PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

NETSPOT®

40 microgram kit for the preparation of gallium (^{68}Ga) oxodotreotide for injection

Diagnostic Radiopharmaceutical Kit

Novartis Pharmaceuticals Canada Inc.

700 Saint-Hubert St., Suite 100
Montreal, Quebec
H2Y 0C1

Date of Initial Authorization:
Jul 03, 2019

Date of Revision:
Feb 28, 2024

Submission Control Number: 282568

RECENT MAJOR LABEL CHANGES

4 Dosage and Administration, 4.4 Administration	06/2021
4 Dosage and Administration, 4.7 Instructions for Preparation and Use	06/2021
4 Dosage and Administration, 4.8 Radiation Dosimetry	06/2021
7 Warnings and Precautions	06/2021

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

RECENT MAJOR LABEL CHANGES 2

TABLE OF CONTENTS 2

PART I: HEALTH PROFESSIONAL INFORMATION 4

1 INDICATIONS 4

1.1 Pediatrics 4

1.2 Geriatrics 4

3 SERIOUS WARNINGS AND PRECAUTIONS BOX 4

4 DOSAGE AND ADMINISTRATION 4

4.1 Dosing Considerations 4

4.2 Recommended Dose and Dosage Adjustment 5

4.4 Administration 5

4.6 Image Acquisition and Interpretation 5

4.7 Instructions for Preparation and Use 5

4.8 Radiation Dosimetry 10

5 OVERDOSAGE 12

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING 12

6.1 Physical Characteristics 13

6.2 External Radiation 14

7 WARNINGS AND PRECAUTIONS 14

7.1 Special Populations 15

7.1.1 Pregnant Women 15

7.1.2 Breast-feeding 15

7.1.3 Pediatrics 16

7.1.4 Geriatrics 16

8 ADVERSE REACTIONS 16
8.1 Adverse Reaction Overview 16
8.5 Post-Market Adverse Reactions 16
9 DRUG INTERACTIONS 17
9.3 Drug-Behavioural Interactions 17
9.4 Drug-Drug Interactions 17
9.5 Drug-Food Interactions 17
9.6 Drug-Herb Interactions 17
9.7 Drug-Laboratory Test Interactions 17
10 CLINICAL PHARMACOLOGY 17
10.1 Mechanism of Action 17
10.2 Pharmacodynamics 17
10.3 Pharmacokinetics 17
11 STORAGE, STABILITY AND DISPOSAL 18
12 SPECIAL HANDLING INSTRUCTIONS 18
PART II: SCIENTIFIC INFORMATION 20
13 PHARMACEUTICAL INFORMATION 20
14 CLINICAL TRIALS 21
14.1 Trial Design and Study Demographics 21
15 MICROBIOLOGY 22
16 NON-CLINICAL TOXICOLOGY 22
PATIENT MEDICATION INFORMATION 25

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

NETSPOT® [kit for the preparation of gallium (^{68}Ga) oxodotreotide injection], after radiolabeling with gallium (^{68}Ga), is indicated for:

- Use with positron emission tomography (PET), as an adjunct to other diagnostic tests for localization of somatostatin receptor-positive neuroendocrine tumours (NETs).

1.1 Pediatrics

Pediatrics (<18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of Netspot in pediatric patients has not yet been established, therefore, Health Canada has not authorized a specific indication for pediatric use (see 7.1.3 Pediatrics).

1.2 Geriatrics

Geriatrics (> 65 years of age): Clinical studies of Netspot did not include sufficient numbers of subjects aged 65 and over, to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- Radiopharmaceuticals should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Drug Preparation

Netspot requires reconstitution and radiolabeling prior to use. Following reconstitution and radiolabeling, handle gallium (^{68}Ga) oxodotreotide injection with appropriate safety measures to minimize radiation exposure (see 7 WARNINGS AND PRECAUTIONS).

Prior to use, visually inspect the prepared gallium (^{68}Ga) labelled Netspot injection behind a lead glass shield for radioprotection purposes. Only use solutions that are clear without visible particles. Using a single-dose syringe fitted with a sterile needle and protective shielding, aseptically withdraw the prepared gallium (^{68}Ga) oxodotreotide injection prior to administration.

Patient Preparation

Patients should have discontinued all medications that could interfere with uptake of Netspot (see 9.4 Drug-Drug Interactions).

Instruct patients to drink a sufficient amount of water to ensure adequate hydration prior to administration of gallium (^{68}Ga) oxodotreotide (see 7 WARNINGS AND PRECAUTIONS).

4.2 Recommended Dose and Dosage Adjustment

In adult patients, the recommended amount of radioactivity to be administered for PET imaging is 2 MBq/kg of body weight (0.054 mCi/kg), up to a total of 200 MBq (5.4 mCi).

4.4 Administration

Gallium (^{68}Ga) oxodotreotide is to be administered by intravenous bolus injection.

Prior to injection, verify the injected radioactivity by measuring the radioactivity of the vial containing the gallium (^{68}Ga) oxodotreotide injection with a dose calibrator before administration to the patient. Ensure that the injected radioactivity is within $\pm$ 10% of the recommended dose.

Accidental extravasation may cause local irritation, due to the acidic pH of the gallium (^{68}Ga) oxodotreotide solution. In case of extravasation, the injection must be stopped, the site of injection must be changed and the affected area should be irrigated with sodium chloride solution.

4.6 Image Acquisition and Interpretation

For gallium (^{68}Ga) oxodotreotide PET imaging, the acquisition must include a whole-body acquisition from skull to mid-thigh. Images can be acquired 40 to 90 minutes after the intravenous administration of the gallium (^{68}Ga) oxodotreotide. Adapt imaging acquisition delay and duration according to the equipment used, and the patient and tumour characteristics, in order to obtain the best image quality possible.

Gallium (^{68}Ga) oxodotreotide binds to somatostatin receptors. Based upon the intensity of the signals, PET images obtained using gallium (^{68}Ga) oxodotreotide indicate the presence and density of somatostatin receptors in tissues. Tumours that do not bear somatostatin receptors will not be visualized (see 7 WARNINGS AND PRECAUTIONS).

4.7 Instructions for Preparation and Use

The Netspot kit is supplied as two vials (see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING) which allows for direct preparation of gallium (^{68}Ga) oxodotreotide injection with the eluate from the following Germanium 68/Gallium 68 (^{68}Ge/^{68}Ga) generator that is authorized by Health Canada.

- 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

The ^{68}Ge/^{68}Ga generators are not supplied with the Netspot kit.

Components of the kit:

- **Vial 1** (reaction vial with lyophilized powder) contains: 40 µg oxodotreotide; 5 µg 1,10-phenanthroline; 6 µg gentisic acid; 20 mg mannitol; and
- **Vial 2** (buffer vial) contains: 60 mg formic acid; 56.5 mg sodium hydroxide; and water for injection.

