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Revised 2010 (Resolution 26)*

ACR–ASTRO PRACTICE GUIDELINE FOR THE PERFORMANCE OF THERAPY WITH UNSEALED RADIOPHARMACEUTICAL SOURCES

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic and radiation oncology care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment.

Therefore, it should be recognized that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

This guideline was revised by the American College of Radiology (ACR), and the American Society for Radiation Oncology (ASTRO).

This guideline is intended to guide appropriately trained and licensed physicians performing therapy with unsealed radiopharmaceutical sources. Such therapy requires close cooperation and communication between the physicians who are responsible for the clinical management of the patient and those who administer radiopharmaceutical therapy and manage the attendant side effects. Adherence to this guideline should help to maximize the efficacious use of these procedures, maintain safe conditions, and ensure compliance with applicable regulations.

Application of this guideline should be in accordance with the [ACR–SNM Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals](#) [1], as that guideline relates to the handling of radiopharmaceuticals, radiation safety, and radiation protection of patients, personnel, and the public. There must also be compliance with applicable laws and regulations.

II. DEFINITION

Therapy with unsealed sources involves administration of radiopharmaceuticals for the treatment of medical conditions.

III. GOAL

The goal of therapy with unsealed radiopharmaceutical sources is to provide either cure or effective palliation of disease while minimizing untoward side effects and complications.

IV. INDICATIONS

Examples of therapy with unsealed radiopharmaceutical sources include, but are not limited to:

1. Iodine-131 (sodium iodide) for treatment of hyperthyroidism.
2. Iodine-131 (sodium iodide) for ablation of post-operative thyroid remnant and for therapy of iodine-avid thyroid cancer.
3. Phosphorus-32 (sodium phosphate) for treatment of myeloproliferative disorders such as polycythemia vera and thrombocytosis.
4. Phosphorus-32 (colloidal chromic phosphate) for intracavitary therapy of malignant ascites, malignant pleural effusions, malignant pericardial effusions, and malignant brain cysts.
5. Strontium-89 (strontium chloride) and samarium-153 lexidronam ethylene diamine tetra methylene phosphonic acid (EDTMPA) for adjuvant and palliative treatment of painful skeletal metastases when these metastases are radiotracer-avid on a diagnostic bone scan.
6. Yttrium-90 ibritumomab tiuxetan and iodine-131 tositumomab, murine monoclonal antibodies that target the CD20 antigen, for treatment of patients with CD20 positive follicular B-cell non-Hodgkin's lymphoma, with or without transformation, including but not limited to disease that is refractory to rituximab and has relapsed following chemotherapy. On Sept 3, 2009 the FDA granted expanded approval for the use of yttrium-90 ibritumomab tiuxetan in patients with previously untreated follicular non-Hodgkin's lymphoma who have demonstrated partial or complete response to first-line chemotherapy (consolidation after chemotherapy) [2,3].

For more information on radioembolization, see the [ACR–ASTRO–SIR Practice Guideline for Radioembolization with Microsphere Brachytherapy Device \(RMBD\) for Treatment of Liver Malignancies](#) [4].

V. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

The qualifications and responsibilities of physicians and other personnel performing these therapeutic procedures should be in accordance with the [ACR–SNM Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals](#) [1] and/or the [ACR Practice Guideline for Radiation Oncology](#) [5]. In addition, training and experience must be in compliance with the applicable laws and regulations.

VI. SPECIFICATIONS OF THE EXAMINATION AND TREATMENT

The written or electronic request for a radiopharmaceutical procedure should provide sufficient information to demonstrate the medical necessity of the examination and allow for its proper performance.

Documentation that satisfies medical necessity includes 1) signs and symptoms and/or 2) relevant history (including known diagnoses). Additional information regarding the specific reason for the procedure or diagnosis would be helpful and may at times be needed to allow for the proper performance of the procedure.

The request for the procedure must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should be provided by a physician or other appropriately licensed health care provider familiar with the patient's clinical problem or question and consistent with the state's scope of practice requirements. (ACR Resolution 35, adopted in 2006)

A. General Procedures

1. Clinical evaluation - The initial evaluation includes review of the patient's history, physical examination, and pertinent diagnostic studies and reports. A complete history of all previous radiotherapy and radiopharmaceutical therapy and communication with the referring physician and other physicians involved in the patient's care are also recommended. For the radiopharmaceutical treatments that are potentially marrow-toxic, a complete blood count with differential and platelet count should be part of the initial evaluation and of each pretreatment examination.

2. Quality management - In order to use radiopharmaceuticals as unsealed sources for therapy, a “quality management” program must be in place as required by the Nuclear Regulatory Commission (NRC) or agreement state³ regulations. Key elements of this program are: written directives; duplicative procedures for identifying patients; careful record keeping to ensure prescribed administered activity; minimization of the possibility of infiltration for agents that are administered intravenously; procedures for minimizing radiation exposure or radiopharmaceutical contamination of personnel, family members of patients, and the public (e.g., alerts regarding possible current or future pregnancy); procedures for containment of radioactivity; and an audit mechanism to ensure compliance with the program.
3. Informed consent - Informed consent must be obtained and documented. See the [ACR Practice Guideline on Informed Consent – Radiation Oncology](#) [6].
4. Treatment - The procedure and follow-up should be performed according to an established system of procedural steps that may be unique for each type of application.
5. Female patients should not be pregnant, breast-feeding, or lactating at the time radiopharmaceutical therapy is orally, intravenously, or intraperitoneally administered. Pregnancy should be ruled out by a negative human chorionic gonadotropin (hCG) test obtained prior to administration of the radiopharmaceutical or by documented history of hysterectomy or by a postmenopausal state with absence of menstrual bleeding for 2 years, or by premenarche in a child age 10 or younger. Breast-feeding should be completely discontinued prior to the therapy and should not be resumed until subsequent pregnancy. Other national regulatory bodies may have similar recommendations. In addition, postpartum lactating patients should not undergo treatment, even if not breast-feeding, for a period of at least 3 months, or until lactation ceases, because the lactating breasts may accumulate significant amounts of iodine-131 or other unsealed therapeutic radiopharmaceuticals, resulting in a significant radiation dose to the patient’s breasts. The treating physician should also bear in mind that the immediate

postlactating breast may still concentrate iodine-131, resulting in breast radiation dose.

6. Radiation precautions - Radiation precautions and patient release criteria may be regulated federally by the NRC in many states, or by the state (with regulations that are closely patterned on the federal regulations and may be more restrictive). The radiation safety officer, medical physicist or health physicist for the local facility can provide information on the applicable regulations. Details on the federal regulations can be obtained at the NRC web site, www.nrc.gov, or by telephone (301-415-7000).

