

Cyanocobalamin Co 57 Capsules

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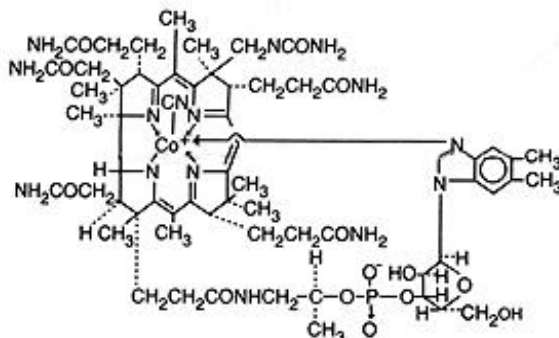
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Diagnostic—For Oral Administration Only

DESCRIPTION

Cyanocobalamin Co 57 is available for diagnostic use in opaque blue and white gelatin capsules for oral administration. Each capsule contains approximately 18.5 kilobecquerels (0.5 microcurie) cyanocobalamin Co 57 having a specific activity ranging from 18.5 to 37 kilobecquerels (0.5 to 1 microcurie) per microgram of cyanocobalamin. Cyanocobalamin has the following chemical structure:



PHYSICAL CHARACTERISTICS

Cobalt-57 decays by electron capture with a physical half-life of 270.9 days. Photons that are useful for detection are listed in Table 1.

Table 1. Principal Radiation Emission Data¹

Radiation	Mean Percent Per Disintegration	Energy (KeV)
Gamma-2	85.51	122.1
Gamma-3	10.60	136.5

The specific gamma ray constant² for cobalt-57 is 0.5657 R/hr-mCi at 1 cm. The half-value thickness of lead (Pb) for cobalt-57 is 0.02 cm.

To correct for physical decay of cobalt-57, the fractions that remain at selected time intervals after the day of calibration are shown in Table 2.

Table 2. Physical Decay Chart: Cobalt-57,
Half-Life 270.9 Days

Days	Fraction Remaining	Days	Fraction Remaining
0*	1.000	90	0.794
5	0.987	105	0.764
10	0.975	120	0.736
15	0.962	135	0.708
30	0.926	150	0.681
45	0.891	165	0.656
60	0.858	180	0.631
75	0.825		

*Calibration Day

CLINICAL PHARMACOLOGY

Orally administered cyanocobalamin is normally complexed to intrinsic factor and absorbed by the distal ileum.

INDICATIONS

Cyanocobalamin Cobalt Co 57 is used for diagnosis of Addisonian (pernicious) anemia and as a diagnostic adjunct in other defects of intestinal absorption.

CONTRAINDICATIONS

None known.

WARNINGS

None known.

PRECAUTIONS

General

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

The test should not be started within 24 hours of a therapeutic dose (1000 µg) of Vitamin B₁₂ or within 24 hours of a loading dose of Vitamin B₁₂ for the Schilling Test.

Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides produced by nuclear reactor or particle accelerator and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential, or whether this drug affects fertility of males or females.

Pregnancy Category C

Adequate reproduction studies have not been performed in animals to determine whether this drug affects fertility in males or females, has teratogenic potential, or has other adverse effects on the fetus. This drug should be used in pregnant women only when 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 onset of menses.

Nursing Mothers

It is not known whether this drug is excreted in human milk during lactation. Because many drugs are excreted in human milk, as a general rule nursing should not be undertaken when a patient has been administered radioactive material.

Pediatric Use

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

No adverse reactions specifically attributed to the use of this drug have been reported.

DOSAGE AND ADMINISTRATION

The suggested dose range employed for oral administration in the average patient (70 kg) is up to 37 kilobecquerels (1.0 microcurie) of Cyanocobalamin Cobalt Co 57.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

See section on DIRECTIONS FOR USE.

RADIATION DOSIMETRY

The estimated absorbed radiation doses³ to an average patient (70 kg) from an oral administration of 37 kilobecquerels (1 microcurie) of Cyanocobalamin Cobalt Co 57 are shown in Table 3.

Table 3. Absorbed Radiation Doses

Tissue	Cyanocobalamin CobaltCo 57			
	Normal		Pernicious Anemia	
	mGy/ MBq	rads/ mCi	mGy/ MBq	rads/ mCi
Liver	1.4	0.14*	0.26	0.026
Stomach	0.0016	0.00016	0.0022	0.00022
Small Intestine	0.0023	0.00023	0.0070	0.00070
Upper Large Intestine	0.0057	0.00057	0.017	0.0017
Lower Large Intestine	0.015	0.0015	0.044	0.0044
Testes	0.063	0.0063	0.0065	0.00065
Ovaries	0.048	0.0048	0.0012	0.00012
Total body	0.10	0.010	0.013	0.0013

*The administration of a flushing dose of nonradioactive Vitamin B₁₂ will decrease the dose to the liver, gonads, and total-body from cobalt-57 by about 30 percent.

