CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: 020123/S015

Trade Name: OMNISCAN INJECTION

Generic Name: GADODIAMIDE

Sponsor: NYCOMED INCORPORATED

Approval Date: 10/3/97

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: 020123/S015

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Pharmacology Review(s)	X			
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Bioequivalence Review(s)				
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Correspondence				

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: 020123/S015

APPROVAL LETTER

Div FM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-123/S-015

OCT 3 1997

Nycomed Inc.
Attention: Judith A. Magner
466 Devon Park Drive
PO Box 6630
Wayne, PA 19087-8630

Dear Ms. Magner:

Please refer to your supplemental new drug application dated April 7, 1997, received April 8, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OMNISCAN, (gadodiamide), Injection.

The supplemental application provides a compilation for scientific publications which demonstrate the safety and effectiveness of OMNISCAN in the pediatric population.

We have completed the review of this supplemental application, including the submitted draft labeling, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use in pediatric patients over the age of 2 years as recommended in the enclosed marked-up draft labeling. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed marked-up draft labeling.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL PRINTED LABELING" for approved supplemental NDA 20-123/S-015. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

In addition, please submit three copies of the introductory promotional material that you

propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications, HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Should a letter communicating important information about this drug product (i.e., a "Dear Doctor" letter) be issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20852-9787

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Kyong Cho, Pharm. D., Consumer Safety Officer, at (301) 443-1560.

Sincerely yours,

APPEARS THIS WAY
ON ORIGINAL

Patricia Y. Love, M.D., M.B.A.
Director, Division of Medical Imaging and Radiopharmaceutical Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE

APPEARS THIS WAY
ON ORIGINAL

cc:
Original NDA 20-123
HFD-160/Div. files
HFD-160/CSO/K.Cho
HFD-160/Love/Jones/Udo/Lee/Melograna/Meyers
DISTRICT OFFICE
HF-2/Medwatch (with labeling)
HFD-92/DDM-DIAB (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFD-735/DPE (with labeling) - for all NDAs and supplements for adverse reaction changes.
HFD-560/OTC (with labeling - for OTC Drug Products Only)
HFI-20/Press Office (with labeling)

Drafted by: kc/October 2, 1997/n20123.sap
Initialed by:
final:

APPROVAL (AP)

10/03/97

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FINAL PRINTED LABELING HAS NOT BEEN SUBMITTED TO THE FDA.

DRAFT LABELING IS NO LONGER BEING SUPPLIED SO AS TO ENSURE ONLY CORRECT AND CURRENT INFORMATION IS DISSEMINATED TO THE PUBLIC.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020123/S015

MEDICAL REVIEW(S)

DIV

SEP 16 1997

NDA 20-123/S015
DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS
HFD-160
CLINICAL TEAM LEADER REVIEW

This is amended from a filing review dated May 15, 1997

NDA 20-123 SLR-015 SUBMITTED APRIL 7, 1997

OMNISCAN (gadodiamide injection)
NYCOMED INC.
PEDIATRIC LABELING SUPPLEMENT

INDICATIONS AND USAGE (proposed by sponsor):

CNS (Central Nervous System)
Omniscan is indicated for intravenous use in MRI for adult and pediatric patients to visualize lesions with abnormal vascularity (or those thought to cause abnormalities in the blood-brain barrier) in the brain (intra cranial lesions), spine, and associated tissues.

Body (Intrathoracic [noncardiac], Intra-abdominal, Pelvic and Retroperitoneal Regions)

Omniscan is indicated for intravenous administration for use in MRI in adults and pediatric patients to facilitate the visualization of lesions with abnormal vascularity within the thoracic (noncardiac), abdominal, pelvic cavities, and the retroperitoneal space.

CURRENT INDICATIONS: (quote from the package insert):

CNS (Central Nervous System)
Omniscan is indicated for intravenous use in MRI for adults and children 2 years of age and older to visualize lesions with abnormal vascularity (or those thought to cause abnormalities in the blood-brain barrier) in the brain(intracranial lesions), spine, and associated tissues.

BODY [Intrathoracic (noncardiac), Intra-abdominal, Pelvic and Retroperitoneal Regions]
Omniscan is indicated for intravenous administration for use in adults to facilitate the visualization of lesions with abnormal vascularity within the thoracic (noncardiac), abdominal, pelvic cavities, and the retroperitoneal space.

CURRENT DOSAGE: (quote fom the labeling).

