RadioGenix® System
(technetium Tc 99m generator)

**Indication**¹

- The RadioGenix® System is a technetium Tc-99m generator used to produce Sodium Pertechnetate Tc-99m Injection, USP. Sodium Pertechnetate Tc-99m Injection is a radioactive diagnostic agent and can be used in the preparation of FDA-approved diagnostic radiopharmaceuticals.
- Sodium Pertechnetate Tc-99m Injection is also indicated in
- Adults for Salivary Gland Imaging and Nasolacrimal Drainage System Imaging (dacryoscintigraphy).
- Adults and pediatric patients for Thyroid Imaging and Vesicoureteral Imaging (direct isotopic cystography) for detection of vesicoureteral reflux.

¹ RadioGenix® System [package insert]. Beloit, WI: NorthStar Medical Radioisotopes, LLC; March, 2018
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Important Risk Information

- Allergic reactions (skin rash, hives, or itching) including anaphylaxis have been reported following the administration of Sodium Pertechnetate Tc-99m Injection. Monitor all patients for hypersensitivity reactions.

- Radiation risks associated with the use of Sodium Pertechnetate Tc-99m Injection are greater in children than in adults and, in general, the younger the child, the greater the risk owing to greater absorbed radiation doses and longer life expectancy. These greater risks should be taken firmly into account in all benefit-risk assessments involving children. Long-term cumulative radiation exposure may be associated with an increased risk of cancer.

- Temporarily discontinue breastfeeding. A lactating woman should pump and discard breastmilk for 12 to 24 hours after Sodium Pertechnetate Tc-99m Injection administration.

- Sodium Pertechnetate Tc-99m Injection should be given to pregnant women only if the expected benefits to be gained clearly outweigh the potential hazards.

- Follow step by step directions for use provided in the RadioGenix® System Operator Guide. Only use potassium molybdate Mo-99, processing reagents, saline and other supplies, including kits, provided by NorthStar Medical Radioisotopes. Do not administer Sodium Pertechnetate Tc-99m Injection after the 0.15 microCi of Mo-99/mCi of Tc-99m limit has been reached or when the 12 hour expiration time from elution is reached, whichever occurs earlier.

- Sodium Pertechnetate Tc-99m Injection contributes to a patient’s long-term cumulative radiation exposure. Ensure safe handling to protect patients and health care workers from unintentional radiation exposure. Use the lowest dose of Sodium Pertechnetate Tc-99m Injection necessary for imaging and ensure safe handling and preparation to protect the patient and health care worker from unintentional radiation exposure. Encourage patients to drink fluids and void as frequently as possible after intravenous or intravesicular administration. Advise patients to blow their nose and wash their eyes with water after ophthalmic administration.

NorthStar Medical Radioisotopes, LLC

Our Mission: Transforming Medical Radioisotopes

- Approved by the FDA in early 2018, the RadioGenix® System is the first of its kind - an innovative, intelligent radioisotope separation platform for use in producing medically important technetium-99m (Tc-99m) from non-uranium produced molybdenum-99 (Mo-99)
Technetium-99m (Tc-99m)

- Approx. 80% of nuclear medicine imaging procedures use Tc-99m
- More than 40,000 Tc-99m procedures are performed daily in the U.S.
- Tc-99m based radiopharmaceuticals are used to diagnose and stage heart disease, cancer, infection, inflammation and other conditions
- Short half-life: ~6 hours
  - Low radiation dose to patient
  - Radiopharmaceuticals must be replenished daily

Molybdenum-99 (Mo-99)

- Worldwide demand for medical use ≈ 42,000 Ci per week
- U.S. demand ≈ 21,000 Ci per week
- Short (66 hour) half-life
- Parent of Tc-99m
- NorthStar provides Mo-99 by neutron activation of Mo-98
  - $^{98}\text{Mo (n,}\gamma)\ 99\text{Mo}$
  - Natural molybdenum consists of ~24% Mo-98
NorthStar Licensed Facilities

- NorthStar has three facilities used for licensed activities
  - Beloit, WI
  - Madison, WI
  - Columbia, MO

- Beloit, WI
  - NorthStar Headquarters
  - Sufficient property for growth
  - FDA approved manufacturing facility
  - Two WI radioactive materials licenses:
    - Use and Service
    - Manufacturing and Distribution
NorthStar Licensed Sites

• Madison, WI
  • WI research & development radioactive materials license.