Under the guidelines of federal code 10 CFR 35.75 [7] and NRC Regulatory Guide 8.39 [8], the patient may be released if the total effective dose equivalent to any other individual who is exposed to the patient is not likely to exceed 5 mSv (0.5 rem), assuming all other regulatory requirements for patient instructions and record keeping are met. NUREG-1556, Vol 9, “Consolidated Guidance about Materials Licenses: Program-Specific Guidance about Medical Use Licenses,” describes methods for calculating doses to other individuals and contains tables of activities not likely to cause doses exceeding 5 mSv (0.5 rem). Agreement states may have specific rules and regulations regarding release of patients with significant residual activity.

Most radiation meters measure exposure rates in milliroentgens/hour (mR/h). For low-linear-energy-transfer-rate radiation (including beta particles and most X-rays and gamma rays), the exposure rate in mR/h will be equivalent to the dose rate in 0.01 mSv/h (1 mrem/h). Thus, an exposure rate of 7.0 mR/h at 1 meter is assumed to give a dose rate of 0.07 mSv/h (7.0 mrem/h).

For treatments outside the United States, regulations of the corresponding national regulatory bodies may apply, and all applicable laws and regulations must be followed.

If confinement in a health care facility is needed, it is not usually necessary to store body effluents such as urine, stool, or vomitus. For effluent disposal the toilet should be flushed two or three times after each use to ensure sufficient dilution of radioactivity. Food trays and linens should be stored in the room until monitored and cleared by radiation safety staff. All routine blood work and laboratory specimens should be obtained prior to treatment with the radiopharmaceutical.

³An agreement state is any state with which the U.S. Nuclear Regulatory Commission or the U.S. Atomic Energy Commission has entered into an effective agreement under Subsection 274.b of the Atomic Energy Act of 1954, as amended (73 Stat. 689).

The patient must stay in the room except in a medical or nonmedical (e.g., fire) emergency, and access by personnel and visitors must be limited. All trash and residual nondisposable items must be monitored after the patient's release and stored until radiation levels reach the statutory level defined for safe disposal or reuse. Once all known contamination is removed from the room, the room must be surveyed to verify that the radiation levels are sufficiently low to permit its general use. The room may not be used until this survey is performed.

If the admitting physician is different from the physician who administers the radiopharmaceutical, there must be a mechanism to prevent premature discharge or release of the patient from confinement.

B. Iodine-131 (sodium iodide) Therapy for Hyperthyroidism

The basic disease entities treated are: diffuse toxic goiter (Graves' disease), toxic nodular goiter, and solitary toxic nodule.

Administered Dose		Radiation Absorbed Dose	
SI Units	Traditional	SI Units	Traditional
3.7 GBq	100 mCi	1 Sv	100 rem
37 MBq	1 mCi	1 cSv	1 rem
3.7 MBq	100 μ Ci	1 mSv	100 mrem
37 kBq	1 μ Ci	0.01 mSv	1 mrem

1. Diffuse toxic goiter

- a. Patient - A recent radioiodine thyroid uptake should be available (see the [ACR–SNM–SPR Practice Guideline for the Performance of Thyroid Scintigraphy and Uptake Measurements](#) [9]). The size of the thyroid gland should be noted. Optimally, the patient's system should be free of iodide-containing medications, iodinated contrast agents, exogenous thyroid hormone, and antithyroid medications. The patient should avoid foods containing very large amounts of iodine for the week prior to therapy; however, a strict low-iodine diet is usually unnecessary.
- b. Administered activities - Initial activity of 1.85 to 7.4 MBq (50 to 200 μ Ci) per gram of thyroid (after adjusting for current 24-hour radioiodine uptake) may be administered. Generally the likelihood of residual hyperthyroidism is greater for lower administered activity, and the likelihood of hypothyroidism is greater for higher administered activity. There are also data to support empiric adult dosing with a "fixed"

dose of 185 to 555 MBq (5 to 15 mCi). The measurement of radioiodine uptake before radioiodine therapy is necessary even when a fixed dose is planned, to prevent the inappropriate administration of radioactive iodine. Each treating physician, often in consultation with the referring physician, should decide on an appropriate activity to be administered (see section VI.A.6 for radiation precautions).

- c. Side effects/complications - Side effects are usually minor. Patients may occasionally experience neck tenderness and/orodynophagia from radiation thyroiditis. Serious complications are rare. However, on occasion patients with severe hyperthyroidism may experience exacerbation of symptoms within the first 2 weeks following iodine-131 therapy. These symptoms usually respond to short term beta blocker therapy, but rarely may progress to frank thyroid storm. Patients should be instructed to contact their referring physician or seek immediate medical care should such symptoms occur. Hypothyroidism is often considered to be a likely or even desired outcome of successful therapy of Graves' disease or toxic nodular goiter and can occur within the first few months following therapy or even decades later, with a small, ongoing annual incidence. Hypothyroidism is treated with carefully monitored hormone replacement therapy. Based on previous multicenter trials, there is no evidence of increased risk of thyroid carcinoma or other malignancy, infertility, or increased incidence of birth defects following iodine-131 therapy for hyperthyroidism.
- d. Ideally, patients should not receive thioamide medications (e.g., propylthiouracil or methimazole) for at least 5 to 7 days prior to therapy.
- e. Subsequent therapies - In patients who have not adequately responded to prior iodine-131 therapy, subsequent treatments may be given. An equal or higher treatment dose is generally used for retreatment. Dose considerations should balance the total activity against the relative risks of residual disease versus hypothyroidism. Repeat therapies are usually not indicated until at least 3 months after a radioiodine treatment to allow the assessment of the effect of therapy.

2. Toxic nodular goiter and solitary toxic nodule
 - a. Patient - See section VI.B.1.a.
 - b. Administered activity - These conditions tend to be more resistant to radioiodine therapy. Activity of up to 1.11 GBq (30 mCi) or more for outpatient treatment may be administered provided that the radioiodine uptake is sufficient.
 - c. Prior thionamide therapy - The effect of thionamide on the responsiveness of the thyroid to radioiodine therapy is similar to that in diffuse toxic goiter. The treating physician should consider having the patient discontinue the medication to allow for systemic clearance or, if this is not feasible, using an activity in the upper end of the administered activity range.
 - d. Side effects/complications - See section VI.B.1.c. If a solitary toxic nodule has fully suppressed the function of the remaining thyroid, the risk of resulting hypothyroidism is decreased, but hypothyroidism may still occur.
 - e. Treatment failures - Rarely, it may be necessary to administer an activity larger than 1.22 GBq (33.0 mCi) (see section VI.A.6).
 - f. In rare cases, radioiodine therapy may be indicated in other nonsurgical patients with benign thyroid disease.