BODY [Intrathoracic (noncardiac), Intra-abdominal, Pelvic and Retroperitoneal Regions]
Omniscan is indicated for intravenous administration for use in adults to facilitate the visualization of lesions with abnormal vascularity within the thoracic (noncardiac), abdominal, pelvic cavities, and the retroperitoneal space.

CURRENT DOSAGE: (quote fom the labeling).

CNS (Central Nervous System)

ADULTS: The recommended dose of Omniscan is 0.2 mL/kg (0.1 mmol/kg) administered as a bolus intravenous injection. An additional 0.4 mL/kg (o.2 mmol/kg) can be given within 20 minutes of the first dose. (See the dosage chart.)

CHILDREN (2-18 YEARS): The recommended dose of Omniscanis 0.2 mL/kg (0.1 mmol/kg) administered as a bolus intravenous injection. (See dosage chart.)

Body [Intrathoracic (noncardiac), Intra-abdominal, Pelvic and Retroperitoneal Regions]

For the kidney, the recommended dose of Omniscan is 0.1mL/kg (0.05 mmol/kg). For the intrathoracic (noncardiac), intra-abdominal, and pelvic cavities, the recommended dose of Omniscan is 0.2 mL/kg (0.1 mmol/kg). (See the dosage chart.)

Comment:

The sponsor has presented

CNS (Central Nervous System)

ADULTS: The recommended dose of Omniscan is 0.2 mL/kg (0.1 mmol/kg) administered as a bolus intravenous injection. An additional 0.4 mL/kg (0.2 mmol/kg) can be given within 20 minutes of the first dose. (See the dosage chart.)

CHILDREN (2-18 YEARS): The recommended dose of Omniscanis 0.2 mL/kg (0.1 mmol/kg) administered as a bolus intravenous injection. (See dosage chart.)

Body [Intrathoracic (noncardiac), Intra-abdominal, Pelvic and Retroperitoneal Regions]

For the kidney, the recommended dose of Omniscan is 0.1mL/kg (0.05 mmol/kg). For the intrathoracic (noncardiac), intra-abdominal, and pelvic cavities, the recommended dose of Omniscan is 0.2 mL/kg (0.1 mmol/kg). (See the dosage chart.)

Comment:

The sponsor has presented

to support the approval of this supplement. The sponsor's statement correctly noted that Omniscan is not metabolized

The sponsor also noted that "Specific studies in relevant categories do not seem necessary, since no major differences between adult and pediatric populations, such as metabolic or elimination pathways, are known to exist for Omniscan".

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The sponsor did not review and analyze each publication provided in this supplement.

The osmolality of Omniscan is 789 mOsmol/kg water

REVIEW DEFICIENCIES:

1. This supplement provided no original safety data for pediatric patients. Omniscan is approved for CNS use in patients from two years up to sixteen years

4. The sponsor provided pharmacokinetics (referenced by publications 1 and 2) which described studies in adults

CONCLUSION:

It is reasonable to utilize existing data in adults as well as the approved pediatric indication for the use of a dose of Omniscan (0.1 mmol/kg) for the evaluation of the CNS, as a basis for considering a wider indication for use.

RECOMMENDATION:

It is reasonable to approve this submission for a "body indication" claim (excluding heart) in subjects between 2 years up to 16 years of age.

9/16/97

A. Eric Jones M.D.
Team Leader, HAD-160

CC
NDA 20-123
Div/File
CSO K. Cho
Deputy Dir. V. Raczkowski M.D.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020123/S015

PHARMACOLOGY REVIEW(S)

SEP 23 1997

NDA 20-123
Review #7

John Melograna
Reviewing Toxicologist

Documents covered in this review:

Doc date	Doc type
4/7/97	SLR 015
4/22/97	S-015, BL
5/9/97	S-015, BL

REVIEW AND EVALUATION OF PHARMACOLOGY AND TOXICOLOGY DATA

Division of Medical Imaging and Radiopharmaceutical Drug Products (HFD-160)

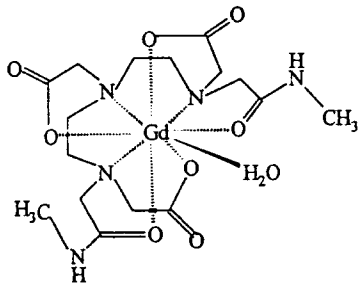
SPONSOR: Nycomed, Inc.
Wayne, PA

DRUG PRODUCT: **Omniscan**

OTHER NAMES: Gadodiamide Injection

CHEMICAL NAME: gadolinium diethylenetriamine pentaacetic acid bismethylamide (Gadodiamide)

