Society of Nuclear Medicine Procedure Guideline for Palliative Treatment of Painful Bone Metastases

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I. Purpose

The purpose of this guideline is to assist nuclear medicine practitioners in evaluating patients who might be candidates for ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam (^{153}Sm-EDTMP) radiopharmaceutical treatment of bone pain due resulting from osteoblastic metastases, to provide information for performing this treatment, and to assist in understanding the sequelae of therapy.

II. Background Information and Definitions

A. Definitions

1. ^{89}Sr therapy means the intravenous injection of the radionuclide ^{89}Sr as strontium chloride. ^{89}Sr-chloride emits a β particle with maximum energy 1.46 MeV, mean energy 0.58 MeV, average soft-tissue range 2.4 mm, and 0.01% abundant γ emission with a photopeak of 0.91 MeV. It has a 50.5-d physical half-life.
2. ^{153}Sm-lexidronam therapy means the intravenous injection of the radionuclide ^{153}Sm chelated to ethylene diamine tetramethylene phosphonate. ^{153}Sm emits a β particle with maximum energy 0.81 MeV, mean energy 0.23 MeV, average soft-tissue range 0.6 mm, and 28% abundant γ emission with a photopeak of 0.103 MeV. It has a 1.9-d physical half-life.
3. ^{32}P therapy means the intravenous injection or oral administration of the radionuclide ^{32}P as sodium phosphate. ^{32}P-sodium phosphate emits a β particle with maximum energy of 1.71 MeV, mean energy 0.70 MeV, average soft-tissue range 3.0 mm, and no γ emission. It has a 14.3-d physical half-life.
4. "Osteoblastic" or "osteoblastic metastases" means a focus or foci of increased activity on bone scintigraphy caused by osseous reaction to tumor in bone. These may appear osteoblastic or osteolytic on radiographs.

B. Background

Intravenous injection of ^{89}Sr-chloride and ^{153}Sm-lexidronam and intravenous or oral administration of ^{32}P-sodium phosphate have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of bone pain resulting from osteoblastic metastases as defined by bone scan. Physicians involved in treating such patients should have an understanding of the natural history of the disease process and should be able to collaborate closely with the physician (or group of physicians) handling the overall management of the patient's disease.

The administration of these agents falls under the guidelines of the Nuclear Regulatory Commission (NRC), Title 10 CFR Part 35.300 or Agreement State Institutional License. Institutional licenses must specifically list individuals licensed to use Section 35.300 materials.

As other radiopharmaceuticals are approved by the FDA for the treatment of bone pain resulting from osteoblastic metastases, they will be added to the guideline.

III. Common Indications

^{32}P-sodium phosphate, ^{89}Sr-chloride, and ^{153}Sm-lexidronam (and the other unsealed β or conversion electron-emitting radiopharmaceuticals under development or approved in countries outside the United States, e.g., ^{186}Re-etidronate) are indicated for the treatment of bone pain resulting from a metastatic malignancy that has involved multiple skeletal sites and has evoked an osteoblastic response on bone scintigraphy. Where there is danger of either spinal cord compression from vertebral metastases or pathologic fracture in the extremities, ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam therapy should only be used in conjunction with other forms of management directed at these complications and after management of the acute presentation.

IV. Procedure

A. Facility / Personnel

1. ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam may be administered only in a facility with a valid radioactive materials license incorporating Section 35.300 or comparable Agreement State license.
2. All administering physicians (the physician writing the prescription and injecting the dose) must be listed on the NRC or Agreement State license or specifically designated under a broad license.
3. Patients should be seen in consultation by the administering / treating physician in collaboration with the physician assuming overall patient management.
4. Practitioners should be aware of the wide variations that occur between national jurisdictions with respect to who may administer radioisotope therapy.
5. The administering physician should participate in the care of the patient as part of the patient management team.
6. The facility in which the treatment is performed must have proper radiation safety procedures, including waste disposal, handling of contamination of personal belongings, etc. Information sheets should be available.

