CardioGen-82 PI to FDA_July-27-2010_CLEAN.doc

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CARDIOGEN-82 safely and effectively. See full prescribing information for CARDIOGEN-82.

CARDIOGEN-82® (rubidium Rb 82 Generator)
To produce rubidium Rb 82 chloride injection for intravenous use
Initial U.S. Approval: 1989

----------RECENT MAJOR CHANGES----------

Indications and Usage: (1)	07/2010
Warnings and Precautions: (5.2)	07/2010

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

CardioGen-82® is a closed system used to produce rubidium Rb 82 chloride injection for intravenous use. Rubidium Rb 82 chloride injection is a radioactive diagnostic agent indicated for Positron Emission Tomography (PET) imaging of the myocardium under rest or pharmacologic stress conditions to evaluate regional myocardial perfusion in adult patients with suspected or existing coronary artery disease. (1)

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

- Use CardioGen-82® with a specific infusion system. (2.6)
- The usual adult (70 kg) dose of rubidium Rb 82 chloride injection is 1480 MBq (40 mCi), with a range of 1110-2220 MBq (30-60 mCi) infused intravenously at a rate of 50 mL/minute, not to exceed a total volume of 100 mL. Do not exceed a single dose of 2220 MBq (60 mCi). (2.3)
- Start imaging acquisition 60-90 seconds after completion of the infusion; if a longer circulation time is anticipated, wait for 120 seconds. Image acquisition is typically 5 minutes long.
- To obtain rest and stress images, wait 10 minutes after completion of the rest image acquisition then administer the pharmacologic stress agent in accordance with its prescribing information. Three minutes after administration of the pharmacologic stress agent, infuse the second dose of rubidium Rb 82 chloride and complete the stress image acquisition. (2.3)

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

CardioGen-82® consists of strontium Sr 82 adsorbed on a hydrous stannic oxide column with an activity of 90-150 millicuries Sr-82 at calibration time.(3)

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

None (4)

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

- Rubidium Rb 82 chloride contributes to the cumulative radiation exposure, with the long term risks for cancer. Use the lowest dose necessary for imaging and ensure safe handling to protect the patient and health care worker. (5.1)
- Pharmacologic induction of cardiovascular stress may be associated with serious adverse events such as myocardial infarction, arrhythmia, hypotension, bronchoconstriction, and cerebrovascular events. Perform testing in accordance with the pharmacologic stress agent's prescribing information. (5.2)
- Circulatory volume overload may result from administration of rubidium chloride injection to patients with congestive heart failure. Observe these patients for several hours following injection. (5.3)

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

Clinical trials and post-marketing experience have identified no adverse reactions to rubidium Rb 82 chloride injection. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Bracco Diagnostics Inc at 1-800-257-8151 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------

- Specific drug-drug interactions have not been studied. (7)

----------USE IN SPECIFIC POPULATIONS----------

- Pregnancy: No human or animal studies have been performed. (8.1)
- Nursing Mothers: Caution should be exercised when administered to a nursing mother. (8.3)
- Pediatric Use: Safety and effectiveness in pediatric patients have not been established. (8.4)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 07/2010

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

CardioGen-82® is a closed system used to produce rubidium Rb 82 chloride injection for intravenous administration. Rubidium Rb 82 chloride injection is indicated for Positron Emission Tomography (PET) imaging of the myocardium under rest or pharmacologic stress conditions to evaluate regional myocardial perfusion in adult patients with suspected or existing coronary artery disease.

2 DOSAGE AND ADMINISTRATION

2.1 Use Lowest Dose Necessary for Cardiac Visualization

Use the lowest dose of rubidium Rb 82 chloride injection necessary to obtain adequate cardiac visualization. A lower dose provides less patient radiation and is consistent with the achievement of the dosing goal of As Low As Reasonably Achievable (ALARA). Most procedures do not require the maximum recommended dose of rubidium Rb 82 chloride; carefully individualize the dose and consider factors such as body size, and the equipment and technique to be employed *[see Warnings and Precautions (5.2)]*.

2.2 Infusion System

Use CardioGen-82 only with an infusion system specifically designed for use with the generator and capable of accurate measurement and delivery of doses of rubidium Rb 82 chloride injection, not to exceed a single dose of 2220 MBq (60 mCi) and a cumulative dose of 4440 MBq (120 mCi) at a rate of 50 mL/min with a maximum volume per infusion of 100 mL and a cumulative volume not to exceed 200 mL. These limitations for a single rest and stress session reflect the conditions of use under which the drug development clinical trials were conducted.

