LOCAMETZ- kit for the preparation of gallium ga 68 gozetotide injection, powder, lyophilized, for solution
Advanced Accelerator Applications USA, Inc

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LOCAMETZ safely and effectively. See full prescribing information for LOCAMETZ.

LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection), for intravenous use
Initial U.S. Approval: 2020

RECENT MAJOR CHANGES

Indications and Usage (1)	3/2025
Dosage and Administration, Image Interpretation (2.8)	3/2025
Warnings and Precautions, Risk for Misinterpretation (5.1)	3/2025

INDICATIONS AND USAGE

LOCAMETZ, after radiolabeling with gallium-68, is a radioactive diagnostic agent indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA)-positive lesions in men with prostate cancer:

- with suspected metastasis who are candidates for initial definitive therapy
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level
- for selection of patients who are indicated for PSMA-directed therapy as described in the prescribing information of the therapeutic products. (1)

DOSAGE AND ADMINISTRATION

- Use appropriate radiation safety measures and aseptic precautions while handling and administering gallium Ga 68 gozetotide injection. (2.1)
- The recommended amount of radioactivity is 111 MBq to 259 MBq (3 mCi to 7 mCi). Administered as slow intravenous injection. (2.2)
- Advise patients to be well hydrated prior to the administration and to void immediately prior to and frequently after image acquisition. (2.3)
- A diuretic expected to act within the uptake time period may be administered at the time of radiotracer injection. (2.6)
- Acquire PET whole body images 50 minutes to 100 minutes after administration. (2.7)
- See the full prescribing information for detailed instructions on preparation, administration, imaging, and radiation dosimetry. (2)

DOSAGE FORMS AND STRENGTHS

- Kit for the preparation of gallium Ga 68 gozetotide injection supplied in a multiple-dose vial containing 25 mcg of gozetotide as a white lyophilized powder. After radiolabeling with gallium-68, the vial contains a sterile solution of gallium Ga 68 gozetotide at a strength up to 2,590 MBq (70 mCi) in up to 10 mL at calibration date and time. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Risk for Misinterpretation: Gallium Ga 68 gozetotide uptake may occur in other tumor types and in non-malignant processes. Interpretation of LOCAMETZ PET imaging with histopathology and/or other diagnostic procedures is recommended. (5.1)
- Radiation Risk: Gallium Ga 68 gozetotide contributes to a patient's overall long-term cumulative radiation exposure. Ensure safe handling and preparation procedures to protect patients and health care workers from unintentional radiation exposure. (5.2)

ADVERSE REACTIONS

The adverse reactions (incidence ≥ 0.5%) are fatigue, nausea, constipation, and vomiting. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 3/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Radiation Safety – Drug Handling
2.2 Recommended Dosage
2.3 Patient Preparation
2.4 Drug Preparation
2.5 Specifications and Quality Control
2.6 Administration
2.7 Image Acquisition
2.8 Image Interpretation
2.9 Radiation Dosimetry
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Risk for Misinterpretation
5.2 Radiation Risk
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
10 OVERDOSAGE
11 DESCRIPTION
11.1 Chemical Characteristics
11.2 Physical Characteristics
11.3 Radiation Attenuation
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
14.1 Imaging Prior to Initial Definitive Therapy
14.2 Imaging Prior to Suspected Recurrence Therapy

14.3 Imaging to Select Patients for PSMA-Directed Therapy
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

LOCAMETZ, after radiolabeling with gallium-68, is indicated for positron emission tomography (PET) of prostate-specific membrane antigen (PSMA)-positive lesions in men with prostate cancer:

- with suspected metastasis who are candidates for initial definitive therapy.
- with suspected recurrence based on elevated serum prostate-specific antigen (PSA) level.
- for selection of patients who are indicated for PSMA-directed therapy as described in the prescribing information of the therapeutic products.

2 DOSAGE AND ADMINISTRATION

2.1 Radiation Safety – Drug Handling

After reconstitution and radiolabeling of LOCAMETZ, the vial contains gallium Ga 68 gozetotide injection. Handle the gallium Ga 68 gozetotide injection with appropriate safety measures to minimize radiation exposure *[see Warnings and Precautions (5.2)]*. Use waterproof gloves, effective radiation shielding, and other appropriate safety measures when preparing and handling gallium Ga 68 gozetotide injection.

Radiopharmaceuticals should be used by or under the control of health care providers who are qualified by specific training and experience in the safe use and handling of radionuclides, and whose experience and training have been approved by the governmental agency authorized to license the use of radionuclides.

2.2 Recommended Dosage

In adults, the recommended amount of radioactivity to be administered for PET is 111 MBq to 259 MBq (3 mCi to 7 mCi) by slow intravenous injection.

2.3 Patient Preparation

Advise patients to be well hydrated prior to gallium Ga 68 gozetotide injection administration and to void immediately prior to and frequently during the first hours after image acquisition to reduce radiation exposure *[see Warnings and Precautions (5.2)]*.

2.4 Drug Preparation

LOCAMETZ allows the direct preparation of gallium Ga 68 gozetotide injection with the

eluate from one of the following generators (see below for specific instruction for use with each generator):

- Eckert & Ziegler GalliaPharm germanium-68/gallium-68 (^{68}Ge/^{68}Ga) generator
- IRE ELiT Galli Eo germanium-68/gallium-68 (^{68}Ge/^{68}Ga) generator
- ITM Medical Isotopes GeGant germanium-68/gallium-68 (^{68}Ge/^{68}Ga) generator

The instructions for use provided by the germanium-68/gallium-68 generator manufacturer should also be followed.

Prepare gallium Ga 68 gozetotide injection according to the following aseptic procedure:

a. Use suitable shielding to reduce radiation exposure.

b. Wear waterproof gloves.

c. Flip the cap off the LOCAMETZ vial and swab the septum with an appropriate antiseptic, then allow the septum to dry.

d. Pierce the LOCAMETZ vial septum with a sterile needle connected to a 0.2-micron sterile air venting filter to maintain atmospheric pressure within the vial during the reconstitution process.

e. Place the LOCAMETZ vial in a lead shield container.

f. Follow the generator specific procedures below. Schematic diagrams are provided in Figures 1, 2 and 3.

Preparation with Eckert & Ziegler GalliaPharm Generator

1) Connect the male luer of the outlet line of the generator to a sterile elution needle (size 21G to 23G).

2) Connect the LOCAMETZ vial directly to the outlet line of the generator by pushing the elution needle through the rubber septum.

3) Elute directly from the generator into the LOCAMETZ vial.