Prepare gallium (^{68}Ga) oxodotreotide for injection according to the following aseptic procedure:

Set-up

a) Use suitable shielding to reduce radiation exposure (see 12 SPECIAL HANDLING INSTRUCTIONS).
b) Wear waterproof gloves.
c) Test periodically (weekly) the ^{68}Ga chloride eluate for ^{68}Ge breakthrough by suitable method. ^{68}Ge breakthrough and other gamma emitting radionuclides should be < 0.001%.

d) Set the temperature of a shielded dry bath to 95°C, and wait for the temperature to reach the set point and stabilize.
e) Prepare syringes for elution and reconstitution steps per Table 1 below.
f) Radiolabeling of carrier molecules with gallium (^{68}Ga) chloride is very sensitive to the presence of trace metal impurities. Only syringes and syringe needles able to minimize trace metal impurity levels (for example, non-metallic or coated silicone needles - not supplied) should be used.
g) A low dead space 1-mL plastic syringe must be used in order to precisely measure the adequate volume of reaction buffer to be added during the preparation. Glass syringe must not be used.
h) Prior to piercing vial septums, flip-off cap and swab top of vial closure with an appropriate antiseptic to disinfect the surface, and allow the stopper to dry.

Table 1 – Solutions for Generator Elution and Radiolabeling Reaction

Solutions for use with Eckert & Ziegler GalliaPharm generator		
Syringe	**Solution**	**Purpose**
5-mL sterile syringe	5 mL of 0.1 N sterile HCl supplied by the generator manufacturer	For elution of the generator
1-mL sterile syringe	**Vial 2 buffer** Calculate the volume (in mL) by multiplying the volume of HCl used for the elution of the generator in mL by its molarity: Reaction buffer volume in mL = HCl volume in mL x HCl molarity (5 mL x 0.1 N = 0.5 mL of reaction buffer)	For radiolabeling reaction
Solutions for use with IRE Galli Eo generator		
Syringe	**Solution**	**Purpose**
5-mL sterile syringe	3.9 mL sterile water for injection	For preliminary dilution of **Vial 1**
N/A	1.1 mL $^{68}GaCl_3$ in HCl (0.1 M) eluate from generator	Add eluate directly into **Vial 1**
1-mL sterile syringe	**Vial 2 buffer** Calculate the volume (in mL) by multiplying the volume of HCl eluate from the generator in mL by its molarity: Reaction buffer volume in mL = HCl volume in mL x HCl molarity (1.1 mL x 0.1 N = 0.11 mL of reaction buffer)	For radiolabeling reaction

i) Pierce the **Vial 1** septum with a sterile needle connected to a 0.2 µm sterile vented filter (not supplied) to maintain atmospheric pressure within the vial during the reconstitution process.
j) ***Follow the generator specific reconstitution procedures below. Then continue with incubation step k.***

Reconstitution with Eckert & Ziegler GalliaPharm generator

A schematic representation of the radiolabeling procedure is shown in Figure 1.

- Connect the male luer of the outlet line of the GalliaPharm generator to a sterile needle.
- Connect **Vial 1** to the outlet line of the GalliaPharm generator by pushing the needle through the rubber septum and place the vial in a lead shield container.
- Elute the generator directly into the **Vial 1** through the needle according to the instructions for use of the GalliaPharm generator that are supplied by Eckert & Ziegler, in order to reconstitute the lyophilized powder with 5 mL of eluate. Perform the elution manually or by means of a pump.
- At the end of the elution, disconnect the generator from **Vial 1** by removing the needle from the rubber septum, and immediately (do not delay buffer addition more than 10 minutes) add the kit reaction buffer in the 1-mL sterile syringe (the amount of reaction buffer as determined in Table 1).
- Withdraw the syringe and the 0.2 µm sterile air venting filter.

Reconstitution with IRE Galli Eo generator

A schematic representation of the radiolabeling procedure is shown in Figure 2.

- Set the generator for the elution according to manufacturer instructions. Connect a sterile needle to the outlet tube of the generator, turn the button by 90º to loading position then wait 10 seconds before turning the button back to the initial position.
- Reconstitute **Vial 1** with the 3.9 mL of sterile water for injection as per Table 1.
- Add the 0.1 mL reaction buffer to **Vial 1** as per Table 1.
- Connect **Vial 1** to the outlet line of the generator by pushing the needle through the rubber septum.
- Connect one end of the two male luer ends of the sterile extension line to the 0.2 µm sterile vent filter inserted into **Vial 1**.
- Assemble a sterile needle on the second male luer end of the sterile extension line and connect it to a sterile evacuated vial (17 mL minimum volume) by pushing the needle through the rubber septum. The generator elution will start.
- Wait for the elution to be completed (minimum 3 minutes, according to the generator manufacturer instructions for use).
- At the end of the elution, first withdraw the needle from the evacuated vial in order to establish atmospheric pressure into **Vial 1**, then disconnect **Vial 1** from the generator by removing the needle from the rubber septum and remove the 0.2 µm sterile vent filter from **Vial 1**.

Incubation

k) Using a tong, move **Vial 1** to the heating hole of the dry bath, and leave the vial at 95°C (not to exceed 98°C) for at least 7 minutes (do not exceed 10 minutes heating) without agitation or stirring.

l) After 7 minutes, remove the vial from the dry bath, place it in an appropriate lead shield and let it cool down to room temperature for approximately 10 minutes.

m) Assay the whole vial containing the gallium (^{68}Ga) oxodotreotide injection for total radioactivity concentration using a dose calibrator and record the result.

n) Perform the quality controls according to the recommended methods in order to check the compliance with the specifications (see Directions for Quality Control).

o) Prior to use, visually inspect the solution behind a shielded screen for radioprotection purposes. Only use solutions that are clear without visible particles.

p) Keep the vial containing the gallium (^{68}Ga) oxodotreotide injection upright in a radio-protective shield container at a temperature below 25°C until use.
q) After addition of gallium (^{68}Ga) chloride to the reaction vial, use gallium (^{68}Ga) oxodotreotide injection within 4 hours.