C. Iodine-131 (Sodium Iodide) for Ablation of Postoperative Thyroid Remnant and for Therapy of Iodine-Avid Thyroid Cancer

Iodine-avid thyroid cancers frequently take up radioiodine in the absence of significant amounts of residual normal thyroid tissue. In order to optimize ablative radioiodide therapy for residual or metastatic disease, or in selected cases to facilitate the follow-up for patients with good prognosis, the thyroid remnant should be eliminated by surgery and/or radioiodine treatment, if possible. In planning therapy for a suspected thyroid remnant or metastasis, a total body iodine scan with iodine-123 or iodine-131 may be of assistance in assessing extent of disease.

1. Ablation of thyroid remnant
 - a. Patient - The serum TSH must be elevated, usually to a level in excess of 30 μ IU/mL, either by withholding oral thyroid hormone to induce endogenous TSH secretion or by injecting recombinant human TSH (rhTSH) to raise the patient's blood level of this hormone before therapy. If a remnant is suspected, thyroid scintigraphy with iodine-131 or iodine-123 may be performed to

determine how avidly the thyroid remnant is accumulating radioiodide. If a large thyroid remnant is present, performing a completion thyroidectomy before the iodine-131 therapy should also be considered. Documentation of an elevated TSH level as well as adherence to a low iodine diet for 1 to 2 weeks prior to treatment is recommended. Optimally, the patient's system should be free of iodide-containing medications, iodinated contrast agents, exogenous thyroid hormone, and antithyroid medications. No age limits apply. Administration of more than 74 to 185 MBq (2 to 5 mCi) of iodine-131 may interfere with subsequent uptake of iodine-131 for several days to several weeks. This "stunning" effect, if it occurs, may be minimized by administering the therapeutic dose shortly after the diagnostic radionuclide dosage.

- b. Administered activity - Activities of 1.11 to 3.7 GBq (30 to 100 mCi) of iodine-131 (sodium iodide) administered orally are most often used. Higher doses may be used for more extensive disease. Prior to administration, the patient should be fasting and should abstain from eating for at least 2 hours after taking an oral dose. The patient may need to be placed on radiation precautions (see section VI.A.6 for radiation precautions).
- c. Side effects/complications - Side effects include radiation dysphagia and sialadenitis, both of which are activity related and self-limited. To address sialadenitis, measures may be taken to maintain a high level of hydration and stimulate saliva flow following therapy, such as recommending administration of a sialogogue or other agent that stimulates the salivary gland for as long as 6 days [10]. With larger activities or multiple administrations, xerostomia may rarely occur. Patients given 3.7 GBq (100 mCi) or more may develop mild treatment-related symptoms such as headache, nausea, and vomiting that begin about 4 hours after iodine-131 administration and resolve within 72 hours. Diarrhea has occasionally been noted. A single dose of 1.85 to 3.7 GBq (50 to 100 mCi) may deliver sufficient radiation to the testes to cause transient testicular failure of uncertain long-term consequence. Discussion of fertility issues should be considered, particularly in young patients who may need multiple treatments. There is some evidence that female fertility may be decreased after activities in excess of 22.2

GBq (600 mCi). Transient myelosuppression may occur with oral doses of iodine-131 in excess of 5.55 to 7.4 GBq (150 to 200 mCi), and dosimetry is suggested when such doses are used, especially in older patients. Leukemogenesis and carcinogenesis (salivary glands, kidney, bladder, and gastrointestinal tract) have been described in patients following very high dose iodine-131 therapy, i.e., 11.1 to 14.8 GBq (300 to 400 mCi).

2. Known or suspected residual thyroid cancer
 - a. Patient - See section VI.B.1.a. An elevated thyroglobulin level or a whole body survey performed with iodine-131, iodine-123, FDG-PET, or other radiopharmaceuticals that show abnormal concentration of tracer indicates recurrence (see the [ACR–SNM–SPR Practice Guideline for the Performance of Thyroid Scintigraphy and Uptake Measurements](#) [9]).
 - b. Administered activity - For residual tumor in the thyroid bed without evidence of distant metastasis, activities of 3.7 to 5.55 GBq (100 to 150 mCi) are usually administered. Complications, side effects, and radiation precautions are similar to those described in section VI.C.1.c.
3. Distant metastases
 - a. Patient - See section VI.C.1.a.
 - b. Activities of 3.7 to 9.25 GBq (100 to 250 mCi) are usually administered. Complications, side effects, and radiation precautions are similar to those described in sections VI.A.6 and VI.B.1.c. Activity administered can be based on fixed doses, depending on the clinical situation, or based on quantitative iodine-131 dosimetry. Dosimetry calculations of dose to the whole blood and of total lung activity at 48 hours should be considered when the highest activities are used. When larger activities are administered, bone marrow suppression becomes a concern. There are reports of pulmonary fibrosis and/or pneumonitis resulting from therapy for widespread lung metastases when the administered activity delivers a dose of 6 Sv (600 rem) or more to the lung. Pulmonary function studies should be considered prior to treatment if there are widespread pulmonary metastases.
 - c. After successful remnant ablation, a measurable serum thyroglobulin level suggests functioning iodine avid tissue, the possibility of recurrent disease, and may be an indication for additional treatment.

However, both high and low thyroglobulin levels are unreliable in the presence of antithyroglobulin antibodies. In particular, falsely low thyroglobulin levels may occur in antibody-positive patients; therefore antibody assays should accompany all thyroglobulin measurements. Even when a diagnostic whole-body scan is negative, if the stimulated thyroglobulin level is greater than about 10 ng/mL or there is other evidence of disease, empiric therapy with 3.7 to 5.55 MBq (100 to 150 mCi) can be considered.

- d. In the setting of a negative whole-body scan and suspected metastatic disease, an FDG-PET/CT scan may be helpful to localize recurrent/metastatic disease that would potentially be amenable to surgical management.
4. Interactions with other forms of treatment
 - a. Patients with a high risk of local/regional recurrent disease may be treated with both iodine-131 and external beam irradiation. The use of external beam irradiation prior to or alternating with radioactive iodine treatment has not been shown to be associated with a subsequent reduction in tumor uptake of radioactive iodine. Therefore external beam irradiation, if indicated, need not be delayed. The toxicity, acute and late, is likely to be additive within the field of irradiation. Dosimetry calculations should be considered if iodine-131 therapy and external beam radiotherapy are both being considered or have previously been performed in patients with spinal lesions, to avoid potential radiation-induced spinal cord damage.
 - b. Distant metastatic lesions that are painful or are a threat to life or function may be treated with external beam irradiation or surgery in addition to iodine-131.

