LOCAMETZ®
Kit for the preparation of gallium Ga 68 gozetotide
INJECTION FOR INTRAVENOUS USE

Radiolabeling Guide

Directions for using the Eckert & Ziegler GalliaPharm® or IRE ELiT Galli Eo™ Ge 68/Ga 68 Generator

Indication

LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection), 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.

IMPORTANT SAFETY INFORMATION

Risk for Misinterpretation

Image interpretation errors can occur with LOCAMETZ PET. Negative imaging does not rule out the presence of prostate cancer and a 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 nonmalignant processes. Clinical correlation, which may include histopathological evaluation of the suspected prostate cancer site, is recommended.

Please see additional Important Safety Information on pages 2 and 20-21 and full Prescribing Information.

PSMA PET imaging unlocks a single biomarker-based approach to diagnosis and treatment of eligible patients with metastatic prostate cancer

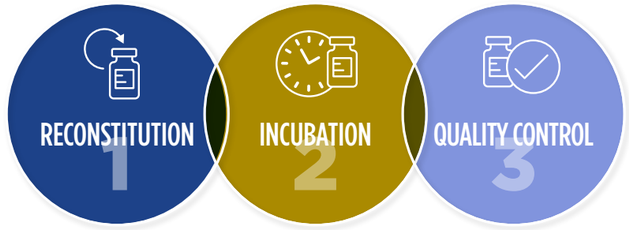
Prostate-specific membrane antigen (PSMA) is a biomarker that is overexpressed in >80% of men with prostate cancer, making it an ideal diagnostic and therapeutic target [1-5]

PSMA positron emission tomography (PET) imaging using gallium Ga 68 gozetotide has been studied in multiple trials and approved for certain prostate cancer patients[6-9]

LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection) is available as a kit for radiopharmaceutical preparation of gallium Ga 68 gozetotide solution for injection[10]

LOCAMETZ must be prepared at a central radiopharmacy and delivered to the hospital ready to inject, or prepared at the radiopharmacy on site at the hospital.

Radiolabeling of LOCAMETZ is accomplished in a 3-step process[10]



This guide provides an illustrated, step-by-step walk-through of the radiolabeling process for LOCAMETZ using the Eckert & Ziegler GalliaPharm® or IRE ELiT Galli Eo™ germanium 68/gallium 68 (Ge 68/Ga 68) generators.

IMPORTANT SAFETY INFORMATION (continued)

Risk for Misinterpretation (continued)

The performance of LOCAMETZ seems to be affected by serum PSA levels and by site of disease for imaging of biochemically recurrent prostate cancer, and by Gleason score for imaging of metastatic pelvic lymph nodes prior to initial definitive therapy.

Radiation Risk

Gallium Ga 68 gozetotide contributes to a patient's long-term cumulative radiation exposure, which 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 administration and to void immediately prior to and frequently during the first hours after image acquisition to reduce radiation exposure.

Please see additional Important Safety Information on pages 20-21 and full Prescribing Information.

Table of contents

Important

This guide is provided for informational purposes only and is not intended, nor should it be used, to establish a legal standard of care. It is important to adhere to the full Prescribing Information and your institutional guidelines when administering LOCAMETZ.

This guide lists materials and visuals to illustrate certain portions of the LOCAMETZ Prescribing Information. The instructions for use provided by the Ge 68/Ga 68 generator manufacturer must also be followed.

STEP 1: RECONSTITUTION

Eckert & Ziegler GalliaPharm® Generator

Reconstitution must be performed in compliance with aseptic procedures, local regulations, and instructions from the generator supplier.

Materials you will need to reconstitute LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection)[10,11]

The materials and equipment shown here are required for the reconstitution of LOCAMETZ using the Eckert & Ziegler GalliaPharm Ge 68/Ga 68 generator.