B. Patient Preparation

1. Before administration of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam, the patient should have had recent bone scintigraphy (less than 8 wk) documenting increased osteoblastic activity in the painful sites.

   Radiographs taken within 8 wk demonstrating osteosclerotic lesions are not adequate, because there are rare cases in which the increased bone density has occurred slowly and bone scintigraphy shows little increased activity. In such cases, ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam uptake will be inadequate. In the presence of osteolytic metastases on bone radiographs, but with a positive bone scan, these β-emitters will often be taken up at the tumor site.
2. Bone scintigraphic abnormalities should be correlated with appropriate physical examination and imaging studies to ascertain that osseous or soft-tissue abnormalities, which might cause cord or other nerve compression or pathologic fracture in an extremity, are not present. ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam would be indicated in these circumstances only in conjunction with local radiation therapy or surgical intervention and especially if there are other painful bone metastases. These β-emitters may also be effective if pain persists at the single treated site.
3. In general, patients should not have received long-acting myelosuppressive chemotherapy (e.g., nitrosoureas) for 6–8 wk, and full doses of other forms of myelosuppressive chemotherapy or systemic radioisotope therapy for approximately 4 wk before administration of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam and for about 12 wk after administration of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam because of the potential for severe leukopenia or thrombocytopenia. Caution should be used if ^{32}P-sodium phosphate,

   ^{89}Sr-chloride, or ^{153}Sm-lexidronam is used in conjunction with myelosuppressive chemotherapy.
4. The patient should not have received external beam hemibody radiation within 2–3 mo before administration of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam to reduce the probability of combined myelotoxicity from the external and internally distributed radiopharmaceuticals during this period, except for radiotherapy to local areas performed to prevent fracture or spinal compression.
5. Complete blood counts should be obtained, preferably on the day of, and not more than 7 d before, administration of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam. The patient's platelet count should probably exceed 60,000 / μL and preferably 100,000 / μL; the leukocyte count should probably exceed 2,400–3,000 / μl and preferably 5,000 / μL; the absolute granulocyte count should exceed 2,000 / μL; and the hemoglobin count should be more than 10g / dL to receive ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam. Results below these blood count levels are not absolute contraindications to treatment but raise the chance of infection or bleeding. Practitioners should be aware of counts over the preceding weeks; a rapid recent fall without signs of recovery should be considered a probable contraindication.
6. The presence or absence of nonandrogenic hormone therapy is irrelevant to administration of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam. Bone pain could be

worsening while hormone therapy is controlling other sites of tumor, so hormone therapy need not be discontinued. ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam can be of value after failure of hormone therapy to control the pain of osseous metastases.