4) Perform the elution manually or by means of a pump according to the generator instructions for use.

5) Reconstitute the lyophilized powder with 5 mL of eluate.

6) At the end of the elution, disconnect the LOCAMETZ vial from the generator by removing the elution needle and the vent needle with the 0.2-micron sterile air venting filter from the rubber septum. Then, invert LOCAMETZ vial once and place it upright.

7) Incubate the LOCAMETZ vial upright between 20°C to 30°C (68°F to 86°F) for at least 5 minutes without agitation or stirring.

8) After 5 minutes, assay the vial containing the gallium Ga 68 gozetotide injection for total radioactivity using a dose calibrator, calculate the radioactivity concentration and record the result.

9) After radiolabeling, gallium Ga 68 gozetotide injection may be diluted with Sterile Water for Injection, USP or 0.9% Sodium Chloride Injection, USP up to a final volume of 10 mL.

10) Perform quality controls according to the recommended methods in order to check compliance with the specifications *[see Dosage and Administration (2.5)]*.

11) Store the LOCAMETZ vial containing the gallium Ga 68 gozetotide injection upright in a lead shield container below 30°C (86°F) until use.

12) After addition of gallium-68 chloride to the LOCAMETZ vial, use gallium Ga 68 gozetotide injection within 6 hours.

Preparation with IRE ELiT Galli Eo Generator

1) Connect the male luer of the outlet line of the generator to a sterile elution needle (size 21G to 23G).

2) Connect the LOCAMETZ vial directly to the outlet line of the generator by pushing the elution needle through the rubber septum.

3) Connect the LOCAMETZ vial through the vent needle with 0.2-micron sterile air venting filter to a vacuum vial (25 mL minimum volume) by means of a sterile needle (size 21G to 23G) or to a vacuum pump to start the elution.

4) Elute directly from the generator into the LOCAMETZ vial.

5) Reconstitute the lyophilized powder with 1.1 mL of eluate.

6) At the end of the elution, first withdraw the sterile needle from the vacuum vial or disconnect the vacuum pump in order to establish atmospheric pressure into the LOCAMETZ vial, then disconnect the vial from the generator by removing both the elution needle and the vent needle with the 0.2-micron sterile air venting filter needle from the rubber septum. Inversion of the LOCAMETZ vial is not needed.

7) Incubate the LOCAMETZ vial upright between 20°C to 30°C (68°F to 86°F) for at least 5 minutes without agitation or stirring.

8) After 5 minutes, assay the vial containing the gallium Ga 68 gozetotide injection for total radioactivity using a dose calibrator, calculate the radioactivity concentration and record the result.

9) After radiolabeling, gallium Ga 68 gozetotide injection may be diluted with Sterile Water for Injection, USP or 0.9% Sodium Chloride Injection, USP up to a final volume of 10 mL.

10) Perform quality controls according to the recommended methods in order to check compliance with the specifications *[see Dosage and Administration (2.5)]*.

11) Store the LOCAMETZ vial containing the gallium Ga 68 gozetotide injection upright in a lead shield container below 30°C (86°F) until use.

12) After addition of gallium-68 chloride to the LOCAMETZ vial, use gallium Ga 68 gozetotide injection within 6 hours.

Preparation with ITM Medical Isotopes GeGant Generator

1) Connect the male luer of the outlet line of the generator to a sterile elution needle (size 21G to 23G).

2) Connect the LOCAMETZ vial directly to the outlet line of the generator by pushing the elution needle through the rubber septum.

3) Elute directly from the generator into the LOCAMETZ vial.

4) Perform the elution manually or by means of a pump according to the generator instructions for use.

5) Reconstitute the lyophilized powder with 4 mL of eluate.

6) At the end of the elution, disconnect the LOCAMETZ vial from the generator by removing the elution needle and the vent needle with the 0.2-micron sterile air venting filter from the rubber septum. Then, invert LOCAMETZ vial once and place it upright.

7) Incubate the LOCAMETZ vial upright between 20°C to 30°C (68°F to 86°F) for at least 5 minutes without agitation or stirring.

8) After 5 minutes, assay the vial containing the gallium Ga 68 gozetotide injection for total radioactivity using a dose calibrator, calculate the radioactivity concentration and record the result.

9) After radiolabeling, gallium Ga 68 gozetotide injection may be diluted with Sterile Water for Injection, USP or 0.9% Sodium Chloride Injection, USP up to a final volume of 10 mL.

10) Perform quality controls according to the recommended methods in order to check compliance with the specifications *[see Dosage and Administration (2.5)]*.

11) Store the LOCAMETZ vial containing the gallium Ga 68 gozetotide injection upright in a lead shield container below 30°C (86°F) until use.

12) After addition of gallium-68 chloride to the LOCAMETZ vial, use gallium Ga 68 gozetotide injection within 6 hours.

