK0/2.5, BK4/2.5, ***BGK4/0, BGK4/2.5***, BGK4/3.5, BGK 2/3.5, ***BGK2/0, BK0/3.5***, BK0/0	Mode of therapy, solute formulation, flow rates and length of therapy depend on the clinical condition of the patient: *Adults and adolescents:* [redacted] *Children:* [redacted]	NA
Prismasate	Continuous Renal Replacement therapy (CRRT). ***BK0/3.5***, ***BGK2/0***, ***BGK4/0***, ***BGK4/2.5***, B22GK4/0, BK2/0	Mode of therapy, solute formulation, flow rates and length of therapy depend on the clinical condition of the patient.	LA
Pramasone	Hydrocortisone Acetate and Pramoxine Hydrochloride Cream: 0.5 %/1 % and 1 %/1 % Lotion: 1 %/1 % and 2.5 %/ 1 %	As directed.	LA
Primidone	Primidone Tablets: 50 mg and 250 mg	100 mg to 750 mg three to four times a day. Maximum dose of 2 g/day.	LA
Premasol	Amino Acids: Sulfite-free Amino Acids Injection: 6% and 10%	*<10 kg weight*: 2-4 g/kg/day *>10 kg weight:* 20-25 g/day for the first 10 kg, plus 1-1.23 g/kg/day for weight over 10 kg.	LA/SA
Pravachol	Pravastatin Sodium Tablets: 10 mg, 20 mg, 40 mg, and 80 mg	*Adults*: 10 mg to 80 mg/ daily. *Age 8-13*: inclusive: 20 mg/day. *Age 14-18* inclusive: 40 mg/day.	LA
Primsol	Trimethoprim Hydrochloride Oral Solution: 50 mg/5 mL	*Uncomplicated UTI:* 100 mg every 12 hours to 200 mg every 24 hours. *Chronic UTI:* 100 mg qhs. *Traveler's diarrhea:* 200 mg bid *Pneumocystis Carinii Pneumonia:* 5 mg/kg/ t.i.d.	LA/SA
Prednisol TBA	Prednisolone Tebutate Injection 20 mg/mL suspension	Intra-articular, intralesional or soft tissue administration: 4 mg to 40 mg	SA
Prednisol	Prednisolone Sodium Phosphate Ophthalmic Solution 1%	One or two drops every one to six hours.	SA

*Frequently used, not all-inclusive.
**L/A (look-alike), S/A (sound-alike)

B. FDA DATABASE SEARCHES

Since Prismasate (K013448) was approved for use as a dialysate in Continuous Renal Replacement Therapy (approval date January 15, 2002), DMETS conducted a search of the FDA Adverse Event Reporting System (AERS), Drug Quality Reporting System (DQRS), and the Manufacturer User Facility and Distributor Experience database (MAUDE) databases.

1. MANUFACTURER USER FACILITY AND DISTRIBUTOR EXPERIENCE (MAUDE), Prismasate Device

The Center for Device and Radiological Health conducted a search of the MAUDE system using the search term 'Prismasate'. This search revealed three cases related to the Prismasate device. In three of the cases the 'frangible pins' were identified as the reason for the alarming of the dialysis machine.

a. The first case (User Report Number 3400610000-2003-9030), was received on February 05, 2004, and identifies the design of the dialysate solution bag (Prismasate) as a problem. This report identified the failure to break the second frangible pin that allows the solution to go to the tubing for administration. The report states that the instructions do not mention the need to break the second pin. The reporter suggests that the second pin be colored in the same manner as the first pin. The reporter also states that the second pin is clear which does not allow the user to see if the pin is broken and also suggests that the instructions include a step that refers to the breaking of the second pin. In this report, the patient died from complications unrelated to this event.

b. The second case (User Report Number 0533050000-2004-9007), was received on December 23, 2004, with a follow-up report on February 03, 2005, and identifies the design of the dialysate solution bag (Prismasate) as the issue. The reporter states that there are two 'cones' that need to be broken to allow for administration, and that partial breakage will not allow full flow of the solution through the system without warning. In this case, the 'cones', or pins, were not broken and as a result the machine shut off automatically. The patient expired shortly after the machine stopped.

c. The third case (Manufacturer Report Number 1051129-2006-00002), was received on February 1, 2006 and identifies the pins inside the Prismasate bag as the issue. The reporter states that when breaking the pin it blocks the flow of the solution. No patient outcome is reported.