CHEMICAL STRUCTURE:



GADODIAMIDE

PERTINENT DATES:

Official Summary Draft Completed: 9/23/97

Official Summary Completed: 9/23/97

RELATED DOCUMENTS:

OBJECTIVE OF THIS REVIEW:

Pediatric indications for Omniscan will be evaluated in this review. The following table shows which doses and indications are approved and which are currently being proposed in the various age groups:

Proposed Doses and Indications of Omniscan by Age Group				
Indication =imaging of:		children (2-12 yr)	adolescents (12-16 yr)	adults (>16 yr)
kidney				**0.05**
body organs		0.1	0.1	**0.1**
CNS		**0.1**	0.1	**0.1+0.2**
***Bolded dosages are approved. Unbolded dosages are proposed in this submission.**				

EVALUATION:

2. Body organ imaging in children and adolescents at the 0.1 mmole/kg dose will be considered.

3. 0.1 mmole/kg is already approved for CNS imaging in children and adolescents.

4. Since the dose and route of administration under consideration for approval are the same as already approved, pharm/tox evaluation is not necessary.

COMMENTS TO THE REVIEW TEAM:

1. Since Omniscan is eliminated by glomerular filtration, it may be more appropriate to dose pediatric patients based on body surface area (mmole/m^2).

2. Note that the previously approved dose for kidney imaging in adults is half the dose for whole body imaging (0.05 mmole/kg). If kidney imaging is approved along with whole body imaging, the dose for kidney imaging in pediatric patients should be clarified in any correspondence to the Sponsor.

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3/23/97

John Melograna
Reviewing Toxicologist

Orig. NDA 20-123
HFD-160/Division File
HFD-160/Chem/Place
HFD-160/Medical/Jones
HFD-160/CSO/Cho
HFD-160/Pharm/Melograna

I concured with the evaluation and comments.

P/T Tim Leader 9-23-97

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020123/S015

ADMINISTRATIVE DOCUMENTS

Div

DIVISION DIRECTOR MEMO TO THE FILE

NDA:	20123/S-015
DRUG:	OMNISCAN (gadodiamide) Injection
INDICATION:	Pediatric Labeling Expansion for MRI Contrast Enhancement
CATEGORY:	Labeling Supplement
SPONSOR:	Nycomed, Inc.
SUBMITTED:	April 23, 1997
DUE DATE:	October 3, 1997
COMPLETED:	October 3,1997

10/3/97

RELATED REVIEWS:

Clinical Team Leader - AE Jones 9/16/97
Pharmacokinetics - D. Udo, PhD, 9/25/97, D. Lee, PhD 9/26/97
Pharmacology - J Melograna, PhD 9/23/97
Project Manager - K. Cho, PhD

BACKGROUND:

OMNISCAN (gadodiamide) for injection is a gadolinium complex, nonionic drug that is intravenously administered to enhance magnetic resonance contrast. It is formulated as a hypertonic, solution with an osmolality of 789 mOsmol/kg at 37°C (approximately 2.8 times that of plasma).[1] OMNISCAN is marketed by Nycomed, Inc. for MRI contrast enhancement in the CNS (central nervous system) of adults and pediatric patients ≥2 years of age, and in the body (intrathoracic [nocardiac], intra-abdominal, pelvic and retroperitoneal regions of adults. Nycomed has submitted a labeling supplement

to dose with 0.05 to 0.1 mmol/kg depending upon the organ being imaged.

In support of the above pediatric labeling changes, Nycomed submitted a position paper that presented a proposal for predicting the renal elimination of OMNISCAN on the basis of the general knowledge about glomerular filtration in pediatrics, and pharmacokinetics modeling information derived from Also submitted were 23 literature references. Seven (7) of these references discussed the safety and tolerability of gadodiamide in pediatrics. The other 16 addressed the general handling and elimination of gadodiamide, the use gadodiamide to evaluate GFR, and the pharmacokinetics of gadodiamide in adults with renal insufficiency. None of the 23 literature articles were comprehensively summarized by Nycomed.

[1]Adapted from OMNISCAN package insert.