7. Before using ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam, the pain usually should be severe enough to limit activity and/or to require narcotic analgesia for control of symptoms. There are no definitive data on the efficacy of the treatment of asymptomatic or minimally painful osteoblastic metastatic disease in terms of delaying the time to the onset of future clinically significant bone pain.
8. Active disseminated intravascular coagulation (DIC) may be a risk factor for severe thrombocytopenia post-therapy. Deaths have been reported in patients with DIC after therapy with β-emitting radiopharmaceuticals, and this potential risk must be sought and carefully considered before administering ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam in the presence of DIC, especially if a rapid recent fall in platelet count has occurred.
9. Hypercalcemia should not deter ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam treatment unless accompanied by renal failure. Recent administration of etidronate or other bisphosphonates may decrease the uptake of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam at the tumor site and, consequently, decrease the effectiveness of pain palliation. If bisphosphonates have been administered within 2 wk before the planned therapy, a bone scan should be considered to confirm adequate uptake at the tumor site. Bisphosphonate therapy probably should not be given for at least 48 hr after ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam therapy. The patient should remain well hydrated before, during, and after the procedure.
10. The patient need not fast before administration of the radiopharmaceutical.
11. The radiopharmaceutical should be administered slowly through an intravenous catheter or a running intravenous line to avoid infiltration, to reduce the hand dose to the injecting physician, and to permit flushing of the syringe so that all of the ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam is injected. A plastic syringe shield or equivalent is suggested for administration of the radiopharmaceutical. Flush the syringe and intravenous line from the syringe to the patient with saline from the running intravenous line or a saline-filled syringe attached to a 3-way stopcock.
12. Hospitalization is not required for the administration of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam.
13. A patient who has a life expectancy of less than 4–6 wk is unlikely to benefit from ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam, and, at his/her death, the pathologist will require certain precautions (goggles, double gloving) if an autopsy is performed less than 1 wk after administration. There is no problem with cremation if the crematorium annually handles bodies containing less than 2 mCi of all radionuclides except ^{131}I, which has a 200 mCi/y limit.
14. The usual administered activity of ^{89}Sr-chloride ranges from 1.5–2.2 MBq/kg (40–60 μCi/kg) or 148 MBq (4 mCi). The usual administered activity of ^{153}Sm-lexidronam is 1 mCi/kg. The usual administered activity of ^{32}P-sodium phosphate is 185–370 MBq (5–10 mCi) intravenously (often in divided doses) or 370–444 MBq (10–12 mCi) orally. Some physicians calculate the activity based on lean body mass, reduce the activity given in patients with azotemia, or slightly increase the administered activity with diffuse widespread metastases. There are no unequivocal data on these adjustments. Some data support the administration of higher doses of these radiopharmaceuticals with autologous stem cell support, but these are not definitive for showing a significantly greater reduction in bone pain. Patients have responded to up to 7 dosages of radiotracer if needed, but the risk of marrow toxicity rises with each subsequent dosage.
15. The procedure may be repeated 12 or more wk after the first injection if blood counts are at the suggested levels. The response rate after the second treatment is about 50% and may occur even if there was no response to the first treatment.
16. There is no unequivocal evidence that the addition of nonmyelotoxic chemotherapy (e.g., cisplatin) enhances the efficacy of treatment with these bone-seeking radiopharmaceuticals.
17. A few patients who have failed to respond to the first ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam injection have had pain

reduction with a second injection 12 wk later.

C. Information Pertinent to Performing the Procedure
   1. Patient demographics (age, sex, weight, height, diagnosis).
   2. Indications for therapy.
   3. Current medications, especially those affecting coagulation and bisphosphonates.
   4. Extent of disease on bone scan obtained 4–8 wk before therapy.
   5. Complete blood count, d-dimer or fibrin split products, and serum creatinine within 1 wk before therapy.
   6. Relevant radiographs and/or MR imaging of painful sites to exclude cord compression or severe lytic lesions, which carry an increased risk of pathologic fracture.
   7. Life expectancy estimate.
   8. Pregnancy and breast feeding are absolute contraindications to therapy.