2. MANUFACTURER USER FACILITY AND DISTRIBUTOR EXPERIENCE (MAUDE), Prisma Dialysis Machine Device

Cases relating to the Prisma Device were obtained from the Center for Device and Radiological Health (CDRH). The report generated by CDRH yielded one additional potential case that references the design of the Prismasate device as the potential cause of the problem. In this case, the 'seal' of the infusion bag was not completely broken, and the flow of the hemofiltration solution coming from the bag was not correct, however, the flow from the patient continued.

3. DRUG QUALITY REPORTING SYSTEM (DQRS)

DQRS was searched using the search term '%prism%' to identify any cases regarding the Prismasate device. This search yielded one case involving Prismasate.

One case was received (M 139940 12May2004) where a physician ordered a patient to receive several 3 liters bags of dialysate with a final volume of 3 meq of potassium per liter. The pharmacist verifying the electronic physician order did not realize that the 5000 mL dialysate bags from Gambro already contained 2 meq of potassium per liter. As a result, potassium was added to the premixed bags giving an incorrect final volume of 5 meq instead of 3 meq per liter. The reporter suggests that Gambro should make the electrolyte contents on the bag with larger or bolder letters.

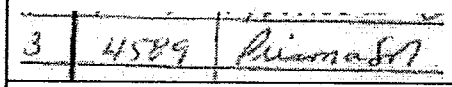
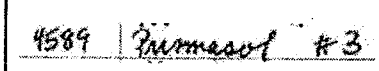
4. ADVERSE EVENT REPORTING SYSTEM (AERS)

AERS was searched to identify any errors involving Prismasate. One case was received (ISR#: 4356294-4) which is a duplicate of the DQRS case discussed above.

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of PrismaSol 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. These studies employed a total of 125 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. Two pharmacy requisition orders were written, each consisting of a combination of marketed and unapproved drug products and a requisition for PrismaSol (see below). These requisition orders were optically scanned and one requisition was delivered to a random sample of the participating health professionals via e-mail. In addition, verbal requisitions for a combination of marketed and unapproved drug products were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal requisitions, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Requisition #1:  	Order Code: 4589 Prismasol #3
Requisition #2:  	

2. Results:

One respondent from the verbal study interpreted the proposed name as Prednisol which is a currently marketed U.S. drug product. Additionally, one respondent from the inpatient written and one from the verbal study interpreted the proposed name as Primasol, which looks and sound similar to the currently marketed U.S. drug products, Primsol and Premasol. See appendix A for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, PrismaSol, the primary concerns related to look-alike and sound-alike confusion with Prismasate, Primasone, Primidone, Premasol, Pravachol, and Primsol.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was confirmation that PrismaSol could be confused with Prednisol which is a currently marketed U.S. drug product. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population. Although there are limitations to the predictive value of these studies, primarily due to sample size, we have acquired safety concerns due to the positive interpretation with this drug product.

1. Look-alike and sound-alike concerns

   a. Premasol was identified as a name with potential look-alike and sound-alike similarities to PrismaSol. Premasol is indicated in the nutritional support of infants and young children requiring Total Parenteral Nutrition (TPN) via either central or peripheral infusion routes.

      Both names begin with letters that may sound and look similar when pronounced or written (Pre vs. Pri). They also end in the same five letters (masol). These similarities in spelling contribute to an overall similarity in the pronunciation and orthographic appearance of each name. Additionally, they both contain the same seven letters in the same sequence and location (first two letters and last five letters) (see below). The potential for orthographic confusion is enhanced further when the first 's' in PrismaSol is written in close proximity to the 'm' and appears to be one of the three 'humps' (see below). Contributing further to the phonetic similarities is the potential for the 's' in PrismaSol to be slurred or not even be included in the pronunciation.

      Adding to the potential for confusion even further, are some overlapping product characteristics, such as: route of administration (intravenous), dosage form (injection), and storage location (large volume parenterals). Moreover, the similarities in the spelling of each of these names would lead these two items to be stored in close physical proximity to each other either in a pharmacy or sterile central supply unit. This has the potential to result in restocking or selection errors. Although the strengths of these two products are different (BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0 vs. 6% and 10%), a stock requisition for 'Prismasol IV 0/0' that indicates the intravenous product with no potassium or calcium, could potentially be misinterpreted and stocked as 'Premasol 10%'. See below. The overwhelming orthographic and phonetic similarities in addition to the overlapping product characteristics increase the potential for confusion involving these two products.

