CHROMITOP® Sodium Sodium Chromate Cr 51 Injection USP

DESCRIPTION
Chromitope Sodium (Sodium Chromate Cr 51 Injection USP) is a diagnostic radiopharmaceutical (or intravenous administration. This agent provides radioactive chromium 51 in the form of starito, nonpyrogenic aqueous solution of sodium chromate (Na₂CrO₄). The solution also contains 6 mg/mL benzyl alcohol as a preservative and sodium chloride for isotonicity; the pH has been adjusted to 7.5-8.5 with hydrochloric acid or sodium bicarbonate.

PHYSICAL CHARACTERISTICS
Chromium 51 decays by electron capture and gamma emission with a physical half-life of 27.7 days. The principal photon that is useful for detection and imaging studies is listed in Table 1.

TABLE 1

<table>
<thead>
<tr>
<th>Principal Radiation Emission Data</th>
<th>Radiation Mean % per Disintegration</th>
<th>Mean Energy (KeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma-1</td>
<td>9.83</td>
<td>320.1</td>
</tr>
</tbody>
</table>


External Radiation
The specific gamma ray constant for Cr 51 is 0.19 R/bour-millicurie at 1 cm. The first half-value layer is 0.20 cm lead (Pb). Values for the relative attenuation of the radiation emitted by the radionuclide that result from interposition of two thicknesses of Pb are shown in Table 2. To facilitate control of the radiation exposure from millicurie amounts of this radionuclide, the use of a 0.60 cm thickness of lead will attenuate the radiation emitted by a factor of about 10.

TABLE 2

<table>
<thead>
<tr>
<th>Radiation Attenuation by Lead Shielding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shield Thickness (Pb/cm)</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>0.20</td>
</tr>
<tr>
<td>0.60</td>
</tr>
</tbody>
</table>

To correct for physical decay of Cr 51, the fraction* that remain at selected intervals before and after the time of calibration as shown in Table 3.

<table>
<thead>
<tr>
<th>Physical Decay</th>
<th>Faction Remaining</th>
<th>127.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0 1</td>
<td>1.000 0.975</td>
<td>25 30</td>
</tr>
<tr>
<td>Day 2</td>
<td>0.975</td>
<td>35 40</td>
</tr>
<tr>
<td>Day 4</td>
<td>0.905</td>
<td>40 45</td>
</tr>
<tr>
<td>Day 8</td>
<td>0.819</td>
<td>45 50</td>
</tr>
<tr>
<td>Day 15</td>
<td>0.687 0.606</td>
<td>50 55</td>
</tr>
</tbody>
</table>

*Calibration time

CLINICAL PHARMACOLOGY
The chromium in this agent is present as the dianionic chromate ion in which form it appears to bind to the red blood cell in two steps, initially by a rapid but reversible attachment to the cell membrane followed by a slower nearly irreversible binding to intracellular hemoglobin and reduction to the anion state. It has been suggested that the slow rate of uptake is dependent on the rate at which chromate can penetrate the cell membrane. Binding is maintained until the red blood cells are sequestered by the spleen or until elution of the chromium occurs into the plasma. The chromium is then readily excreted mainly in the urine. Once liberated by alunox or erythrocyte senescence, chromium 51 is not available for relabeling of red cells.

In normal individuals the erythrocyte survival half-time (T_½) as measured by the chromium 51 "random labeling" technique, generally ranges between 25 and 35 days. This apparent short survival time, when compared to the 120 day life span of the red blood cells, is due to the elution of chromium from the cells and to cell damage that probably occurs during the process of withdrawing them from the body and labeling. Subnormal T_½ may be indicative of blood loss. Sequestration of red blood cells by the spleen, shortened cell viability, as occurs in hemolytic anemia.

INDICATIONS AND USAGE
Chromitope Sodium (Sodium Chromate Cr 51 Injection USP) is indicated for use in determining red blood cell volume or mass, studying red blood cell survival time (in conditions such as hemolytic anemia), and evaluating blood loss.

CONTRAINDICATIONS
None known.

PRECAUTIONS

In the use of any radioactive material, care should be taken to insure minimum radiation exposure to the patient and occupational workers consistent with proper patient management.

Nuclear medicine procedures involving withdrawal and reinfection of blood have the potential for transmission of blood borne pathogens. Procedures should be implemented to avoid administration errors and viral contamination of personnel during blood product labeling. A system of checks similar to the ones used (or administering blood transfusions should be routine.

In order to obviate or minimize the possibility of contamination and of increased fragility of the labeled red blood cells, sterile techniques should be employed throughout the collection, laboring, rinsing, suspending, and injection of red blood cells. In addition, the number of washes and transfers should be kept to a minimum and only sterile, non-pyogenic isotonic diluent should be employed throughout the labeling procedure.

Radiopharmaceuticals should be used only by 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.

Carcinogen—La, Mutagenemia, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate carcinogenic or mutagenic potential, or whether this agent may impair fertility in males or females.