Follow instructions in the Infusion System User's Guide for the set up and intravenous infusion of rubidium chloride injection dose(s).

2.3 Rubidium Rb 82 Chloride Injection Dosage

Rubidium Rb 82 chloride injection obtained from CardioGen-82 is intended only for intravenous administration using an appropriate infusion system. The usual adult (70 kg) single dose is 1480 MBq (40 mCi) with a range of 1110-2220 MBq (30-60 mCi); a single dose of 2220 MBq (60 mCi) should not be exceeded. Administer the single dose at a rate of 50 mL/minute through a catheter inserted into a large peripheral vein, not to exceed a total volume of 100 mL. Two single doses are used to complete a rest and stress imaging session, as follows:

For rest imaging

- Administer a single ("resting") rubidium Rb 82 chloride dose as described above.
- Start imaging 60-90 seconds after completion of the infusion of rubidium chloride injection; if a longer circulation time is anticipated (e.g., in a patient with severe left ventricular dysfunction), wait for 120 seconds. Image acquisition is typically 5 minutes long.

For stress imaging

- Begin the stress imaging study 10 minutes after completion of the resting dose infusion, to allow for sufficient isotope decay.
- Administer a pharmacologic stress agent in accordance with its prescribing information.
- After an interval of 3 minutes, infuse a single ("stress") rubidium Rb 82 chloride dose, as described above.
- Start imaging 60-90 seconds after completion of the stress dose infusion; if a longer circulation time is anticipated (e.g., in a patient with severe left ventricular dysfunction), wait for 120 seconds. Image acquisition is typically 5 minutes long.

2.4 Radiation Dosimetry

Table 1 shows the estimated absorbed radiation doses to an average adult patient (70 kg) from an intravenous injection of a recommended dose of 2220 MBq (60 mCi) of rubidium Rb 82 chloride.

TABLE 1

Adult Absorbed Radiation Doses*		
Organ	mGy/2220 MBq	rads/60 mCi
Adrenals	2.15	0.22
Stomach	1.91	0.19
Small Intestine	3.11	0.32
Upper Large Intestine	1.91	0.19
Lower Large Intestine	1.91	0.19
Heart Wall	4.22	0.42
Kidneys	19.1	1.92
Liver	1.91	0.19
Lungs	3.77	0.38
Ovaries	0.84	0.084
Pancreas	1.38	0.14
Trabecular Bone	0.0055	0.00055
Cortical Bone	0.0091	0.0009
Red Marrow	0.84	0.084
Testes	0.67	0.066
Total Body	0.95	0.096

*Calculated by the Internal Dosimetry Center at Oak Ridge Associated Universities based on data collected by Ryan et al. in two human subjects[1] and on rat data of Kearfott[2] Contaminant levels of Sr-82 and Sr-85 assumed to be 10^{-7} and 2.5 X 10^{-7} relative to Rb-82.

For strontium, assumed distribution and retention:
Bone 50% $t_b = \infty$ (uniformity distributed throughout volume)
Testes 0.5% t_b = 1.5 day
Remainder 49.5% t_b = 1.5 day

2.5 Drug Handling

- Limit the use of radiopharmaceuticals to physicians who are qualified by 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.
- Wear waterproof gloves and effective shielding when handling rubidium Rb 82 chloride injection and the infusion system.
- Observe aseptic techniques in all drug handling.
- Use only additive-free Sodium Chloride Injection USP to elute the generator.
- Visually inspect the drug for particulate matter and discoloration prior to administration whenever solution and container permit. Do not administer eluate from the generator if there is any evidence of foreign matter.

2.6 Directions for Eluting Rubidium Rb 82 Chloride Injection

Assay the eluate for rubidium Rb 82 and strontium Sr-82 and Sr-85 breakthrough each day the generator is used *[see Dosage and Administration (2.7)]*.

Use of CardioGen-82 requires an appropriate infusion system. Consult the Infusion System User's Guide for detailed directions on generator hookup, elution, and patient administration. Prior to use with patients,

establish a thorough understanding of the use and performance of the system. Consult the applicable User's Guide for the infusion system before beginning elution.

When eluting the CardioGen-82 generator:

- Wear waterproof gloves during the preparation and elution processes.
- Employ aseptic techniques throughout the preparation and elution processes.
- Allow at least 10 minutes between elutions for regeneration of Rb-82.
- Elute with additive-free Sodium Chloride Injection USP only.
- Discard the first 50 mL eluate each day the generator is eluted. Employ proper safety precautions since the eluate contains radioactivity.