Prismasol
Premasol

Premasol 10%

Premasol

Table 2: Comparison of PrismaSol and Prismasate

PrismaSol	Replacement solution [redacted] Continuous Renal Replacement Therapy 5000 mL dual chambered bag BGK0/2.5, BK4/2.5, ***BGK4/0***, ***BGK4/2.5***, BGK4/3.5, BGK 2/3.5, ***BGK2/0***, ***BK0/3.5***, BK0/0	Mode of therapy, solute formulation, flow rates and length of therapy depend on the clinical condition of the patient: *Adults and adolescents:* [redacted] *Children:* [redacted]
Prismasate	Continuous Renal Replacement therapy (CRRT). 5000 mL dual chambered bag ***BK0/3.5***, ***BGK2/0***, ***BGK4/0***, ***BGK4/2.5***, B22GK4/0, BK2/0	Mode of therapy, solute formulation, flow rates and length of therapy depend on the clinical condition of the patient.

b. Prismasate was identified as a name with similar appearance to PrismaSol when written. PrismaSol and Prismasate are the same product except that Prismasate is a device used in the treatment of patients undergoing dialysis. As a result of a new route of administration (intravenous), Prismasate is being submitted as a new drug application (NDA) under the name PrismaSol.

Both names begin with the same seven letters (Prismas) and end with letters that may look similar when written (ate vs. ol). Although there is a 'cross-bar' for the 't' in Prismasate, its location may not be clearly obvious or spurious in placement. Additionally, the last letter 'e' may not be clear in the presentation. Thus, these may not be distinguishing factors and as a result both names may look similar when scripted.

There are many overlapping product characteristics, such as product composition, dose (patient and/or protocol specific), frequency of administration (continuous), dosage form (injection), storage location (large volume parenterals), [redacted] container (dual chambered bag), and location of use and patient population (dialysis unit/patients). Although Prismasate is supplied in six different electrolyte combinations, three of these combinations overlap with PrismaSol. Both products contain the same ingredients and are packaged similarly. [redacted]

This has the potential to increase confusion further and potentially result in stocking and/or selection errors. Although both Prismasate and Prismasol are the same product, one is a device and one is a drug. After speaking with the microbiologist and the medical officer, DMETS determined that a patient would not experience an adverse event from the administration of one product versus the other. However, confusion by health care practitioners over the similar names could result in the wrong product being administered despite the lack of adverse outcome. This could be compounded by the fact that the products will be labeled with different routes of administration leading health care practitioners to believe that they are two different products. Thus, DMETS considers that the potential for confusion between these two products significant enough that we recommend that only one name be used and the

routes of administration be clearly placed on the principal display panel. Marketing both products under the same name will also allow for better education on product differences. Also, perhaps the bags and labels could be differentiated in order to avoid selection errors.

Primsol
Primsol

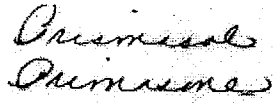
c. Primsol was identified as a name that has may look and sound similar to PrismaSol when spoken or written. Primsol is indicated in the treatment of urinary tract infections, Traveler's diarrhea, and Pneumocystis Carinii Pneumonia.

Both names contain the same seven letters in the same order (Primsol vs. Pri _ m _ sol). Although there are additional letters in PrismaSol (s and a), they may or may not be noticeable when spoken or written, particularly if they are slurred in the pronunciation or scripted close to the other letters and are not clearly obvious (see below). The similar spelling contributes to the similar phonetic pronunciation and orthographic appearance of each name. Although there are some phonetic and orthographic similarities involving these two products, there are some product characteristics that may help to differentiate these two products when ordered. They include dose (patient laboratory value dependent vs. 100 mg to 200 mg or 5 mg/kg), frequency of administration (continuous vs. once or twice daily), product strength (BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0 vs. 50 mg/5 mL), route of administration (intravenous vs. oral), dosage form (injection vs. oral solution), storage location (large volume parenterals vs. oral liquids), and indication of use (dialysis vs. infection). Although the indication of use would not necessarily be included in an order for an oral solution, orders for dialysis solutions may include 'per protocol' or 'per dialysis protocol', or 'as directed'. Moreover, Primsol is not likely to include a direction such as 'use as directed'. This additional information would help to differentiate between these two products when ordered. Additionally, the final dose of Primsol and/or the volume to be administered along with the frequency of administration, would need to be included in an order. This may also help to differentiate these two products when ordered. Moreover, PrismaSol will likely be stocked in the dialysis unit and not designated for specific patients, whereas, Primsol will be patient specific. Despite the differentiating product characteristics, DMETS objects to the use of the name Prismasol because its spelling and pronunciation are too similar to that of Primsol. Per 21 CFR 201.10(c)(5) "The labeling of a drug may be misleading by reason (among other reasons) of: Designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient."