Figure 1. Preparation with Eckert & Ziegler GalliaPharm Generator

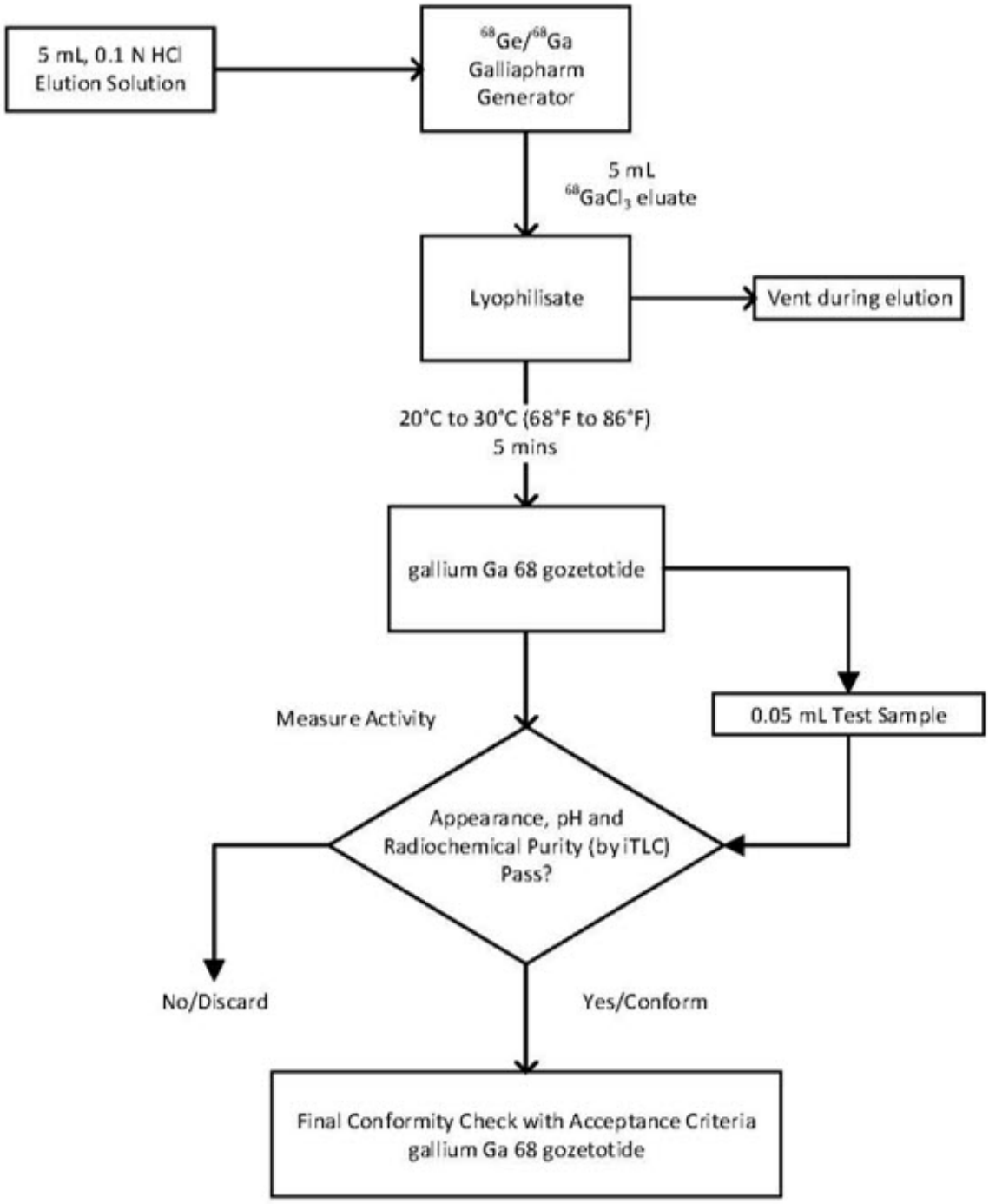


Figure 2. Preparation with IRE ELiT Galli Eo Generator

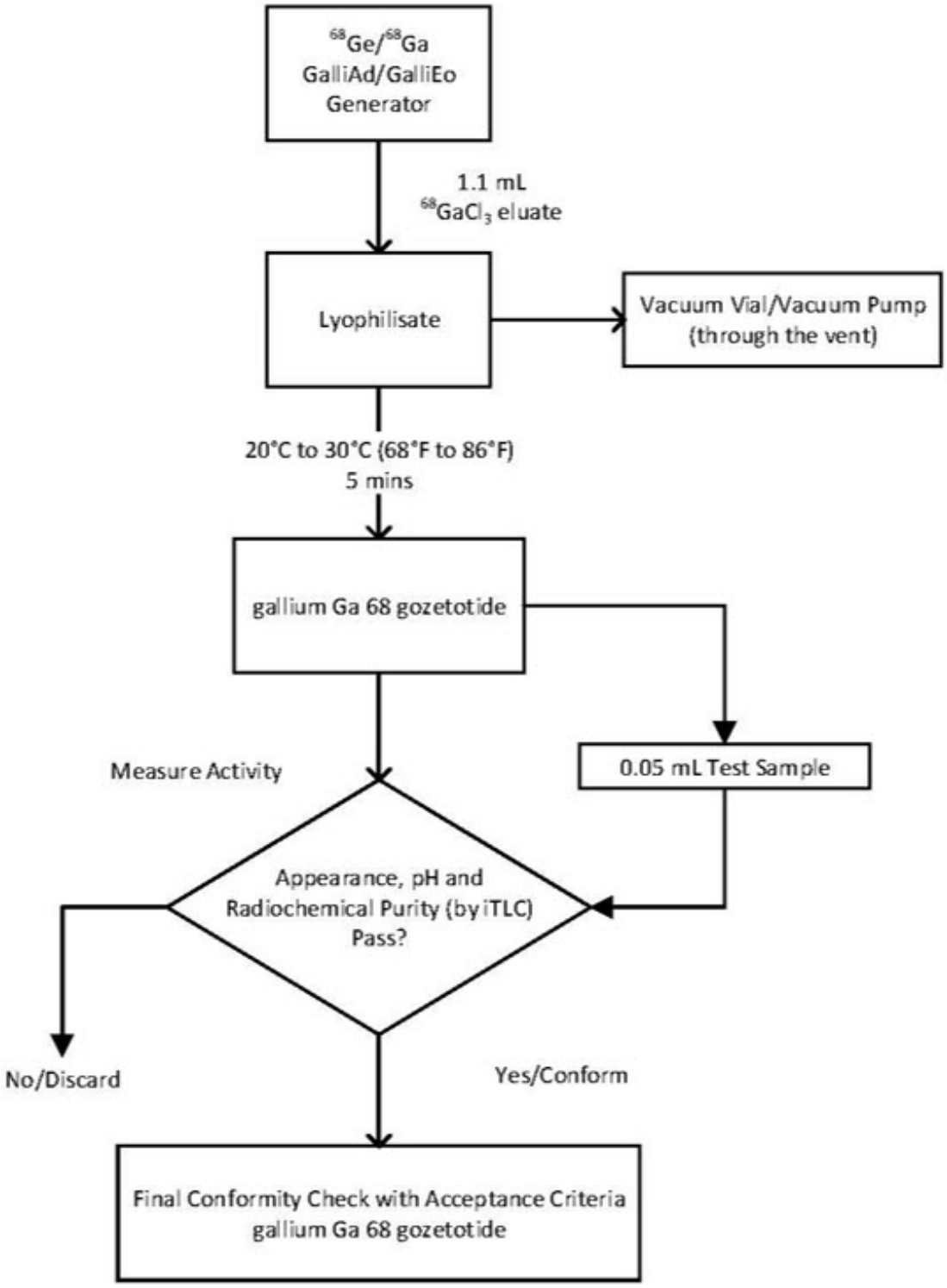
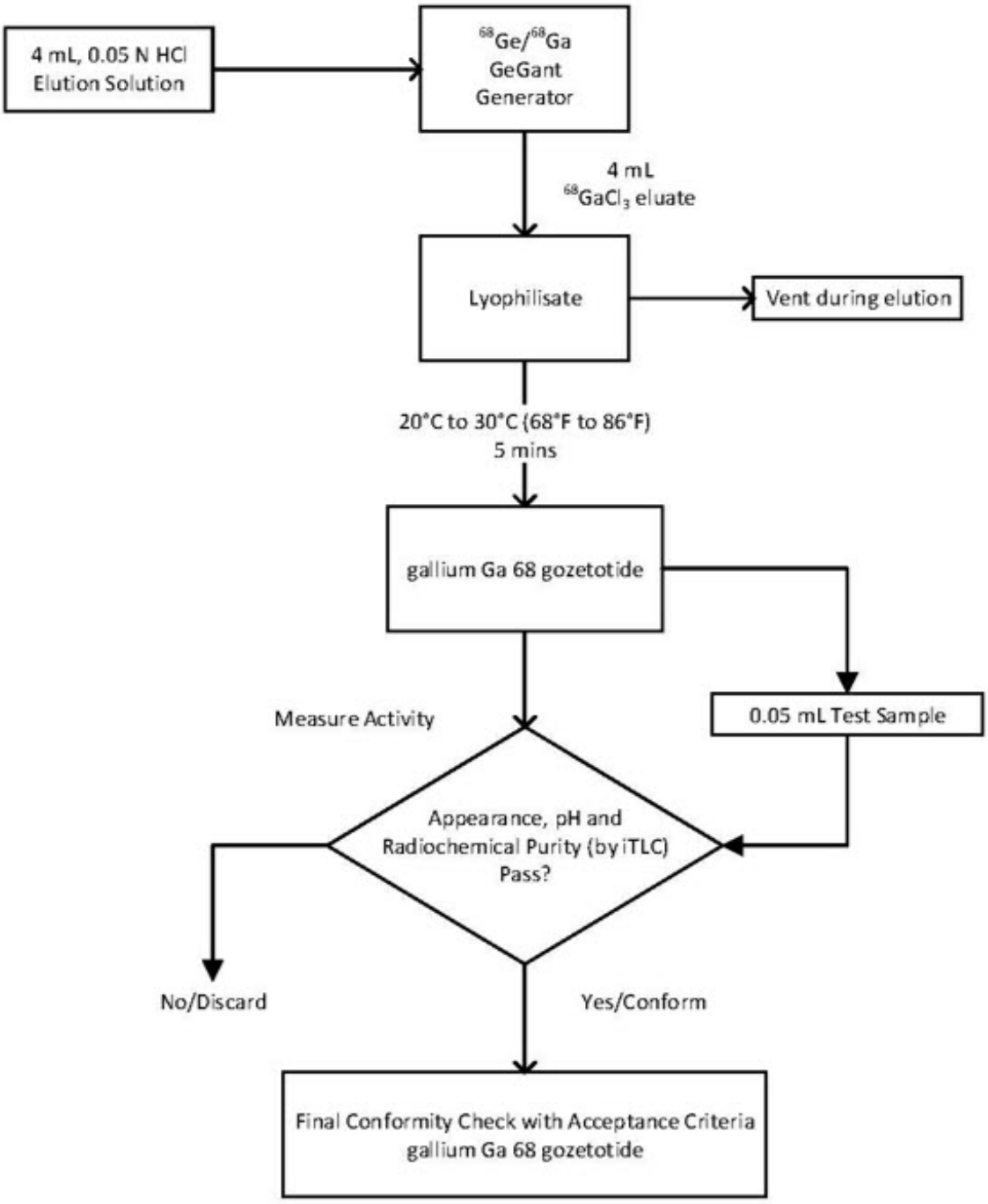