Figure 1 – Reconstitution Procedure for Eckert & Ziegler GalliaPharm generator

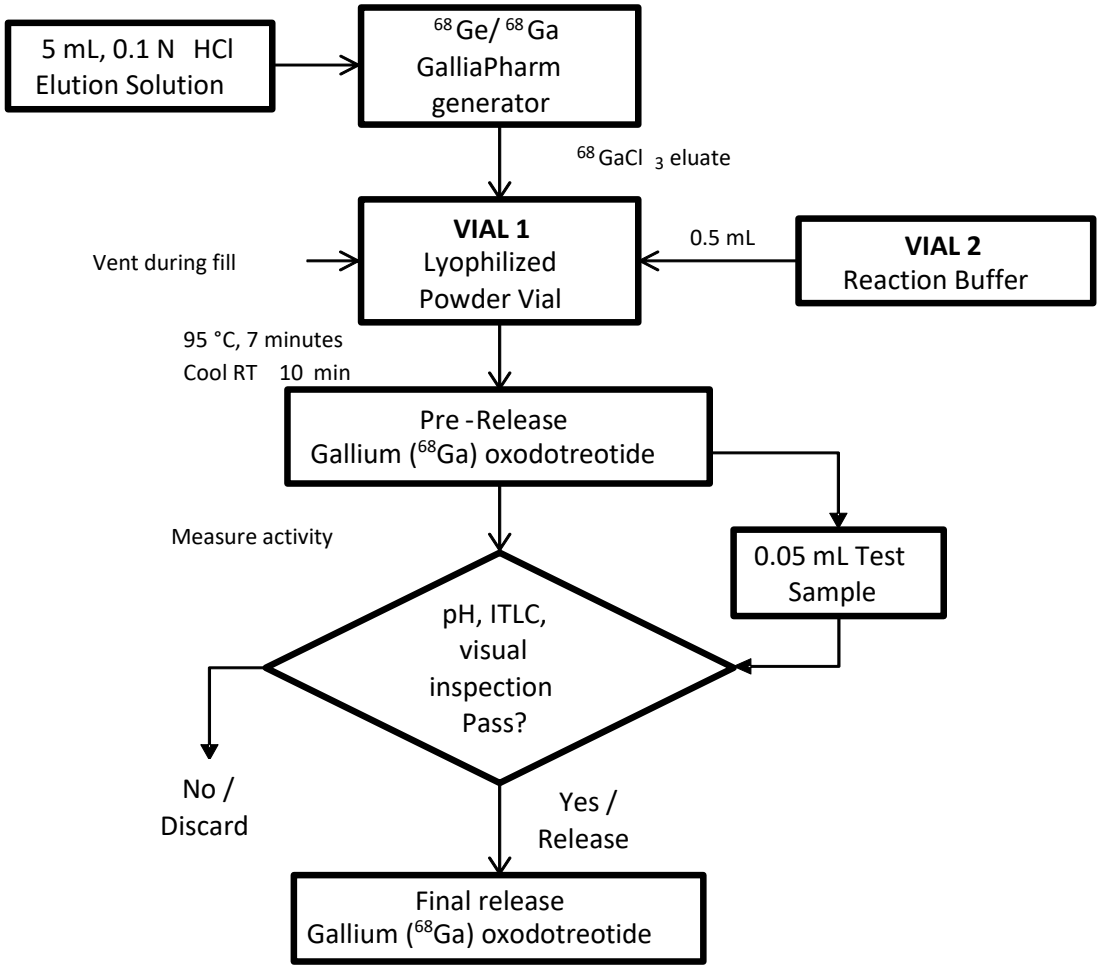
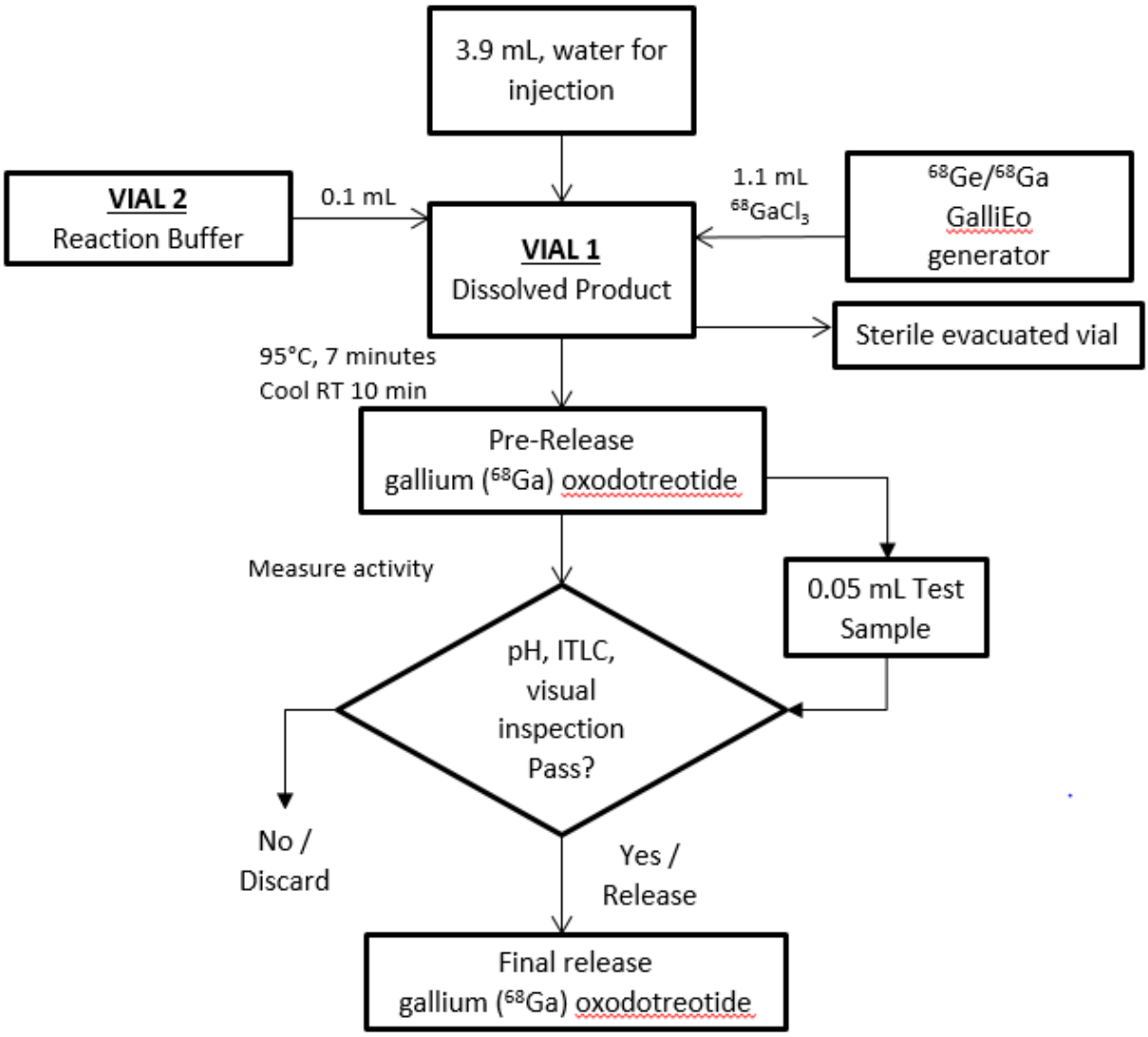


Figure 2 – Reconstitution Procedure for IRE Galli Eo generator



Directions for Quality Control

Perform the quality controls in Table 2 behind a lead glass shield for radioprotection purposes.

Table 2 – Specifications of the Radiolabeled Imaging Product Gallium (^{68}Ga) Oxodotreotide

Test	Acceptance Criteria	Method
Appearance	Colourless and particulate free	Visual Inspection
pH	3.2 to 3.8	pH indicator strips
Labelling Efficiency	gallium (^{68}Ga) oxodotreotide ≥ 95% and Other Ga 68 species ≤ 5%	Thin layer chromatography (ITLC, see details below)

Determine labeling efficiency of gallium (^{68}Ga) oxodotreotide applying one of the following recommended methods.

Obtain the following materials:

- ITLC SA or ITLC SG;
- Ammonium acetate 1M: Methanol (1:1 V/V);
- Developing tank; and
- Radiometric ITLC scanner.

ITLC Method 1 – using ITLC SA or ITLC SG (longer development length)

Perform the following:

a) Pour ammonium acetate 1M: Methanol (1:1 V/V) solution to a depth of 3 to 4 mm in the developing tank, cover the tank, and allow it to equilibrate.
b) Apply a drop of the gallium (^{68}Ga) oxodotreotide injection on a pencil line 1 cm from the bottom of the ITLC strip.
c) Place the ITLC strip in the developing tank and allow it to develop for a distance of 10 cm from the point of application (i.e. to the top pencil mark).
d) Scan the ITLC with a radiometric ITLC scanner.
e) Calculate radiochemical purity (RCP) by integration of the peaks on the chromatogram. Do not use the reconstituted product if the RCP is less than 95%.
f) The retention factor (Rf) specifications are as follows for ITLC SA or ITLC SG:
ITLC SA: Non-complexed ^{68}Ga species, Rf = 0 to 0.1; gallium (^{68}Ga) oxodotreotide, Rf = 0.6 to 0.8.
ITLC SG: Non-complexed ^{68}Ga species, Rf = 0 to 0.1; gallium (^{68}Ga) oxodotreotide, Rf = 0.8 to 1.