Drs' Jones (medical team leader), Lee (Biopharmaceutics Team Leader) and Udo (Biopharmaceutic's reviewer) reviewed the submitted literature and recommend a limited expansion of the pediatric indication to include the addition of pediatric use to the body indication. However, they recommend continuing age range at ≥ 2 years of age. I agree with these recommendations. The basis for these actions is summarized below.

1. Expansion of the Body Indication to Include Pediatric Patients.

The use of OMNISCAN is approved for CNS use pediatric patients ≥ 2 years of age as a bolus dose of 0.1 mmol/kg. The adult Body indication doses are 0.05 mmo/kg in the kidney and 0.1 mmol/kg for the other intra-abdominal, pelvic, retroperitoneal or intrathoracic organs. Therefore, the safety of the intravenous injection in pediatrics population over 2 years of age is established on the basis of the existing safety data used to support the CNS indication. The efficacy in the body is based upon the adult clinical trials.

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ASSESSMENT:

The safety of OMNISCAN in pediatric patients is supported by the data from the existing pediatric indication for CNS imaging. The efficacy for use in the body is supported by the adult adequate and well controlled trials.

ACTION: Approval of the expansion of the body indication to the pediatric population over 2 years of age.

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ATTACHMENT - PEDIATRIC REFERENCE ASSESSMENT

Pediatric Data from OMNISCAN

18. Abstract (one page):

This abstract reported on 4 clinical trials in a total of 294 pediatric patients who received either OMNISCAN or Magnevist. Of those who received OMNISCAN the demographics are: 1) 57 patients from 2 - 18 years, 2) 50 patients from 2 - 17 years. The ages were not further subdivided and the adverse events were reported as a pool. Overall 10 patients had adverse events that included bradycardia, shortness of breath, diarrhea, nausea, convulsion, fever, headache, pain, and flushing. Methodology for collecting AEs is not described; vital signs were not reported. The indication for the studies was central nervous system (CNS) evaluations (i.e., the pediatric indication that is already approved).

19.

20.

21.

22

23 This article reported on a 2 part clinical study of 174 patients from 2- 18 who received OMNISCAN(84) OMNISCAN . Although the article attempts to separate the adverse events into these two age groups, the numbers in the do not appear to be consistent with the articles descriptions. The article says for all patients in part 1 and 2. Therefore the sample size should be 84 + 13 = 97.

Thus far this is correct. But, the number of patients with adverse events in table one is 3 and in table number 3 the number of patients with adverse events is 9. Since all of the patients in table 3 should be counted in table 2, there must be an error somewhere. The information in the article is not sufficient to determine the source of the problem.

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SEP 30 1997

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS

LABELING REVIEW

NDA: 20-123/S-015

SPONSOR: Nycomed, Inc.

DRUG: Omniscan (gadodiamide) Injection

DATE OF SUBMISSION: April 7, 1997

BACKGROUND: This supplement provides a compilation of scientific publications which demonstrate the safety and effectiveness of OMNISCAN in the pediatric population. A comparison between the most recently approved labeling for NDA 20-123/S-013 and the proposed labeling for S-015 was completed. Any differences between the 2 labelings are noted below:

1. **CLINICAL TRIALS** Section, 6th sentence:

   Currently approved labeling (S-013) reads:

   "A blinded comparison of the results from the noncontrast enhanced MRI, the OMNISCAN 0.1 mmol/kg enhanced and the cumulative OMNISCAN 0.3 mmol/kg (0.1 followed by 0.2 mmol/kg) enhanced MRI's was performed."

   Proposed labeling (S-015) reads:

   "The results of the noncontrast enhanced MRI, the OMNISCAN 0.1 mmol/kg enhanced, and the cumulative OMNISCAN 0.3 mmol/kg (0.1 followed by 0.2 mmol/kg) enhanced MRIs **were compared blindly**."

ACCEPTABLE ▩ **UNACCEPTABLE** ▩ _____ Patricia Y, Love, M.D.

2. **CLINICAL TRIALS**, under **CNS (Central Nervous System)-Pediatric (2-18 years)**:

Currently approved labeling (S-013) reads:

CNS (Central Nervous System)-Pediatric (2-18 years)

"OMNISCAN was evaluated in two double-blind, parallel studies with MAGNEVIST® (gadopentetate dimeglumine) in a total of 173 children who were referred for a CNS MRI. The children received either OMNISCAN or MAGNEVIST® in a single 0.1 mmol/kg dose. OMNISCAN was administered to 84 children (45 boys and 39 girls) with a mean age of 8.9 (2-18) years; of these patients, 92% were Caucasian, 7% Black, and 1% other races. The demographics were similar for the 89 children who received MAGNEVIST®. Postcontrast MRI results showed that added diagnostic information, diagnostic confidence, and new patient management information were provided in approximately 76%, 67% and 52%, respectively of children who received OMNISCAN. These findings were similar to those of MAGNEVIST®. CT of histopathology was performed in 70/173 (42%) children who received OMNISCAN and MAGNEVIST®. Of these, 69/70 (98.6%) were confirmed.