Figure 3. Preparation with ITM Medical Isotopes GeGant Generator



2.5 Specifications and Quality Control

Perform the quality controls in Table 1 behind a lead glass shield for radioprotection purposes.

Table 1. Specifications of Gallium Ga 68 Gozetotide Injection

Test	Acceptance criteria	Method
Appearance	Clear, colorless and free from particulate matter	Visual inspection

pH	3.2 to 6.5	pH-indicator strips
Radiochemical purity	gallium Ga 68 gozetotide ≥ 95% Non-complexed gallium-68 species ≤ 5%	Instant thin layer chromatography (ITLC, see details below)

Determine radiochemical purity of gallium Ga 68 gozetotide injection by performing instant thin layer chromatography (ITLC).

Perform ITLC using ITLC SG strips and using ammonium acetate 1M: Methanol (1:1 V/V) as mobile phase.

ITLC Method

a. Develop the ITLC SG strip for a distance of 6 cm from the point of application (i.e., to 7 cm from the bottom of the ITLC strip).

b. Scan the ITLC SG strip with a radiometric ITLC scanner.

c. Calculate radiochemical purity by integration of the peaks on the chromatogram. Do not use the reconstituted product if the percentage (%) of non-complexed gallium-68 species is higher than 5%.

The retention factor (Rf) specifications are as follows:
- Non-complexed gallium-68 species, Rf = 0 to 0.2;
- Gallium Ga 68 gozetotide, Rf = 0.8 to 1.

2.6 Administration

a. Use aseptic technique and radiation shielding when withdrawing and administering gallium Ga 68 gozetotide injection.

b. Calculate the necessary volume to administer based on calibration time and required dose.

c. Inspect the prepared gallium Ga 68 gozetotide injection for particulate matter and discoloration behind a lead glass shield for radioprotection purposes. Use only solutions that are clear, colorless and free from particulate matter.

d. Using a single-dose syringe fitted with a sterile needle (size 21G to 23G) and protective shielding, aseptically withdraw the prepared gallium Ga 68 gozetotide injection.

e. Verify the total radioactivity in the syringe with a dose calibrator immediately before and after gallium Ga 68 gozetotide injection administration to the patient. The dose calibrator must be calibrated with NIST traceable standards.

f. After injection of gallium Ga 68 gozetotide, administer an intravenous flush of sterile 0.9% Sodium Chloride Injection, USP to ensure full delivery of the dose.

g. Dispose of any unused gallium Ga 68 gozetotide injection in a safe manner in compliance with applicable regulations.

h. If clinically necessary, a diuretic expected to act within the uptake time period may be administered at the time of radiotracer injection to potentially decrease artifact from radiotracer accumulation in the urinary bladder and ureters.

2.7 Image Acquisition

Begin PET scanning 50 minutes to 100 minutes after the intravenous administration of gallium Ga 68 gozetotide injection. Patients should void immediately prior to image acquisition and image acquisition should begin at the mid-thighs and proceed cranially to the skull base or skull vertex. Adapt imaging technique according to the equipment used and patient characteristics in order to obtain the best image quality possible.