HOW SUPPLIED

Catalog Number

397 Intrinsic Factor Concentrate Capsules, each containing 60 milligrams.

402 Cyanocobalamin Cobalt Co 57 Capsules are supplied in plastic vials containing 3 or 5 opaque blue and white gelatin capsules. Each capsule contains approximately 18.5 kilobecquerels (0.5 microcurie) Cyanocobalamin Cobalt Co 57 having a specific activity ranging from 18.5 to 37 kilobecquerels (0.5 to 1 microcurie/microgram of cyanocobalamin).

Cyanocobalamin Cobalt Co 57 Capsules may not be used after 6 months from the date of manufacture. The expiration date for the product is stated on the label.

403 Cyanocobalamin Cobalt Co 57 Reference Standard, approximately 0.185 kilobecquerel (0.005 microcurie) (1 percent of Catalog No. 402).

406 Schilling Test Kit. Kit contains:

5 capsules - Cyanocobalamin Cobalt Co 57, 18.5 kilobecquerels (0.5 microcurie) each.

1 x 4 mL vial - Cobalt Co 57 Reference Standard, 1 percent of capsule activity.

1 x 10 mL vial - Cyanocobalamin Injection (Vitamin B₁₂), 1000 micrograms per milliliter.

2 capsules - Intrinsic Factor Concentrate, 60 milligrams each.

5 counting vials

STORAGE

Store at room temperature (Below 86°F/30°C).

DIRECTIONS FOR USE

Urinary Excretion (Schilling) Test

The following General Procedure may be employed in conducting this test:

1. To determine that no interfering gamma-emitting radioisotopes are present from previous studies, a control urine specimen is recommended. Collect a 12-hour urine specimen from approximately 7:00 p.m. of the preceding day to 7:00 a.m. of the test day. Check for radioactivity. If radioactivity is present, repeat this procedure until none is found in the urine.
2. Administer one Cyanocobalamin Cobalt Co 57 Capsule containing approximately 18.5 kilobecquerels (0.5 microcurie) cobalt-57. The patient should have fasted for at least 8 to 12 hours prior to receiving the test dose. Following ingestion of the test dose, a light breakfast may be given. Normal noon and evening meals are permitted.
3. One to two hours later, a dose of 1000 micrograms of non-radioactive cyanocobalamin should be administered intramuscularly.
4. Collect the total urine excretion for the next 24 hours following Step 2. The patient's bladder should be voided immediately prior to the administration of the test dose and at the termination of the 24-hour collection period.
5. Dilute the collected urine with water to a convenient total urine volume, e.g., 2000 mL, using a volumetric flask.
6. Obtain an accurately measured aliquot of diluted urine and count in an appropriate instrument such as a well-type scintillation counter for 5 to 15 minutes. Obtain a background count, by counting for the same length of time employed for the urine sample. Subtract the background count from the sample count to obtain the net sample count.
7. Count a cobalt-57 Standard having the identical volume and geometry as the test urine sample counted in Step 6. Mallinckrodt Cyanocobalamin Co 57 Reference Standard (Cat. No. 403) may be employed. This standard is prepared to be equivalent to 1% of the total radioactivity of a single Cyanocobalamin Cobalt Co 57 Capsule bearing the same lot number. It is supplied in a total volume of 4 mL. If this reference standard is employed, the test urine sample aliquot (Step 6) must also be 4 mL.

An alternate standard may be prepared by using a capsule containing the same amount of radioactivity (cobalt-57) as administered to the patient. This may be accomplished by thoroughly dissolving the capsule in about 50 mL of hot water. The resulting solution should be diluted to a convenient volume (e.g., 100 mL) and accurate aliquots obtained to represent a known percentage of the total administered dose. The aliquot must be diluted to the identical volume and counted under the same conditions as the test urine sample in Step 6. Obtain a background count and subtract from the standard count to determine the net count for the reference standard.

8. Determine the percent of Cyanocobalamin Cobalt Co 57 excretion by the following:

Percent Cobalt-57 Excreted In Urine=

$$\text{Net Urine Sample CPM} \times \frac{\text{Total Urine Volume (mL)}}{\text{Urine Sample Volume (mL)}} \times 100$$

$$\text{Net Standard CPM} \times 100 *$$

*This correction factor is necessary if a Mallinckrodt 1% Reference Standard is employed. If the standard is prepared from a Cyanocobalamin Co 57 Capsule, the net standard count must be multiplied by the appropriate factor to obtain a value equivalent to the administered dose. For example, if a Cyanocobalamin Co 57 Capsule is diluted up to 100 mL and a 2 mL aliquot is removed to prepare the standard, the factor is 50 ($100 \div 2 = 50$).