Prismasol
Primsol

d. Pramasone was identified as a name that has may look similar to PrismaSol when scripted. Pramasone is a topical product and is indicated in the relief of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

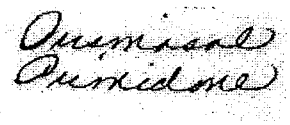
Both names begin with letters that may look similar (Prisma vs. Prama) when scripted. Although PrismaSol has an additional letter at the beginning of the name (s), it may be written in close proximity to the letter 'm' and appear to be one of the humps of the letter 'm'. Despite the potential for orthographic similarities involving the beginning of each name, the upstroke for the letter 'l' at the end of PrismaSol may help to differentiate these two names when written. There are also some product characteristics that may also help to differentiate these two products, such as dose (patient laboratory value and clinical status dependent vs. small amount), frequency of administration (continuous vs. two to four times a day), product strength (BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0 vs. 0.5 %/1 %, 1 %/1 %, 2.5 %/1 %), route of administration (intravenous vs. topical), and storage location (large volume parenterals vs. topicals). It would be possible for either product to be written 'as directed' since it is not an uncommon practice when ordering topical products, and since the particular replacement solution _____ for each patient is based upon their clinical status and/or electrolyte levels. Since it is possible that the strengths of PrismaSol may be written so that they appear as a percentage (e.g. 0/0), this possibility and the potential for confusion may be mitigated by the fact that none of the strengths of either drug have overlapping numerals. Despite the potential for orthographic similarities involving this name pair, the different product strengths, frequencies of administration, and usual dose will help to decrease confusion.



e. Primidone was identified as a name that may look similar to PrismaSol when scripted. Primidone is indicated in the treatment of epilepsy.

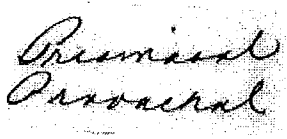
Both names begin with letters that may look similar when written (Prisma vs. Primi). Although PrismaSol contains an additional letter 's', its presence may not be obvious if it is scripted close to the letter 'm' and misinterpreted as one of the 'humps' of the letter 'm'. This would result in the orthographic appearance of the beginnings of each name looking similar (see below). However, the different placements for the upstrokes of the letter 'd' in Primidone and the letter 'l' in PrismaSol might help to differentiate each name when written. There are some product characteristics that may help to differentiate these two products. They include dose (patient laboratory value and clinical status dependent vs. 50 mg to 500 mg or 10 mg/kg/day to 25 mg/kg/day), frequency of administration (continuous vs. one to six times a day), product strength (BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0 vs. 50 mg and 250 mg), route of administration (intravenous vs. oral), dosage form (injection vs. tablet), and storage location (large volume parenterals vs. oral solids). There is the potential for the product strength, flow rates, frequency and route of administration to be omitted in an order for PrismaSol and result in being ordered 'per protocol, per dialysis protocol, or as directed'. This would indicate that the pre-existing protocols based on patient

laboratory values, clinical condition, etc., should be followed. Primidone has only one route of administration and one dosage form, thus an order for Primidone may omit this information. However, orders for Primidone would need to include the dose and frequency of administration. This additional information would help to differentiate these two products when ordered. Despite the potential for some look-alike similarities, the dose and frequency of administration will help to differentiate these two products when written.



f. Pravachol may look similar to PrismaSol when scripted. Pravachol is indicated in the treatment of patients at increased risk for atherosclerosis-related clinical events as a function of cholesterol levels.

Both names begin with letters that may look similar (Prisma vs. Prava). Although both names also end in the same two letters (ol), the additional upstroke for the letter 'h' in Pravachol may help to differentiate these two names when written. There are also product characteristics that may help to differentiate these two products such as dose (patient laboratory and clinical status dependent vs. 20 mg to 80 mg), frequency of administration (continuous vs. daily), product strength (BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0 vs. 10 mg, 20 mg, 40 mg, and 80 mg), route of administration (intravenous vs. oral), dosage form (injection vs. tablet), storage location (large volume parenterals vs. oral solids), and indication of use. Since PrismaSol is ordered and administered per patient clinical condition and clinical laboratory results, orders for PrismaSol may omit the frequency of administration, product strength, and dose, and be written 'per protocol, per dialysis protocol, or as directed'. However, since Pravachol is supplied in multiple strengths (10 mg, 20 mg, 40 mg, and 80 mg) and has a variable dosing profile, orders for Pravachol would need to include a desired dose. This additional information may help to differentiate these two products when ordered.



g. Prednisol was identified as a name that may sound similar to PrismaSol when spoken. Prednisol is indicated for the treatment of steroid responsive inflammatory conditions of the eye.

Both names begin with similar sounding letters (Prisma vs. Predni) which may be pronounced 'Prismuh vs. Prednuh'. Additionally, the last three letters are the same (sol). The similar pronunciations of these two names was evidenced through the verbal prescription studies where one respondent misinterpreted the name as 'Prednisol'.

