June 10, 2010

Colleen Casey
U.S. Nuclear Regulatory Commission
Region III Materials Licensing Branch
2443 Warrenville Road
Suite 210
Lisle, Illinois 60532-4352

Re: Information request to Radioactive Material License 13-16558-01, Reference Control #317990 and #318764.

Dear Ms. Casey,

We are in receipt of your faxed communication dated April 20, 2010 regarding your request for additional information for our request for amendment to our byproduct materials license. As discussed in the telephone conversation on Wednesday, June 9th, we offer the following additional information:

1. Regarding the clarification of our request to replace Iodine-131 as iodobenzyl-guanidine with Iodine-123 MIGB, under 10 CFR 35.200 sub-items Nos. 6 through 9B, we would like to validate our request for license amendment for authorization for use of Iodine-131 MIBG. We have included documentation regarding the FDA approval of Iobenguane I 123 injection and our hospital approved protocol regarding the use of this agent. Supporting documents include:
    a. Communication from GE Healthcare dated September 19, 2008.
    b. Communication from FDA Advisory Committee dated August 11, 2008.
    c. Communication dated September 30, 2008 regarding FDA approval.
    d. Communication from Nuclear Pharmacy Newsletter dated September, 2008.
    e. Package insert.
    f. Methodist Hospitals Nuclear Medicine departmental protocol.

2. Regarding the deletion of certain sealed sources in accordance with 10 CFR 30.41 and 30.51, we apologize for the error of previous communications categorizing these sources under sub-item 7D. These sources were check sources used for Nuclear Medicine, not brachytherapy sources as previously indicated. We have included documentation regarding the inventory of sealed sources that were deleted. Documents include:
    a. Documentation to Indiana State Department of Health dated April 4, 2008 regarding the disposal of seven (7) sources in regular trash, based upon guidelines for disposal of low level waste NUREG/BR-0216.

METHODIST HOSPITALS

Northlake Campus
600 Grant Street
Gary, Indiana 46402

Midlake Campus
2269 West 25th Avenue
Gary, Indiana 46404

Southlake Campus
8701 Broadway
Merrillville, Indiana 46410

b. Documentation to our Methodist Hospital, Gary location, from International Isotope Inc validating the receipt on 03/14/2008 of Isotope Co-57, serial number 1154-161, with labeled activity of 20 mCi.
c. Documentation to our Methodist Hospital, Southlake or Merrillville location, from International Isotopes Inc validating the receipt on 03/14/2008 of Isotope Co-57, serial number 1154-163, with labeled activity of 20 mCi.

We would also like to apologize to the NRC for any confusion regarding the Methodist Hospitals name and campus locations. The Methodist Hospitals has two campuses, the Northlake Campus in Gary, Indiana, and the Southlake Campus in Merrillville, Indiana. Again, we apologize for any confusion in the use of these campus designations.

We are hopeful this additional information will satisfactorily address the request by NRC. We remain available to respond to any questions or concerns. Please feel free to contact me at 219-886-4540, or you may feel free to contact Gary Dillon, Radiation Safety Officer, at 219-738-5598.

Sincerely,

Denise Dillard, Vice-President
Government and External Affairs
T&R Officer

Cc: Gary Dillon
Mary Jo Hagan

April 4, 2008

Indiana State Department of Health,
Indoor & Radiological Health
2 North Meridian Street SF
Indianapolis, IN 46204

Re: Radioactive Source Disposal
Site ID# XN000233

To Whom It May Concern:

This letter is to inform you of the disposal of nine (9) radioactive sources from our facilities. The following changes should be made for our Material Registration Form.

Isotope Products Laboratories, Co-57 sheet source
Calibrated at 20mCi as of March 1, 2006
Model #NES 8450
Serial # 1154-161
Gary Campus
Returned to International Isotopes Idaho, Inc. on March 12, 2008 by Fed Ex
Wipe test-PASSED
Survey 0.07 mr/hr at surface in leaded case

Isotope Products Laboratories, Co-57 sheet source
Calibrated at 20mCi as of March 1, 2006
Model #NES 8450
Serial #1154-163
Merrillville Campus
Returned to International Isotopes Idaho, Inc. on March 1, 2008 by FedEx
Wipe test-PASSED
Survey 0.05 mr/hr at surface in leaded case

North American Scientific sheet source
Model# Med3709
Serial # B1638
Calibrated at 20mCi as of Jan 23, 2000
Merrillville Campus
Disposed of in regular trash having decayed past 10 half-lives
Wipe test-PASSED
Survey-0.04mr/hr @ surface

DuPont/Pharma sheet source
Model# NES 8450
Serial# S8450188-02
Calibrated at 20mCi as of Feb 15, 1999
Merrillville Campus
Disposed of in regular trash having decayed past 10 half-lives
Wipe test-PASSED
Survey-0.02mr/hr @ surface

Two (2) Co-57 button sources DuPont
Model: NES 289
50uCi each as of Nov. 1998
Merrillville Campus
disposed of in regular trash having decayed past 10 half-lives
Wipe test-PASSED
Survey-0.00mr/hr

Three (3) Co-57 button sources
50uCi each as of Feb 2000
Serial# W 11836-1-28
Serial# W 11836-1-29
Serial# W 11836-1-30
Merrillville Campus
Disposed of in regular trash having decayed past 10 half-lives
Wipe test-PASSED
Survey-0.00mr/hr

Survey Equipment

Victoreen THYAC *III survey meter Serial # 2962*
Instrument calibrated Sept 5, 2007
Merrillville campus
Victoreen Deluxe Wipe Test Counter, Model 05-578
Merrillville campus
Victoreen 498 survey meter Serial # 238
Instrument calibrated June 13, 2007
Gary campus
Victoreen Deluxe Wipe Test Counter, Model 05-578
Gary campus

ANY QUESTIONS, PLEASE CALL SHARON HAMILTON, RT, CNMT AT 219-738-5600

Sharon K. Hamilton, RT., CNMT

Sources disposed with the assistance of Stan A.Huber Consultants, Inc.

Erica Kluegel
Stan A. Huber Consultants, Inc

International Isotopes Inc.

To: GARY METHODIST HOSPITAL

Attn: SHARON HAMILTON

Fax: 219-738-6668

By sending this letter, International Isotopes, Inc, NRC license number 11-27680-01, acknowledges the receipt and transfer of possession of the radioactive source(s) described below. International Isotopes, Inc. received the source(s) at our facility located in Idaho Falls, Idaho.

Isotope	Manufacturer	Reference Date	Labeled Activity	Serial Number	Date Received	RA Number
Co-57	IPL	03/01/2006	20 mCi	1154-161	03/14/2008	None

International Isotopes Inc.
4137 Commerce Circle

Idaho Falls, Idaho 83401
Phone: 208-524-5300

800-699-3108

Fax: 208-524-1411
Website: www.internationalisotopes.com

International Isotopes Inc.

To: SOUTHLAKE METHODIST HOSPITAL

Attn: SHARON HAMILTON

Fax: 219-738-6668

By sending this letter, International Isotopes, Inc, NRC license number 11-27680-01, acknowledges the receipt and transfer of possession of the radioactive source(s) described below. International Isotopes, Inc. received the source(s) at our facility located in Idaho Falls, Idaho.

Isotope	Manufacturer	Reference Date	Labeled Activity	Serial Number	Date Received	RA Number
Co-57	IPL	03/01/2006	20 mCi	1154-163	03/11/2008	None

International Isotopes Inc.
4137 Commerce Circle

Idaho Falls, Idaho 83401
Phone: 208-524-5300

800-699-3108

Fax: 208-524-1411
Website: www.internationalisotopes.com

News and Events

FDA APPROVES GE HEALTHCARES ADREVIEW (LOBENGUANE I 123 INJECTION) DIAGNOSTIC AGENT FOR DETECTING NEUROENDOCRINE TUMORS IN CHILDREN, ADULTS

For More Information Contact
Ryan Fitzgerald
ryan.fitzgerald@ge.com
GE Healthcare, Americas
office: 414-721-2628
cell: 414-530-2735

September 19, 2008

PRINCETON, NJ – September 19, 2008 – GE Healthcare, a unit of General Electric Company (NYSE: GE), today announced that the Food and Drug Administration (FDA) has approved AdreView™ (Iobenguane I 123 Injection), a molecular imaging agent for the detection of rare neuroendocrine tumors in children and adults. AdreView provides high quality images that allow physicians to detect tumors, both at the time of initial diagnosis and at later examinations when relapse or recurrence is suspected.