2.8 Image Interpretation

Gallium Ga 68 gozetotide binds to PSMA. Based on the intensity of the signals, PET images obtained using gallium Ga 68 gozetotide injection indicate the presence of PSMA in tissues.

Imaging Prior to Initial Definitive or Suspected Recurrence Therapy

Lesions should be considered suspicious if uptake is greater than physiologic uptake in that tissue or greater than adjacent background if no physiologic uptake is expected. Tumors that do not bear PSMA will not be visualized. Increased uptake in tumors is not specific for prostate cancer *[see Warnings and Precautions (5.1)].*

Imaging to Select Patients for PSMA-Directed Therapy

For instructions on patient selection, refer to the prescribing information of the PSMA-directed therapeutic product.

2.9 Radiation Dosimetry

Estimated radiation absorbed doses per injected activity for organs and tissues of 13 adult male patients with an early stage of disease following an intravenous bolus of gallium Ga 68 gozetotide injection are shown in Table 2.

The effective radiation dose resulting from the administration of 259 MBq (7 mCi) is 4.4 mSv. The radiation doses for this administered dose to the critical organs, which are the kidneys, urinary bladder, and spleen, are 96.2 mGy, 25.4 mGy, and 16.8 mGy, respectively.

These radiation doses are for gallium Ga 68 gozetotide injection alone. If CT or a transmission source are used for attenuation correction, the radiation dose will increase by an amount that varies by technique.

Table 2. Estimated Mean Radiation Absorbed Doses per Activity of Intravenously Administered Gallium Ga 68 Gozetotide Injection in Selected Organs and Tissues

	Absorbed dose (mGy/MBq)	
Organ	**Mean**	**SD**
Adrenals	0.0156	0.0014
Brain	0.0104	0.0011
Breasts	0.0103	0.0011
Gallbladder	0.0157	0.0012

Lower colon	0.0134	0.0009
Small intestine	0.014	0.002
Stomach	0.0129	0.0008
Heart	0.012	0.0009
Kidneys	0.3714	0.0922
Liver	0.0409	0.0076
Lungs	0.0111	0.0007
Muscle	0.0103	0.0003
Pancreas	0.0147	0.0009
Red marrow	0.0114	0.0016
Skin	0.0091	0.0003
Spleen	0.065	0.018
Testes	0.0111	0.0006
Thymus	0.0105	0.0006
Thyroid	0.0104	0.0006
Urinary bladder	0.0982	0.0286
Total body	0.0143	0.0013
Effective dose (mSv/MBq)	**0.0169**	**0.0015**

3 DOSAGE FORMS AND STRENGTHS

LOCAMETZ is a kit for the preparation of gallium Ga 68 gozetotide injection supplied in a multiple-dose vial containing 25 micrograms of gozetotide as a white lyophilized powder.

Gallium-68 is obtained from one of the following generators:
- Eckert & Ziegler GalliaPharm (Ge 68/Ga 68) generator
- IRE ELiT Galli Eo (Ge 68/Ga 68) generator
- ITM Medical Isotopes GeGant (Ge 68/Ga 68) generator

After radiolabeling with gallium-68, each vial contains a sterile, clear, colorless solution free from particulate matter of gallium Ga 68 gozetotide at an activity of up to 2,590 MBq (70 mCi) in up to 10 mL at calibration date and time.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Risk for Misinterpretation

Image interpretation errors can occur with LOCAMETZ PET. Negative imaging does not rule out the presence of prostate cancer and positive imaging does not confirm the presence of prostate cancer. Gallium Ga 68 gozetotide uptake is not specific for

prostate cancer and may occur with other types of cancer as well as non-malignant processes, such as Paget's disease, fibrous dysplasia, and osteophytosis. Clinical correlation, which may include histopathological evaluation of the suspected prostate cancer site, is recommended.

The performance of LOCAMETZ for imaging of biochemically recurrent prostate cancer seems to be affected by serum PSA levels and by site of disease. The performance of LOCAMETZ for imaging of metastatic pelvic lymph nodes prior to initial definitive therapy seems to be affected by Gleason score *[see Clinical Studies (14.1, 14.2)]*.

5.2 Radiation Risk

Gallium Ga 68 gozetotide contributes to the patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe handling to minimize radiation exposure to the patient and health care workers. Advise patients to be well hydrated prior to gallium Ga 68 gozetotide injection administration and to void immediately prior to and frequently during the first hours after image acquisition to reduce radiation exposure *[see Dosage and Administration (2.1, 2.3)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of LOCAMETZ has been established based on three prospective studies of gallium Ga 68 gozetotide in patients with prostate cancer (i.e., Studies 1, 2, and 3). Adverse reactions from these studies are reported below.

In Studies 1 and 2 using another formulation of gallium Ga 68 gozetotide injection, 960 patients received one dose of gallium Ga 68 gozetotide intravenously with the amount (mean ± SD) of radioactivity 188.7 ± 40.7 MBq (5.1 ± 1.1 mCi) *[see Clinical Studies (14.1, 14.2)]*. The most commonly reported adverse reactions were nausea, diarrhea and dizziness, occurring at a rate of < 1%.

In a randomized, multicenter, open-label clinical study (NCT03511664, referred to as Study 3) in which gallium Ga 68 gozetotide was used to identify PSMA-positive patients on PET imaging to determine eligibility for PSMA-directed therapy, 1,003 patients with progressive metastatic castration-resistant prostate cancer (mCRPC) received one dose of gallium Ga 68 gozetotide intravenously with the amount of radioactivity 167.1 ± 23.1 MBq (4.52 ± 0.62 mCi). Patients were males with median age of 70 years (range, 40 to 94 years), were White (87%), Black or African American (7%), or Asian (2.4%), and had median baseline PSA levels of 74 ng/mL (range, 0 to 8995 ng/mL).

Adverse reactions occurring at ≥ 0.5% in patients with metastatic prostate cancer who received gallium Ga 68 gozetotide injection in Study 3 are presented in Table 3.

Table 3. Adverse Reactions (≥ 0.5%) in Patients with Metastatic Prostate

Cancer Who Received Gallium Ga 68 Gozetotide Injection in Study 3

Adverse reactions	Gallium Ga 68 Gozetotide Injection N = 1003 n (%)
General disorders	
Fatigue	12 (1.2)
Gastrointestinal disorders	
Nausea	8 (0.8)
Constipation	5 (0.5)
Vomiting	5 (0.5)

Adverse reactions occurring at a rate of < 0.5% in the study were diarrhea, dry mouth, injection site reactions including injection site hematoma and injection site warmth, and chills.