There are some product characteristics that may help to minimize confusion involving this name pair. They include dose (patient laboratory value and clinical status dependent vs. one or two drops), frequency of administration (continuous vs. every

one to four hours), product strength (BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0 vs. 1%), and indication of use (dialysis vs. steroid responsive inflammatory conditions of the eye). Although most medications do not include an indication of use, an order for PrismaSol may be written to 'use per dialysis protocol', or 'as directed' which would indicate to follow the prescribed protocol. Conversely, an order for Prednisol would most likely include information as to into which eye to administer the medication. This type of information may help to differentiate these two products when ordered. Despite the potential for phonetic similarities between these two names, the product characteristics will help to minimize confusion.

h. Prednisol TBA was identified as a name that has may sound similar to PrismaSol when spoken. Prednisol TBA is indicated in the treatment of Multiple Sclerosis.

Both names begin with similar sounding letters (Prisma vs. Predni) which may be pronounced 'Prismuh vs. Prednuh'. Additionally, they contain the same three letters as the third syllable (sol). Although Prednisol TBA contains a modifier (TBA), it may be omitted in an order and result in the name Prednisol being ordered. The similar pronunciations of these two names was evidenced through the verbal prescription studies where one respondent misinterpreted the name as 'Prednisol', which sounds similar to Prednisol TBA. Although both products are injectables, they include different routes of administration (intravenous vs. intra-articular, intralesional or soft tissue administration).

There are product differences that may help to differentiate them when ordered. They include dose (patient laboratory value and clinical status dependent vs. 4 mg to 40 mg), frequency of administration (continuous vs. once), product strength (BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0 vs. 20 mg/mL), and indication of use (dialysis vs. Multiple Sclerosis). Although most medications do not include an indication of use, an order for PrismaSol may be written to 'use per dialysis protocol', or 'as directed' which would indicate to follow the prescribed protocol for the individual patient. Conversely, an order for Prednisol would most likely not include this general direction of use and would include a specific dose and route of administration. This type of information may help to differentiate these two products when ordered. Despite the potential for phonetic similarities between these two names, the product characteristics will help to minimize confusion.

2. Other safety concerns

This product was previously marketed as a device (Prismasate). Thus, in a hospital setting, it would most likely have been primarily dispensed and/or administered by healthcare practitioners working in the hospitals' central supply department and/or the dialysis unit. Although, these individuals would be familiar with the Prismasate labels and labeling, it is unlikely that other practitioners in the hospital would be familiar with these labels and labeling. Moreover, since this product is not administered intravenously, any supplemental additives could be added to the bag in the dialysis unit. In contrast, when additives are added to stock solutions in the pharmacy they are usually done using aseptic techniques under a laminar flow hood.

The sponsor now proposes to market this product (Prismasol) both as a device and a drug using the same labels and labeling. If the 'drug' needs additives, it would most likely be done in the pharmacy under sterile conditions, thus widening the exposure to include pharmacy personnel. Additionally, since it is an intravenous product it could potentially be administered to the patient when they return to the ward thereby exposing the ward nurses to this product. Therefore, this product may be used by healthcare practitioners that are not currently familiar with the presentation of the active ingredients and strength. This may create confusion for these healthcare practitioners.

The presentation of the active ingredients and/or strength is not in a format commonly used for drug products. Abbreviations are used to represent the active ingredients. Additionally, these abbreviations are not the standard abbreviations used for the chemical compounds. For example, in the product Prismasate BGK 0/2.5 'B' refers to sodium bicarbonate, 'G' refers to glucose, and 'K' refers to potassium chloride. The number zero indicates that there is no potassium chloride, whereas the 2.5 indicates that there are 2.5 mEq of calcium in each 5000 mL. This difference in presentation of the active ingredients and strength is not commonly recognized. Moreover, the lack of active ingredients in a drug product is not commonly designated by a zero content. The presentation of the active ingredients in this manner is problematic and confusing.

With the potential for unfamiliarity of what the current abbreviations refer to, it is possible that errors may occur in the preparation of the infusate. This particular problem was demonstrated by the medication error that occurred when a pharmacist did not realize that Prismasate already contained potassium and subsequently added more potassium. Thus, using the unfamiliar presentation of the active ingredients and strength, the configuration of the bag (i.e., activation) and similarly named device and drug product increases the potential for confusion and medication error significantly.

III. COMMENTS TO THE SPONSOR

DMETS does not recommend the use of the proprietary name, PrismaSol. In reviewing the proprietary name, the primary concerns related to look-alike and/or sound-alike confusion with Premasol, Prismasate, and Primsol.