- Kit containing LOCAMETZ vial only
- 5-mL and 10-mL syringes
- Sterile needles (21G-23G)
- Vent needle with 0.2-µm sterile air venting filter
- Optional: Sterile water for injection or sodium chloride 9 mg/mL (0.9%) solution for infusion

See LOCAMETZ Prescribing Information, *Drug Preparation*, section 2.4

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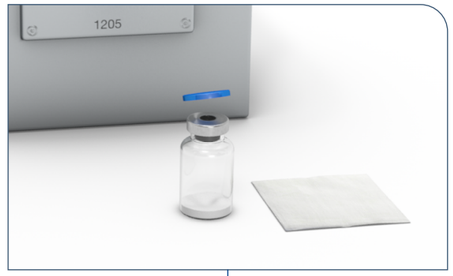
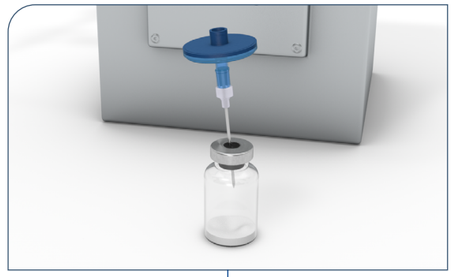
Getting started: Setting up for the elution process[10]

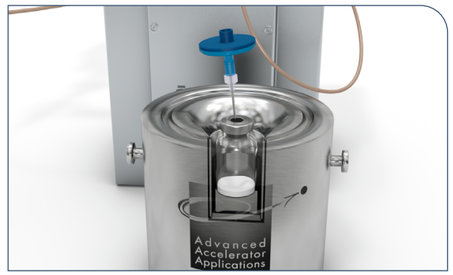
When preparing and handling LOCAMETZ, use waterproof gloves, effective radiation shielding, and appropriate safety measures to avoid unintentional radiation exposure to the patient and health care workers. Prepare LOCAMETZ according to the aseptic procedure shown.



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



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

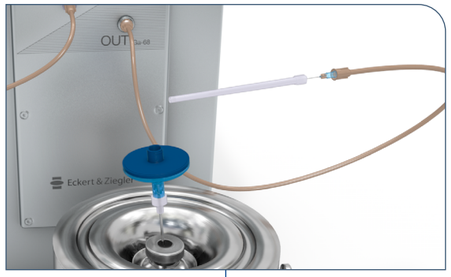


Place the LOCAMETZ vial in a lead-shield container.

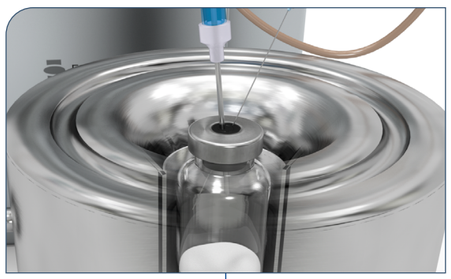
STEP 1: RECONSTITUTION

Eckert & Ziegler GalliaPharm® Generator

Getting started: Setting up for the elution process[10] (continued)



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



Connect the LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection) vial directly to the outlet line of the generator by pushing the elution needle through the rubber septum.

The elution can be performed directly from the generator into the LOCAMETZ vial.

LOCAMETZ®
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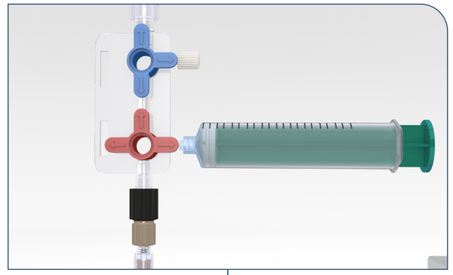
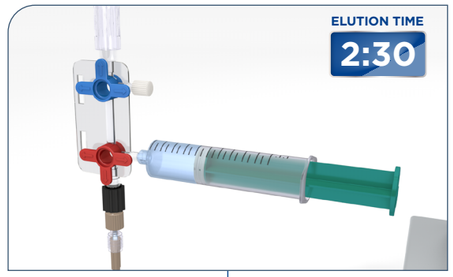
Eluting LOCAMETZ with gallium-68[10,11]



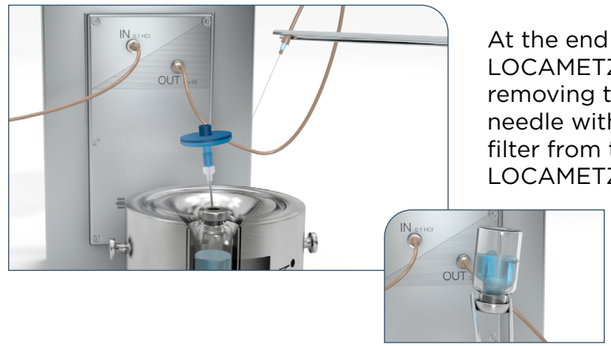
Perform the elution manually or by means of a pump according to the generator instructions for use.