2.7 Assay for Rubidium Rb 82 and Measurement of Sr-82 and Sr-85 Breakthrough

Determine the eluate rubidium Rb 82 content and strontium Sr 82 and strontium Sr 85 breakthrough using an ionization chamber-type dose calibrator. Perform procedure 1 through 11 below daily prior to the administration of rubidium Rb 82 chloride injection to any patients.

Assay the eluate for rubidium Rb 82 as follows:

1. Set a dose calibrator for Rb-82 as recommended by the manufacturer or use the Co-60 setting and divide the reading obtained by 0.548. Obtain the reading from the instrument in millicuries.
2. Aseptically elute the generator with 50 mL of Sodium Chloride Injection USP and discard the eluate (first elution).
3. After allowing at least 10 minutes for the regeneration of Rb-82, aseptically elute the generator with 50 mL of Sodium Chloride Injection USP at a rate of 50 mL/min and collect the eluate in a stoppered glass vial (plastic containers are not suitable). Note the exact time of end of elution (E.O.E.).
4. Using the dose calibrator, determine the activity of Rb 82 and note the time of the reading. Correct the reading for decay to the E.O.E. using the appropriate decay factor for Rb 82 (see Table 6). Note: If the reading is taken 2 1/2 minutes after E.O.E., multiply the dose calibrator reading by 4 to correct for decay.

Measure the Sr-82 breakthrough in the eluate as follows:

5. Using the sample obtained for the Rb-82 activity determination, allow the sample to stand for at least one hour to allow for the complete decay of Rb-82.
6. Measure the activity of the sample in a dose calibrator at the setting recommended by the manufacturer for Rb-82 and/or Sr-82. As an alternative, use the Co-60 setting and the reading obtained divided by 0.548. Obtain the reading from the instrument in microcuries.
7. Calculate the ratio (R) of Sr-85/Sr-82 on the date of measurement using the Sr-85/Sr-82 ratio chart below (Table 2) and the ratio of Sr-85/Sr-82 on the day of calibration provided on the generator label. Determine R using the following equation:

   $$R = \frac{[\text{Sr-85}]}{[\text{Sr-82}]} \text{ on calibration date x ratio factor on the date of measurement}$$
8. Use a correction factor (F) of 0.478 to compensate for the contribution of Sr-85 to the reading.
9. Calculate the amount of Sr-82 in the sample using the following equation:

$$\text{Sr-82 } (\mu\text{Ci}) = \frac{\text{dose calibration reading } (\mu\text{Ci})}{[1 + (R)\,(F)]}$$

Example: dose calibrator reading (μCi) = 0.80
Sr-85/Sr-82 ratio (R) = (1.48)
Correction factor (F) = 0.478

$$\text{Sr-82 } (\mu\text{Ci}) = \frac{0.80}{}$$

$$[1 + (1.48)(0.478)]$$

$$\text{Sr-82 } (\mu\text{Ci}) = 0.47$$

10. Determine the Sr-82 breakthrough by dividing the µCi of Sr-82 by the mCi of Rb-82 at E.O.E.
    Example:
    0.47 µCi of Sr-82
    50 mCi of Rb-82 E.O.E.

$$\frac{0.47\ \mu\text{Ci Sr-82}}{50\ \text{mCi Rb-82}} = 0.0094 = 9.4 \times 10^{-3}\ \mu\text{Ci/mCi Rb-82}$$

The Sr-82 content must not be more than 2×10^{-2}µCi/mCi of Rb-82 at E.O.E. If the Sr-82 breakthrough is above specified limits, discontinue use of the generator and contact Bracco Diagnostics Inc.

11. Determine the Sr-85 breakthrough by multiplying the result obtained in step 10 by (R) Sr-85/Sr-82 ratio.

    Example:
    $9.4 \times 10^{-3} \times 1.48 = 1.4 \times 10^{-2}$ µCi Sr-85/mCi Rb-82

The Sr-85 content must not be more than 0.2 µCi/mCi of Rb-82 at E.O.E. If the Sr-85 breakthrough is above specified limits, discontinue use of the generator and contact Bracco Diagnostics Inc.