"AdreView will have an immediate impact on improving diagnostic assessment of pediatric cancer patients with neuroblastoma," said Dr. Arnold Jacobson, MD, PhD, GE's clinical project leader for the AdreView program. "AdreView also will provide reliable imaging data to aid in identifying primary and metastatic pheochromocytoma, a predominantly adult tumor that often presents diagnostic challenges for clinicians. The introduction of AdreView is a reflection of our commitment to provide new and improved molecular imaging solutions for physicians and their patients."

Neuroblastoma is the most common extra-cranial solid tumor of young children up to 5 years of age, while pheochromocytoma is a rare tumor typically affecting adults. Both tumors usually arise from tissues of the sympathetic nervous system, most commonly in the adrenal glands. Neuroblastoma and pheochromocytoma can be difficult to detect at an early stage because symptoms may be non-specific when the tumors are small. AdreView images reflect the functional behavior of the tumor cells, thus allowing clearer characterization of even small tumors in comparison to similar appearing but non-malignant tissues. AdreView provides valuable adjunctive information to complement anatomic imaging procedures such as CT and MRI.

GE Healthcare expects to begin supplying this important new imaging agent to hospitals and imaging centers throughout the United States in the coming weeks. It will mark the first time this imaging agent, manufactured to the high standards required by FDA, is available

throughout the country. AdreView will also permit imaging of these tumors with a lower radiation dose than other agents that have been available for this purpose. AdreView also can be used with Single Photon Emission Computed Tomography (SPECT) imaging, a valuable addition for localizing sites of disease in the body.

"AdreView is just the first of many new products we are developing to deliver on the promise of molecular medicine," said Don Black, MD, vice-president of research and development for GE Healthcare's Medical Diagnostics business. "We are invested in making imaging agents that will make new medical breakthroughs a reality".

GE Healthcare began developing AdreView in 2004, and the agent was granted orphan-drug status by the FDA in December 2006. In May 2008, AdreView received priority review status from the FDA.

Important Safety Information

AdreView contains benzyl alcohol (10.3 mg/mL) which may cause serious reactions in premature or low birth-weight infants. Benzyl alcohol has been associated with a fatal "Gasping Syndrome" in premature infants and infants of low birth weight. Have anaphylactic and hypersensitivity treatment measures available prior to AdreView administration. AdreView is cleared by glomerular filtration and is not dialyzable. The radiation dose to patients with severe renal impairment may be increased due to the delayed elimination of the drug. Adreview is contraindicated in patients with known hypersensitivity to lobenguane or lobenguane sulfate. In clinical trials the most common adverse reactions seen were dizziness, rash, puritis, flushing or injection site hemorrhage reported in less than 1% of patients.

Please see full prescribing information www.md.gehealthcare.com

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ABOUT GE HEALTHCARE

GE Healthcare provides transformational medical technologies and services that are shaping a new age of patient care. Our broad expertise in medical imaging and information technologies, medical diagnostics, patient monitoring systems, drug discovery, biopharmaceutical manufacturing technologies, performance improvement and performance solutions services help our customers to deliver better care to more people around the world at a lower cost. In addition, we partner with healthcare leaders, striving to leverage the global policy change necessary to implement a successful shift to sustainable healthcare systems. Our "healthymagination" vision for the future invites the world to join us on our journey as we continuously develop innovations focused on reducing costs, increasing access and improving quality and efficiency around the world. Headquartered in the United Kingdom, GE Healthcare is a $17 billion unit of General Electric Company (NYSE: GE). Worldwide, GE Healthcare employs more than 46,000 people committed to serving healthcare professionals and their patients in more than 100 countries. For more information about GE Healthcare, visit our website at www.gehealthcare.com

11 August 2009

FDA ADVISORY COMMITTEE RECOMMENDS DaTSCAN™ (Ioflupane I 123 Injection)

PRINCETON, NJ--GE Healthcare announced today that the Peripheral Central Nervous System Drugs advisory committee of the U.S. Food an Drug Administration (FDA) has voted to recommend DaTSCAN (Ioflupa 123 Injection) to the FDA. The panel determined DaTSCAN has a favor risk to benefit profile, voting 11 to two with one abstention.

The proposed indication for DaTSCAN is for the visualization of the dopamine transporter (DaT) distribution within the striata by single phot emission computed tomography (SPECT) imaging in patients presentin with symptoms or signs suggestive of dopaminergic neurodegeneration.

In May 2009, the FDA accepted the New Drug Application and granted DaTSCAN priority review, a designation identified for areas of unmet medical need. If approved, DaTSCAN will be the first radiopharmaceuti agent available to detect DaT distribution within the brain.

"We are pleased that the committee has recognized the potential benefi DaTSCAN," said Don Black, MD, head of R&D for GE Healthcare Medi Diagnostics. "Making DaTSCAN available in the U.S. would be an important milestone for GE Healthcare and improved patient care."

The Prescription Drug User Fee Act (PDUFA) date for DaTSCAN is September 9, 2009.

About DaTSCAN
DaTSCAN has been available in Europe since 2000 and has been used more than 200,000 patients in 32 countries. It has been administered to nearly 1,000 patients in clinical trials.

About GE Healthcare
GE Healthcare provides transformational medical technologies and services that are shaping a new age of patient care. Our broad expertis medical imaging and information technologies, medical diagnostics, pati monitoring systems, drug discovery, biopharmaceutical manufacturing technologies, performance improvement and performance solutions services help our customers to deliver better care to more people aroun the world at a lower cost. In addition, we partner with healthcare leaders striving to leverage the global policy change necessary to implement a successful shift to sustainable healthcare systems.

Our "healthymagination" vision for the future invites the world to join us our journey as we continuously develop innovations focused on reducin costs, increasing access and improving quality and efficiency around th world. Headquartered in the United Kingdom, GE Healthcare is a $17 billion unit of General Electric Company (NYSE: GE). Worldwide, GE Healthcare employs more than 46,000 people committed to serving healthcare professionals and their patients in more than 100 countries. more information about GE Healthcare, visit our website at www.gehealthcare.com.

PRESS CONTACTS

Download All Assets

New Gamma-Scintigraphy Agent Approved by FDA for the Detection of Neuroendocrine Tumors

September 30, 2008

Iobenguane I 123 injection (AdreViewâ„¢ | GE Healthcare), a diagnostic radiopharmaceutical agent for gamma-scintigraphy, has recently been approved by the US Food and Drug Administration (FDA) for the detection of rare neuroendocrine tumors, both during the initial diagnosis as well as for subsequent examinations of suspected recurrence in adults and children.

The premium imaging quality of AdreView offers consistent imaging data that would be helpful in detecting primary and metastatic pheochromocytoma in adults, and would be essentially beneficial in improving the diagnosis of neuroblastomas in pediatric patients. The unambiguous images provided by AdreView, using the functional behavior of even small tumors, aids in differentiating such tumors from similar appearing non-malignant tissues. It has been approved for use as an adjunctive to other diagnostic tests since the information provided by AdreView complements other anatomic imaging procedures such as magnetic resonance imaging (MRI), computed tomography (CT) and single photon emission computed tomography (SPECT) imaging. Another major advantage of the AdreView over other imaging agents is that it facilitates tumor imaging with lower radiation doses.

Recently, Rozovsky and colleagues (*American Journal of Roentgenology*, 2008) conducted a study to assess the effect of SPECT/CT fusion images in correlation with metaiodobenzylguanidine (MIBG) scintigraphy (iobenguane) and image analysis in neuroblastoma and pheochromocytoma. Subjects comprised of three adult patients with pheochromocytoma and eight children with neuroblastoma undergoing ^{123}I-MIBG scintigraphy and computed tomography at an interval of 2 to 30 days between MIBG scintigraphy and diagnostic CT, during treatment follow-up. Discordance in data between SPECT/CT and diagnostic CT was observed in nine out of 15 imaging studies, while six studies had demonstrated concordant results of planar MIBG and diagnostic CT. Results demonstrated that the localization of the pathologic sites was possible by MIBG SPECT/CT, which was otherwise difficult to identify using diagnostic CT. The researchers observed that the use of MIBG SPECT/CT had enhanced the diagnostic certainty in 89% of studies where data were discordant.

Pheochromocytomas are benign tumors formed in chromaffin cells of the body, especially inside the adrenal gland, leading to excess release of catecholamine hormones. Although, pheochromocytomas are non-cancerous, they may lead to other health problems such as hypertension, heart palpitations, flushing of the face, pounding headaches, nausea, and vomiting. Neuroblastoma, a cancer of immature nerve tissues, usually begins in the adrenal glands, but may also form in neck, chest or spinal cord during early childhood. According to the American Cancer Society, neuroblastoma accounts for 6.7% of all childhood cancers and the 5-year survival rate for neuroblastoma patients is estimated to be 69%. X-rays, ultrasound, CT, MRI, PET, MIBG and bone scans are the main imaging techniques used to diagnose pheochromocytoma and neuroblastoma.