D. Instructions for Patients
   1. The patient should be told that ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam has a 25%–80% probability (depending on how the subjective pain response is measured) of reducing bone resulting from cancer spread in bone but that the chance of relieving pain completely is low but real.
   2. The patient should be told that this is not a curative treatment for cancer but a treatment to palliate pain, even though some cancer cells may be killed.
   3. The patient should be told that the 2 most common side effects are:
      a. An increase in bone pain ("flare") occurring most often within 72 h of injection but, rarely, up to 21 d after injection and lasting 2–5 d. Flare is unusual after the second week and can be treated by increasing doses of analgesia, if required.
      b. The likelihood that the leukocyte and platelet counts may decrease by 30%–70% of baseline values or possibly to even lower levels, which could lead to infection if leukocytes are too low or bleeding if the platelets are too low. Bleeding or the risk of bleeding could require platelet transfusion. Marrow replacement by tumor, ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam therapy, chemotherapy, and external beam radiotherapy have additive effects on myelosuppression, and the presence of 2 or more of these risk factors increases the possibility of clinically significant marrow suppression.
   4. A written consent form is strongly suggested, to include indications and success rate and the risks of severe infection, bleeding, and death. Local hospital policies and state regulations should be followed. The patient should be told that pain reduction is unlikely before the first week, more probable in the second week, and could occur as late as 25 d or longer after injection.
   5. The patient should be told that he/she may continue with a normal diet, should be careful to avoid soiling underclothing or areas around toilet bowls for 2 wk postinjection, and should wash separately any underclothing that is significantly soiled with urine. Sitting down to urinate is recommended, because this will reduce the possibility of contamination. A double toilet flush should be adequate after urination. Urinary excretion is greatest (80%–90%) during the first 48 hr postinjection. Patients should wash their hands thoroughly after urination.
   6. If the patient is being cared for in a hospital, then his/her attendants should wear gloves and gowns if contact with urine, feces, saliva, or blood is anticipated. Catheter bags should be transferred quickly to the toilet for emptying, with the attendant wearing gloves. Gloves also should be worn at home if soiled garments are to be handled. (There is no significant salivary secretion of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam, so no other precautions are required.)
   7. In patients who are incontinent, plastic mattress covers and adult urine-absorbing undergarments are recommended; condom drainage or bladder catheterization also should be considered for several days to a week.

E. Precautions
   1. The degree of leukopenia and thrombocytopenia present should not be severe, as noted in IV.B.5.
   2. Previous (especially recent) chemotherapy or wide-field radiation can worsen ^{32}P-sodium phosphate-, ^{89}Sr-chloride-, or ^{153}Sm-lexidronam-induced leukopenia or thrombocytopenia.
   3. Renal failure may require reducing the activity injected.
   4. Exclude spinal cord compression or soft-tissue tumor as the cause of the pain that is being treated.
   5. Do not use ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam alone with ≥50% destruction of an involved bone (especially of

an arm or leg) or for pain resulting from pathologic fracture.

6. Careful injection technique must be used to avoid infiltration. No specific therapy is available if infiltration occurs, but local heat may increase the rate of reabsorption and therefore decrease the local radiation dose.
7. Exclude active disseminated intravascular coagulation.
8. In women of childbearing age, the pregnancy test must be negative.
9. The patient and caregivers should be educated as to how to minimize contamination (see IV.D.5–D.7).

F. Radiopharmaceuticals

1. ^{32}P
   a. Usual therapeutic administered activity is 185–370 MBq (5–10 mCi) intravenously (often in divided doses) or 370–444 MBq (10–12 mCi) orally.

^{32}P Radiation Dosimetry[1]

Organ	mGy/MBq	rad/mCi
Bone Surface	10	37
Red Bone Marrow	7.6	28
Lower Bowel Wall	0.001	0.003
Bladder Wall	0.001	0.003
Testes	0.001	0.003
Ovaries	0.001	0.003
Uterine Wall	0.001	0.003
Kidneys	0.001	0.003

[1] Radiation Internal Dose Information Center, 1995.

2. ^{89}Sr
   a. Usual therapeutic administered activity is 1.5–2.2 MBq / kg (40–60 μCi / kg)
3. ^{153}Sm
   a. Usual therapeutic administered activity is 1 mCi / kg.

G. Guidelines for Measuring the Activity of ^{32}P-Sodium Phosphate, ^{89}Sr-Chloride, or ^{153}Sm-Lexidronam to be Administered:

Either of the following 2 methods can be used to measure the amount of ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam to be administered:

1. Follow the manufacturers recommendations for the calibration of ^{89}Sr-chloride injection USP; or

^{89}Sr Radiation Dosimetry[1]

Organ	mGy/MBq	rad/mCi
Bone Surface	17.0	63.0
Red Bone Marrow	11.0	40.7
Lower Bowel Wall	4.7	17.4
Bladder Wall	1.3	4.8
Testes	0.8	2.9
Ovaries	0.8	2.9
Uterine Wall	0.8	2.9
Kidneys	0.8	2.9

[1]International Commission on Radiological Protection and Measurements. *Radiation Dose to Patients from Radiopharmaceuticals.* ICRP report no. 53. London, UK: ICRP; 1988:171; and Amersham package insert.