ITLC Method 2 – using ITLC SG (shorter development length)

Perform the following:

a) Pour ammonium acetate 1M: Methanol (1:1 V/V) solution to a depth of 3 to 4 mm in the developing tank, cover the tank, and allow it to equilibrate.
b) Apply a drop of the gallium (^{68}Ga) oxodotreotide injection on a pencil line 1 cm from the bottom of an ITLC SG strip.
c) Place the ITLC SG strip in the developing tank and allow it to develop for a distance of 6 cm from the point of application (e.g. to 7 cm from the bottom of the ITLC strip).
d) Scan the ITLC SG strip with a radiometric ITLC scanner.
e) Calculate radiochemical purity (RCP) by integration of the peaks on the chromatogram. Do not use the reconstituted product if the RCP is less than 95%.
f) The retention factor (Rf) specifications are as follows:
Non-complexed ^{68}Ga species, Rf = 0 to 0.1, gallium (^{68}Ga) oxodotreotide, Rf = 0.8 to 1.

4.8 Radiation Dosimetry

Estimated radiation dose per injected activity for organs and tissues of adult patients following an intravenous bolus of gallium (^{68}Ga) oxodotreotide are shown in Table 3. The estimates were taken from different sources (Sandstrom 2013, Josefsson 2018). The absorbed doses for the tissues with higher absorbed dose per unit activities (adrenals, kidney, liver, gall bladder wall, urinary bladder wall, pituitary gland) are those reported by Josefsson (2018), obtained using more updated formalisms, based on ICRP 110 reference voxel phantoms. For the other tissues, the estimated absorbed doses are those reported by Sandstrom (2013), which were obtained using standard phantom-based dosimetry (Stabin 1996 and Stabin 2005).

Estimated radiation effective doses per injected activity for adult and pediatric patients following an intravenous bolus of gallium (^{68}Ga) oxodotreotide are shown in Table 4 (Soares Machado 2016). These effective dose estimates were calculated starting from available gallium (^{68}Ga) oxodotreotide biokinetic data for adults (Sandstrom 2013), using Cristy-Eckerman age-dependent phantoms provided by OLINDA/EXM software.

Gallium (^{68}Ga) decays with a half-life of 68 minutes to stable zinc (^{68}Zn):

- 89% through positron emission with a mean energy of 836 keV followed by photonic annihilation radiations of 511 keV (178%);
- 10% through orbital electron capture (X-ray or Auger emissions); and
- 3% through 13 gamma transitions from five excited levels.

The effective radiation dose resulting from the administration of 150 MBq (4.05 mCi) [within the range of the recommended gallium (^{68}Ga) oxodotreotide injection dose] to an adult weighing 75 kg, is about 3.45 mSv. For an administered activity of 150 MBq (4.05 mCi), the typical radiation dose to the critical organs, which are the urinary bladder wall, the spleen, kidneys and adrenals, are about 6, 37.5, 21 and 16.5 mGy, respectively. Since the spleen has one of the highest physiological uptakes, higher uptake and radiation dose to other organs or pathologic tissues may occur in patients with spleen disorders (e.g. splenectomy and splenosis) (see 7 WARNINGS AND PRECAUTIONS).

Table 3 – Estimated Radiation Absorbed Dose per Unit Activity and Total Injected Activity in Selected Organs and Tissues of Adults after a Gallium (^{68}Ga) Oxodotreotide Injection Dose in Adults

Absorbed Dose per Injection Activity in Selected Organs and Tissues of Adults	mGy/MBq		mGy/150 MBq
	Mean	SD	
Adrenals*	0.11	0.037	16.50
Brain	0.010	0.002	1.50
Breasts	0.010	0.002	1.50
Gallbladder wall*	0.043	0.008	6.45
Lower large intestine wall	0.015	0.002	2.25
Small intestine	0.025	0.004	3.75
Stomach wall	0.013	0.002	1.95
Upper large intestine wall	0.021	0.003	3.15
Heart wall	0.018	0.003	2.70
Kidneys*	0.14	0.048	21.00
Liver*	0.084	0.019	12.60
Lungs	0.006	0.001	0.90
Muscle	0.012	0.002	1.80
Ovaries	0.016	0.001	2.40
Pancreas	0.015	0.002	2.25
Red marrow	0.015	0.003	2.25
Osteogenic cells	0.021	0.005	3.15
Skin	0.010	0.002	1.50

Absorbed Dose per Injection Activity in Selected Organs and Tissues of Adults	mGy/MBq		mGy/150 MBq
	Mean	SD	
Spleen	0.25	0.097	37.50
Testes	0.010	0.001	1.50
Thymus	0.012	0.002	1.80
Thyroid	0.011	0.002	1.65
Pituitary gland*	0.15	0.062	22.50
Urinary bladder wall*	0.040	0.011	6.00
Uterus	0.015	0.002	2.25
Total body	0.014	0.002	2.10
Effective dose per injection activity	**mSv/MBq**		**mSv/150 MBq**
	0.023	0.003	3.45

*Absorbed dose values from Josefsson 2018. The others are taken from Sandstrom 2013.

Table 4 – Estimated Radiation Effective Dose per Unit Injected Activity after a Gallium (^{68}Ga) Oxodotreotide Injection Dose

Age	Effective Dose per Unit Injected Activity (mSv/MBq)
Adult	0.023
15 years	0.025
10 years	0.040
5 years	0.064
1 year	0.13
Newborn	0.35

Table 4 indicates how the effective dose per unit injected activity scales with body habitus in computational models of adult and pediatric patients.

5 OVERDOSAGE

In the event of a radiation overdose, the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body using reinforced hydration and frequent bladder voiding. A diuretic might also be considered. If possible, an estimate of the radioactive dose given to the patient should be performed.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 5 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous	Kit for the preparation of	Vial 1: 5 µg 1,10-phenanthroline; 6 µg gentisic

	gallium (^{68}Ga) oxodotreotide **Vial 1:** 40 µg lyophilized oxodotreotide **Vial 2:** buffer vial	acid; 20 mg D-mannitol Vial 2: 60 mg formic acid; 56.5 mg sodium hydroxide; water for injection

Netspot is supplied as a single-dose kit, containing two vials for preparation of gallium (^{68}Ga) oxodotreotide injection:

- **Vial 1** (reaction vial with lyophilized powder): 40 µg of oxodotreotide; 5 µg of 1,10-phenanthroline; 6 µg gentisic acid; and 20 mg D-mannitol for injection as a white lyophilized powder in a 10-mL glass vial with light-blue flip-off cap.
- **Vial 2** (buffer vial): clear, and colourless reaction buffer solution (60 mg formic acid, 56.5 mg sodium hydroxide in approximately 1 mL volume) in a 10-mL olefin polymer vial with a yellow flip-off cap.

Gallium (^{68}Ga) is obtained from a Germanium 68/Gallium 68 (^{68}Ge/^{68}Ga) generator that is authorized by Health Canada.