Simplified Procedure Using the Schilling Test Kit

NOTE: Please refer to statements on interfering gamma-emitting radioisotopes and pretest fasting in Steps 1 and 2 under General Procedure above.

1. Administer orally one Cyanocobalamin Cobalt Co 57 Capsule.
2. One to two hours later administer 1000 micrograms of Vitamin B₁₂ intramuscularly.
3. Collect ALL urine for 24 hours.
4. Measure total 24-hour urine volume.
5. Pipette 4 mL of urine into a counting vial. If the urine is collected in more than one container, volumes should be thoroughly mixed prior to pipetting.
6. Count 4-mL urine sample for a minimum of 15 minutes, but preferably 30 minutes and divide the counts by the counting time to get counts per minute (cpm).
7. Count the background for the same length of time that you count the urine sample and divide by the counting time to get cpm.
8. Subtract the background from the sample count to get Net Urine cpm.
9. Count the standard for 3 minutes and divide by 3. Subtract the background from step 7 to get Net Standard cpm.

Percent Cobalt-57 Excreted In Urine =

$$\frac{\text{Net Urine cpm} \times \text{Total Urine Volume (mL)}}{4 \times \text{Net Standard cpm}}$$

Interpretation: Generally, pernicious anemia can be ruled out if the amount of cobalt-57 found in the urine is greater than 6 to 10 percent of the administered dose. A value in the range of 0 to 3 percent normally indicates pernicious anemia or other conditions resulting in a lack of Vitamin B₁₂ absorption. Results in the 3 to 5 percent range are somewhat questionable and usually require further analysis.

If a low value is obtained, the test is repeated after 48 to 72 hours, following the same procedure described above except that a dose of 60 milligrams of Intrinsic Factor Concentrate is administered along with the Cyanocobalamin Cobalt Co 57. If, in the presence of intrinsic factor, the urinary excretion of cobalt-57 increased to the normal range, the diagnosis of pernicious anemia is confirmed.

Various factors may affect the accuracy and interpretation of the test. Please refer to the section under PRECAUTIONS for a discussion of these points.

Fecal Excretion Test

The extent of Vitamin B₁₂ absorption can also be determined by the difference in the administered dose and the amount recovered in the feces. The test is considerably more time consuming, however, and requires a great deal more patient cooperation than the urinary excretion method.

The following general procedure is employed in conducting this test:

1. Following administration of one capsule of Cyanocobalamin Cobalt Co 57, collect all stools in individual containers. Stool must not be contaminated with urine. Continue to count each container separately until less than 1% of the dose administered is found in two successive samples. A period of 5 to 15 days is normally required.
2. Homogenize the combined stool samples and dilute as needed to an appropriate counting volume. Determine the total radioactivity present.
3. Dilute the Mallinckrodt 1% Reference Standard or one prepared as described in Step 7 under the Urinary Excretion (Schilling) Test: General Procedure, to a volume equal to the combined stool sample. Count the standard and the stool sample, correcting both values for background.
4. Determine the amount of radioactivity recovered in the stools as a percentage of the administered dose as follows:

Percent of Administered Dose =

$$\frac{\text{Net Stool Sample cpm}}{\text{Net Standard cpm} \times 100^*} \times 100$$

*This correction factor is necessary if a Mallinckrodt 1% Reference Standard is employed. If the standard is prepared from a Cyanocobalamin Co 57 Capsule, the net standard count must be multiplied by the appropriate factor to obtain a value equivalent to the administered dose. For example, if a Cyanocobalamin Co 57 Capsule is diluted up to 100 mL and a 2 mL aliquot is removed to prepare the standard, the factor is 50 ($100 \div 2 = 50$).

Interpretation: In normal patients, approximately 50% or less of the administered dose will be recovered in the feces. Patients with impaired absorption will excrete from 75 to 100 percent of the administered dose. A diagnosis of pernicious anemia can be established in those patients who exhibit a normal absorption following a repeat study in which intrinsic factor is administered.

Dosage: For the diagnosis of pernicious anemia using either of the above two procedures, the usual dosage of Cyanocobalamin Cobalt Co 57 is a single capsule containing approximately 18.5 kilobecquerels (0.5 microcurie) cobalt-57.

¹ Kocher, David C., "Radioactive Decay Data Tables," DOE/TIC 11026, 77 (1981)

² From Radiopharmaceutical Internal Dosimetry Information Center, Oak Ridge Associated Universities, Oak Ridge, TN 37831-0117, February 1995.

³ Method of calculation: "S", Absorbed Dose per Unit Calculated Activity for Selected Radionuclides and Organs, MIRD Pamphlet No. 11 (1975).

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