The approval of AdreView injection provides for improved diagnostic assessment of neuroendocrine tumors with better quality imaging, both in children and adults. The advantages of AdreView, such as imaging with lesser irradiation dosages and adjunctive use with single photon emission computed tomography (SPECT) imaging, will allow better localization of the lesions.

About GE Healthcare â€“ UK-based GE Healthcare, a unit of General Electric Company, offers transformational medical technologies such as imaging and information technologies, diagnostics, patient monitoring systems, and drug discovery and manufacturing technologies.

References

1. FDA Approves GE Healthcares AdreView (Lobenguane I 123 Injection) Diagnostic Agent For Detecting Neuroendocrine Tumors In Children, Adults. News and Events. *GE Healthcare*. Last Accessed September 25, 2008.

2. Rozovsky K, Koplewitz BZ, Krausz Y, et al. Added value of SPECT/CT for correlation of MIBG scintigraphy and diagnostic CT in neuroblastoma and pheochromocytoma. *AJR Am J Roentgenol*. 2008 Apr;190(4):1085-90.

Written by · Filed Under Basic Sciences, Drug Development, Endocrinology, Lab Medicine, Medical Technology, Oncology, Pathology, Pediatrics, Pharma, Pharma Industry, Ultrasound

Comments

Got something to say?

You must be logged in to post a comment.

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  - ALERT: Herpes Zoster Ophthalmicus Diagnosis, an Indicator for Increased Stroke Risk
  - Dramatic Rise in Nonmelanoma Skin Cancer Prevalence Seen Across the US
  - Study Substantiates Effectiveness of Prophylactic Mastectomy in *BRCA*1/2 Mutation Carriers
  - ALERT: Disrupted CSF Levels of Tau Protein could Help in Early Detection of Alzheimer Disease
  - ALERT: Dopamine-based MRI Sensor could Revolutionize Conventional Brain Imaging
  - Researchers Validate Use of Artificial Neural Networks in Predicting AD Progression
  - Study Validates Long-term Safety and Efficacy of Proximal Gastrectomy for Upper-third Early Gastric Carcinoma
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Nuclear Pharmacy eNewsletter

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In This Issue

Nuclear Facts

Large Hadron Collider

September 10th the first beams were circulated through the new world's largest and highest-energy particle accelerator. However, the collider will be down until next spring following technical problems within the first two days of operation. The collider is contained in a circular tunnel with a 17 mile circumference crossing the border between Switzerland and France. To learn more about this exciting experimental facility see Wikipedia and view a great rap video on YouTube!

Case Study

Dear Nuclear Medicine Professional,

Murphy's Law has been in effect lately with the world's supply of molybdenum from nuclear reactors. The Nordion reactor in Canada (one of the few up and running) was hit by lightening and had to be shut down early compounding the shortage problem. Hopefully , we will have an increased supply by next week so that we can celebrate Nuclear Medicine Week!

Nuclear Reactor Update

The world's supply of molybdenum is fluctuating from week to week depending on reactor production. Typically, reactors run for about 3.5 weeks before a scheduled maintenance period which may run 3-4 days to a couple of weeks. When reactors are down and maintenance periods overlap, the Mo-99 supply is affected. The HFR reactor is anticipated to be down through November, but the BR2 reactor should be back in service about Oct. 21. Covidien will be posing an update to the situation in the next couple of days. Check their website for updates. You can also get additional informaton about the reactor update from the NRG website.

FDA Approves AdreView

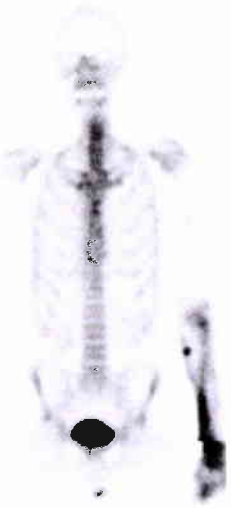
GE Healthcare received FDA approval for I-123 lobenquane (AdreView, I-123 MIBG) for neuroendocrine tumor imaging. GE received orphan-drug status to develop this agent in 2004. I-123 MIBG is also used in investigational studies as a diagnostic tool to assess cardiac sympathetic innervation.

Hepatobiliary CE - Free

A free CE on-demand webcourse titled Hepatobiliary Scintigraphy in Gall Bladder Disease is available from www.ProCE.com. This is an excellent program sponsored by Bracco Diagnostics that you will find very informative.

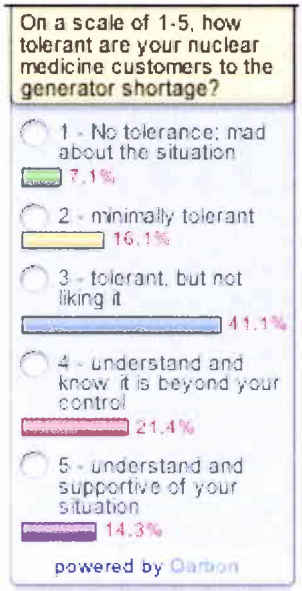
Generic Sestamibi Available

Covidien is first to the market with generic sestamibi. FDA approval was received on Sept. 23rd. (If we only have the technetium to make it!)



A 61 year old man was recently diagnosed with prostate cancer. A bone scan was ordered
continued...

Online Poll Results



Quick Links...

Nuclear Education Online
The Nuclear Pharmacy
Nuclear Job Postings
DOT Training
Basic Radiation Safety
BPS Website
APhA website

Online Poll

Have you witnessed any downturn in business that you can attribute to the current economic situation?

Vote Online

Calendar of Events

Oct 1-31	American Pharmacists Month
Oct. 4	Board Certification Exam Date
Oct. 3-5	Missouri Valley Chapter, SNM Meeting, Omaha, NE
Oct. 6-10	Nuclear Medicine Week
Oct. 11	MidEastern Chapter Fall Meeting, Annapolis, MD
Oct. 16-18	Eastern Great Lakes Chapter Meeting, Niagara Falls, NY
Oct. 16-19	Western Regional SNM Meeting, Portland, OR
Oct. 18-19	Florida Pharmacists Assoc Mid-Year, Orlando
Oct. 24-26	NE Regional Meeting, NY & New England Chapters, Newport, RI
Oct. 25-26	What's "Nu" in Nuclear Medicine, Grand Rapids, MI
Oct. 31-Nov.1	Practical PET Imaging, Las Vegas

neo Nuclear Education Online

Nicki Hilliard, PharmD, BCNP
Professor of Nuclear Pharmacy

If you have problems viewing the eNewsletter go to
http://www.nuclearonline.org/newsletter/Sept08.htm

Previous eNewsletters
Aunt Minnie
NANP website

Join Our Mailing List!

Basic Radiation Safety Training

Only $45

The Nuclear Education Online program is offering a Basic Radiation Safety Course for those workers that need a basic introductory course to Radiation Safety. Great for drivers and support staff. A great way to document their training.

Click here for more information.

GE Healthcare

AdreView™
Iobenguane I 123 Injection

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

AdreView (Iobenguane I 123 Injection) for Intravenous Use
Initial U.S. Approval: 2008

INDICATIONS AND USAGE

AdreView is a diagnostic radiopharmaceutical agent for gamma-scintigraphy. It is indicated for use in the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests. (1)

DOSAGE AND ADMINISTRATION

- AdreView emits radiation and must be handled with appropriate safety measures. (2.1, 2.6)
- Administer thyroid blockade medications prior to AdreView. (2.2, 5.4)
- Measure patient dose by a suitable radioactivity calibration system immediately prior to administration. (2.4)
- For patients ≥ 16 years of age or < 16 years of age and ≥ 70 kg: administer 10 mCi (370 MBq). (2.4, 2.5)
- For patients < 16 years of age and < 70 kg: amount scaled to the adult reference activity based on weight. (2.5)

DOSAGE FORMS AND STRENGTHS

5 mL of sterile solution for intravenous injection in a single use vial (2 mCi/mL at calibration time). (3)

CONTRAINDICATIONS

Known hypersensitivity to iobenguane or iobenguane sulfate. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity reactions have followed AdreView administration. Have anaphylactic and hypersensitivity treatment measures available prior to AdreView administration. (5.1)
- AdreView contains benzyl alcohol (10.3 mg/mL) which may cause serious reactions in premature or low birth-weight infants. (5.2)
- Patients with severe renal impairment may have increased radiation exposure and decreased quality of AdreView images. (5.3)
- Failure to block thyroid iodine uptake may result in iodine 123 accumulation in the thyroid. (5.4)
- Drugs which block norepinephrine uptake or deplete norepinephrine stores may decrease AdreView uptake in neuroendocrine tumors. When medically feasible, stop these drugs before AdreView administration and monitor patients for withdrawal signs and symptoms. (5.5)