After reconstitution with gallium (^{68}Ga) and pH adjustment with Reaction Buffer, Vial 1 contains a sterile solution of gallium (^{68}Ga) oxodotreotide at a strength up to 218 MBq/mL (5.89 mCi/mL).

Description

6.1 Physical Characteristics

Netspot is supplied as a sterile, single-dose kit for preparation of gallium (^{68}Ga) oxodotreotide for injection.

After reconstitution and radiolabeling (see 4 DOSAGE AND ADMINISTRATION), gallium (^{68}Ga) oxodotreotide injection also contains hydrochloric acid as an excipient derived from the generator eluate. The prepared gallium (^{68}Ga) oxodotreotide for injection is a sterile, pyrogen-free, clear, colourless, buffered solution, with a pH between 3.2 and 3.8, having the following physical properties.

Physical data

Gamma constant:	0.67 mrem/hr per mCi at 1 metre [1.8E-4 mSv/hr per MBq at 1 metre]
Specific activity:	Maximum 4.1E7 Ci/g [1.51E18 Bq/g] max

6.2 Table 6 and External Radiation

Table 7 provide the principle radiation emission data, radiation attenuation by lead shielding and physical decay of gallium (^{68}Ga).

Table 6 – Principal Radiation Emission Properties (>1%) of Gallium (^{68}Ga)

Radiation/Emission	% Disintegration	Mean Energy (MeV)
beta+	88%	0.8360
beta+	1.1%	0.3526
Gamma	178%	0.5110

Radiation/Emission	% Disintegration	Mean Energy (MeV)
Gamma	3%	1.0770
X-ray	2.8%	0.0086
X-ray	1.4%	0.0086

6.3 External Radiation

Table 7 – Physical Decay Chart for Gallium (^{68}Ga)

Minutes	Fraction Remaining
0	1.000
15	0.858
30	0.736
60	0.541
90	0.398
120	0.293
180	0.158
360	0.025

7 WARNINGS AND PRECAUTIONS

Please see the 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

General

Netspot should only be handled, prepared and administered by authorized persons in designated clinical settings (see 12 SPECIAL HANDLING INSTRUCTIONS).

Gallium (^{68}Ga) oxodotreotide should be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patients consistent with proper patient management, and to minimize radiation exposure to occupational workers (see 4 DOSAGE AND ADMINISTRATION).

Immune

Hypersensitivity associated symptoms (erythema, pruritus, rash and urticaria) have been rarely reported following Netspot administration. Prior to administration, the patient should be questioned for a history of reactions to Netspot or to other somatostatin analogues.

Radiation Risk

Gallium (^{68}Ga) oxodotreotide contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. To reduce radiation exposure, ensure patients are well hydrated prior to administration of gallium (^{68}Ga)

oxodotreotide and advise patients to drink and void frequently during the first hours following administration.

Patients should be instructed to avoid close contact with infants and pregnant women during the first 12 hours following gallium (^{68}Ga) oxodotreotide administration.

Risk for Image Misinterpretation

The uptake of gallium (^{68}Ga) oxodotreotide reflects the level of somatostatin receptor density in NETs. However, uptake can also be seen in some other tumour types. Increased uptake might also be seen in other pathologic conditions (e.g. thyroid disease or subacute inflammation) or it might occur as a normal physiologic variant (e.g. uncinated process of the pancreas).

The spleen has one of the highest physiological uptakes, therefore spleen disorders (e.g. splenectomy and splenosis) should be considered as a relevant factor for an accurate interpretation of gallium (^{68}Ga) oxodotreotide PET images (see 4.8 Radiation Dosimetry). PET images with gallium (^{68}Ga) oxodotreotide should be interpreted visually and the uptake may need to be confirmed by histopathology or other assessments (see 4 DOSAGE AND ADMINISTRATION).

Long-term endogenous hypercortisolism (e.g. Cushing syndrome) may down regulate somatostatin receptor expression and negatively influence the results of somatostatin receptor imaging with gallium (^{68}Ga) oxodotreotide. Thus, in patients with gastroenteropancreatic neuroendocrine tumours (GEP-NETs) and hypercortisolism, normalization of cortisol levels should be attempted before performing PET with gallium (^{68}Ga) oxodotreotide.

7.1 Special Populations

7.1.1 Pregnant Women

Risk Summary

There are no studies with gallium (^{68}Ga) oxodotreotide in pregnant women to inform any drug-associated risks. However, all radiopharmaceuticals, including gallium (^{68}Ga) oxodotreotide, have the potential to cause fetal harm. Animal reproduction studies have not been conducted with gallium (^{68}Ga) oxodotreotide.

In the Canadian general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is estimated at 3.85% and 5%, respectively.

Clinical Considerations

All female patients of reproductive age should be questioned on the possibility of being pregnant. A pregnancy test should be considered if clinically indicated. Ideally examinations using radiopharmaceuticals, especially those elective in nature in women of childbearing capability should be performed during the first 10 days following the onset of menses.

7.1.2 Breast-feeding

Risk Summary:

There is no information on the presence of gallium (^{68}Ga) oxodotreotide in human milk, the effect on the breastfed infant, or the effect on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for gallium (^{68}Ga) oxodotreotide injection and any potential adverse effects on the breastfed child from gallium (^{68}Ga)

oxodotreotide injection or from the underlying maternal condition.

Clinical Considerations:

Advise a lactating woman to interrupt breastfeeding and pump and discard breast milk for 12 hours after gallium (^{68}Ga) oxodotreotide administration in order to minimize radiation exposure to a breastfed infant. Formula feeding in place of breast feeding may also be considered.

7.1.3 Pediatrics

As documented by available bibliographic data, the safety and efficacy of gallium (^{68}Ga) oxodotreotide in children and adolescents below 18 years of age have not yet been established. The use in children and adolescents must be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group. The effective dose resulting from administration of gallium (^{68}Ga) oxodotreotide may be higher in children than in adults (see 4.8 Radiation Dosimetry).

7.1.4 Geriatrics

Clinical studies of gallium (^{68}Ga) oxodotreotide did not include sufficient numbers of subjects aged 65 and over, to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Clinical trials are conducted under very specific conditions. Therefore, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

The safety of gallium (^{68}Ga) oxodotreotide was evaluated in a survey of the scientific literature. No serious adverse reactions were identified in these studies.

Deppen 2016 reported safety data from a clinical study of 97 patients (41 males, 56 females) with mean age of 54 years. Of these patients, 90 had a proven diagnosis of neuroendocrine tumour (NET) (see 14 CLINICAL TRIALS). Patients were treated with a single dose gallium (^{68}Ga) oxodotreotide (196 MBq, 5.3 mCi), the amount of oxodotreotide peptide administered was 50 µg or less. Safety and toxicity were assessed by comparing vital signs and laboratory values before and after the administration of gallium (^{68}Ga) oxodotreotide. No serious adverse events were observed and no participants had a trial related event requiring additional medical care. Events that were considered clinically relevant were as follows: mild tachycardia in one patient; hyperglycemia in two patients; and increased aspartate aminotransferase in one patient. Other observed variances in blood and physiological measurements were transitory and minor or did not vary out of normal ranges.

8.5 Post-Market Adverse Reactions

The following adverse reactions have been identified during post-approval use of Netspot. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to the drug.

Gastrointestinal Disorders: Nausea and vomiting.

General Disorders and Administration Site Conditions: Injection site pain and burning sensation.