D. Strontium-89 and Samarium-153 Lexitronam Therapy for Bone Pain Caused by Skeletal Metastases [11]

1. Patient - Patients with multiple osseous metastases that show increased tracer uptake on bone scintigraphy, who are obtaining diminishing relief from other methods of pain management (e.g., analgesics, bisphosphonates, external beam irradiation), and whose bone marrow is competent, are candidates for radiopharmaceutical therapy. Complete blood cell count with platelets should be obtained within 7 days prior to therapy. Platelet count

should be greater than 60,000 to 100,000/ μ L, leukocyte count greater than 2,400 to 5,000/ μ L absolute granulocyte count greater than 2,000/ μ L. Patients with disseminated intravascular coagulation (DIC) must be excluded from therapy. Patients should have an expected life span of greater than 3 months. Others may be treated after a case-by-case evaluation as adjuvant therapy to delay symptomatic skeletal metastases. Urinary incontinence is not a contraindication to treatment, although the patient or caregiver should be instructed on how to minimize radiation contamination from spilled urine. For samarium-153 lexidronam and strontium-89, bladder catheterization should be considered for patients incontinent of urine, to minimize the risk of radioactive contamination.

2. Administered activity - For strontium-89 the standard activity is 1.48 to 2.22 MBq (40 to 60 μ Ci per kilogram of body weight, (approximately 4 mCi [148 MBq] for standard weight) given by intravenous infusion over several minutes. The recommended samarium-153 lexidronam activity is 37.0 MBq (1.0 mCi) per kilogram of body weight, given intravenously, also over several minutes. When samarium-153 lexidronam is used, whole body gamma camera imaging may also be performed between 2 and 24 hours postinjection.
3. Complications - A “flare” phenomenon occurs in some patients, with transient worsening of pain within several days after treatment. This is a self limited process, although it can be severe. Patients should be counseled concerning the possibility of a flare phenomenon. The pain associated with the flare phenomenon can usually be managed with analgesics or steroidal medication. For intravenously administered radiotherapy, extravasation of the radiopharmaceutical should be avoided. It is imperative to have excellent intravenous access that is confirmed prior to injection. Although local skin damage is unusual, some experts believe it is prudent to follow a vesicant protocol for radiotherapy infusion [12]. Bone marrow depression occurs transiently, with a nadir at about 3 to 6 weeks and with recovery in about 3 to 6 additional weeks. Complete blood and platelet counts should be followed routinely for 8 to 12 weeks.
4. Interactions with other forms of treatment
 - a. Hormone administration need not be discontinued before the administration of

radiopharmaceutical therapy, since it does not interfere with the mechanism of action and does not potentiate any side effects.

- b. External beam radiation therapy may be used in concert with radiopharmaceutical therapy for local treatment of selected sites, especially those in which pathologic fracture or cord compression might occur. Careful evaluation of complete blood and platelet counts is required when these therapies are combined.
 - c. The patient should not have received long-acting myelosuppressive chemotherapy for 6 to 8 weeks and other forms of myelosuppressive chemotherapy for at least 4 weeks prior to radiopharmaceutical administration, also because of potential marrow toxicity.
5. Radiation precautions - There are none for strontium-89 as long as the patient is continent of urine and feces. For samarium-153 lexidronam, the patient may be released if the total effective dose equivalent to any other individual who is exposed to the patient is not likely to exceed 5 mSv (0.5 rem) per year. If state or facility regulations are more restrictive, they should be followed.
 6. Retreatment - Retreatment may be administered if initial treatment fails or symptoms recur. Special attention should be paid to recovery of bone marrow and blood counts. Retreatment may be given after adequate bone marrow recovery occurs, which is typically 2 to 3 months.
 7. As with all other forms of therapy with unsealed sources, patient management should be coordinated with clinical services and with other involved parties, especially radiation oncology, if external beam irradiation has been used or is being considered.

E. Phosphorus-32 (sodium phosphate) for Polycythemia Rubra Vera associated with Thrombocytosis

Phosphorus-32 (sodium phosphate) is approved for treatment of thrombocytosis associated with polycythemia vera. The diagnosis must be confirmed prior to therapy. The activities should be based on body surface area (85 MBq [2.3 mCi] per square meter intravenously) but may be standardized to a dose of 111 to 185 MBq [3.0 to 5 mCi] intravenously but should not exceed 185 MBq (5.0 mCi). Relapse or failure to respond within 12 weeks may require retreatment with dosages up to 259 MBq (7.0 mCi). Phosphorus-32 should not be given if the platelet

count is less than 100,000/ μ L or the leukocyte count is less than 3,000/ μ L.

F. Phosphorus-32 (colloidal chromic phosphate) for Malignant Ascites, Pleural Effusion or as an Adjunct to Treatment of Borderline Ovarian Neoplasms

The usual activity for intracavitary therapy is 222 to 555 MBq (6 to 15 mCi) in the pleural cavity and 370 to 740 MBq (10 to 20 mCi) in the peritoneum. The ability of the radiopharmaceutical to spread uniformly throughout the affected cavity should be documented using technetium-99m sulfur colloid (see the [ACR–SNM–SPR Practice Guideline for the Performance of Gastrointestinal Scintigraphy](#) [13]) as an intraperitoneal or intrapleural injection followed by appropriate imaging. The patient should be turned to distribute the imaging agent. After documented dispersal, i.e., no evidence of loculation or penetration into the bowel, the patient may be treated. The combination of intraperitoneal phosphorus-32 colloidal chromic phosphate and external irradiation to the pelvis has been reported to be associated with a high incidence of morbidity, particularly bowel obstruction; accordingly, caution must be observed when this combination of therapies is used.

G. Yttrium-90 Ibritumomab Tiuxetan and Iodine-131 Tositumomab for Radioimmunotherapy of Non-Hodgkin's Lymphoma

1. Agents

Yttrium-90 ibritumomab tiuxetan consists of ibritumomab, the murine IgG1 kappa monoclonal antibody from which rituximab was developed, and tiuxetan, which stably chelates indium-111 for imaging and yttrium-90 for therapy. Iodine-131 tositumomab is a murine IgG2a lambda monoclonal antibody covalently linked to iodine-131. Both antibodies are directed against the CD20 antigen which is found on the surface of normal and malignant B lymphocytes.