Reconstitute the lyophilized powder with 5 mL of eluate.

Elution time:

2:30



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-µm sterile air venting filter from the rubber septum. Then, invert LOCAMETZ vial once and place it upright.

STEP 1: RECONSTITUTION

IRE ELiT Galli Eo™ Generator

Reconstitution must be performed in compliance with aseptic procedures, local regulations, and instructions from the generator supplier.

Materials you will need to reconstitute LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection)[10,11]

The materials and equipment shown here are required for the reconstitution of LOCAMETZ using the IRE ELiT Galli Eo Ge 68/Ga 68 generator.

- Kit containing product vial only
- 1 syringe (5 mL or 10 mL)
- Sterile needles (21G-23G)
- Vent needle with 0.2-µm sterile air venting filter
- Optional: Sterile water for injection or sodium chloride 9 mg/mL (0.9%) solution for infusion
- Vacuum vial (at least 25 mL)
- Sterile tube
- Male-male adapter

See LOCAMETZ Prescribing Information, *Drug Preparation*, section 2.4

Please see Important Safety Information on pages 20-21 and full Prescribing Information.

LOCAMETZ®
Kit for the preparation of gallium Ga 68 gozetotide
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Getting started: Setting up for the elution process[10]

When preparing and handling LOCAMETZ, use waterproof gloves, effective radiation shielding, and appropriate safety measures to avoid unintentional radiation exposure to the patient and health care workers. Prepare LOCAMETZ according to the aseptic procedure shown.

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

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

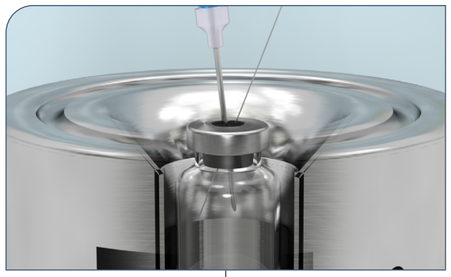
Place the LOCAMETZ vial in a lead-shield container.

STEP 1: RECONSTITUTION

IRE ELiT Galli Eo™ Generator

Getting started: Setting up for the elution process[10] (continued)

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



Connect the LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection) vial directly to the outlet line of the generator by pushing the elution needle through the rubber septum.

The elution can be performed directly from the generator into the LOCAMETZ vial.

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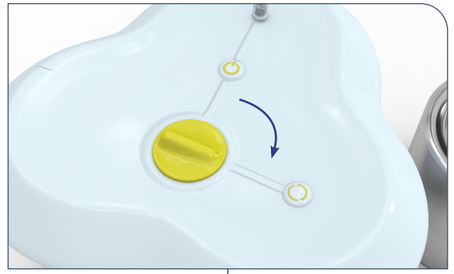
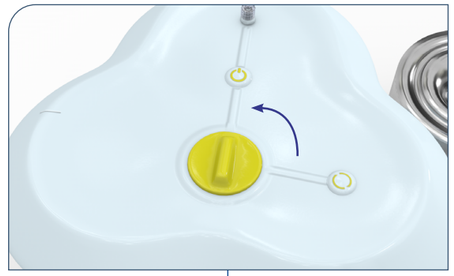
Begin eluting LOCAMETZ with gallium-68[10,12]

Prepare the generator.

For proper use of the IRE ELiT Galli Eo generator, follow the instructions for use provided by the manufacturer.