Skin and subcutaneous tissue disorders: Erythema, pruritus, rash and urticaria.

9 DRUG INTERACTIONS

9.3 Drug-Behavioural Interactions

As gallium (^{68}Ga) decays rapidly, interactions with lifestyle factors are not expected.

9.4 Drug-Drug Interactions

Somatostatin analogs
Non-radioactive somatostatin analogs competitively bind to the same somatostatin receptors as gallium (^{68}Ga) oxodotreotide. To prevent interference in visualization, image patients with gallium (^{68}Ga) oxodotreotide PET just prior to dosing with long-acting analogs of somatostatin. Short-acting analogs of somatostatin can be used up to 24 hours before imaging with gallium (^{68}Ga) oxodotreotide.

Corticosteroids
Some evidence exists that corticosteroids can induce down-regulation of somatostatin subtype 2 receptors (SSTR2) receptors. Repeated administration of high-doses of glucocorticosteroids prior to gallium (^{68}Ga) oxodotreotide administration may cause insufficient SST2 receptor expression for adequate visualization of somatostatin receptor-positive NETs.

9.5 Drug-Food Interactions

As gallium (^{68}Ga) oxodotreotide is administered by the intravenous route, interactions with food are not expected.

9.6 Drug-Herb Interactions

As gallium (^{68}Ga) decays rapidly, interactions with herbal products are not expected.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Gallium (^{68}Ga) oxodotreotide binds to somatostatin receptors, with highest affinity for subtype 2 receptors (SSTR2). It binds to cells that express somatostatin receptors including malignant cells, which overexpress SSTR2 receptors. Gallium (^{68}Ga) is a ß+ emitting radionuclide with an emission yield that allows PET imaging.

10.2 Pharmacodynamics

The relationship between gallium (^{68}Ga) oxodotreotide plasma concentrations and successful imaging was not explored in clinical trials.

10.3 Pharmacokinetics

Absorption

Netspot prepared gallium (^{68}Ga) oxodotreotide is administered intravenously, it is thus immediately and completely bioavailable.

Distribution

Gallium (^{68}Ga) oxodotreotide distributes at varying levels in SSTR2-expressing organs such as pituitary, thyroid, spleen, adrenals, kidney, pancreas, prostate, liver, and salivary glands. There is no significant uptake in the cerebral cortex or in the heart, and usually thymus and lung uptakes are low.

Elimination

A total of 12% of the injected dose is excreted in urine in the first four hours post-injection.

Special Populations and Conditions

No studies evaluating the pharmacokinetics of gallium (^{68}Ga) oxodotreotide in special populations were conducted.

11 STORAGE, STABILITY AND DISPOSAL

Netspot is supplied as a single-dose kit for preparation of a single-dose of gallium (^{68}Ga) oxodotreotide for injection. The radionuclide is not part of the kit. Before reconstitution and radiolabeling with gallium (^{68}Ga), the contents of this kit are not radioactive.

The expiry date is indicated on the original outer packaging, and on the vials. This medicinal product must not be used beyond the date indicated on the packaging.

For prolonged storage, store Netspot in its original packaging at room temperature below 25°C (do not freeze). After reconstitution and radiolabeling (see 4 DOSAGE AND ADMINISTRATION) with activities of up to 1110 MBq (30 mCi), keep gallium (^{68}Ga) oxodotreotide injection upright with an appropriate shielding to protect from radiation, at a temperature below 25°C (do not freeze), and for a maximum of 4 hours.

The storage of the radiolabeled product must comply with regulatory requirements for radioactive materials.

12 SPECIAL HANDLING INSTRUCTIONS

Netspot is supplied as a single-dose kit for preparing a single-dose of gallium (^{68}Ga) oxodotreotide for injection. The radionuclide is not part of the kit. Before reconstitution and radiolabeling with gallium (^{68}Ga), the contents of the kit are not radioactive.

Netspot should be prepared, administered and disposed only by authorized persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of the competent official organization.

Always use the principles of time, distance and shielding to minimize the radiation dose, especially to the person administering gallium (^{68}Ga) oxodotreotide.

Recommended protective measures:

- Use disposable plastic, latex or rubber gloves;

- Wear a lab coat, which must be monitored for radioactivity before taken from the laboratory;
- Wear safety glasses;
- Minimize handling time;
- Use tongs to handle unshielded sources and potentially contaminated vessels; and
- Use disposable absorbent liners on trays.

Radiation shielding information:

1. Shielding
   Lead [Pb] Half Value Layer [HVL]: 6 mm

   Tenth Value Layer [TVL]: 17 mm

Table 8 – Radiation Attenuation of 511 keV Photons by Lead (Pb) Shielding

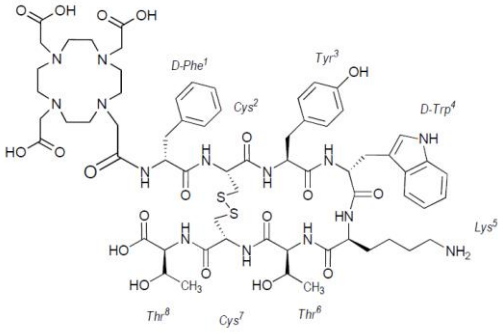
Shield Thickness (Pb) mm	Coefficient of Attenuation
6	0.5
12	0.25
17	0.1
34	0.01
51	0.001

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Oxodotreotide, also known as dotatate or DOTA-0-Tyr3-Octreotate, is a cyclic 8 amino acid peptide with a covalently bound metal chelator (DOTA). The peptide has the amino acid sequence: H-D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH, and contains one disulfide bond. Oxodotreotide has a molecular weight of 1435.6 Daltons and its chemical structure is shown below.

Proper name:	oxodotreotide
Chemical name:	[(4,7,10-Tricarboxymethyl-1,4,7,10-tetrazacyclododec-1-yl)acetyl]-(D)-Phenylalanyl-(L)Cysteinyl-(L)-Tyrosyl-(D)-Tryptophanyl-(L)-Lysyl-(L)-Threoninyl-(L)-Cysteinyl-(L)-Threonine-cyclic(2-7)disulfide]
Structural formula:	

Product Characteristics:

NETSPOT® is a kit with the following components:

- **Vial 1** (10-mL Ultra inert Type I Plus glass vial, light-blue flip-off cap): 40 µg of oxodotreotide; 5 µg 1,10-phenanthroline; 6 µg gentisic acid; and 20 mg mannitol as lyophilized powder.
- **Vial 2** (10-mL cyclic olefin polymer vial, with a yellow flip-off cap): reaction buffer solution (approximately 1 mL volume); 60 mg formic acid; 56.5 mg sodium hydroxide; and water for injection.

After reconstitution and radiolabeling (see 4 DOSAGE AND ADMINISTRATION), gallium (^{68}Ga) oxodotreotide injection also contains hydrochloric acid as an excipient derived from the generator eluate. The prepared gallium (^{68}Ga) oxodotreotide for injection, is a sterile, pyrogen-free, clear, colourless, buffered solution with a pH between 3.2 to 3.8.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

The safety and clinical benefit of Netspot is based on a systematic review of the scientific literature on the use of gallium (^{68}Ga) oxodotreotide as a radiodiagnostic agent in the management of patients with NETs. No serious adverse reactions were identified in these literature reports.

The efficacy of gallium (^{68}Ga) oxodotreotide was investigated in three clinical studies as described below.