A. Premasol was identified as a name with potential look-alike and sound-alike similarities to PrismaSol. Premasol is indicated in the nutritional support of infants and young children requiring Total Parenteral Nutrition (TPN) via either central or peripheral infusion routes.

Both names begin with letters that may sound and look similar when pronounced or written (Pre vs. Pri). They also end in the same five letters (masol). These similarities in spelling contribute to an overall similarity in the pronunciation and orthographic appearance of each name. Additionally, they both contain the same seven letters in the same sequence and location (first two letters and last five letters) (see below). The potential for orthographic confusion is enhanced further when the first 's' in PrismaSol is written in close proximity to the 'm' and appears to be one of the three 'humps' (see below). Contributing further to the phonetic similarities is the potential for the 's' in PrismaSol to be slurred or not even be included in the pronunciation.

Adding to the potential for confusion even further, are some overlapping product characteristics, such as: route of administration (intravenous), dosage form (injection), and storage location (large volume parenterals). Moreover, the similarities in the spelling of each of these names would lead these two items to be stored in close physical proximity to each other either in a pharmacy or sterile central supply unit. This has the potential to result in restocking or selection errors. Although the strengths of these two products are different (BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0 vs. 6% and 10%), a stock requisition for 'Prismasol IV 0/0' that indicates the intravenous product with no potassium or calcium, could potentially be misinterpreted and stocked as 'Premasol 10%'. See below. The overwhelming orthographic and phonetic similarities in addition to the overlapping product characteristics increase the potential for confusion involving these two products.

Premasol Prismasol

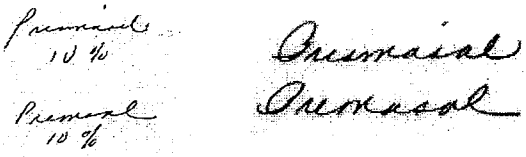


Table 2: Comparison of PrismaSol and Prismasate

PrismaSol	Replacement solution [redacted] Continuous Renal Replacement Therapy 5000 mL dual chambered bag BGK0/2.5, BK4/2.5, ***BGK4/0***, ***BGK4/2.5***, BGK 4/3.5, BGK 2/3.5, ***BGK2/0***, ***BK0/3.5***, BK0/0	Mode of therapy, solute formulation, flow rates and length of therapy depend on the clinical condition of the patient. *Adults and adolescents:* [redacted] *Children:* [redacted]
Prismasate	Continuous Renal Replacement therapy (CRRT). 5000 mL dual chambered bag ***BK0/3.5***, ***BGK2/0***, ***BGK4/0***, ***BGK4/2.5***, B22GK4/0, BK2/0	Mode of therapy, solute formulation, flow rates and length of therapy depend on the clinical condition of the patient.

B. Prismasate was identified as a name with similar appearance to PrismaSol when written. PrismaSol and Prismasate are the same product except that Prismasate is a device used in the treatment of patients undergoing dialysis. As a result of a new route of administration (intravenous), Prismasate is being submitted as a new drug application (NDA) under the name PrismaSol.

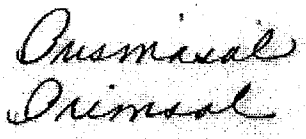
Both names begin with the same seven letters (Prismas) and end with letters that may look similar when written (ate vs. ol). Although there is a 'cross-bar' for the 't' in Prismasate, its location may not be clearly obvious or spurious in placement. Additionally, the last letter 'e' may not be clear in the presentation. Thus, these may not be distinguishing factors and as a result both names may look similar when scripted.

There are many overlapping product characteristics, such as product composition, dose (patient and/or protocol specific), frequency of administration (continuous), dosage form (injection), storage location (large volume parenterals), indication of use (dialysis), container (dual chambered bag), and location of use and patient population (dialysis unit/patients). Although Prismasate is supplied in six different electrolyte combinations, three of these combinations overlap with PrismaSol. Both products contain the same ingredients and are packaged similarly. Additionally, since [redacted] solutions, they would be stored and dispensed from the same location. This has the potential to increase confusion further and potentially result in stocking and/or selection errors. Although both Prismasate and Prismasol are the same product, one is a device and one is a drug. After speaking with the microbiologist and the medical officer, DMETS determined that a patient would not experience an adverse event from the administration of one product versus the other. However, confusion by health care practitioners over the similar names could result in the wrong product being administered despite the lack of adverse outcome. This could be compounded by the fact that the products will be labeled with different routes of administration leading health care practitioners to believe that they are two different products. Thus, DMETS considers that the potential for confusion between these two products significant enough that we recommend that only one name be used and the routes of administration be clearly placed on the principal display panel. Marketing both products under the same name will also allow for better education on product differences. Also, perhaps the bags and labels could be differentiated in order to avoid selection errors.