7 DRUG INTERACTIONS

Androgen Deprivation Therapy and Other Therapies Targeting the Androgen Pathway

Androgen deprivation therapy (ADT) and other therapies targeting the androgen pathway, such as androgen receptor antagonists, can result in changes in uptake of gallium Ga 68 gozetotide in prostate cancer. The effect of these therapies on performance of LOCAMETZ PET has not been established.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

LOCAMETZ is not indicated for use in females. There are no available data with gallium Ga 68 gozetotide use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. All radiopharmaceuticals, including LOCAMETZ, have the potential to cause fetal harm depending on the fetal stage of development and the magnitude of radiation dose. Animal reproduction studies have not been conducted with gallium Ga 68 gozetotide.

8.2 Lactation

Risk Summary

LOCAMETZ is not indicated for use in females. There are no data on the presence of gallium Ga 68 gozetotide in human milk, the effect on the breastfed infant, or the effect on milk production.

8.4 Pediatric Use

The safety and effectiveness of gallium Ga 68 gozetotide in pediatric patients have not been established.

8.5 Geriatric Use

The efficacy of LOCAMETZ in geriatric patients with prostate cancer is based on data from three prospective studies.

Of the total number of patients in Studies 1 and 2 *[see Clinical Studies (14.1, 14.2)]*, 691 of 960 (72%) were 65 years of age and older while 195 (20%) were 75 years of age and older.

Of the total number of patients in Study 3 *[see Adverse Reactions (6.1)]*, 752 of 1,003 (75%) were 65 years of age and older while 284 (28%) were 75 years of age and older.

The efficacy and safety profiles of gallium Ga 68 gozetotide appeared similar in younger adult and geriatric patients with prostate cancer and other reported clinical experience has not identified differences in responses between the elderly and younger patients.

10 OVERDOSAGE

In the event of an overdose of gallium Ga 68 gozetotide, reduce the radiation absorbed dose to the patient where possible by increasing the elimination of the radioactivity from the body by hydration and frequent bladder voiding. A diuretic might also be considered. If possible, an estimate of the effective radiation dose exposure to the patient should be made.

11 DESCRIPTION

11.1 Chemical Characteristics

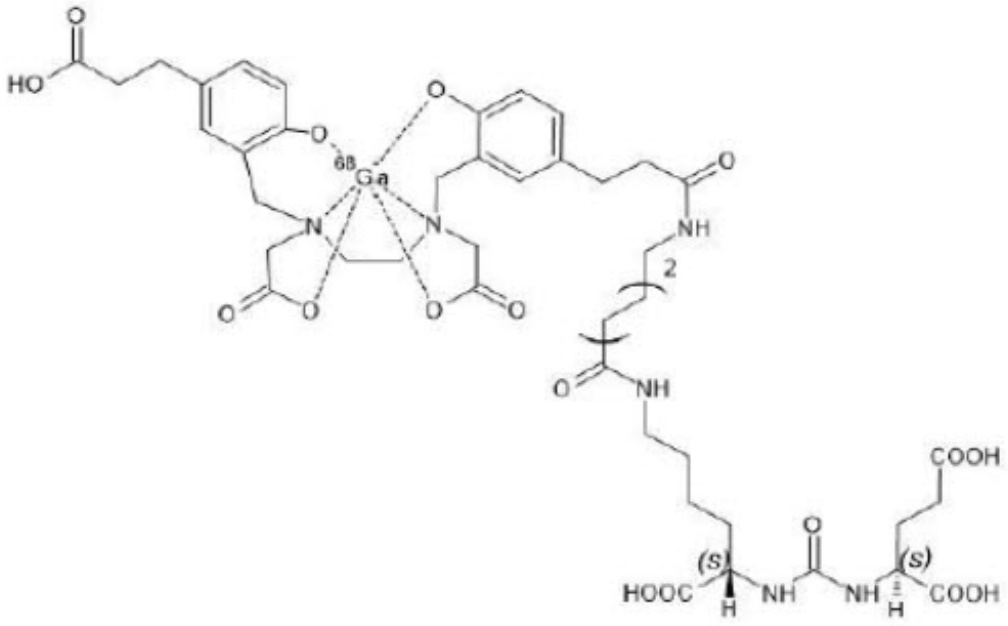
LOCAMETZ (kit for the preparation of gallium Ga 68 gozetotide injection) is a sterile, radioactive diagnostic agent for intravenous administration after radiolabeling. Each vial contains 25 micrograms of gozetotide, 1 mg gentisic acid, 78 mg of sodium acetate trihydrate, and 40 mg sodium chloride. Gozetotide is also known as PSMA-11.

After reconstitution and radiolabeling of LOCAMETZ, the vial contains gallium Ga 68 gozetotide injection at a radioactivity of up to 2,590 MBq (70 mCi) in up to 10 mL at calibration date and time. The vial also contains hydrochloric acid derived from the gallium-68 chloride solution. Gallium Ga 68 gozetotide injection has a pH between 3.2 to 6.5.

Gallium Ga 68 gozetotide is a urea based peptidomimetic that has a covalently bound chelator (HBED-CC). The peptide has amino acid sequence OH-Glu-CO-Lys(Ahx-CC-HBED)-OH.

Gallium Ga 68 gozetotide has a molecular weight of 1011.91 g/mol. The chemical structure is shown in Figure 4.

Figure 4. Chemical Structure of Gallium Ga 68 Gozetotide



11.2 Physical Characteristics

Gallium-68 decays with a half-life of 68 minutes to stable zinc-68. Table 4 and Table 5 display the principle radiation emission data, and physical decay of gallium-68.

Table 4. Principal Radiation Emission Data (> 1%) for Gallium-68

Radiation/Emission	% Disintegration	Mean energy (MeV)
beta+	88%	0.8360
beta+	1.1%	0.3526
Gamma	178%	0.5110
Gamma	3%	1.0770
X-ray	2.8%	0.0086
X-ray	1.4%	0.0086

Table 5. Physical Decay Chart for Gallium-68

Minutes	Fraction remaining
0	1
15	0.858
30	0.736
60	0.541
90	0.398
120	0.293
180	0.158
240	0.086
360	0.025

11.3 Radiation Attenuation

Table 6 displays the radiation attenuation by lead shielding of gallium-68.