Deppen 2016

In Deppen 2016, 97 adult patients (41 male, 56 female) with known or suspected NETs were evaluated with gallium (^{68}Ga) oxodotreotide PET. Mean age was 54 ± 11 years. Patients received a single i.v. dose of 196 MBq gallium (^{68}Ga) oxodotreotide and PET/CT images were collected beginning at 65 minutes (range 55-93 minutes) after injection. The gallium (^{68}Ga) oxodotreotide images were read by two independent readers blinded to clinical information. The reads were compared to CT and/or MR images and to indium (^{111}In) pentetreotide images obtained with Single Photon Emission Computed Tomography (SPECT) within previous three years.

Among 78 patients in whom CT and/or MRI images and indium (^{111}In) pentetreotide images were available, gallium (^{68}Ga) oxodotreotide PET was in agreement with the reference standard in 74 patients. Out of 50 patients with NETs as per the reference standard, gallium (^{68}Ga) oxodotreotide was positive in 48 patients including 13 patients in whom indium (^{111}In) pentetreotide was negative. Gallium (^{68}Ga) oxodotreotide was negative in 26 out of 28 patients in whom the reference standard was negative.

Haug 2012

Haug 2012 reported results from a study in 104 patients (52 men, 52 women) with suspected NETs due to clinical symptoms, elevated levels of tumour markers, or indeterminate tumours suggestive of NET. Mean age ± SD was 57.6 ± 16.1 years (range 1-83 years). Patients received a single 200 MBq dose of gallium (^{68}Ga) oxodotreotide and PET/CT scans were taken 60 minutes later. Diagnostic performance of gallium (^{68}Ga) oxodotreotide PET in localizing tumour sites was retrospectively assessed using a reference standard – histopathology (n=49) or clinical follow-up of up to five month duration (n=55). Images were interpreted by consensus between two on-site readers who were not blinded to clinical information. NET sites were localized by reference standard in 36 patients (all by histopathology). Out of these, gallium (^{68}Ga) oxodotreotide was positive, correctly identifying a NET site, in 29 out of 36 patients and was falsely negative in seven. In 68 patients with no NET identified by a reference standard, the images were negative in 61 and falsely positive in seven patients.

Haug 2014

Haug 2014 reported results of a study which involved 63 adult patients (34 men, 29 women) evaluated for NET recurrence using gallium (^{68}Ga) oxodotreotide PET/CT scans. Patients were treated with a single 200 MBq i.v. dose and PET/CT scans were taken 60 minutes later. Gallium (^{68}Ga) oxodotreotide images were interpreted independently by two central readers blinded to clinical information.

Reader 1 correctly localized NETs in 23 out of 29 reference standard-positive patients and reader 2 correctly localized NETs in 22 such patients. In 34 patients with no NET identified by a reference standard, reader 1 was correct in 29 patients and reader 2 in 32.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

The safety of gallium (^{68}Ga) oxodotreotide was assessed in an extensive non-clinical package including safety pharmacology, toxicology and genotoxicity studies conducted with the non-radioactive surrogate lutetium (^{175}Lu) oxodotreotide, and the results showed that the product has a favourable safety profile. Due to the lower mass dose of DOTA-peptide in a single dose of gallium (^{68}Ga) oxodotreotide compared to lutetium (^{177}Lu) dotatate administered to patients, the safety margin of the DOTA-peptide relative to the gallium (^{68}Ga) dotatate is even higher compared to lutetium (^{177}Lu) dotatate.

Regarding the potential toxicity related to the radioactivity, this is based on dosimetric assessments in animals and humans, and on the clinical experience showing a good safety profile for this agent. The radiation absorbed doses in the different organs and the total effective dose are known for humans (see 4.8 Radiation Dosimetry).

General Toxicology

- An acute toxicity study was conducted in female rats using a non-radioactive form of lutetium (^{177}Lu) oxodotreotide (lutetium (^{175}Lu) oxodotreotide). The compound was given intravenously, as a bolus, to three groups of three animals each at increasing doses (1.2, 4.8 and 20.5 mg/kg, respectively) at an administration volume of 5 mL/kg. The administered doses were about 40, 170 and 700 fold the recommended human dose. Animals were observed for 11 to 14 days after the treatment.

  The results of the study showed that the compound was well tolerated after single i.v. administration, without inducing any toxicity signs, up to the highest tested dose. Therefore, the Maximum Tolerated Dose (MTD) in female rats is higher than 20.5 mg/kg.

- In the MTD study conducted in male and female dogs, lutetium (^{175}Lu) oxodotreotide formulation was administered intravenously, as a bolus, at ascending doses from 0.4 to 3.2 mg/kg (0.4, 0.8, 1.6 and 3.2 mg/kg, that is about 50 to 400 fold the recommended human dose) to a group of one male and two female dogs, and as single doses of 6.4 mg/kg and 10 mg/kg (about 800 and 1200 fold the intended human dose) to two groups of one male and one female dog each. The administration volume was 2.5 mL/kg. Animals were observed for a 13 to 15 day period following administration.

  The results of this MTD study in dogs show that intravenous bolus of lutetium (^{175}Lu) oxodotreotide did not induce mortality and any evident drug-related signs of toxicity in male and female Beagle dogs, except for soft to liquid faeces observed on the days following treatment at all doses, and spread red (at 0.4 to 3.2 mg/kg) or dark red (at 6.4 and 10 mg/kg) areas on the mucosa of the gastro-intestinal tract (jejunum, duodenum or rectum). No changes on haematology, coagulation and clinical chemistry parameters were observed. Based on the results of this study, the doses chosen for the repeated dose toxicity study in dogs were 0.08, 0.5 and 3.2 mg/kg.

- In the repeat dose toxicity study in rats lutetium (^{175}Lu) oxodotreotide formulation was administered intravenously at 1.25, 5 or 20 mg/kg (that is, 40, 170, and 700 fold the recommended human dose) for four times, once every two weeks, to mimic the schedule applied in human but with a reduced time between treatments to increase the possibility of occurrence of any toxic effects linked to the non-radioactive compound. The treatment groups were composed of 10 male and 10 female rats. The study included additional animals (five males and five females)

administered with the vehicle and with the highest dose, in order to study the reversibility, persistence or delayed occurrence of toxic effects for three months post-treatment.

The compound induced no mortality and no major signs of toxicity. The primary target organ was the pancreas, a high SSTR2 expressing organ. Pancreatic acinar apoptosis occurred at lutetium (^{175}Lu) oxodotreotide intermediate and high doses (≥ 5 mg/kg). These findings were consistent with high uptake of the peptide in the pancreas in animal biodistribution studies.

Therefore, the no-observed-effect level (NOEL) corresponds to 1.25 mg/kg that is around 40 times the human dose.

- A repeated dose toxicity study was also conducted in dogs. Lutetium (^{175}Lu) oxodotreotide formulation was administered intravenously four times, once every two weeks, at three different doses (0.08, 0.5 and 3.2 mg/kg, corresponding to about 10, 65 and 400 fold the recommended human dose).

  The compound induced no mortality and no major signs of toxicity at any dose tested. The signs observed (salivation, vocalisation and soft to liquid faeces, associated at the highest dose to slight increase in body temperature and a slight decrease of food consumption) were mild and reversible. As for rats, the primary target organ was the pancreas. Moderate and reversible pancreatic acinar apoptosis occurred in few animals at doses ≥ 0.5 mg/kg.