2. Patient

- a. Patients with CD20 positive follicular B-cell non-Hodgkin's lymphoma, with or without transformation, including patients who are refractory to rituximab, are candidates for radioimmunotherapy.
- b. The principal toxicity of anti-CD20 radioimmunotherapy is hematologic. A careful hematologic evaluation needs to be performed prior to therapy. Since lymphoma in the bone marrow will increase the dose to the marrow, a recent bone marrow biopsy must be evaluated by an experience hematopathologist.

- c. Patients should have diagnostic scanning prior to the therapeutic dose delivery in order to verify individual biodistribution. Indium-111 ibritumomab tiuxetan is used for diagnostic studies prior to treatment with yttrium-90 ibritumomab tiuxetan, and a diagnostic activity of iodine-131 tositumomab is used prior to the therapeutic dose delivery of that radiopharmaceutical. Patients with altered biodistribution as described in section 3 below should not be treated with these radiopharmaceuticals. The pretreatment scans are also used to calculate the therapeutic dose for iodine-131 tositumomab.
- d. Patients treated with iodine-131 tositumomab are at risk for hypothyroidism. To reduce this probability, they must be treated with either a saturated solution of potassium iodide (SSKI) four drops orally a day, Lugol's solution 20 drops orally three times a day, or potassium iodide tablets 130 mg orally once a day, starting at least 24 hours prior to initiating the iodine-131 tositumomab dosimetric dose. Thyroid blockade must continue until 2 weeks after administration of the iodine-131 tositumomab therapeutic dose. If the patient is not required to remain in the hospital, he or she may need to receive appropriate counseling concerning limitation of dose to other individuals.

3. Dosimetry and assessment of biodistribution

- a. Altered biodistribution is uncommon. Biodistribution is considered to be altered if indium-111 ibritumomab tiuxetan blood pool concentration is not well visualized, indicating rapid clearance by reticuloendothelial system. It can be represented by any of the following conditions: urinary obstruction; diffuse lung uptake greater than that of the blood pool, or intense areas of bowel uptake that is comparable to that of the liver.
- b. Patients treated with iodine-131 tositumomab have total body counts and images obtained by gamma camera scanning on day 0 (within 1 hour of administration, before the patient voids), on days 2 to 4, and on day 6 or 7 if necessary. The biodistribution is evaluated with the same criteria used above. Total body residence times of less than 50 hours or more than 150 hours represent altered biodistribution. The total body residence time is used as a factor in calculating the dose of iodine-131

tositumomab, which is calculated using a nomogram provided by the manufacturer.

4. Administered activity

- a. For both yttrium-90 ibritumomab tiuxetan and iodine-131 tositumomab, administration should occur during a specified period of time after the first diagnostic scan.
- b. According to manufacturer's instructions, the therapeutic dose of yttrium-90 ibritumomab tiuxetan is administered on days 7 to 9, with day 1 being the day of the first dosimetric scan. Iodine-131 tositumomab administration is recommended to occur on day 7 (up to day 14), with day 0 being the day of the first dosimetric scan.
- c. Biodistribution of both diagnostic and therapeutic administration is improved by concurrent administration of unlabeled agents in order to saturate readily accessible CD20 positive sites, including circulating B-cells and cells in the spleen. Biodistribution of radiolabeled ibritumomab tiuxetan is improved with the prior administration of rituximab. Unlabeled tositumomab is used for this purpose with iodine-131 tositumomab administration.
- d. The therapeutic dose for yttrium-90 ibritumomab tiuxetan, after an infusion of rituximab, is 14.8 MBq/kg (0.4 mCi/kg) for patients with a platelet count >150,000 cells/ μ L and 11.1 MBq/kg (0.3 mCi/kg) for patients with platelet count of 100,000 to 149,000 cells/ μ L. The maximum allowable dose of yttrium-90 ibritumomab tiuxetan is 1.184 GBq (32.0 mCi).
- e. For iodine-131 tositumomab, the administered activity is that calculated to provide a prescribed total body dose of 0.75 Gy (75 rad) for patients with a platelet count >150,000 cells/ μ L and 0.65 Gy (65 rad) cGy for patients with platelet count of 100,000 to 149,000 cells/ μ L. Patients should not be treated if the platelet count is <100,000 cells/ μ L.
- f. Since yttrium-90 is a pure beta emitter, on-site administered-dose measurement can be very difficult. A precise technique with careful attention to detail should be established with the help of a radiopharmacist or a medical physicist.

5. Complications

- a. Hypersensitivity reactions occur and may be severe. Patients who have received murine proteins should be screened for human

antimouse antibodies (HAMA). Patients who are positive are likely to be at increased risk of anaphylaxis and serious hypersensitivity and may show altered biodistribution of the antibody. Known hypersensitivity to rituximab or murine proteins is considered a contraindication to administration of yttrium-90 ibritumomab tiuxetan. Premedication with acetaminophen and diphenhydramine is recommended and should be considered prior to diagnostic and therapeutic infusions. Reactions to the unlabeled antibody infusion of rituximab or unlabeled tositumomab are common. Although reactions to subsequently infused iodine-131 tositumomab or indium-111 or yttrium-90 ibritumomab tiuxetan are uncommon, a physician must be present. Medications for the treatment of hypersensitivity reactions (e.g., epinephrine, antihistamines, and corticosteroids) and equipment for resuscitation should be immediately available.

- b. The most common serious adverse reactions associated with both yttrium-90 ibritumomab tiuxetan and iodine-131 tositumomab are severe or life-threatening cytopenias. With yttrium-90 ibritumomab tiuxetan, approximately 85% of patients are expected to experience grade 3 or 4 cytopenia. Cytopenias are influenced by initial bone marrow reserve as evidenced by baseline platelet count. With iodine-131 tositumomab, 71% of 230 patients enrolled in clinical studies experienced grade 3 or 4 cytopenias. The nadir can occur from 1 to more than 3 months after administration, and the duration of cytopenias can be from 3 to 5 weeks. Precautions include not treating patients who have more than 25% of bone marrow involved, or who have poor bone marrow reserve (including but not limited to prior stem-cell or bone marrow transplant, absolute neutrophil count <1,500 cells/ μ L, or previous failure of stem cell collection). The dose is modified according to the pretreatment platelet counts. Blood counts are monitored weekly or more frequently as needed until recovery occurs, for at least 10 to 12 weeks. Stem cell support and/or transfusions are provided as necessary, and cases of febrile neutropenia or infection are treated as appropriate.
- c. In patients treated with iodine-131 tositumomab, hypothyroidism occurs approximately 5% of the time, despite thyroid protection.