TABLE 2

Sr-85/Sr-82 Ratio Chart

Days	Ratio Factor	Days	Ratio Factor
0*	1.00	16	1.31
1	1.02	17	1.34
2	1.03	18	1.36
3	1.05	19	1.38
4	1.07	20	1.41
5	1.09	21	1.43
6	1.11	22	1.46
7	1.13	23	1.48
8	1.15	24	1.51
9	1.17	25	1.53
10	1.19	26	1.56
11	1.21	27	1.59
12	1.23	28	1.61
13	1.25	29	1.64
14	1.27	30	1.67
15	1.29		

*Day of calibration

3 DOSAGE FORMS AND STRENGTHS

CardioGen-82 is a closed system used to produce rubidium Rb 82 chloride injection for intravenous use. CardioGen-82 consists of strontium Sr 82 adsorbed on a hydrous stannic oxide column with an activity of 90-150 millicuries Sr-82 at calibration time.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Radiation Risks

Rubidium Rb 82 chloride contributes to the cumulative radiation exposure, with the long term risks for cancer. When considering administration of rubidium Rb 82 chloride injection to women of child-bearing potential, always seek information about pregnancy and consider the radiation risks for a fetus *[see Use in Specific Populations (8.1)]*.

Use the lowest dose necessary for imaging and ensure safe handling to protect the patient and health care worker *[see Dosage and Administration (2.3, 2.4)]*. Encourage voiding as soon as a study is completed and as often as possible thereafter for at least one hour.

5.2 Risks Associated with Pharmacologic Stress

Pharmacologic induction of cardiovascular stress may be associated with serious adverse events such as myocardial infarction, arrhythmia, hypotension, bronchoconstriction, and cerebrovascular events. Perform pharmacologic stress testing in accordance with the pharmacologic stress agent's prescribing information and only in the setting where cardiac resuscitation equipment and trained staff are readily available.

5.3 Volume Overload

Use caution during infusion as patients with congestive heart failure may experience a transitory increase in circulatory volume load. Observe these patients for several hours following rubidium chloride injection administration to detect delayed hemodynamic disturbances.

6 ADVERSE REACTIONS

A review of the published literature, publicly available reference sources, adverse drug reaction reporting system, and post-marketing experience reported no adverse reactions to rubidium Rb 82 chloride injection.

7 DRUG INTERACTIONS

Specific drug-drug interactions have not been studied.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Animal reproductive studies have not been conducted with rubidium Rb 82 chloride injection. It is also not known whether rubidium Rb 82 chloride injection can cause fetal harm when administered to a pregnant woman; however, all radiopharmaceuticals have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of the radiation dose. If considering rubidium Rb 82 chloride injection administration to a pregnant woman, inform the patient about the potential for adverse pregnancy outcomes based on the radiation dose from rubidium Rb 82 and the gestational timing of exposure.

8.3 Nursing Mothers

It is not known whether rubidium Rb 82 chloride is excreted in human milk. Due to the short half-life of rubidium Rb 82 (75 seconds) it is unlikely that the drug would be excreted in human milk during lactation. However, because many drugs are excreted in human milk, caution should be exercised when rubidium Rb 82 chloride injection is administered to nursing women. Do not resume breastfeeding until one hour after the last infusion.

8.4 Pediatric Use

Rubidium Rb 82 chloride injection safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Reported clinical experience has not identified differences in safety or effectiveness between elderly and younger subjects. In elderly patients with a clinically significant decrease in cardiac function, lengthen the delay between infusion and image acquisition *[see Dosage and Administration (2.3)]*. Observe these patients for the possibility of fluid overload from the infusion *[see Warnings and Precautions (5.3)]*.

8.6 Renal and/or Hepatic Impairment

Reductions in renal or hepatic function are not anticipated to alter clearance of rubidium Rb 82 chloride injection because rubidium Rb 82 decays to stable Kr-82 with a half-life of 75 seconds and Kr-82 is exhaled through the lungs.

11 DESCRIPTION

11.1 Chemical Characteristics

CardioGen-82 contains accelerator-produced strontium Sr 82 adsorbed on stannic oxide in a lead-shielded column and provides a means for obtaining sterile nonpyrogenic solutions of rubidium Rb 82 chloride injection. The chemical form of rubidium 82 is ^{82}RbCl.

The amount (millicuries) of Rb-82 obtained in each elution will depend on the potency of the generator. When eluted at a rate of 50 mL/minute, each generator eluate at the end of elution should not contain more than 0.02 microcurie of strontium Sr 82 and not more than 0.2 microcurie of strontium Sr 85 per millicurie of rubidium Rb 82 chloride injection, and not more than 1 microgram of tin per mL of eluate.