^{153}Sm Radiation Dosimetry[1]

Organ	mGy/MBq	rad/mCi
Bone Surface	6.8	25.0
Red Bone Marrow	1.5	5.7
Lower Bowel Wall	0.01	0.04
Bladder Wall	1.0	3.60
Testes	0.01	0.02
Ovaries	0.01	0.03
Kidneys	0.02	0.07

[1]Berlex package insert; and Eary JF, Collins C, Stabin M, et al. Samarium-153-EDTMP biodistribution and dosimetry estimation. *J Nucl Med.* 1993:34:1031–1036.

2. Use a dose calibrator specially configured to quantitate β emissions. (^{153}Sm-lexidronam has a γ emission at 103 keV for calibration.)
3. Advice may be sought, but it is also possible to use certified standards of ^{32}P-sodium phosphate and ^{89}Sr-chloride to calibrate (and recalibrate) well counters, similar to those used for ^{90}Y.

H. Interventions

Not applicable.

I. Processing

Not applicable.

J. Interpretation Criteria

There is no image to be described, so there are no interpretation criteria to which to adhere. Although bone imaging is possible with ^{153}Sm-lex-

idronam, the preliminary diagnostic scan should be performed with a ^{99m}Tc-bisphosphonate.

K. Reporting
   1. The report to the referring physician should include the fact that informed consent was obtained and that the patient is aware of leukopenia, thrombocytopenia, and death as possibilities (this should alert the referring physician to monitor the patient). The need for leukocyte and platelet count monitoring may be mentioned on the report, usually beginning 2 wk postinjection and then every 1–3 wk for a total of 12–16 wk. The physician performing the therapy is urged to monitor the blood counts, if possible.
   2. The referring physician may be reminded that pain reduction does not occur until 1–3 wk have passed.
   3. The physician should not assume the patient has failed ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam therapy until a full 4 wk after injection.

L. Quality Control
   1. The institutional Quality Management Program mandated by the Nuclear Regulatory Commission should be followed.
   2. There should be close coordination with the referring physician in all aspects of patient work-up and follow-up.
   3. The relevant patient information (see IV.C.) should be reviewed before ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam injection.

M. Sources of Error
   1. Improper use of dosage calibrator. The use of the ^{32}P setting on the modern dosage calibrator approximates that of the ^{89}Sr-chloride or ^{153}Sm setting. The radioactivity must be measured in geometry and in containers consistent with previous calibration of the dosage calibrator.
   2. The radiopharmaceutical should be injected through a running intravenous line or intravenous catheter to avoid infiltration of the material injected, to reduce hand dose, and to permit flushing of all ^{32}P-sodium phosphate, ^{89}Sr-chloride, or ^{153}Sm-lexidronam activity out of the syringe and into the patient.

V. Issues Requiring Further Clarification

1. Relative response rates of osteoblastic metastasis from different primary cancers. Preliminary data are available on this topic (see Taylor, 1994, in bibliography).
2. Which is the optimal radiopharmaceutical in terms of safety and efficacy?
3. Should high- and low-dose-rate radiopharmaceuticals be combined in 1 injection?
4. Is split-dose therapy with any of these radiopharmaceuticals efficacious?
5. What is the best way to objectively rate a reduction in pain?
6. Should these radiopharmaceuticals be combined with radiosensitizing chemotherapy?
7. Is there really a dose–response relationship justifying high-dose radiopharmaceutical administration with stem cell support?
8. Is it efficacious to treat asymptomatic bone metastases?
9. Do any of these radiopharmaceuticals prolong life?
10. How often is a second treatment efficacious when the first treatment is not?
11. Are these radiopharmaceuticals better than bisphosphonate therapy for bone pain resulting from osseous metastases?
12. Is there any additive effect from using a bisphosphonate plus a radiopharmaceutical?
13. Are there additional toxicities (e.g., renal)?