Proposed labeling S-015 reads:

'CNS (Central Nervous System) **and Body -Pediatric**

ACCEPTABLE ▒ **UNACCEPTABLE** ▒ _____Patricia Y. Love, M.D.

3. **CLINICAL TRIALS**, under **Body (Intrathoracic [noncardiac], Intra-abdomian, Pelvic and Retroperitoneal) - Adults**, 4th sentence:

   Currently approved labeling (S-013) reads:

   "A blinded comparison of the pre-and post OMNISCAN images were evaluated for the degree of contrast, lesion detection and diagnostic value."

   Proposed labeling (S-015) reads:

   "Pre- and post-OMNISCAN images were evaluated blindly for the degree of contrast, diagnostic value, and lesion detection."

ACCEPTABLE ☒ **UNACCEPTABLE** ☒ _____Patricia Y. Love, M.D.

4. **CLINICAL TRIALS**, under **Body (Intrathoracic [noncardiac], Intra-abdominal, Pelvic and Retroperitoneal) - Adults**, 7th sentence:

   Currently approved labeling (S-013) reads:

   "These findings were similar to those of MAGNEVIST® 0.1 mmol/kg."

   Proposed labeling S-015 reads:

   "These findings were similar to those of MAGNEVIST **(gadopentetate dimeglumine)** 0.1 mmol/kg."

ACCEPTABLE ☒ **UNACCEPTABLE** ☒ _____Patricia Y. Love, M.D.

5. **INDICATIONS AND USAGE**, under **CNS (Central Nervous System)**, 1st sentence:

   Current approved labeling (S-013):

   "OMNISCAN is indicated for intravenous use in MRI for adults and children 2 years of age and older to visualize lesions with abnormal vascularity (or those thought to cause abnormalities in the blood-brain barrier) in the brain (intracranial lesions), spine, and associated tissues."

Proposed labeling S-015 reads:

ACCEPTABLE ▒UNACCEPTABLE ▒ _____Patricia Y. Love, M.D.

6. **INDICATIONS AND USAGE**, under **Body (Intrathoracic [noncardiac], Intra-abdominal, Pelvic and Retroperitoneal Regions)**, 1st sentence:

Current approved labeling (S-013) reads:

"OMNISCAN is indicated for intravenous administration for use in MRI in adults to facilitate the visualization of lesions with abnormal vascularity within the thoracic (noncardiac), abdominal, pelvic cavities, and the retroperitoneal space."

Proposed labeling S-015 reads:

ACCEPTABLE UNACCEPTABLE ▒ _____Patricia Y. Love, M.D.

7. **PRECAUTIONS**, under **General**, 2nd paragraph:

Current approved labeling (S-13) reads:

"OMNISCAN is cleared from the body by glomerular filtration. Significant hepatobiliary enteric pathway excretion has not been demonstrated. Dose adjustments in renal or hepatic impairment have not been studied. Caution should be exercised in patients with impaired renal insufficiency with or without hepatic impairment."

Proposed labeling S-015 reads:

ACCEPTABLE ▒ UNACCEPTABLE X _____David Lee, Ph.D.

8. **PRECAUTIONS**, under **Pediatric Use**, 1st paragraph:

Current approved labeling (S-013) reads:

"The safety and efficacy of OMNISCAN at a single dose of 0.1 mmol/kg have been established in children 2 years of age and older (See INDICATIONS and USAGE and DOSAGE and ADMINISTRATION). The safety and efficacy for doses >0.1 mmol/kg and for repeat procedures have not been studied in children."

Proposed labeling S-015 reads:

ACCEPTABLE ▒ UNACCEPTABLE ▒ _____Patricia Y. Love, M.D.

9. **PRECAUTIONS**, under **Pediatric Use**, 2nd paragraph:

Current approved labeling (S-013) reads:

"The safety and efficacy for children under 2 years of age have not been established."

Proposed labeling S-015 reads:

ACCEPTABLE ▒ **UNACCEPTABLE** ▒ _____David Lee, Ph.D.