Turn the button 90° clockwise to the loading position.[12]



Then, turn the button back to the initial position.[12]

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

STEP 1: RECONSTITUTION

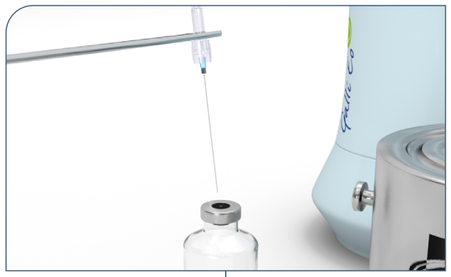
IRE ELiT Galli Eo™ Generator

Begin eluting LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection) with gallium-68[10,12] (continued)

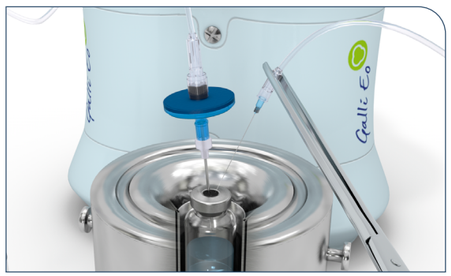
Reconstitute the lyophilized powder with 1.1 mL of eluate.

Elution time:

3:00



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-µm sterile air venting filter needle from the rubber septum. Inversion of the LOCAMETZ vial is not needed.

Please see Incubation and Quality Control instructions starting on page 13.

Please see Important Safety Information on pages 20-21 and full Prescribing Information.

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STEP 2: INCUBATION

Eckert & Ziegler GalliaPharm® Generator and IRE ELiT Galli Eo™ Generator

Preparing for radioactivity measurement[10]

Step 2 of the process is incubation. Following reconstitution, a 5-minute incubation period is required before measuring the vial radioactivity.

These are the materials you will need for incubation.

- Lead pot
- Dose calibrator
- Monitor

See LOCAMETZ Prescribing Information, *Drug Preparation*, section 2.4

Incubating and calibrating LOCAMETZ[10]

Incubate the LOCAMETZ vial upright between 68°F and 86°F for at least 5 minutes without agitation or stirring.

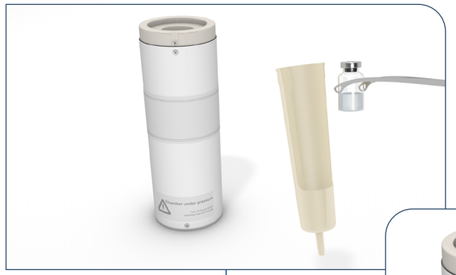
Incubation time:

5:00

STEP 2: INCUBATION

Eckert & Ziegler GalliaPharm® Generator and IRE ELiT Galli Eo™ Generator

Incubating and calibrating LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection)[10] (continued)



After 5 minutes, assay the vial containing the gallium Ga 68 gozetotide injection for total radioactivity using a dose calibrator. Calculate the radioactivity concentration.

Record the result.

Please see Important Safety Information on pages 20-21 and full Prescribing Information.

STEP 3: QUALITY CONTROL

Eckert & Ziegler GalliaPharm® Generator and IRE ELiT Galli Eo™ Generator

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Materials required for quality control[10]

The final step is quality control. Quality control consists of 3 standard tests—appearance, pH, and labeling efficiency.

For these tests, you will need the required materials shown here.

- Instant thin layer chromatography (ITLC) developing tank with lid
- ITLC silica gel (SG) strip
- Ruler
- Pencil
- pH-indicator strips
- Pipette with fitted tip
- 1-mL single-dose syringe and sterile needle (21G-23G)
- Radiometric ITLC scanner

See LOCAMETZ Prescribing Information, *Specifications and Quality Control,* section 2.5.

STEP 3: QUALITY CONTROL

Eckert & Ziegler GalliaPharm® Generator and IRE ELiT Galli Eo™ Generator

Quality control specifications for LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection)[10]

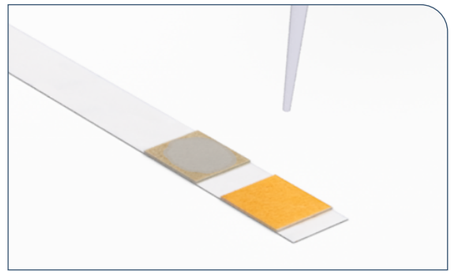
Perform quality controls according to each of the 3 recommended methods below in order to check compliance with the specifications. These tests should be performed behind a lead-glass shield for radioprotection purposes.