NorthStar Licensed Facilities

• NorthStar-Columbia, Columbia, MO
  • Located at Missouri University Research Reactor (MURR®)
  • 10 MW – largest research reactor
  • Excellent operational track record
  • Operations are performed under the MURR® reactor license
  • MURR® irradiates molybdenum and produces Mo-99 for NorthStar use

Image provided by MURR®
NorthStar Mo-99 Production

• NorthStar – Columbia fills source vessels (SV) with up to 7.5 curies of Mo-99 solution, which meets or exceeds European Pharmacopeia standards
• SV are custom shielded Type A containers

NorthStar Mo-99 Production

• NorthStar – Columbia packages SV into certified Type A containers that are shipped from MURR® directly to customers.
• SV Packages are currently sent as Radioactive Yellow II.
NorthStar Mo-99 Production

• NorthStar has been shipping Mo-99 in NorthStar Type A containers without incident since 2016
  • More than 3300 curies of Mo-99 shipped in over 550 SV
  • Packaging has performed exceptionally well
    • No contamination on or in the SV package upon receipt
    • No changes with TI
    • SV and package labeling are accurate

Mo-99 Supply Disruptions

• 2009 – 2010: Severe Mo-99 shortages due to two production reactors (NRU and HFR) down simultaneously
  • Resulted in an 65% reduction of Mo-99 supplies world-wide
• Current supply chain for Mo-99 is fragile
• In 2018 alone there have been 30+ weeks with supply disruptions, for reasons including:
  • Unscheduled reactor shutdowns
  • Mo-99 spills
  • Flight delays
Promotion of Domestic Mo-99 Production

- American Medical Isotope Production Act (2012)
  - Enacted to establish a reliable, domestic supply of Mo-99
- Objectives:
  - Meet U.S. patient needs
  - Eliminate the use of highly-enriched uranium-235 (U-235)
- Support from National Labs
- Technology neutral
- Financial assistance

Domestic Production of Mo-99

- Mo-99 was produced for patient use by molybdenum irradiation at MURR through the mid-1970’s.
- Process produced low-specific activity Tc-99m. Physicians wanted high-specific activity (HSA) Tc-99m.
- Replaced by irradiation of highly-enriched U-235 targets
- NorthStar’s solution…
NorthStar’s RadioGenix® System

- The RadioGenix® System eluant meets the requirements of the USP monograph for Sodium Pertechnetate Tc-99m Injection
  - Equivalent activity concentration as existing generators
  - Unique, on-demand, point-of-use liquid ozone sterilization system
  - Holds up to 4 source vessels

Advantages of the RadioGenix® System

- No irradiation of uranium (no HEU or LEU)
- Conventional radioactive material licenses
- Rigorously tested protocols automate operation
- Integrated safety features
Advantages of the RadioGenix® System

- Shipped directly to radiopharmacies
- Low volume of short-lived waste
- Customers return SV to NorthStar to be recycled
  - Shipping packages and return kits are supplied

Irradiation of Enriched Mo-98 (eMo)

- NorthStar building facility at Beloit site to manufacture Mo-99 Source Vessels using enriched (>98%) Mo-98 (eMo).
Processing Enriched Mo-98 (eMo)

- MURR will irradiate eMo
- eMo target processed at either MURR or transported to Beloit in NorthStar Type B container
- eMo processed to fill SV with Mo-99
- SV packaged & shipped to customers

Advantages of Enriched Mo-98 (eMo)

- Mo-99 activity X4 from natural Mo irradiation.
- Able to ship Mo-99 to customers from Beloit and MURR
- Mo-98 can be recovered for target re-manufacturing
- Radioactive waste profile is further reduced
Accelerator Irradiation of Mo-100

- Planning for constructing an electron accelerator building in Beloit underway
- Photon irradiation of enriched Mo-100 produces Mo-99
  - $^{100}\text{Mo} (\gamma,n)^{99}\text{Mo}$
- Allows for recovery of Mo-100 for target re-manufacturing
- Minimal, short-lived waste production

NorthStar Mo-99 Production Advantages

- Both methods capable of meeting NNSA target production of 3000 6-day Ci without using uranium
- No uranium (HEU or LEU) target material = no fission waste stream
- RadioGenix® System incorporates a unique, on-demand, point-of-use liquid ozone sterilization system
- Production of short-lived radioactive byproducts and minimal chemical waste
NorthStar Mo-99 Production Advantages

• The RadioGenix® System is a patented platform technology potentially applicable to other medical isotope pairs such as actinium-225/bismuth-213, tungsten-188/rhenium-188, germanium-68/gallium-68, etc. (all of which will require additional regulatory approvals)

• First U.S. producer of Mo-99 in >25 years