10. **PRECAUTIONS**, under **Adverse Events**, under **Skin and Appendage Disorders**:

Current approved labeling (S-013) reads:

"Pruritis, rash, erythematous rash, skin discoloration, sweating, urticaria."

Proposed labeling S-015 reads:

"Pruritis, rash, erythematous rash, skin discoloration, sweating **increased**, urticaria."

ACCEPTABLE ▒ **UNACCEPTABLE** ▒ _____Patricia Y. Love, M.D.

APPEARS THIS WAY ON ORIGINAL

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11. **DOSAGE ADMINISTRATION**, under **CNS (Central Nervous System)**, 2nd paragraph:

Current approved labeling (S-013) reads:

CHILDREN (2-18 years): The recommended dose of OMNISCAN is 0.2 mL/kg (0.1 mmol/kg) administered as a bolus intravenous injection. (See the Dosage Chart).

Proposed labeling S-015 reads:

ACCEPTABLE ▒ **UNACCEPTALBE** ▒ _____Patricia Y. Love, M.D.

12. **DOSAGE AND ADMINISTRATION**, under **Body (Intrathoracic [noncardiac], Intra-abdominal, Pelvic, and Retroperitoneal Regions)**:

Current approved labeling (S-013) reads:

"For the kidney, the recommended dose of OMNISCAN is 0.1 mL/kg (0.05 mmol/kg). For the intrathoracic (noncardiac), intra-abdominal, and pelvic cavities, the recommended dose of OMNISCAN is 0.2 mL/kg (0.1 mmol/kg). (See the Dosage Chart)."

Proposed labeling S-015 reads:

"**Adult and Pediatric Patients**: For the kidney, the recommended dose of OMNISCAN is 0.1 mL/kg (0.05 mmol/kg). For the intrathoracic (noncardiac), intra-abdominal, and pelvic cavities, the recommended dose of OMNISCAN is 0.2 mL/kg (0.1 mmol/kg). (See the Dosage Chart)."

ACCEPTABLE ▒ **UNACCEPTALBE** ▒ _____Patricia Y. Love, M.D.

13. **DOSAGE AND ADMINISTRATION**, under **Dosage Chart**:

Current approved labeling (S-013) reads:

BODY WEIGHT kg	BODY WEIGHT lb	PEDIATRIC 0.1 (mmol/kg)	ADULTS 0.05 (mmol/kg)	ADULTS 0.1 (mmol/kg)	ADULTS 0.2 (mmol/kg)
		VOLUME (mL)	VOLUME (mL)		
12	26	2.4	-	-	-
14	31	2.8	-	-	-
16	35	3.2	-	-	-
18	40	3.6	-	-	-
20	44	4.0	-	-	-
22	48	4.4	-	-	-
24	53	4.8	-	-	-
26	57	5.2	-	-	-
28	62	5.6	-	-	-
30	66	6.0	-	-	-
40	88	8.0	4.0	8.0	16.0
50	110	10.0	5.0	10.0	20.0
60	132	12.0	6.0	12.0	24.0
70	154	14.0	7.0	14.0	28.0
80	176	16.0	8.0	16.0	32.0
90	198	-	9.0	18.0	36.0
100	220	-	10.0	20.0	40.0
110	242	-	11.0	22.0	44.0
120	264	-	12.0	24.0	48.0
130*	286	-	13.0	26.0	52.0

* The heaviest patient in clinical studies weighed 136 kg.

Proposed labeling S-015 reads:

120	264	-	-	12.0	24.0	48.0
130*	286	-	-	13.0	26.0	~~52.0~~

* The heaviest patient in clinical studies weighed 136 kg.

ACCEPTABLE ▩ **UNACCEPTABLE** ▩ David Lee, Ph.D.

Recommendation: Pending that all changes to the labelings are found acceptable the supplement and the proposed labeling can be approved. If the proposed changes are not found acceptable the supplement can be approved on marked-up draft labeling.

9/3-/97

Kyong Cho, Pharm.D.
Consumer Safety Officer

9/30/97

Concur:
David Lee, Ph.D.
Biopharmaceutics Team Leader

Concur:
Patricia Y. Love, M.D., M.B.A.
Director, Division of Medical Imaging and
Radiopharmaceutical Drug Products

cc:
Orig. NDA 20-123/S-015
HFD-160/Div. File
HFD-160/K.Cho

(NDA 20-123 labeling review)