Table 6. Radiation Attenuation of 511 keV Photons by Lead (Pb) Shielding

Shield thickness (Pb) mm	Coefficient of attenuation
6	0.5
12	0.25
17	0.1
34	0.01
51	0.001

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Gallium Ga 68 gozetotide binds to PSMA. It binds to cells that express PSMA, including malignant prostate cancer cells, which usually overexpress PSMA. Gallium-68 is a β+ emitting radionuclide that allows PET.

12.2 Pharmacodynamics

The relationship between gallium Ga 68 gozetotide plasma concentrations and successful imaging was not explored in clinical trials.

12.3 Pharmacokinetics

Distribution

Intravenously injected gallium Ga 68 gozetotide is cleared from the blood and is accumulated preferentially in the liver (15%), kidneys (7%), spleen (2%), and salivary glands (0.5%). Gallium Ga 68 gozetotide uptake is also seen in the adrenals and prostate. There is no uptake in the cerebral cortex or in the heart, and usually lung uptake is low.

Gozetotide exhibits a mean blood-to-plasma ratio (% CV) of 0.71 (26%) and is approximately 33% bound to human plasma proteins at 1 mcg/mL to 5 mcg/mL *in vitro*.

Elimination

A total of 14% of the injected dose is excreted in urine in the first 2 hours post-injection.

In Vitro Drug Interaction Studies

CYP450 enzymes

Gozetotide is not a substrate of cytochrome P450 (CYP450) enzymes, not an inhibitor of CYP1A2, CYP2B6, CYP2C8, CYP2C19, CYP2D6 and CYP3A4, and not an inducer of CYP1A2, CYP2B6 and CYP3A4 *in vitro*.

Transporters

Gozetotide is not a substrate of BCRP, P-gp, MATE1, MATE2-K, OAT1, OAT3 or OCT2. Gozetotide is not an inhibitor of BCRP, P-gp, MATE1, MATE2-K, OAT1, OAT3, OATP1B1, OATP1B3, OCT1 or OCT2 *in vitro*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No studies on mutagenic, carcinogenic potential or fertility have been conducted with gallium Ga 68 gozetotide.

14 CLINICAL STUDIES

14.1 Imaging Prior to Initial Definitive Therapy

The efficacy of LOCAMETZ for PET of PSMA-positive lesions in men with prostate cancer with suspected metastasis who are candidates for initial definitive therapy has been established based on a study of another formulation of gallium Ga 68 gozetotide injection. Below is a display of the results of the prospective, open label study PSMA-PreRP (NCT03368547 and NCT02919111, referred to as Study 1).

This two-center study enrolled 325 patients with biopsy-proven prostate cancer who were considered candidates for prostatectomy and pelvic lymph node dissection. All enrolled patients met at least one of the following criteria: serum PSA of at least 10 ng/mL, tumor stage cT2b or greater, or Gleason score greater than 6. Each patient received a single gallium Ga 68 gozetotide PET/CT or PET/MR from mid-thigh to skull base.

A total of 123 patients (38%) proceeded to standard-of-care prostatectomy and template pelvic lymph node dissection and had sufficient histopathology data for evaluation (evaluable patients). Three members of a pool of six central readers independently interpreted each PET scan for the presence of abnormal gallium Ga 68 gozetotide uptake in pelvic lymph nodes located in the common iliac, external iliac, internal iliac, and obturator subregions bilaterally as well as in any other pelvic location. The readers were blinded to all clinical information except for the history of prostate cancer prior to definitive treatment. Extrapelvic sites and the prostate gland itself were not analyzed in this study. For each patient, gallium Ga 68 gozetotide PET results and reference standard histopathology obtained from dissected pelvic lymph nodes were compared by region (left hemipelvis, right hemipelvis, and other).

For the 123 evaluable patients, the mean age was 65 years (range, 45 to 76 years), and 89% were White. The median serum PSA was 11.8 ng/mL. The summed Gleason score was 7 for 44%, 8 for 20%, and 9 for 31% of the patients, with the remainder of the patients having Gleason scores of 6 or 10.

Table 7 compares majority PET reads to pelvic lymph node histopathology results at the patient-level with region matching, such that at least one true positive region defines a true positive patient. As shown, approximately 24% of patients studied were found to have pelvic nodal metastases based on histopathology (95% CI: 17, 32).

Table 7. Patient-Level Performance of Gallium Ga 68 Gozetotide PET for Detection of Pelvic Lymph Node Metastasis[a] in Men with Prostate Cancer with Suspected Metastasis in Study 1 (n = 123)

		Histopathology		Predictive value % (95% CI)
		Positive	**Negative**	
PET scan	**Positive**	14	9	PPV 61% (41, 81)
	Negative	16	84	NPV 84% (79, 91)
Total		30	93	
Diagnostic performance % (95% CI)		Sensitivity 47% (29, 65)	Specificity 90% (84, 96)	

Abbreviations: CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.
[a]With region matching where at least one true positive region defines a true positive patient.

Among the pool of six readers, sensitivity ranged from 36% to 60%, specificity from 83% to 96%, positive predictive value from 38% to 80%, and negative predictive value from 80% to 88%.

In an exploratory subgroup analysis based on summed Gleason score, there was a numerical trend toward more true positives in patients with Gleason score of 8 or higher compared to those with Gleason score of 7 or lower.

An exploratory analysis was performed to estimate the sensitivity and specificity for pelvic nodal metastasis detection in all scanned patients, including the patients who were lacking histopathology reference standard. An imputation method was used based on patient-specific factors. This exploratory analysis resulted in an imputed sensitivity of 47%, with a 95% confidence interval (CI) ranging from 38% to 55%, and an imputed specificity of 74%, with a 95% CI ranging from 68% to 80% for all patients imaged with gallium Ga 68 gozetotide PET.

14.2 Imaging Prior to Suspected Recurrence Therapy

The efficacy of LOCAMETZ for PET of PSMA-positive lesions in men with prostate cancer with suspected recurrence based on elevated serum PSA level has been established based on studies of another formulation of gallium Ga 68 gozetotide injection. Below is a display of the result of the prospective, open label study PSMA-BCR (NCT02940262 and NCT02918357, referred to as Study 2).

This two-center study enrolled 635 patients with biochemical evidence of recurrent prostate cancer after definitive therapy, defined by serum PSA of > 0.2 ng/mL more than 6 weeks after prostatectomy or by an increase in serum PSA of at least 2 ng/mL

above nadir after definitive radiotherapy. All patients received a single gallium Ga 68 gozetotide PET/CT or PET/MR from mid-thigh to skull base. Three members of a pool of nine independent central readers evaluated each scan for the presence and regional location (20 subregions grouped into four regions) of abnormal gallium Ga 68 gozetotide uptake suggestive of recurrent prostate cancer. The readers were blinded to all clinical information other than type of primary therapy and most recent serum PSA level.