Pregnancy: Teratogenic Effect
Catalofy C
Animal reproduction studies have not been conducted with Sodium Chromate Cr 51 Injection. It is also not known whether this agent can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. A suspension of chromium 51-labeled red blood cell containing Sodium Chromate Cr 51 Injection and Bracco A-C-D Solution Modified (Anticoagulant Citrate Dextrose Solution Modified) should be
administered to a pregnant woman only if clearly needed.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of a woman of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses.

Nursing Mothers
Caution should be exercised when Sodium Chromate Cr 51 Injection is administered to a nursing woman since chromium 51 is excreted in human milk during lactation. Therefore, formula feedings should be substituted for breast feedings.

Pediatric Us
Safety of the chromium 51-labeled suspension of red blood cells in children has not been established.

ADVERSE REACTIONS
No adverse reactions specifically attributable to Sodium Chromate Cr 51 Injection have been reported.

DOSEAGE AND ADMINISTRATION
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

The usual doses to the average patient (70 kg) are as follows:

- Determination of red blood cell volume or mass-0.37 to 1.11 microcuries (10 to 30 microcuries).
- Study of red blood cell survival time-5.55 microcuries (150 microcuries).
- Evaluation of blood loss-7.40 microcuries (200 microcuries).

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration. The specific activity should be not less than 370 microcuries (10 milliunits) per mg [0.37 microcuries (10 microcuries) per g] of Sodium Chromate at the time of use.

It is essential that the user adhere to strict aseptic procedures during the preparation, withdrawal and administration of the labeled red blood cells. Waterproof gloves are to be worn during the labeling procedure to prevent the possibility of radioactive contamination of the hands. Shielded syringes should be used when adding the Chromitope Sodium to the reaction vial and for the withdrawal and administration of the labeled red blood cells. To maintain adequate shielding during the life of the labeled preparation, a lead vial shield and lead cover must remain in place on the reaction vial.

Red Blood Cell Labeling Procedure
Labeling may be performed without washing or centrifugation steps directly in the silicone-coated reaction vial of Bracco A-C-D Solution Modified.*

A 30 to 50 mL sample of whole blood is withdrawn from the patient and added aseptically to a vial of Bracco A-C-D Solution Modified. 1.85 to 5.55 microcuries (50 to 150 microcuries) of Chromitope Sodium (Sodium Chromate Cr 51 Injection USP) is then injected into the reaction vial using a shielded syringe. The amount of radioactivity added to the vial will depend on the intended use of the labeled red blood cells. The suspension is incubated for 30 to 60 minutes at room temperature with frequent gentle agitation. After incubation, 100 mg Ascorbic Acid Injection USP is injected into the vial. The ascorbic acid reduces any remaining unbound dianionic chromium 51 to the anionic state which does not penetrate red blood cells; thus in vivo labeling of red blood cells is prevented.

The extent of chromium 51 labeling is influenced by hematocrit values; hematocrits below 35 percent will result in a higher degree of

<table>
<thead>
<tr>
<th>Tissue</th>
<th>mGy/7.40 MBq</th>
<th>rads/200 uCi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>2.0 26.4</td>
<td>0.20 2.64</td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tests</td>
<td>0.66</td>
<td>0.066</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.66</td>
<td>0.066</td>
</tr>
<tr>
<td>Whole body</td>
<td>0.55</td>
<td>0.055</td>
</tr>
</tbody>
</table>

HOW SUPPLIED
Chromitope Sodium (Sodium Chromate Cr 51 Injection USP) is available in multiple dose vials containing 9.25 microcuries (250 microcuries) and 37 microcuries (1.0 milliunit) at the time of calibration. Complete assay data for each vial are provided on the container.

Storage
Store the product as supplied at 20-25 °C (68-77 °F) [See USP]; avoid excess heat.

DISPOSAL
Any unused portion of the labeled preparation must be stored and disposed of in accordance with the conditions of NRC radioactive material license pursuant to Agreement State Regulation.

The U.S. Nuclear Regulatory Commission has approved this prepared radiopharmaceutical for distribution to persons licensed to use, byproduct material identified in 535.100 of 10 CFR Part 35, to persons who hold an equivalent license issued by an Agreement State, and, outside the United States, to persons authorized by the appropriate authority.

Rx only
Manufactured for
Bracco Diagnostics Inc.
Princeton, NJ 08543
by Nycomed Amersham plc
Little Chalfont, England

Revised October 1999

Chromate Cr 51 Injection USP is then injected into the reaction vial using a shielded syringe. The amount of radioactivity added to the vial will depend on the intended use of the labeled red blood cells. The suspension is incubated for 30 to 60 minutes at room temperature with frequent gentle agitation. After incubation, 100 mg Ascorbic Acid Injection USP is injected into the vial. The ascorbic acid reduces any remaining unbound dianionic chromium 51 to the anionic state which does not penetrate red blood cells; thus in vivo labeling of red blood cells is prevented.

The extent of chromium 51 labeling is influenced by hematocrit values; hematocrits below 35 percent will result in a higher degree of