6. Interactions with other forms of treatment
 - a. A time interval sufficient to allow for bone marrow recovery after cytotoxic chemotherapy is recommended. Concomitant use of chemotherapy with yttrium-90 ibritumomab tiuxetan or iodine-131 tositumomab therapy has not been fully evaluated and should be considered with caution when not performed in conjunction with a defined research protocol.
 - b. Prior to radiopharmaceutical therapy, external beam radiation therapy may be necessary for local treatment of selected sites, especially when life-threatening or function-threatening involvement such as fracture or spinal cord compression exists or is likely to occur without such treatment. Careful consideration must be given to the amount of bone marrow treated, as treatment of a large percentage of the patient's bone marrow is likely to significantly affect the ability to tolerate radioimmunotherapy.

7. Radiation precautions
 - a. Lead shielding is used for the storage and handling of radiolabeled indium-111 (a gamma emitter), a required injection before yttrium-90. For yttrium-90 ibritumomab tiuxetan there are no special precautions, beyond the usual care taken to minimize radiation exposure to patients and to medical personnel, consistent with institutional radiation safety practices and patient management procedures. Yttrium-90 is a pure beta emitter, and safety precautions for medical professionals are universal precautions, with the addition of acrylic shielding for the yttrium-90 ibritumomab tiuxetan. Patients may be released immediately, with basic instructions, after administration of yttrium-90 ibritumomab tiuxetan.
 - b. Iodine-131 tositumomab is both a beta and a gamma emitter, and lead shielding is required during storage, preparation, and administration. Under the guidelines of federal code 10 CFR 35.75, the patient may be released if the total effective dose equivalent to any other individual who is exposed to the patient is not likely to exceed 5 mSv (0.5 rem), assuming all other regulatory requirements for patient instructions and record keeping are met. Assessment includes a calculation based on the patient's measured total body residence time (a function of the antibody clearance rate) and dose rate at 1 meter, as well as the individual's living and working situation

and ability to comply with instructions. If state or facility regulations are more restrictive, they should be followed.

8. As with all other forms of therapy with unsealed sources, patient management should be coordinated with clinical services and with other involved parties, especially medical and radiation oncology.

H. Follow-Up After Treatment

Physicians using unsealed radiopharmaceutical sources for therapy should participate with the patient's primary physician in the follow up and management of all patients treated with curative, adjuvant, or palliative intent and should document the outcome of therapy, including results of treatment (tumor control, survival, degree of palliation, time to retreatment) and significant sequelae [11].

VII. DOCUMENTATION

Reporting should be in accordance with the [ACR Practice Guideline for Communication: Radiation Oncology](#) [14].

The report should include the radiopharmaceutical used and the dose and route of administration, as well as any other pharmaceuticals administered, also with dose and route of administration.

VIII. ACR STATEMENT ON THERAPEUTIC USE OF UNSEALED RADIOPHARMACEUTICAL SOURCES

It is the position of the American College of Radiology that both nuclear medicine physicians and radiation oncologists are particularly well qualified by training and experience to administer unsealed radiopharmaceutical sources for treatment and that either can do so independently. Often, the preferred approach is for the nuclear medicine physician and radiation oncologist to work together as a physician team. The approach that is chosen may vary from patient to patient depending on the type of cancer being treated, local expertise, and patient-related issues. Whichever approach is used, it is important that patient selection as well as overall treatment planning and follow-up be performed by physicians with training and expertise in cancer management, basic radiation safety, and radiation physics.

IX. RADIATION SAFETY

Radiologists, imaging technologists, and all supervising physicians have a responsibility to minimize radiation dose to individual patients, to staff, and to society as a whole, while maintaining the necessary diagnostic image quality. This concept is known as "as low as reasonably achievable (ALARA)."

Facilities, in consultation with the radiation safety officer, should have in place and should adhere to policies and procedures for the safe handling and administration of radiopharmaceuticals, in accordance with ALARA, and must comply with all applicable radiation safety regulations and conditions of licensure imposed by the Nuclear Regulatory Commission (NRC) and by state, and/or other regulatory agencies. Quantities of radiopharmaceuticals should be tailored to the individual patient by prescription or protocol.

X. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION

Policies and procedures related to quality control and improvement, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education appearing under the heading *Position Statement on QC & Improvement, Safety, Infection Control, and Patient Education* on the ACR web page (<http://www.acr.org/guidelines>).

Equipment performance monitoring should be in accordance with the [ACR Technical Standard for Medical Nuclear Physics Performance Monitoring of Gamma Cameras](#).

ACKNOWLEDGEMENTS

This guideline was revised according to the process described under the heading *The Process for Developing ACR Practice Guidelines and Technical Standards* on the ACR web page (<http://www.acr.org/guidelines>) by the Guidelines and Standards Committees of the Commissions on Nuclear Medicine and Radiation Oncology in collaboration with the ASTRO.