A total of 469 patients (74%) had at least one positive region detected by gallium Ga 68 gozetotide PET majority read. The distribution of gallium Ga 68 gozetotide PET positive regions was 34% bone, 25% prostate bed, 25% pelvic lymph node, and 17% extrapelvic soft tissue. Two hundred and ten patients had composite reference standard information collected in a PET positive region (evaluable patients), consisting of at least one of the following: histopathology, imaging (bone scintigraphy, CT, or MRI) acquired at baseline or within 12 months after gallium Ga 68 gozetotide PET, or serial serum PSA. Composite reference standard information for gallium Ga 68 gozetotide PET negative regions was not systematically collected in this study.

In the 210 evaluable patients, the mean age was 70 years (range, 49 to 88 years) and 82% were 65 years of age or older. White patients made up 90% of the group. The median serum PSA was 3.6 ng/mL. Prior treatment included radical prostatectomy in 64% and radiotherapy in 73%.

Of the 210 evaluable patients, 192 patients (91%) were found to be true positive in one or more regions against the composite reference standard (95% CI: 88%, 95%). Among the pool of nine readers used in the study, the proportion of patients who were true positive in one or more regions ranged from 82% to 97%. The prostate bed had the lowest proportion of true positive results at the region-level (76% versus 96% for non-prostate regions).

An exploratory analysis was also performed in which gallium Ga 68 gozetotide PET positive patients who lacked reference standard information were imputed using an estimated likelihood that at least one location-matched PET positive lesion was reference standard positive based on patient-specific factors. In this exploratory analysis, 340 of 475 patients (72%) were imputed as true positive in one or more regions (95% CI: 68%, 76%).

In another exploratory analysis using the same imputation approach for PET positive patients who lacked reference standard information, 340 of 635 patients (54%) were correctly detected as true positive (95% CI: 50%, 57%) among all BCR patients who received a PET scan, whether it was read as positive or negative. The likelihood of identifying a gallium Ga 68 gozetotide PET positive lesion in this study generally increased with higher serum PSA level. Table 8 shows the patient-level gallium Ga 68 gozetotide PET results stratified by serum PSA level. The mean time between PSA measurement and PET scan was 40 days with a range of 0 to 367 days. Percent PET positivity was calculated as the proportion of patients with a positive gallium Ga 68 gozetotide PET out of all patients scanned. Percent PET positivity includes patients determined to be either true positive or false positive as well as those in whom such determination was not made due to the absence of composite reference standard data.

Table 8. Patient-Level Gallium Ga 68 Gozetotide PET Results and Percent PET Positivity Stratified by Serum PSA Level in Men with Prostate Cancer with Suspected

Recurrence in Study 2 (n = 628)[a]

PSA (ng/mL)	PET-positive patients			Without reference standard	PET-negative patients	PET positivity %[b] (95% CI)
	Total	TP	FP			
		With reference standard				
< 0.5	48	11	1	36	87	36% (27, 44)
		12				
≥ 0.5 and < 1	44	15	3	26	35	56% (45, 67)
		18				
≥ 1 and < 2	71	29	1	41	15	83% (75, 91)
		30				
≥ 2	299	137	13	149	29	91% (88, 94)
		150				
Total	462	192	18	252	166	74% (70, 77)
		210				

Abbreviations: PET, positron emission tomography; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; BCR, biochemical recurrence; TP, true positive; FP, false positive.
[a]7 patients were excluded from this table due to protocol deviations.
[b]Percent PET positivity: PET positive patients/total patients scanned.

14.3 Imaging to Select Patients for PSMA-Directed Therapy

Refer to the prescribing information of the PSMA-directed therapy for description of the studies in which the efficacy of LOCAMETZ for selecting patients has been established.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

LOCAMETZ is supplied as a kit for the preparation of gallium Ga 68 gozetotide injection in a carton of 1 vial (NDC# 69488-017-61).

Each multiple-dose vial contains 25 micrograms of gozetotide as white lyophilized powder packaged in a 10 mL type I Plus glass vial closed with a rubber stopper and sealed with a flip-off cap.

Storage and Handling

Before radiolabeling, store at 2°C to 25°C (36°F to 77°F). Do not freeze.

After radiolabeling, store upright with an appropriate lead shielding to protect from radiation, below 30°C (86°F). Do not freeze. After radiolabeling, use within 6 hours.

This preparation is approved for use by persons under license by the Nuclear Regulatory Commission or the relevant regulatory authority of an Agreement State.

17 PATIENT COUNSELING INFORMATION

Adequate Hydration

Advise patients to be well hydrated prior to the administration of gallium Ga 68 gozetotide injection and urge them to urinate immediately prior to image acquisition and frequently during the first hours following administration to reduce radiation exposure *[see Dosage and Administration (2.3), Warnings and Precautions (5.2)]*.

Distributed by:
Novartis Pharmaceuticals Corporation
East Hanover, NJ 07936

©2025 Novartis

LOCAMETZ® is a registered trademark of Novartis AG and/or its affiliates.

U.S. Patent 11369590

T2025-24

PRINCIPAL DISPLAY PANEL

LOCAMETZ®

kit for the preparation of
gallium Ga 68 gozetotide injection
25 mcg per vial gozetotide

For Intravenous Use Only

Radiolabel with gallium-68 chloride before use

RX-Only

NDC 69488-017-61

Advanced Accelerator Applications USA, Inc. Millburn, NJ 07041

LOCAMETZ

kit for the preparation of gallium ga 68 gozetotide injection, powder, lyophilized, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:69488-017
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
GOZETOTIDE (UNII: 9AG41L3AOQ) (GOZETOTIDE - UNII:9AG41L3AOQ)	GOZETOTIDE	25 ug

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM ACETATE (UNII: 4550K0SC9B)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
GENTISIC ACID (UNII: VP36V95O3T)	
WATER (UNII: 059QF0KO0R)	
NITROGEN (UNII: N762921K75)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:69488-017-61	1 in 1 CARTON	03/23/2022	

1		1 in 1 VIAL, MULTI-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA215841	03/23/2022	

Labeler - Advanced Accelerator Applications USA, Inc (051714355)

Registrant - Novartis Pharmaceuticals Corporation (002147023)

Revised: 3/2025 Advanced Accelerator Applications USA, Inc