ADVERSE REACTIONS

Serious hypersensitivity reactions have been reported following AdreView administration. The most common adverse reactions, dizziness, rash, pruritis, flushing and injection site hemorrhage occurred in < 1% of patients. (6.1, 6.2)

To report SUSPECTED ADVERSE REACTIONS, contact GE Healthcare at 1-800-654-0118 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Amitryptiline and derivatives, imipramine and derivatives, other antidepressants that inhibit norepinephrine transporter, antihypertensives that deplete norepinephrine stores or inhibit reuptake, sympathomimetic amines and cocaine: Discontinue for 5 biological half-lives prior to AdreView administration. (7)

USE IN SPECIFIC POPULATIONS

- Pregnancy: any radiopharmaceutical, including AdreView, may cause fetal harm. (8.1)
- Nursing mothers: A decision should be made whether to interrupt nursing after AdreView administration or not to administer AdreView, taking into account the importance of the drug to the mother. (8.3)
- Pediatrics: safety and effectiveness have not been established in pediatric patients < 1 month of age. (8.4)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 09/2008

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

AdreView is a radiopharmaceutical indicated for use in the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests.

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety

AdreView emits radiation and must be handled with appropriate safety measures to minimize radiation exposure to clinical personnel and patients. Radiopharmaceuticals should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides. AdreView dosing is based upon the radioactivity determined using a suitable calibration system immediately prior to administration.

To minimize radiation dose to the bladder, prior to and following AdreView administration, encourage hydration to permit frequent voiding. Encourage the patient to void frequently for the first 48 hours following AdreView administration [*see Clinical Pharmacology (12.2)*].

2.2 Thyroid Blockade

Before administration of AdreView, administer Potassium Iodide Oral Solution or Lugol's Solution (equivalent to 100 mg iodide for adults, body-weight adjusted for children) or potassium perchlorate (400 mg for adults, body-weight adjusted for children) to block uptake of iodine 123 by the patient's thyroid. Administer the blocking agent at least one hour before the dose of AdreView [*see Warnings and Precautions (5.4)*].

2.3 Preparation and Administration

Inspect the AdreView vial for particulate matter and discoloration prior to administration. Use aseptic procedures and a radiation shielding syringe during administration. Administer the dose as an intravenous injection over 1 to 2 minutes. A subsequent injection of 0.9% sodium chloride may be used to ensure full delivery of the dose.

2.4 Recommended Dose for Adults

For adults (≥ 16 years of age), the recommended dose is 10 mCi (370 MBq) [*see Clinical Studies (14.1)*].

2.5 Recommended Dose for Pediatric Patients

For pediatric patients < 16 years of age weighing ≥ 70 kg, the recommended dose is 10 mCi (370 MBq) [*see Clinical Studies (14.1)*].

For pediatric patients < 16 years of age weighing < 70 kg, the recommended dose should be calculated according to patient body weight as shown in Table 1 [*see Clinical Studies (14.1)*]. The benzyl alcohol in AdreView may cause serious adverse reactions in premature or low birth-weight infants [*see Warnings and Precautions (5.2)*].

Table 1
AdreView Dose Preparation for Pediatric Patients*

Weight (kg)	Fraction of adult activity	AdreView (mCi) pediatric dose	AdreView (MBq) pediatric dose
3	0.1	1	37
4	0.14	1.4	52
6	0.19	1.9	70
8	0.23	2.3	85.1
10	0.27	2.7	99.9
12	0.32	3.2	118.4
14	0.36	3.6	133.2
16	0.4	4	148
18	0.44	4.4	162.8
20	0.46	4.6	170.2
22	0.5	5	185
24	0.53	5.3	196.1
26	0.56	5.6	207.2
28	0.58	5.8	214.6
30	0.62	6.2	229.4
32	0.65	6.5	240.5
34	0.68	6.8	251.6
36	0.71	7.1	262.7
38	0.73	7.3	270.1
40	0.76	7.6	281.2
42	0.78	7.8	288.6
44	0.8	8	296
46	0.82	8.2	303.4
48	0.85	8.5	314.5
50	0.88	8.8	325.6
52	0.9	9	333
54	0.9	9	333
56	0.92	9.2	340.4
58	0.92	9.2	340.4
60	0.96	9.6	355.2
62	0.96	9.6	355.2
64	0.98	9.8	362.6
66	0.98	9.8	362.6
68	0.99	9.9	366.3

*Based on a reference activity for an adult scaled to body weight according to the schedule proposed by the European Association of Nuclear Medicine Paediatric Task Group.

2.6 Radiation Dosimetry

The estimated absorbed radiation doses to adults and children from intravenous administration of AdreView are as shown in Table 2.

Table 2
Estimated Absorbed Radiation Dose from AdreView

ORGAN / TISSUE	ABSORBED DOSE PER UNIT ADMINISTERED ACTIVITY											
	ADULT		15-YEAR OLD		10-YEAR OLD		5-YEAR OLD		1-YEAR OLD		NEONATES	
	µGy/MBq	rad/mCi	µGy/MBq	rad/mCi	µGy/MBq	rad/mCi	µGy/MBq	rad/mCi	µGy/MBq	rad/mCi	µGy/MBq	rad/mCi
Adrenals	16	0.059	21	0.078	31	0.115	42	0.155	67	0.248	111	0.411
Brain	3.9	0.014	4.9	0.018	8.1	0.030	13	0.048	24	0.089	55.9	0.207
Breast	4.7	0.017	5.9	0.022	9.4	0.035	15	0.056	28	0.104	65.3	0.242
Gallbladder	20	0.074	24	0.089	34	0.126	51	0.189	95	0.352	200	0.740
GI Tract – Stomach Wall	7.6	0.028	10	0.037	17	0.063	27	0.100	51	0.189	114	0.422
GI Tract – Small Intestine Wall	7.7	0.028	9.8	0.036	16	0.059	25	0.093	46	0.170	104	0.385
GI Tract – Colon Wall	8.1	0.030	10	0.037	16	0.059	26	0.096	46	0.170	104.3	0.386
GI Tract – Upper Large Intestine Wall	8.4	0.031	11	0.041	18	0.067	30	0.111	53	0.196	119	0.440
GI Tract – Lower Large Intestine Wall	7.7	0.028	9.6	0.036	15	0.056	21	0.078	38	0.141	84.9	0.314
Heart Wall	18	0.067	23	0.085	35	0.130	53	0.196	94	0.348	182	0.673
Kidneys	13	0.048	16	0.059	24	0.089	35	0.130	59	0.218	132	0.488
Liver	67	0.248	87	0.322	130	0.481	180	0.666	330	1.221	720	2.664
Lungs	16	0.059	23	0.085	32	0.118	48	0.178	89	0.329	215	0.796
Muscles	6	0.022	7.6	0.028	12	0.044	17	0.063	33	0.122	75.1	0.278
Esophagus	6	0.022	7.6	0.028	11	0.041	18	0.067	32	0.118	72.2	0.267
Osteogenic Cells	16	0.059	21	0.078	31	0.115	47	0.174	100	0.370	254	0.940
Ovaries	7.9	0.029	10	0.037	15	0.056	22	0.081	41	0.152	92.3	0.342
Pancreas	12	0.044	15	0.056	25	0.093	39	0.144	68	0.252	143	0.529
Red marrow	5.6	0.021	6.8	0.025	10	0.037	15	0.056	30	0.111	89.5	0.331
Skin	3.7	0.014	4.4	0.016	7.1	0.026	11	0.041	21	0.078	53.1	0.196
Spleen	20	0.074	27	0.100	42	0.155	64	0.237	110	0.407	282	1.043
Testes	5.4	0.020	7.1	0.026	11	0.041	16	0.059	30	0.111	69.9	0.259
Thymus	6	0.022	7.6	0.028	11	0.041	18	0.067	32	0.118	72.2	0.267
Thyroid	4.7	0.017	6.1	0.023	9.9	0.037	16	0.059	30	0.111	69.4	0.257
Urinary Bladder Wall	66	0.244	84	0.311	110	0.407	110	0.407	200	0.740	478.0	1.769
Uterus	11	0.041	14	0.052	21	0.078	28	0.104	51	0.189	110.0	0.407
Whole Body	8.1	0.030	10	0.037	16	0.059	24	0.089	44	0.163	104.0	0.385
EFFECTIVE DOSE – µSv/MBq	13.7		18.1		26.7		37.6		68		162	
EFFECTIVE DOSE – mSv/mCi	0.507		0.670		0.988		1.39		2.52		6	

*OLINDA/EXM calculation based on biodistribution data from Swanson et al. and Publication 53 of the ICRP (International Commission on Radiological Protection) [Annals of the ICRP 1987; 18 (1-4): 329-331]

The effective dose resulting from an administered activity amount of 10 mCi is 5.07 mSv in an adult.