11.2 Physical Characteristics

Rubidium Rb 82 decays by positron emission and associated gamma emission with a physical half-life of 75 seconds.[3] Table 3 shows the annihilation photons released following positron emission which is useful for detection and imaging studies.

The decay modes of Rb-82 are: 95.5% by positron emission, resulting in the production of annihilation radiation, i.e., two 511 keV gamma rays; and 4.5% by electron capture, resulting in the emission of "prompt" gamma rays of predominantly 776.5 keV. Both decay modes lead directly to the formation of stable Kr-82.[4]

TABLE 3
Principal Radiation Emission Data

Radiation	Mean Percent Per Disintegration	Mean Energy (keV)
Annihilation photons (2)	191.01	511 (each)
Gamma rays	13-15	776.5

The specific gamma ray constant for Rb-82 is 6.1 R/hour-millicurie at 1 centimeter. The first half-value layer is 0.7 centimeter of lead (Pb). Table 4 shows a range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb. For example, the use of a 7.0 centimeter thickness of Pb will attenuate the radiation emitted by a factor of about 1,000.

TABLE 4
Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	Attenuation Factor
0.7	0.5
2.3	10^{-1}
4.7	10^{-2}
7.0	10^{-3}
9.3	10^{-4}

Strontium Sr 82 (half-life of 25 days (600 hrs)) decays to rubidium Rb 82. To correct for physical decay of strontium Sr 82, Table 5 shows the fractions that remain at selected intervals after the time of calibration.

TABLE 5
Physical Decay Chart: Sr-82 half-life 25 days

Days	Fraction Remaining	Days	Fraction Remaining	Days	Fraction Remaining
0*	1.000	11	0.737	21	0.559
1	0.973	12	0.717	22	0.543
2	0.946	13	0.697	23	0.529
3	0.920	14	0.678	24	0.514
4	0.895	15	0.660	25	0.500
5	0.871	16	0.642	26	0.486
6	0.847	17	0.624	27	0.473
7	0.824	18	0.607	28	0.460
8	0.801	19	0.591	29	0.448
9	0.779	20	0.574	30	0.435
10	0.758				

*Calibration time

To correct for physical decay of rubidium Rb 82, Table 6 shows the fraction of rubidium Rb 82 remaining in all 15 second intervals up to 300 seconds after time of calibration.

TABLE 6
Physical Decay Chart: Rb-82 half-life 75 seconds

Seconds	Fraction Remaining	Seconds	Fraction Remaining
0*	1.000	165	.218
15	.871	180	.190
30	.758	195	.165
45	.660	210	.144
60	.574	225	.125
75	.500	240	.109
90	.435	255	.095
105	.379	270	.083
120	.330	285	.072
135	.287	300	.063
150	.250		

*Elution time

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Rb-82 is analogous to potassium ion (K^+) in its biochemical behavior and is rapidly extracted by the myocardium proportional to the blood flow. Rb^+ participates in the sodium-potassium (Na^+/K^+) ion exchange pumps that are present in cell membranes. The intracellular uptake of Rb-82 requires maintenance of ionic gradient across cell membranes. Rb-82 radioactivity is increased in viable myocardium reflecting intracellular retention, while the tracer is cleared rapidly from necrotic or infarcted tissue.

12.2 Pharmacodynamics

In human studies, myocardial activity was noted within the first minute after peripheral intravenous injection of Rb-82. When areas of infarction or ischemia are present in the myocardium, they are visualized within 2-7 minutes after injection as photon-deficient, or "cold", areas on the myocardial scan. In patients with reduced cardiac function, transit of the injected dose from the peripheral infusion site to the myocardium may be delayed *[see Dosage and Administration (2.3)]*.

Blood flow brings Rb-82 to all areas of the body during the first pass of circulation. Accordingly, visible uptake is also observed in other highly vascularized organs, such as the kidneys, liver, spleen and lungs.

12.3 Pharmacokinetics

With a physical half-life of 75 seconds, Rb-82 is very rapidly converted by radioactive decay into a trace amount of stable Kr-82 gas, which is passively expired by the lungs. Renal and hepatic excretion is not anticipated to play an essential role in Rb-82 elimination, although some of the Rb-82 dose may be excreted in the urine prior to radioactive decay.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term studies have been performed to evaluate carcinogenic potential, mutagenicity potential, or to determine whether rubidium Rb 82 chloride injection may affect fertility in males or females.