VI. Concise Bibliography

Collins C, Eary JF, Donaldson G, et al. Samarium-153-EDTMP in bone metastases of hormone refractory prostate carcinoma: a phase I/II trial. *J Nucl Med.* 1993;34:1839–1844.

Edwards GK, Santoro J, Taylor AT, et al. Use of bone scintigraphy to select patients with multiple myeloma for treatment with strontium-89. *J Nucl Med.* 1994;35:1992–1994.

Farhanghi M, Holmes RA, Volkert WA, et al. Samarium-153-EDTMP: Pharmacokinetic, toxicity and pain response using an escalating dose schedule in treatment of metastatic bone cancer. *J Nucl Med.* 1992;33:1451–1458.

Herold TJ, Gross GP, Hung JC. A technique for measurement of strontium-89 in a dose calibrator. *J Nucl Med Technol.* 1995; 23:26–28.

Lamb HM, Faulds D. Samarium-153 Sm-lexidronam. *Drugs & Aging.* 1997;11:413–418.

McCready VR, O'Sullivan JM. Future directions for unsealed source radionuclide therapy for bone metastases. *Eur J Nucl Med.* 2002;29:1271–1275.

McEwan AJ, Amyotte GA, McGowan DG, et al. A retrospective analysis of the cost effectiveness of treatment with Metastron (^{89}Sr-Cl) in patients with prostate cancer metastatic to bone. *Nucl Med Commun.* 1994;15:499–504.

McEwan AJ, Porter AT, Venner PM, et al. An evalu-

ation of the safety and efficacy of treatment with strontium-89 in patients who have previously received wide-field radiotherapy. *Antibod Immunoconj Radiopharm.* 1990;3:91–98.

Porter AT, McEwan AJ, Powe JE, et al. Results of a randomized phase-III trial to evaluate the efficacy of strontium-89 adjuvant to local field external beam irradiation in the management of endocrine resistant metastatic prostate cancer. *Int J Radiat Oncol Biol Phys.* 1993;25:805–813.

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.

Resche I, Chatal JF, Pecking A, et al. A dose-controlled study of ^{153}Sm EDTMP in the treatment of patients with painful bone metastases. *Eur J Cancer.* 1997;33:1583–1591.

Robinson RG, Blake GM, Preston DF, et al. Strontium-89: treatment results and kinetics in patients with painful metastatic prostate and breast cancer in bone. *RadioGraphics.* 1989;9:271–281.

Schmeler K, Bastin K. Strontium-89 for symptomatic metastatic prostate cancer to bone: recommendations for hospice patient. *Hosp J.* 1996;11:1–10.

Sciuto R, Fasta A, Rea S, et al. Effects of low-dose cisplatin on Sr-89 therapy for painful bone metastases for prostate cancer: A randomized clinical trial. *J. Nucl Med.* 2002;43:79–86.

Silberstein EB, Williams C. Strontium-89 therapy for the pain of osseous metastases. *J Nucl Med.* 1985;26:345–348.

Taylor AJ Jr. Strontium-89 for the palliation of bone pain due to metastatic disease. *J Nucl Med.* 1994;35:2054.

Tu SM, Millikan RE, Mengistu B, et al. Bone-targeted therapy for advanced androgen-independent carcinoma of the prostate: a randomized phase II trial. *Lancet.* 2001;357:336–341.

VII. Disclaimer

The Society of Nuclear Medicine has written and approved guidelines to promote the cost-effective use of high-quality nuclear medicine procedures. These generic recommendations cannot be applied to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The spectrum of patients seen in a specialized practice setting may be quite different from the spectrum of patients seen in a more general practice setting. The appropriateness of a procedure will depend in part on the prevalence of disease in the patient population. In addition, the resources available to care for patients may vary greatly from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.