2.7 Imaging Guidelines

Begin whole body planar scintigraphy imaging 24 ± 6 hours following administration of AdreView. Single photon emission computed tomography (SPECT) may be performed following planar scintigraphy, as appropriate [*see Clinical studies* 14.1].

3 DOSAGE FORMS AND STRENGTHS

Single use vials containing 5 mL solution for intravenous injection (2 mCi/mL at calibration time).

4 CONTRAINDICATIONS

AdreView is contraindicated in patients with known hypersensitivity to iobenguane or iobenguane sulfate.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions have been reported following AdreView administration. Prior to administration, question the patient for a history of prior reactions to iodine, an iodine-containing contrast agent or other products containing iodine. If the patient is known or strongly suspected to have hypersensitivity to iodine, an iodine-containing contrast agent or other products containing iodine, the decision to administer AdreView should be based upon an assessment of the expected benefits compared to the potential hypersensitivity risks. Have anaphylactic and hypersensitivity treatment measures available prior to AdreView administration [*see Adverse Reactions (6.2)*].

5.2 Risks for Benzyl Alcohol Toxicity in Infants

AdreView contains benzyl alcohol at a concentration of 10.3 mg/mL. Benzyl alcohol has been associated with a fatal "Gasping Syndrome" in premature infants and infants of low birth weight. Exposure to excessive amounts of benzyl alcohol has been associated with toxicity (hypotension, metabolic acidosis), particularly in neonates, and an increased incidence of kernicterus, particularly in small preterm infants. There have been rare reports of deaths, primarily in preterm infants, associated with exposure to excessive amounts of benzyl alcohol [*see Description (11)*].

Observe infants for signs or symptoms of benzyl alcohol toxicity following AdreView administration. AdreView safety and effectiveness have not been established in neonates (pediatric patients below the age of 1 month).

5.3 Increased Radiation Exposure in Patients with Severe Renal Impairment

AdreView is cleared by glomerular filtration and is not dialyzable. The radiation dose to patients with severe renal impairment may be increased due to the delayed elimination of the drug. Delayed AdreView clearance may also reduce the target to background ratios and decrease the quality of scintigraphic images. These risks importantly may limit the role of AdreView in the diagnostic evaluation of patients with severe renal impairment. AdreView safety and efficacy have not been established in these patients [*see Clinical Pharmacology (12.2)*].

5.4 Thyroid Accumulation

Failure to block thyroid uptake of iodine 123 may result in an increased long term risk for thyroid neoplasia. Administer thyroid blocking medications before AdreView administration [*see Dosage and Administration (2.2)*].

5.5 Risks with Concomitant Medication Withdrawal

Drugs which interfere with norepinephrine uptake or retention may decrease the uptake of AdreView in neuroendocrine tumors and lead to false negative imaging results. When medically feasible, stop these drugs before AdreView administration and monitor patients for the occurrence of clinically significant withdrawal symptoms, especially patients with elevated levels of circulating catecholamines and their metabolites [*see Drug Interactions (7)*].

5.6 Hypertension

Assess the patient's pulse and blood pressure before and intermittently for 30 minutes after AdreView administration. AdreView may increase release of norepinephrine from chromaffin granules and produce a transient episode of hypertension, although this was not observed in the clinical study. Prior to AdreView administration, ensure emergency cardiac and anti-hypertensive treatments are readily available.

6 ADVERSE REACTIONS

6.1 Clinical Study Experience

Serious adverse reactions were not observed in the AdreView clinical study. The data described below reflect AdreView exposure to 251 patients with known or suspected pheochromocytoma or neuroblastoma. The average ages were 49 years (range 17 - 88 years) for adults and, for pediatric patients, 4 years (range 1 month - 16 years). Slightly less than half the patients were male. All patients were monitored for adverse reactions over a 24 hour period following AdreView administration.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse reactions were all mild to moderate in severity and were predominantly isolated occurrences (≤ 2 patients) of one of the following reactions: dizziness, rash, pruritus, flushing or injection site hemorrhage.

6.2 Postmarketing Experience

Because postmarketing reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Hypersensitivity reactions have uncommonly been reported during the postmarketing use of AdreView [*see Warnings and Precautions (5.1)*].

7 DRUG INTERACTIONS

The following drugs have the potential to decrease the uptake of norepinephrine and cause false negative imaging results: antihypertensives that deplete norepinephrine stores or inhibit reuptake (e.g., reserpine, labetalol), antidepressants that inhibit norepinephrine transporter function (e.g., amitriptyline and derivatives, imipramine and derivatives, selective serotonin reuptake inhibitors), sympathomimetic amines (e.g., phenylephrine, phenylpropanolamine, pseudoephedrine and ephedrine), and cocaine. Clinical studies have not determined which specific drugs may cause false negative imaging results nor whether all drugs in any specific pharmacologic class have the same potential to produce the negative imaging results. Increasing the dose of AdreView will not overcome any potential uptake limiting effect of these drugs. Before AdreView administration, discontinue (for at least 5 biological half-lives) drugs known or expected to reduce norepinephrine uptake, as clinically tolerated.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: Any radiopharmaceutical, including AdreView, has a potential to cause fetal harm. It is not known whether AdreView can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Animal reproduction studies have not been conducted with AdreView. AdreView should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

It is not known whether AdreView is excreted into human milk. However, iodine 123 is excreted into human milk. Because many drugs are excreted into human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to interrupt nursing after administration of AdreView or not to administer AdreView, taking into account the importance of the drug to the mother. Based on the physical half-life of iodine 123 (13.2 hours) nursing women may consider interrupting nursing for 6 days after AdreView administration in order to minimize risks to nursing infants.

8.4 Pediatric Use

The safety and effectiveness of AdreView have been established in the age groups 1 month to 16 years [*see Clinical Studies (14.1)*]. Safety and effectiveness in pediatric patients below the age of 1 month have not been established [*see Warnings and Precautions (5.2)*].

8.5 Geriatric Use

The AdreView clinical study did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly population should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

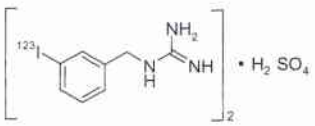
AdreView is excreted by the kidneys, and the risks of adverse reactions, increased radiation dose, and occurrence of falsely negative imaging results may be greater in patients with severely impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and image interpretation. Consider assessment of renal function in elderly patients prior to AdreView administration.

10 OVERDOSAGE

The major manifestations of overdose relate predominantly to increased radiation exposure, with the long term risks for neoplasia.

11 DESCRIPTION

AdreView (Iobenguane I 123 Injection) is a sterile, pyrogen-free radiopharmaceutical for intravenous injection. Each mL contains 0.08 mg iobenguane sulfate, 74 MBq (2 mCi) of I 123 (as iobenguane sulfate I 123) at calibration date and time on the label, 23 mg sodium dihydrogen phosphate dihydrate, 2.8 mg disodium hydrogen phosphate dihydrate and 10.3 mg (1% v/v) benzyl alcohol with a pH of 5.0 – 6.5. Iobenguane sulfate I 123 is also known as I 123 *meta*-iodobenzylguanidine sulfate and has the following structural formula:



11.1 Physical Characteristics

Iodine 123 is a cyclotron-produced radionuclide that decays to Te 123 by electron capture and has a physical half-life of 13.2 hours.

Table 3
Principal Radiation Emission Data – Iodine 123

Radiation	Energy Level (keV)	Abundance (%)
Gamma	159	83

11.2 External Radiation

The specific gamma ray constant for iodine 123 is 1.6 R/mCi-hr at 1 cm. The first half value thickness of lead (Pb) for I 123 is 0.04 cm. The relative transmission of radiation emitted by the radionuclide that results from interposition of various thicknesses of Pb is shown in Table 4 (e.g., the use of 2.16 cm Pb will decrease the external radiation exposure by a factor of about 1,000).