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REFERENCES

1. ACR technical standard for diagnostic procedures using radiopharmaceuticals. *Practice Guidelines and Technical Standards*. Reston, Va.: American College of Radiology;2008:1203-1209.
2. Federal Drug Administration. Supplement Approval Letter (Zevalin). http://www.accessdata.fda.gov/drugsatfda_docs/applletter/2009/125019s0156ltr.pdf. Accessed on October 29, 2009.
3. Federal Drug Administration. Highlights of Prescribing Information (Zevalin). http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/125019s0156.pdf. Accessed on October 29, 2009.
4. Practice guideline for radioembolization with microsphere brachytherapy device (RMBD) for treatment of liver malignancies. *Practice Guideline and Technical Standards*. Reston, Va.: American College of Radiology;2008:1003-1016.
5. ACR practice guideline for radiation oncology. *Practice Guidelines and Technical Standards*. Reston, Va.: American College of Radiology;2008:923-929.
6. ACR practice guideline on informed consent - radiation oncology. *Practice Guidelines and Technical Standards*. Reston, Va.: American College of Radiology; 2008:937-941.
7. United States Nuclear Regulatory Commission. § 35.75 release of individuals containing unsealed byproduct material or implants containing byproduct material, 2007. <http://www.nrc.gov/reading-rm/doc-collections/cfr/part035/part035-0075.html>. Accessed March 18, 2009.
8. United States Nuclear Regulatory Commission. Regulatory guide 8.39, release of patients administered radioactive materials, 1997. http://www.nucmed.com/nucmed/ref/8_39.pdf. Accessed March 18, 2009.
9. ACR practice guideline for the performance of thyroid scintigraphy and uptake measurements. *Practice Guidelines and Technical Standards*. Reston, Va.: American College of Radiology; 2008:845-849.
10. Nakada K, Ishibashi T, Takei T, et al. Does lemon candy decrease salivary gland damage after radioiodine therapy for thyroid cancer? *J Nucl Med* 2005;46:261-266.
11. Schraml FV, Parr LF, Ghurani S, Silverman ED. Autopsy of a cadaver containing strontium-89-chloride. *J Nucl Med* 1997;38:380-382.
12. Williams G, Palmer MR, Parker JA, Joyce R. Extravasation of therapeutic yttrium-90-ibritumomab tiuxetan (zevalin): a case report. *Cancer Biother Radiopharm* 2006;21:101-105.
13. ACR practice guideline for the performance of gastrointestinal scintigraphy. *Practice Guidelines and Technical Standards*. Reston, Va.: American College of Radiology; 2008:863-870.
14. ACR practice guideline for communication: radiation oncology. *Practice Guidelines and Technical Standards*. Reston, Va.: American College of Radiology; 2008:931-936.
15. Bakri YN, Given FT Jr., Peeples WJ, et al. Complications from intraperitoneal radioactive phosphorus in ovarian malignancies. *Gynecol Oncol* 1985;21:294-299.
16. Barbaro D, Boni G, Meucci G, et al. Radioiodine treatment with 30 mCi after recombinant effectiveness for postsurgical remnants ablation. *J Endocrinol Metab* 2003;88:4110-4115.
17. Ben-Josef E, Shamsa F, Williams AO, et al. Radiotherapeutic management of osseous metastases: a survey of current patterns of care. *Int J Radiat Oncol Biol Phys* 1998;40:915-921.
18. Berg G, Lindstedt G, Suurkula M, et al. Radioiodine ablation and therapy in differentiated thyroid cancer under stimulation with recombinant human thyroid stimulating hormone. *J Endocrinol Invest* 2002;25:44-52.
19. *BEXXAR® Prescribing Information*. Glaxo Smith Kline (www.gsk.com) and Corixa Corporation.
20. Brundage MD, Crook JM, Lukka H. Use of strontium-89 in endocrine-refractory prostate cancer metastatic to bone. Provincial Genitourinary Cancer Disease Site Group. *Cancer Prev Control* 1998;2:79-87.
21. Bybel B, Blais M, Vandierendonck R, et al. Radiation safety when a patient dies after therapy. *J Nucl Med Technol* 1998;26:206-207.
22. Cailleux AF, Baudin E, Travagli JP, et al. Is diagnostic iodine-131 scanning useful after total thyroid ablation for differentiated thyroid cancer? *J Clin Endocrinol Metab* 2000;85:175-178.
23. Cholewinski SP, Yoo KS, Klieger PS, et al. Absence of thyroid stunning after diagnostic whole-body scanning with 185 MBq 131I. *J Nucl Med* 2000;41:1198-1202.
24. Coover LR, Silberstein EB, Kuhn PJ, et al. Therapeutic I-131 in outpatients: a simplified method conforming to the Code of Federal Regulations, title 10, part 35.75. *J Nucl Med* 2000;41:1868-1875.
25. Culver CM, Dworkin HJ. Radiation safety considerations for post-iodine-131 thyroid cancer therapy. *J Nucl Med* 1992;33:1402-1405.
26. Currie JL, Bagne F, Harris C, et al. Radioactive chromic phosphate suspension: studies on distribution, dose absorption, and effective

Suggested Reading (Additional articles that are not cited in the document but that the committee recommends for further reading on this topic)

- therapeutic radiation in phantoms, dogs, and patients. *Gynecol Oncol* 1981;12:193-218.
27. Grigsby PW, Siegel BA, Baker S, et al. Radiation exposure from outpatient radioactive iodine (131I) therapy for thyroid carcinoma. *JAMA* 2000;283:2272-2274.
 28. Grigsby PW, Siegel BA, Bekker S, et al. Preparation of patients with thyroid cancer for 131I scintigraphy or therapy by 1-3 weeks of thyroxine discontinuation. *J Nucl Med* 2004;45:567-570.
 29. Harbert JC. *Nuclear Medicine Therapy*. New York, NY: Thieme Medical Publications; 1987.
 30. Hermus AR, Huysmans DA. Treatment of benign nodular thyroid disease. *N Engl J Med* 1998;338:1438-1447.
 31. Janjan NA. Radiation for bone metastases: conventional techniques and the role of systemic radiopharmaceuticals. *Cancer* 1997;80:1628-1645.
 32. Johnson TA, Press OW. Therapy of B-cell lymphomas with monoclonal antibodies and radioimmunoconjugates: the Seattle experience. *Ann Hematol* 2000;79:175-182.
 33. Kaminski MS, Estes J, Zasadny KR, et al. Radioimmunotherapy with iodine (131) I tositumomab for relapsed or refractory B-cell non-Hodgkin lymphoma: updated results and long-term follow-up of the University of Michigan experience. *Blood* 2000;96:1259-1266.
 34. Klassen D, Shelley W, Starreveld A, et al. Early stage ovarian cancer: a randomized clinical trial comparing whole abdominal radiotherapy, melphalan, and intraperitoneal chromic phosphate: a National Cancer Institute of Canada Clinical Trails Group report. *J Clin Oncol* 1988;6:1254-1263.
 35. Knox SJ, Goris ML, Trisler K, et al. Yttrium-90-labeled anti-CD20 monoclonal antibody therapy of recurrent B-cell lymphoma. *Clin Cancer Res* 1996;2:457-470.
 36. Kraeber-Bodere F, Campion L, Rousseau C, et al. Treatment of bone metastases of prostate cancer with strontium-89 chloride: efficacy in relation to the degree of bone involvement. *Eur J Nucl Med* 2000;27:1487-1493.
 37. Kuzel TM, Rosen ST. Radioimmunotherapy of lymphomas and leukemias. In: Henkin RE, Boles MA, Dillehay GL, et al, eds. *Nuclear Medicine*. Vol. 1. St. Louis, Mo: Mosby-Yearbook Inc; 1996:594.
 38. Leslie WD, Ward L, Salamon EA et al. A randomized comparison of radioactive iodine doses in Graves' hyperthyroidism. *J Clin Endocrinol Metab* 2003;88:978-983.
 39. Lugo-Vicente H, Ortiz VN. Pediatric thyroid nodules: insights in management. *Bol Asoc Med P R* 1998;90:74-78.
 40. Mazzaferri EL, Kloos RT. Clinical review 128: Current approaches to primary therapy for papillary and follicular thyroid cancer. *J Clin Endocrinol Metab* 2001;86:1447-1463.
 41. McEwan AJ. Use of radionuclides for the palliation of bone metastases. *Semin Radiat Oncol* 2000;10:103-114.
 42. Nuclear Regulatory Commission. *Program-Specific Guidance About Medical Use Licenses*. NUREG 1556, Vol 9, 2004; 15:28. Accessible at: www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr1556/v9.
 43. Nygaard B, Hegedus L, Nielsen KG, et al. Long-term effect of radioactive iodine on thyroid function and size in patients with solitary autonomously functioning toxic thyroid nodules. *Clin Endocrinol* 1999;50:197-202.
 44. Pacini F, Gasperi M, Fugazzola L, et al. Testicular function in patients with differentiated thyroid carcinoma treated with radioiodine. *J Nucl Med* 1994;35:1418-1422.
 45. Park CH. The role of radioisotopes in radiation oncology. *Semin Oncol* 1997;24:639-654.
 46. Potter ME, Partridge EE, Shingleton HM, et al. Intraperitoneal chromic phosphate in ovarian cancer: risks and benefits. *Gynecol Oncol* 1989;32:314-318.
 47. Press OW, Howel-Clark J, Anderson S, et al. Retention of B-cell-specific monoclonal antibodies by human lymphoma cells. *Blood* 1994;83:1390-1397.
 48. Quilty PM, Kirk D, Bolger JJ, et al. A comparison of the palliative effects of strontium-89 and external beam radiotherapy in metastatic prostate cancer. *Radiother Oncol* 1994;31:33-40.
 49. Robbins RJ, Larson SM, Sinha N, et al. A retrospective review of the effectiveness of recombinant human TSH as a preparation for radioiodine thyroid remnant ablation. *J Nucl Med* 2002;43:1482-1488.
 50. Robinson RG, Preston DF, Baxter KG, et al. Clinical experience with strontium-89 in prostatic and breast cancer patients. *Semin Oncol* 1993;20:44-48.
 51. Rutar FJ, Augustine SC, Colcher D, et al. Outpatient treatment with (131) I anti-B1 antibody: radiation exposure to family members. *J Nucl Med* 2001;42:907-915.
 52. Siegel JA, Kroll S, Regan D, et al. A practical methodology for patient release after tositumomab and (131) I-tositumomab therapy. *J Nucl Med* 2002;43:354-363.
 53. Soper JT, Berchuck A, Dodge R, et al. Adjuvant therapy with intraperitoneal chromic phosphate (³²P) in women with early ovarian carcinoma after comprehensive surgical staging. *Obstet Gynecol* 1992;79:993-997.
 54. Soper JT, Creasman WT, Clarke-Pearson DL, et al. Intraperitoneal chromic phosphate P32 suspension therapy of malignant peritoneal cytology in