14 CLINICAL STUDIES

In a descriptive, prospective, blinded image interpretation study[5] of adult patients with known or suspected coronary artery disease, myocardial perfusion deficits in stress and rest PET images obtained with ammonia N 13 (n = 111) or rubidium 82 (n = 82) were compared to changes in stenosis flow reserve (SFR) as determined by coronary angiography. PET perfusion defects at rest and stress for seven cardiac regions (anterior, apical, anteroseptal, posteroseptal, anterolateral, posterolateral, and inferior walls) were graded on a scale of 0 (normal) to 5 (severe). Values for stenosis flow reserve, defined as flow at maximum coronary vasodilatation relative to rest flow, ranged from 0 (total occlusion) to 5 (normal). With increasing impairment of flow reserve, the subjective PET defect severity increased. A PET defect score of 2 or higher was positively correlated with flow reserve impairment (SFR<3).

A systematic review of published literature was conducted using pre-defined inclusion/exclusion criteria which resulted in identification of 10 studies evaluating the use of Rb 82 PET myocardial perfusion imaging (MPI) for the identification of coronary artery disease as defined by catheter-based angiography. In these studies, the patient was the unit of analysis and 50% stenosis was the threshold for clinically significant coronary artery disease (CAD). Of these 10 studies, 9 studies were included in a meta-analysis for sensitivity (excluding one study with 100% sensitivity) and 7 studies were included in a meta-analysis of specificity (excluding 3 studies with 100% specificity). A random effects model yielded overall estimates of sensitivity and specificity of 92% (95% CI: 89% to 95%) and 81% (95% CI: 76% to 86%), respectively. The use of meta-analysis in establishing performance characteristics is limited, particularly by the possibility of publication bias (positive results being more likely to be published than negative results) which is difficult to detect especially when based on a limited number of small studies.

15 REFERENCES

1. Ryan et al. J Nuc Med 25(5): 94.
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4. Judge, S et. al. Applied Radiation and Isotopes (1987); vol 38, no. 3: pp 185-190.
5. Demer, L.L. K.L.Gould, R.A.Goldstein, R.L.Kirkeeide, N.A.Mullani, R.W. Smalling, A.Nishikawa, and M.E.Merhige. Assessment of coronary artery disease severity by PET: Comparison with quantitative arteriography in 193 patients. Circulation 1989; 79: 825-35.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

CardioGen-82® (Rubidium Rb 82 Generator) consists of strontium Sr 82 adsorbed on a hydrous stannic oxide column with an activity of 90-150 millicuries Sr-82 at calibration time. A lead shield surrounded by a labeled plastic container encases the generator. The container label provides complete assay data for each generator. Directions for determining the activity of rubidium Rb 82 eluted from the generator are described above *[see Dosage and Administration (2.7)]*. Use CardioGen-82 (Rubidium Rb 82 Generator) only with an appropriate, properly calibrated infusion system labeled for use with the generator.

Receipt, transfer, handling, possession or use of this product is subject to the radioactive material regulations and licensing requirements of the U.S. Nuclear Regulatory Commission, Agreement States or Licensing States as appropriate.

16.2 Disposal

Hospital personnel should monitor the amount of radioactivity present within the generator prior to its disposal. Do not dispose of the generator in regular refuse systems. Store and/or dispose of the generator in accordance with the conditions of NRC radioactive materials license pursuant to 10 CFR, Part 20, or equivalent conditions pursuant to Agreement State Regulation.

16.3 Storage

Store the generator at 20-25°C (68-77°F) [See USP].

16.4 Expiration Date

The generator container label provides the expiration date. Due to the short half-life of Rb-82, virtually all the radioactivity in the eluate decays within 15 minutes from the end of elution.

17 PATIENT COUNSELING INFORMATION

17.1 Women of Childbearing Potential

Patients should be advised to inform their physician or healthcare provider if they are pregnant or breast-feeding.

17.2 Post-study Breastfeeding Avoidance

Instruct nursing patients to substitute stored breast milk or infant formula for breast milk for one hour after administration of rubidium Rb 82 chloride injection.

17.3 Post-study Voiding

Instruct patients to void after completion of each image acquisition session and as often as possible for one hour after completion of the PET scan.

Manufactured by:

Manufactured for
Bracco Diagnostics Inc.
Princeton, NJ 08543

by Medi-Physics, Inc.,
South Plainfield, NJ 07080

US Patent 7,504,646

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