Test	Acceptance criteria	Method
Appearance	Clear, colorless, and free from particulate matter	Visual inspection
pH	3.2 – 6.5	pH-indicator strips
Radiochemical Purity	gallium Ga 68 gozetotide ≥95% Non-complexed gallium-68 species ≤5%	ITLC

Performing quality control tests: Appearance[10]

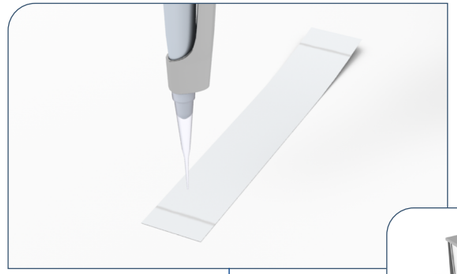
First, visually inspect the prepared LOCAMETZ solution. It should be clear, colorless, and free from particulate matter.

Performing quality control tests: pH[10]

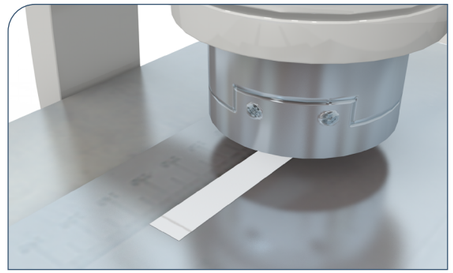


After visually inspecting the product, perform a routine pH test. The acceptable range is between 3.2 and 6.5.

Performing quality control tests: Radiochemical purity[10]



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

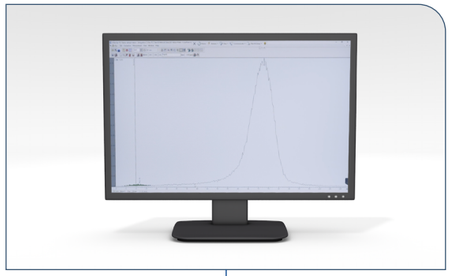


Scan the ITLC SG strip with radiometric ITLC scanner.

STEP 3: QUALITY CONTROL

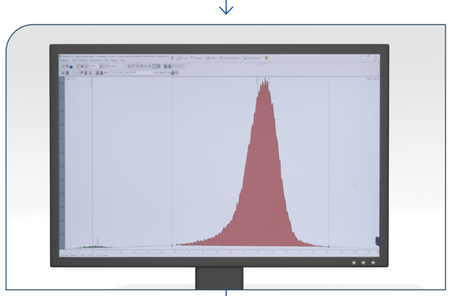
Eckert & Ziegler GalliaPharm® Generator and IRE ELiT Galli Eo™ Generator

Quality control specifications for LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection)[10] (continued)



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
- LOCAMETZ, Rf = 0.8 to 1

Note: Store the LOCAMETZ vial containing the gallium Ga 68 gozetotide injection upright in a lead-shield container below 86°F until use.

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

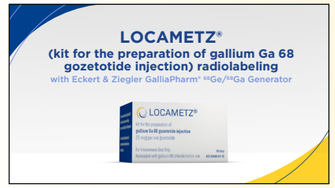
Please see Important Safety Information on pages 20-21 and full Prescribing Information.

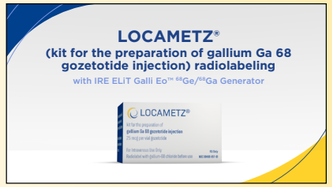
Additional information prior to administration[10]

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

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

Verify the total radioactivity in the syringe with a dose calibrator immediately before administration to the patient. The dose calibrator must be calibrated with NIST traceable standards





Videos for reconstituting and radiolabeling LOCAMETZ are available online

Find videos for the Eckert & Ziegler GalliaPharm and IRE ELiT Galli Eo generators at LOCAMETZ-hcp.com/psma-pet-ct/dosing-and-administration#resources

NIST, National Institute of Standards and Technology; USP, US Pharmacopeia.

INDICATION AND IMPORTANT SAFETY INFORMATION

Indication

LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection), 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.

IMPORTANT SAFETY INFORMATION

Risk for Misinterpretation

Image interpretation errors can occur with LOCAMETZ PET. Negative imaging does not rule out the presence of prostate cancer and a 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 nonmalignant processes. Clinical correlation, which may include histopathological evaluation of the suspected prostate cancer site, is recommended.

The performance of LOCAMETZ seems to be affected by serum PSA levels and by site of disease for imaging of biochemically recurrent prostate cancer, and by Gleason score for imaging of metastatic pelvic lymph nodes prior to initial definitive therapy.