Table 4
Reduction in In-air Collision Kerma Caused by Lead Shielding*

Shield Thickness cm of lead (Pb)	Reduction in In-air Collision Kerma
0.04	0.5
0.13	10^{-1}
0.77	10^{-2}
2.16	10^{-3}
3.67	10^{-4}

*Calculation based on attenuation and energy-transfer coefficients obtained from National Institute of Standards & Technology Report NISTIR 5632.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Iobenguane is similar in structure to the antihypertensive drug guanethedine and to the neurotransmitter norepinephrine (NE). Iobenguane is, therefore, largely subject to the same uptake and accumulation pathways as NE. Iobenguane is taken up by the NE transporter in adrenergic nerve terminals and stored in the presynaptic storage vesicles. Iobenguane accumulates in adrenergically innervated tissues such as the adrenal medulla, salivary glands, heart, liver, spleen and lungs as well as tumors derived from the neural crest. By labeling iobenguane with the isotope iodine 123, it is possible to obtain scintigraphic images of the organs and tissues in which the radiopharmaceutical accumulates.

12.2 Pharmacodynamics

AdreView is a diagnostic radiopharmaceutical which contains a small quantity of iobenguane that is not expected to produce a pharmacodynamic effect [*see Description (11)*]. To minimize radiation dose to the thyroid gland, this organ should be blocked before dosing [*see Dosage and Administration (2.1)*]. Since iobenguane is excreted mainly via the kidneys, patients with severe renal insufficiency may experience increased radiation exposure and impaired imaging results. Frequent voiding should be encouraged after administration to minimize the radiation dose to the bladder [*see Warnings and Precautions (5.3)*]. The calculation of the estimated radiation dose is shown in Table 2 [*see Dosage and Administration (2.5)*].

12.3 Pharmacokinetics

Iobenguane is rapidly cleared from the blood and accumulates in adrenergically innervated tissues [*see Clinical Pharmacology (12.1)*]. Retention is especially prolonged in highly adrenergically innervated tissues (e.g., the adrenal medulla, heart, and salivary glands).

The majority of the iobenguane dose is excreted unaltered by the kidneys via glomerular filtration. A rapid initial clearance of circulating iobenguane is observed, followed by a slow clearance as iobenguane is released from other compartments. In patients with normal renal function, 70 to 90% of the administered dose is recovered unaltered in urine within 4 days. Iobenguane is not cleared by dialysis [*see Warnings and Precautions (5.3)*]. Most of the remaining radioactivity recovered in the urine is in the form of the radioiodinated metabolite *m*-iodohippuric acid (MIHA) (typically ≤ 10%) and free radioiodide (typically ≤ 6%). The enzymatic process responsible for metabolism has not been well characterized and the pharmacologic activity of these metabolites has not been studied. Only a small amount (< 1%) of the injected dose is eliminated via the feces.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Iobenguane hemisulfate was not mutagenic *in vitro* in the Ames bacterial mutation assay and in the *in vitro* mouse lymphoma test, and was negative in the *in vivo* micronucleus test in rats.

Long-term animal studies have not been conducted to evaluate AdreView's carcinogenic potential or potential effects on fertility.

13.2 Animal Toxicology and/or Pharmacology

Iobenguane sulfate testing in dogs revealed electrocardiographic (ECG) changes after administration of 202 times the mg/m² conversion of the maximum human dose for a 60 kg adult; the no observable effect level (NOEL) was not determined. When iobenguane was tested in a cell system stably expressing hERG-1 potassium channels, inhibition of potassium channels was not observed at an 80 µM iobenguane concentration and the IC_{50} was 487 µM.

14 CLINICAL STUDIES

14.1 Pheochromocytomas and Neuroblastomas

The safety and efficacy of AdreView were assessed in an open-label, multicenter, multinational trial of 251 subjects with known or suspected neuroblastoma or pheochromocytoma. Diagnostic efficacy for the detection of metabolically active neuroblastoma or pheochromocytoma was determined by comparison of focal increased radionuclide uptake on planar scintigraphy at 24 ± 6 hours post-administration of AdreView against the definitive diagnosis (standard of truth). Anterior and posterior planar whole-body images, or alternatively whole-body overlapping spot images, were acquired from the head to below the knees. Additional spot images were performed as deemed appropriate at the discretion of the clinical image reviewer. SPECT imaging of the thorax and abdomen was then obtained when possible.

Of the 251 subjects dosed with AdreView, 100 had known or suspected neuroblastoma and 151 had known or suspected pheochromocytoma. The population included 154 adults and 97 pediatric patients; the majority of adults were female (59%), the majority of pediatric subjects were male (58%). The adult subjects had a mean age of 49 years (range 17 to 88 years). The pediatric patients (56 males and 41 females) consisted of 32 infants (1 month up to 2 years of age), 62 children (2 years up to 12 years) and three adolescents (12 years up to 16 years).

The definitive diagnosis (standard of truth) for the presence or absence of metabolically active pheochromocytoma or neuroblastoma was determined by histopathology or, when histopathology was unavailable, a composite of imaging (i.e., CT, MRI, [^{123}I)-*m*IBG scintigraphy), plasma/urine catecholamine and/or catecholamine metabolite measurements, and clinical follow-up.

A standard of truth was available for 211 subjects (127 with pheochromocytoma, 84 with neuroblastoma) and this group comprised the diagnostic efficacy population. For 93 of these subjects, the standard of truth was based solely upon histopathology. Of 211 subjects in the efficacy population, all had planar scintigraphy and 167 subjects had SPECT in addition to planar imaging. All images were assessed independently by three readers blinded to all clinical data. Table 5 summarizes the AdreView performance characteristics, by reader.

Table 5. AdreView Planar Imaging: Sensitivity and Specificity

Outcome	Reader A	Reader B	Reader C
Sensitivity (n = 159)			
Point estimate	0.80	0.77	0.79
95% confidence interval	0.73 - 0.86	0.70 - 0.84	0.71 - 0.85
Specificity (n = 52)			
Point estimate	0.77	0.73	0.69
95% confidence interval	0.63 - 0.87	0.59 - 0.84	0.55 - 0.81

Performance characteristics (sensitivity and specificity) of AdreView planar imaging in patients with known or suspected neuroblastoma were similar to those in patients with known or suspected pheochromocytoma. Among the selected patients who also underwent SPECT imaging, similar performance characteristics of AdreView scintigraphy were observed when SPECT plus planar imaging was compared to planar imaging alone.

16 HOW SUPPLIED/STORAGE AND HANDLING

AdreView is supplied in 10 mL glass vials containing a total volume of 5 mL of solution with a total radioactivity of 370 MBq (10 mCi) at calibration time. Each vial is enclosed in a lead container of appropriate thickness.

NDC 17156-235-01

Storage

Store AdreView at 20°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F) (see USP). This product does not contain a preservative. Store within the original lead container or equivalent radiation shielding.

In accordance with USP recommendations Iobenguane I 123 Injection preparations should not be used after the expiration date and time stated on the label.

Handling

This preparation is approved for use by persons licensed by the Illinois Emergency Management Agency pursuant to 32 Ill. Adm. Code Section 330.260(a) and 355.4010 or equivalent licenses of the Nuclear Regulatory Commission or an Agreement State.

17 PATIENT COUNSELING INFORMATION

Instruct patients to inform their physician or healthcare provider if they:

1. are pregnant or breast feeding.
2. are sensitive to iodine, an iodine-containing contrast agent or other products that contain iodine.
3. are sensitive to Potassium Iodide Oral Solution, or Lugol's Solution.
4. have reduced renal function.

Instruct patients to increase their level of hydration prior to receiving AdreView and to void frequently for the first 48 hours following AdreView administration.

GE Healthcare

Manufactured and Distributed by
GE Healthcare, Medi-Physics, Inc.
Arlington Heights, IL 60004 U.S.A.

METHODIST
HOSPITALS

PROTOCOL: Subject: ADRENAL Imaging with I-123 (MIBG)		PROTOCOL NO.: IMS-NUCM_067
ORIGINAL DATE: 09/1992	SUPERSEDES: 12/2005	PAGE: 1 of 3

I. INDICATION:

MIBG (Brand name ADREVIEW-made by GE) (generic name meta-iodobenzylguaninidine sulfate) is used primarily to image Pheochromocytomas (Paragangliomas) and Neuroblastoma. Other adrenergically innervated tissue line tumors – e.g. carcinoid, and medullary thyroid carcinoma – demonstrate uptake of the tracer less frequently. Adrenal medullary hyperplasia may also be imaged.