Prismacate
Prismasal

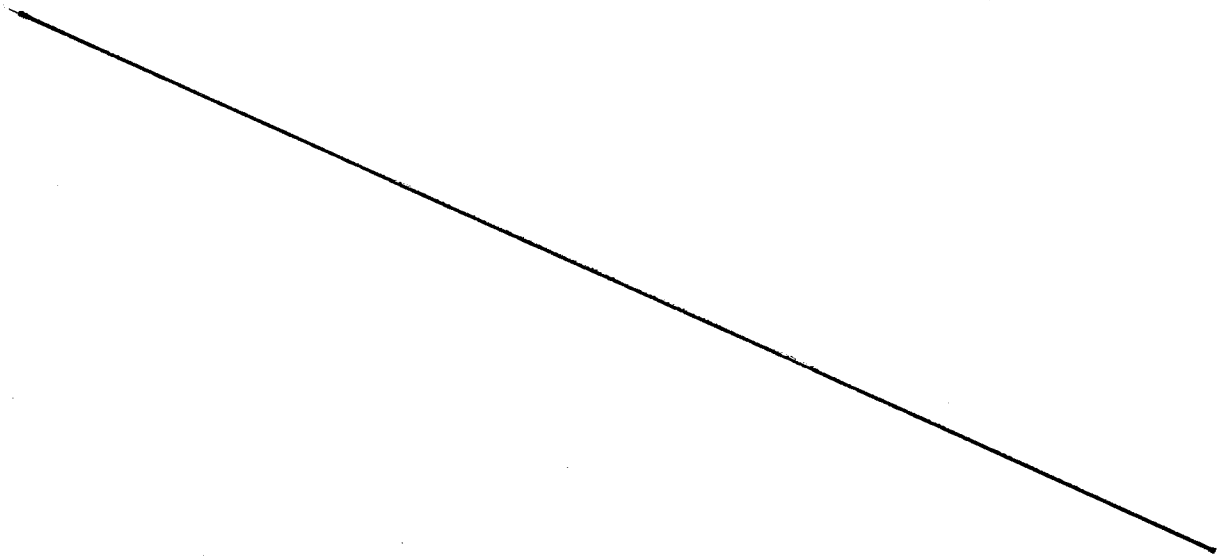
C. Primsol was identified as a name that has may look and sound similar to PrismaSol when spoken or written. Primsol is indicated in the treatment of urinary tract infections, Traveler's diarrhea, and Pneumocystis Carinii Pneumonia.

Both names contain the same seven letters in the same order (Primsol vs. Pri _ m _ sol). Although there are additional letters in PrismaSol (s and a), they may or may not be noticeable when spoken or written, particularly if they are slurred in the pronunciation or scripted close to the other letters and are not clearly obvious (see below). The similar spelling contributes to the similar phonetic pronunciation and orthographic appearance of each name. Although there are some phonetic and orthographic similarities involving these two products, there are some product characteristics that may help to differentiate these two products when ordered. They include dose (patient laboratory value dependent vs. 100 mg to 200 mg or 5 mg/kg), frequency of administration (continuous vs. once or twice daily), product strength (BGK0/2.5, BK4/2.5, BGK4/0, BGK4/2.5, BGK4/3.5, BGK 2/3.5, BGK2/0, BK0/3.5, BK0/0 vs. 50 mg/5 mL), route of administration (intravenous vs. oral), dosage form (injection vs. oral solution), storage location (large volume parenterals vs. oral liquids), and indication of use (dialysis vs. infection). Although the indication of use would not necessarily be included in an order for an oral solution, orders for dialysis solutions may include 'per protocol' or 'per dialysis protocol', or 'as directed'. Moreover, Primsol is not likely to include a direction such as 'use as directed'. This additional information would help to differentiate between these two products when ordered. Additionally, the final dose of Primsol and/or the volume to be administered along with the frequency of administration, would need to be included in an order. This may also help to differentiate these two products when ordered. Moreover, PrismaSol will likely be stocked in the dialysis unit and not designated for specific patients, whereas, Primsol will be patient specific. Despite the differentiating product characteristics, DMETS objects to the use of the name Prismasol because its spelling and pronunciation are too similar to that of Primsol. Per 21 CFR 201.10(c)(5) "The labeling of a drug may be misleading by reason (among other reasons) of: Designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient."