Radiation Risk

Gallium Ga 68 gozetotide contributes to a patient's long-term cumulative radiation exposure, which 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 administration and to void immediately prior to and frequently during the first hours after image acquisition to reduce radiation exposure.

Adverse Reactions

Adverse reactions ≥0.5% in the VISION study were fatigue (1.2%), nausea (0.8%), constipation (0.5%), and vomiting (0.5%). Adverse reactions occurring at a rate of <0.5% were diarrhea, dry mouth, injection site reactions, and chills.

Please see full Prescribing Information.

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References:

1. Hupe MC, Philippi C, Roth D, et al. Expression of prostate-specific membrane antigen (PSMA) on biopsies is an independent risk stratifier of prostate cancer patients at time of initial diagnosis. *Front Oncol.* 2018;8:623. doi:10.3389/fonc.2018.00623. **2.** Pomykala KL, Czernin J, Grogan TR, Armstrong WR, Williams J, Calais J. Total-body ^{68}Ga-PSMA-11 PET/CT for bone metastasis detection in prostate cancer patients: potential impact on bone scan guidelines. *J Nucl Med.* 2020;61(3):405-411. doi:10.2967/jnumed.119.230318. **3.** Hope TA, Aggarwal R, Chee B, et al. Impact of ^{68}Ga-PSMA-11 PET on management in patients with biochemically recurrent prostate cancer. *J Nucl Med.* 2017;58(12):1956-1961. doi:10.2967/jnumed.117.192476. **4.** Tsourlakis MC, Klein F, Kluth M, et al. PSMA expression is highly homogenous in primary prostate cancer. *Appl Immunohistochem Mol Morphol.* 2015;23(6):449-455. doi:10.1097/PAI.0000000000000110. **5.** Minner S, Wittmer C, Graefen M, et al. High level PSMA expression is associated with early PSA recurrence in surgically treated prostate cancer. *Prostate.* 2011;71(3):281-288. doi:10.1002/pros.21241. **6.** Fendler WP, Weber M, Iravani A, et al. Prostate-specific membrane antigen ligand positron emission tomography in men with nonmetastatic castration-resistant prostate cancer. *Clin Cancer Res.* 2019;25(24):7448-7454. doi:10.1158/1078-0432.CCR-19-1050. **7.** Hofman MS, Lawrentschuk N, Francis RJ, et al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multi-centre study. *Lancet.* 2020;395(10231):1208-1216. doi:10.1016/S0140-6736(20)30314-7. Published online March 22, 2020. **8.** Sonni I, Eiber M, Fendler WP, et al. Impact of ^{68}Ga-PSMA-11 PET/CT on staging and management of prostate cancer patients in various clinical settings: a prospective single-center study. *J Nucl Med.* 2020;61(8):1153-1160. doi:10.2967/jnumed.119.237602. **9.** Fendler WP, Calais J, Eiber M, et al. Assessment of ^{68}Ga-PSMA-11 PET accuracy in localizing recurrent prostate cancer: a prospective single-arm clinical trial. *JAMA Oncol.* 2019;5(6):856-863. doi:10.1001/jamaoncol.2019.0096. **10.** Locametz. Prescribing information. Novartis Pharmaceuticals Corp. **11.** GalliaPharm. Summary of Product Characteristics. Berlin, Germany: Eckert & Ziegler Radiopharma GmbH; May 2014. **12.** GalliAd. Summary of Product Characteristics (UK_spc_04E18). Fleurus, Belgium: IRE ELiT Radiopharma.

LOCAMETZ®

Kit for the preparation of gallium Ga 68 gozetotide

INJECTION FOR INTRAVENOUS USE

LOCAMETZ® (kit for the preparation of gallium Ga 68 gozetotide injection) must be prepared at a central radiopharmacy and delivered to the hospital ready to inject, or prepared at the radiopharmacy on site at the hospital.

LOCAMETZ is available as a kit for radiopharmaceutical preparation of gallium Ga 68 gozetotide solution for injection

To learn more about LOCAMETZ, please visit LOCAMETZ-hcp.com

Please see Important Safety Information on pages 20-21 and full Prescribing Information.

NOVARTIS

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