II. PREPARATION:

Patient Preparation:

In order to appropriately prepare the patient, the patient will be informed of the following drugs which interfere with MIBG uptake:

- Cocaine: Avoid for 2 weeks prior to study. Inhibits catecholamine uptake
- Tricyclic antidepressants and related drugs – should be avoided for 6 weeks prior to the study (Desipramine, Amitriptyline (Elavil)) inhibit catecholamine uptake.
- Phenylopropanolamine / Pseudephredine / Phenylephrine – found in over the counter cold preparations and decongestants these agents deplete storage vesicle contents.
- Catecholamine agonists: Sympathomimetics, Amphetamines, and Amphetamine-like compounds. Deplete storage vesicle contents.
- Reserpine: Depletes the catecholamine stores in the neurosecretory storage granules and inhibits vesicle active transport.
- Antipsychotics: Phenothiazines (Thorazine) and thiothixines inhibit catecholamine uptake.
- Adrenergic blockers: Long acting beta-blockers: Labetalol and possibly metoprolol. Labetalol inhibits catecholamine uptake and depletes storage vesicle contents. Should be discontinued for at least 3 weeks prior to scanning. Note: absence of salivary and parotid activity can serve as a clue that patients may be on this medication.
- Possibly some foods. Those which contain vanillin and catecholamine-like compounds such as chocolate and blue-veined cheeses.

(1) 10 drops of saturated solution of Potassium Iodide (SSKI) should be taken orally (in juice or water). the day before the adreview injection and 1 drop should be taken orally on the day of injection and the day after the injection. (2) Encourage hydration prior to examination. Patient should void often for 24-48 hours post injection.

Lugol's solution-SSKI may be ordered for out patients by special order from Walgreen's pharmacy with 2 days advanced notice

II. DEFINITIONS:

mCi – Millicurie, a measure / unit of radioactivity
uCi – Microcurie, a measure / unit of radioactivity
IV – Intra-venous

III. ADVERSE REACTION:

Please see the attached package insert for adverse reactions.

IV. TECHNICAL PROTOCOL:

Action:

1. Verify patient identity by at least 2 means (name and date of birth) prior to beginning the examination.
2. Verify physician order prior to beginning the exam.
3. Explain the procedure to the patient and family beforehand.
4. Inject the patient via IV with 10 mci I-123 MIBG (Adreview) over 30 seconds.
5. **For pediatric dosage, please see the package insert for pediatric dose preparation chart**.
6. The patient will return for imaging at 4 hours and at 24 hours.
7. Position the patient supine on the scan table. Whole body imaging and Anterior and Posterior spot images will be obtained of the head/neck, chest, abdomen and pelvis.
8. These overlapping static images are obtained with 10 minute acquisition times.
9. Spect imaging may be done upon request from radiologist.
10. 48 hours imaging may be done upon request from radiologist

IV. REFERENCE:

V. DOCUMENT INFORMATION

A. Prepared by

Dept. & Title	Date
Nuclear Medicine Supervisor Director of Radiology	1/25/2006

B. Review and Renewal Requirements

This protocol will be reviewed every three years and as required by change of law, practice or standard.

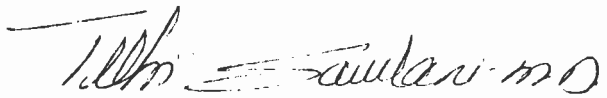
C. Review / Revision History

Reviewed on: 4/2004, 1/2006, 1/2010
Revised on: 2/2001, 3/2002, 12/2005, 05/2010

D. Approvals

1. This Protocol has been reviewed and/or approved by the Radiologist

Radiologist	Date
Dr. T. Sawlani Chief Radiologist	05/21/2010



GE Healthcare

AdreView™
Iobenguane I 123 Injection

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

AdreView (Iobenguane I 123 Injection) for Intravenous Use
Initial U.S. Approval: 2008

INDICATIONS AND USAGE

AdreView is a diagnostic radiopharmaceutical agent for gamma-scintigraphy. It is indicated for use in the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests. (1)

DOSAGE AND ADMINISTRATION

- AdreView emits radiation and must be handled with appropriate safety measures. (2.1, 2.6)
- Administer thyroid blockade medications prior to AdreView. (2.2, 5.4)
- Measure patient dose by a suitable radioactivity calibration system immediately prior to administration. (2.4)
- For patients ≥ 16 years of age or < 16 years of age and ≥ 70 kg: administer 10 mCi (370 MBq). (2.4, 2.5)
- For patients < 16 years of age and < 70 kg: amount scaled to the adult reference activity based on weight. (2.5)

DOSAGE FORMS AND STRENGTHS

5 mL of sterile solution for intravenous injection in a single use vial (2 mCi/mL at calibration time). (3)

CONTRAINDICATIONS

Known hypersensitivity to iobenguane or iobenguane sulfate. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity reactions have followed AdreView administration. Have anaphylactic and hypersensitivity treatment measures available prior to AdreView administration. (5.1)
- AdreView contains benzyl alcohol (10.3 mg/mL) which may cause serious reactions in premature or low birth-weight infants. (5.2)
- Patients with severe renal impairment may have increased radiation exposure and decreased quality of AdreView images. (5.3)
- Failure to block thyroid iodine uptake may result in iodine 123 accumulation in the thyroid. (5.4)
- Drugs which block norepinephrine uptake or deplete norepinephrine stores may decrease AdreView uptake in neuroendocrine tumors. When medically feasible, stop these drugs before AdreView administration and monitor patients for withdrawal signs and symptoms. (5.5)

ADVERSE REACTIONS

Serious hypersensitivity reactions have been reported following AdreView administration. The most common adverse reactions, dizziness, rash, pruritis, flushing and injection site hemorrhage occurred in < 1% of patients. (6.1, 6.2)

To report SUSPECTED ADVERSE REACTIONS, contact GE Healthcare at 1-800-654-0118 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Amitryptiline and derivatives, imipramine and derivatives, other antidepressants that inhibit norepinephrine transporter, antihypertensives that deplete norepinephrine stores or inhibit reuptake, sympathomimetric amines and cocaine: Discontinue for 5 biological half-lives prior to AdreView administration. (7)

USE IN SPECIFIC POPULATIONS

- Pregnancy: any radiopharmaceutical, including AdreView, may cause fetal harm. (8.1)
- Nursing mothers: A decision should be made whether to interrupt nursing after AdreView administration or not to administer AdreView, taking into account the importance of the drug to the mother. (8.3)
- Pediatrics: safety and effectiveness have not been established in pediatric patients < 1 month of age. (8.4)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 09/2008

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

AdreView is a radiopharmaceutical indicated for use in the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests.

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety

AdreView emits radiation and must be handled with appropriate safety measures to minimize radiation exposure to clinical personnel and patients. Radiopharmaceuticals should be used by or under the control of physicians who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides. AdreView dosing is based upon the radioactivity determined using a suitable calibration system immediately prior to administration.

To minimize radiation dose to the bladder, prior to and following AdreView administration, encourage hydration to permit frequent voiding. Encourage the patient to void frequently for the first 48 hours following AdreView administration [*see Clinical Pharmacology (12.2)*].

2.2 Thyroid Blockade

Before administration of AdreView, administer Potassium Iodide Oral Solution or Lugol's Solution (equivalent to 100 mg iodide for adults, body-weight adjusted for children) or potassium perchlorate (400 mg for adults, body-weight adjusted for children) to block uptake of iodine 123 by the patient's thyroid. Administer the blocking agent at least one hour before the dose of AdreView [*see Warnings and Precautions (5.4)*].

2.3 Preparation and Administration

Inspect the AdreView vial for particulate matter and discoloration prior to administration. Use aseptic procedures and a radiation shielding syringe during administration. Administer the dose as an intravenous injection over 1 to 2 minutes. A subsequent injection of 0.9% sodium chloride may be used to ensure full delivery of the dose.

2.4 Recommended Dose for Adults

For adults (≥ 16 years of age), the recommended dose is 10 mCi (370 MBq) [*see Clinical Studies (14.1)*].

2.5 Recommended Dose for Pediatric Patients

For pediatric patients < 16 years of age weighing ≥ 70 kg, the recommended dose is 10 mCi (370 MBq) [*see Clinical Studies (14.1)*].

For pediatric patients < 16 years of age weighing < 70 kg, the recommended dose should be calculated according to patient body weight as shown in Table 1 [*see Clinical Studies (14.1)*]. The benzyl alcohol in AdreView may cause serious adverse reactions in premature or low birth-weight infants [*see Warnings and Precautions (5.2)*].