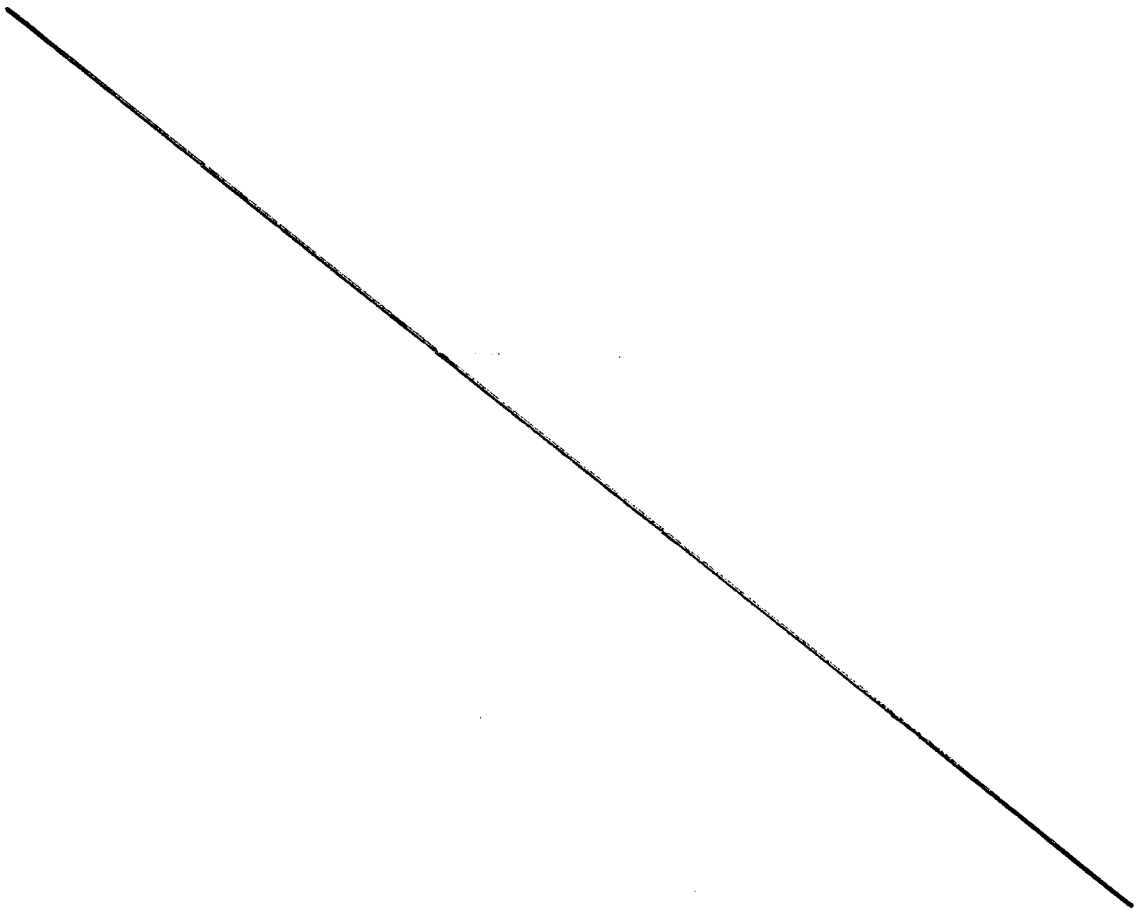


In the review of the container labels, carton and insert labeling of PrismaSol, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENT



B. CONTAINER LABEL (5000 mL bag)



2 Page(s) Withheld

_____ Trade Secret / Confidential

✓ Draft Labeling

_____ Deliberative Process

ODS Consult: 05-0254

Appendix A: PrismaSol

Inpatient Written	Outpatient Written	Verbal
Priama SN	Prismasol	Prednisol
Priama SR or Prism SR	Presmasol	Presonasol
PriamaSol	Presmasol	Primasol
Primasol	Primasol	Prinlasol
Prisma SA	Prismasol	Prislosol
Prisma SN	Prismasol	Prisma SR
Prisma SN	Prismasol	Prismasn
Prismafor	Prismasol	Prismasol
PrismaSA	Prismasol	Prismasol
Prismasn	Prismasol	Prismasol
Prismasn	Prismasol	Prismasol
Prismasn	Prismasol	Prismasol
PrismaSN	Prismasol	Prismasol
PrismaSol	Prismasol	Prismasol
Prismasol	Prismasol	Prismasol
Prismasol	Prismasol	Prismasol
PrismaSol	Prismasol	Prismisol
Prismasol	Prismasol	Prismosal
Prismasol	Prismasol	
Prismasol	Pusmasol	
Prismasor		
Prisonafen		

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

/s/

Linda Wisniewski
6/23/2006 03:24:24 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
6/23/2006 04:07:11 PM
DRUG SAFETY OFFICE REVIEWER
Also signing for Carol Holquist, Director, DMETS, in her absence