- endometrial carcinoma. *Am J Obstet Gynecol* 1985;153:191-196.
55. Sullivan DC, Harris CC, Currie JL, et al. Observations on the intraperitoneal distribution of chromic phosphate (32P) suspension for intraperitoneal therapy. *Radiology* 1983;146:539-541.
 56. Tagesson M, Ljungberg M, Strand SE. A Monte-Carlo program converting activity distributions to absorbed dose distributions in a radionuclide treatment planning system. *Acta Oncol* 1996;35:367-372.
 57. Tedder TF, Engel P, CD20: a regulator of cell-cycle progression of B lymphocytes. *Immunol Today* 1994;15:450-454.
 58. Thrall JH. Endocrine therapy. In: Greenfield LD, Uszler JM, eds. *Nuclear Medicine in Clinical Practice*. Deerfield Beach, Fla: Verlag Chenie International; 1982.
 59. Tubiana M, Schlumberger M, Rougier P, et al. Long-term results and prognostic factors in patients with differentiated thyroid carcinoma. *Cancer* 1985;55:794-804.
 60. Tuttle RM, Becker DV, Hurley JR. Radioiodine treatment of thyroid disease. In: Sandler MP, Coleman RE, Paxton FJ, et al, eds. *Diagnostic Nuclear Medicine*. 4th edition. Philadelphia, Pa: Lippincott Williams; 2003:653-669.
 61. Vermiglio F, Violi MA, Finocchiaro MD, et al. Short-term effectiveness of low-dose radioiodine ablative treatment of thyroid remnants after thyroidectomy for differentiated thyroid cancer. *Thyroid* 1999;9:387-391.
 62. Wagner HN Jr, Wiseman GA, Marcus CS, et al. Administration guidelines for radioimmunotherapy of non-Hodgkin's lymphoma with (90) Y-labeled anti-CD20 monoclonal antibody. *J Nucl Med* 2002;43:267-272.
 63. Wahl RL, Kroll S, Zasadny KR. Patient-specific whole-body dosimetry: principles and a simplified method for clinical implementation. *J Nucl Med* 1998;39:14S-20S.
 64. Wiseman GA, Kornmehl E, Leigh B, et al. Radiation dosimetry results and safety correlations from 90Y-ibritumomab tiuxetan radioimmunotherapy for relapsed or refractory non-Hodgkin's lymphoma: combined data from four clinical trials. *J Nucl Med* 2003;44:465-474.
 65. Wiseman GA, Leigh B, Erwin WD, et al. Radiation dosimetry results for Zevalin radioimmunotherapy of rituximab-refractory non-Hodgkin's lymphoma. *Cancer* 2002;94:1349-1347.
 66. Witzig TE, Flinn IW, Gordon LI, et al. Treatment with ibritumomab tiuxetan radioimmunotherapy in patients with rituximab-refractory follicular non-Hodgkin's lymphoma. *J Clin Oncol* 2002;20:3262-3269.
 67. Young RC, Walton LA, Ellenberg SS, et al. Adjuvant therapy in stage I and stage II epithelial ovarian cancer: results of two prospective randomized trials. *N Engl J Med* 1990;322:1021-1027.
 68. *Zevalin (ibritumomab tiuxetan) Prescribing Information*. San Diego, Calif: IDEC Pharmaceuticals Corporation; 2002.
 69. Zhu X. Radiation safety considerations with yttrium 90 ibritumomab tiuxetan (Zevalin). *Semin Nucl Med* 2004;34:20-23.
 70. Zimmer AM. Logistics of radioimmunotherapy with yttrium 90 ibritumomab tiuxetan (Zevalin). *Seminars in Nuclear Medicine* 2004;34:14-19.

*Guidelines and standards are published annually with an effective date of October 1 in the year in which amended, revised or approved by the ACR Council. For guidelines and standards published before 1999, the effective date was January 1 following the year in which the guideline or standard was amended, revised, or approved by the ACR Council.

Development Chronology for this Guideline

- 1996 (Resolution 11)
- Revised 2000 (Resolution 2 7)
- Revised 2005 (Resolution 21)
- Amended 2006 (Resolution 35)
- Revised 2010 (Resolution 26)