Table 1
AdreView Dose Preparation for Pediatric Patients*

Weight (kg)	Fraction of adult activity	AdreView (mCi) pediatric dose	AdreView (MBq) pediatric dose
3	0.1	1	37
4	0.14	1.4	52
6	0.19	1.9	70
8	0.23	2.3	85.1
10	0.27	2.7	99.9
12	0.32	3.2	118.4
14	0.36	3.6	133.2
16	0.4	4	148
18	0.44	4.4	162.8
20	0.46	4.6	170.2
22	0.5	5	185
24	0.53	5.3	196.1
26	0.56	5.6	207.2
28	0.58	5.8	214.6
30	0.62	6.2	229.4
32	0.65	6.5	240.5
34	0.68	6.8	251.6
36	0.71	7.1	262.7
38	0.73	7.3	270.1
40	0.76	7.6	281.2
42	0.78	7.8	288.6
44	0.8	8	296
46	0.82	8.2	303.4
48	0.85	8.5	314.5
50	0.88	8.8	325.6
52	0.9	9	333
54	0.9	9	333
56	0.92	9.2	340.4
58	0.92	9.2	340.4
60	0.96	9.6	355.2
62	0.96	9.6	355.2
64	0.98	9.8	362.6
66	0.98	9.8	362.6
68	0.99	9.9	366.3

*Based on a reference activity for an adult scaled to body weight according to the schedule proposed by the European Association of Nuclear Medicine Paediatric Task Group

2.6 Radiation Dosimetry

The estimated absorbed radiation doses to adults and children from intravenous administration of AdreView are as shown in Table 2.

Table 2
Estimated Absorbed Radiation Dose from AdreView

		ABSORBED DOSE PER UNIT ADMINISTERED ACTIVITY											
ORGAN / TISSUE		ADULT		15-YEAR OLD		10-YEAR OLD		5-YEAR OLD		1-YEAR OLD		NEONATES	
		µGy/MBq	rad/mCi	µGy/MBq	rad/mCi	µGy/MBq	rad/mCi	µGy/MBq	rad/mCi	µGy/MBq	rad/mCi	µGy/MBq	rad/mCi
Adrenals		16	0.059	21	0.078	31	0.115	42	0.155	67	0.248	111	0.411
Brain		3.9	0.014	4.9	0.018	8.1	0.030	13	0.048	24	0.089	55.9	0.207
Breast		4.7	0.017	5.9	0.022	9.4	0.035	15	0.056	28	0.104	65.3	0.242
Gallbladder		20	0.074	24	0.089	34	0.126	51	0.189	95	0.352	200	0.740
GI Tract	Stomach Wall	7.6	0.028	10	0.037	17	0.063	27	0.100	51	0.189	114	0.422
	Small Intestine Wall	7.7	0.028	9.8	0.036	16	0.059	25	0.093	46	0.170	104	0.385
	Colon Wall	8.1	0.030	10	0.037	16	0.059	26	0.096	46	0.170	104.5	0.386
	Upper Large Intestine Wall	8.4	0.031	11	0.041	18	0.067	30	0.111	53	0.196	119	0.440
	Lower Large Intestine Wall	7.7	0.028	9.6	0.036	15	0.056	21	0.078	38	0.141	84.9	0.314
Heart Wall		18	0.067	23	0.085	35	0.130	53	0.196	94	0.348	182	0.673
Kidneys		13	0.048	16	0.059	24	0.089	35	0.130	59	0.218	132	0.488
Liver		67	0.248	87	0.322	130	0.481	180	0.666	330	1.221	720	2.664
Lungs		16	0.059	23	0.085	32	0.118	48	0.178	89	0.329	215	0.796
Muscles		6	0.022	7.6	0.028	12	0.044	17	0.063	33	0.122	75.1	0.278
Esophagus		6	0.022	7.6	0.028	11	0.041	18	0.067	32	0.118	72.2	0.267
Osteogenic Cells		16	0.059	21	0.078	31	0.115	47	0.174	100	0.370	254	0.940
Ovaries		7.9	0.029	10	0.037	15	0.056	22	0.081	41	0.152	92.3	0.342
Pancreas		12	0.044	15	0.056	25	0.093	39	0.144	68	0.252	143	0.529
Red marrow		5.6	0.021	6.8	0.025	10	0.037	15	0.056	30	0.111	89.5	0.331
Skin		3.7	0.014	4.4	0.016	7.1	0.026	11	0.041	21	0.078	53.1	0.196
Spleen		20	0.074	27	0.100	42	0.155	64	0.237	110	0.407	282	1.043
Testes		5.4	0.020	7.1	0.026	11	0.041	16	0.059	30	0.111	69.9	0.259
Thymus		6	0.022	7.6	0.028	11	0.041	18	0.067	32	0.118	72.2	0.267
Thyroid		4.7	0.017	6.1	0.023	9.9	0.037	16	0.059	30	0.111	69.4	0.257
Urinary Bladder Wall		66	0.244	84	0.311	110	0.407	110	0.407	200	0.740	478.0	1.769
Uterus		11	0.041	14	0.052	21	0.078	28	0.104	51	0.189	110.0	0.407
Whole Body		8.1	0.030	10	0.037	16	0.059	24	0.089	44	0.163	104.0	0.385
EFFECTIVE DOSE	µSv/MBq	13.7		18.1		26.7		37.6		68		162	
	mSv/mCi	0.507		0.670		0.988		1.39		2.52		6	

*OLINDA/EXM calculation based on biodistribution data from Swanson et al. and Publication 53 of the ICRP (International Commission on Radiological Protection) (Annals of the ICRP 1987; 18 (1-4): 329-331)

The effective dose resulting from an administered activity amount of 10 mCi is 5.07 mSv in an adult.

2.7 Imaging Guidelines

Begin whole body planar scintigraphy imaging 24 ± 6 hours following administration of AdreView. Single photon emission computed tomography (SPECT) may be performed following planar scintigraphy, as appropriate [*see Clinical studies 14.1*].

3 DOSAGE FORMS AND STRENGTHS

Single use vials containing 5 mL solution for intravenous injection (2 mCi/mL at calibration time).

4 CONTRAINDICATIONS

AdreView is contraindicated in patients with known hypersensitivity to iobenguane or iobenguane sulfate.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions have been reported following AdreView administration. Prior to administration, question the patient for a history of prior reactions to iodine, an iodine-containing contrast agent or other products containing iodine. If the patient is known or strongly suspected to have hypersensitivity to iodine, an iodine-containing contrast agent or other products containing iodine, the decision to administer AdreView should be based upon an assessment of the expected benefits compared to the potential hypersensitivity risks. Have anaphylactic and hypersensitivity treatment measures available prior to AdreView administration [*see Adverse Reactions (6.2)*].

5.2 Risks for Benzyl Alcohol Toxicity in Infants

AdreView contains benzyl alcohol at a concentration of 10.3 mg/mL. Benzyl alcohol has been associated with a fatal "Gasping Syndrome" in premature infants and infants of low birth weight. Exposure to excessive amounts of benzyl alcohol has been associated with toxicity (hypotension, metabolic acidosis), particularly in neonates, and an increased incidence of kernicterus, particularly in small preterm infants. There have been rare reports of deaths, primarily in preterm infants, associated with exposure to excessive amounts of benzyl alcohol [*see Description (11)*].

Observe infants for signs or symptoms of benzyl alcohol toxicity following AdreView administration. AdreView safety and effectiveness have not been established in neonates (pediatric patients below the age of 1 month).

5.3 Increased Radiation Exposure in Patients with Severe Renal Impairment

AdreView is cleared by glomerular filtration and is not dialyzable. The radiation dose to patients with severe renal impairment may be increased due to the delayed elimination of the drug. Delayed AdreView clearance may also reduce the target to background ratios and decrease the quality of scintigraphic images. These risks importantly may limit the role of AdreView in the diagnostic evaluation of patients with severe renal impairment. AdreView safety and efficacy have not been established in these patients [*see Clinical Pharmacology (12.2)*].

5.4 Thyroid Accumulation

Failure to block thyroid uptake of iodine 123 may result in an increased long term risk for thyroid neoplasia. Administer thyroid blocking medications before AdreView administration [*see Dosage and Administration (2.2)*].

5.5 Risks with Concomitant Medication Withdrawal

Drugs which interfere with norepinephrine uptake or retention may decrease the uptake of AdreView in neuroendocrine tumors and lead to false negative imaging results. When medically feasible, stop these drugs before AdreView administration and monitor patients for the occurrence of clinically significant withdrawal symptoms, especially patients with elevated levels of circulating catecholamines and their metabolites [*see Drug Interactions (7)*].

5.6 Hypertension

Assess the patient's pulse and blood pressure before and intermittently for 30 minutes after AdreView administration. AdreView may increase release of norepinephrine from chromaffin granules and produce a transient episode of hypertension, although this was not observed in the clinical study. Prior to AdreView administration, ensure emergency cardiac and anti-hypertensive treatments are readily available.

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