  At recovery sacrifice, there was no incidence of pancreatic acinar apoptosis in the four male dogs of the control group and male dogs of the group treated with the highest dose. In female dogs there was a single case of pancreatic acinar apoptosis in the highest dose group and also in the control group, both at minimal degree, confirming the reversible nature of this change.

  Acinar apoptosis was the only histological change observed in the high dose group. Therefore, considering also the reversibility of this change after recovery, 3.2 mg/kg was considered to be the no-observed-adverse-effect level (NOAEL) in the repeated dose toxicology study in dogs, which is equivalent to 400 times the human dose.

- In addition to the toxicology studies mentioned above, performed with (^{175}Lu) oxodotreotide, a single-dose toxicity and local tolerability study was performed in rats using gallium (^{68}Ga) oxodotreotide formulation (including all excipients at the final pH of 3.5 ± 0.3). This study showed that the kit formulation is safe and well tolerated, at a dose corresponding to about 450 times the dose in humans.

Carcinogenicity

No long-term animal studies have been performed to evaluate carcinogenic potential of gallium (^{68}Ga) oxodotreotide. However, radiation is a carcinogen and mutagen.

Genotoxicity

As with other radiopharmaceuticals, there may be increased risk of chromosome damage.

Lutetium (^{175}Lu) oxodotreotide formulation was examined for the ability to induce gene mutations in tester strains of *Salmonella typhimurium* and *Escherichia coli*, as measured by reversion of auxotrophic strains to prototrophy. The five tester strains TA1535, TA1537, TA98, TA100 and WP2 uvrA were used. Experiments were performed both in the absence and presence of metabolic activation, using liver S9 fraction from rats.

Lutetium (^{175}Lu) oxodotreotide formulation was also assayed for its ability to induce mutations (5-trifluorothymidine resistance) in L5178Y TK+/- mouse lymphoma cells after *in vitro* treatment, in the absence and presence of S9 metabolizing system, using a fluctuation method.

These genotoxicity studies showed that lutetium (^{175}Lu) oxodotreotide formulation does not induce mutation at the TK locus of L5178Y mouse lymphoma cells *in vitro*, nor reverse mutation in *Salmonella typhimurium* or *Escherichia coli* in the absence or presence of S9 metabolic activation.

Reproductive and Developmental Toxicology

No long-term animal studies have been performed to evaluate whether gallium (^{68}Ga) oxodotreotide affects fertility in males and females.

Special Toxicology

The effects of lutetium (^{175}Lu) oxodotreotide on blood pressure, heart rate, body temperature and electrocardiogram (duration of PR, PQ, QT and QRS) after single i.v. administration were investigated in dogs. The compound did not show any effect on cardiac conduction times or body temperature and did not cause arrhythmia at the doses tested (from 0.08 to 0.8 mg/kg).

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

NETSPOT®

40 microgram kit for preparation of gallium (^{68}Ga) oxodotreotide injection

Read this carefully before you start taking **Netspot®**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Netspot**.

Serious Warnings and Precautions

- Because gallium (^{68}Ga) oxodotreotide injection is a radiopharmaceutical (radioactive substance), it can only be given by doctors and other health professionals who are specially trained and experienced in the safe use and handling of these substances.

What is Netspot used for?

Netspot is a kit used:

- To prepare the radiopharmaceutical (radioactive) product **gallium (^{68}Ga) oxodotreotide injection,** which is used to find and diagnose certain cancer tumours called somatostatin receptor positive neuroendocrine tumours (NETs).

How does Netspot work?

The active ingredient in Netspot is called oxodotreotide. This ingredient binds to tumours that have certain proteins (somatostatin receptors) on their surface. Before it can be used, Netspot must be mixed with another solution and radioactive gallium (^{68}Ga) chloride to make gallium (^{68}Ga) oxodotreotide. This process is called radiolabeling.

Gallium (^{68}Ga) oxodotreotide injection prepared using the Netspot kit contains a small amount of radioactivity. After it is injected into a vein, gallium (^{68}Ga) oxodotreotide can help doctors see parts of the body containing somatostatin receptors on their surface, including some types of tumours. Your doctor will use a procedure called positron emission tomography (PET) to develop a picture of where gallium (^{68}Ga) oxodotreotide has gone in your body. This picture will help your doctor locate tumours and abnormal cells. This picture provides your doctors with valuable information about your disease.

The use of gallium (^{68}Ga) oxodotreotide involves exposure to small amounts of radioactivity. Before you are treated with gallium (^{68}Ga) oxodotreotide, your doctor will determine whether the benefits of gallium (^{68}Ga) oxodotreotide outweigh the potential risks due to radiation exposure.

What are the ingredients in Netspot?

Medicinal ingredients: oxodotreotide, which is combined with the radioactive substance gallium.

Non-medicinal ingredients: 1,10-phenanthroline; gentisic acid; mannitol; formic acid; sodium hydroxide; and water for injection.

Netspot comes in the following dosage forms:

Kit for the preparation of gallium (^{68}Ga) oxodotreotide for injection.

Do not use Netspot if:

- If you are allergic to gallium (^{68}Ga) oxodotreotide or any of the other ingredients of this medicine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Netspot. Talk about any health conditions or problems you may have, including if you:

- Have experienced any signs of allergic reaction after previous administration of Netspot prepared gallium (^{68}Ga) oxodotreotide or other somatostatin analogs;
- Are under 18 years of age;
- Have signs of dehydration (feeling very thirsty) before or after the examination;
- Have any other medical condition as these could affect the interpretation of the image;
- Have been taking other medicines such as somatostatin-type drugs, and glucocorticoids, which may interact with Netspot;
- Are pregnant or believe you may be pregnant; and/or
- Are breast-feeding.

Other warnings you should know about:

Children and adolescents

The safety and efficacy of this medicine in children and adolescents under 18 years of age has not yet been established.

Pregnancy and breast feeding

If you are breast-feeding the nuclear medicine doctor may either delay the medical procedure until you no longer breast-feed or ask you to stop breastfeeding and to collect then discard your milk until there is no radioactivity in your body (usually 12 hours after treatment with Netspot). Be sure to ask your nuclear medicine doctor when you can resume breast-feeding.

Netspot contains sodium

This medicine contains up to 32.4 mg of sodium per dose.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Netspot:

- Other somatostatin drugs – you may be asked to stop and/or change your treatment for a short period of time while receiving gallium (^{68}Ga) oxodotreotide.
- Corticosteroids – speak to your doctor if you are taking a corticosteroid.

How to take Netspot:

- There are strict laws on the use, handling and disposal of radiopharmaceutical products. Netspot prepared gallium (^{68}Ga) oxodotreotide will be given to you by a healthcare professional who is experienced in the use of radiopharmaceuticals.

Usual dose:

The doctor or specialist supervising the procedure will decide on the dose of Netspot prepared gallium (^{68}Ga) oxodotreotide you will receive. The dose will be the smallest amount needed to get the desired information. The dose is based on your weight. The recommended dose for an adult is usually 100 MBq to 200 MBq (MBq = megabecquerel, which is the unit used to express radioactivity).

Administration of Netspot prepared gallium (^{68}Ga) oxodotreotide and conduct of the procedure:

- Netspot prepared gallium (^{68}Ga) oxodotreotide is administered by intravenous injection (directly into the vein);
- A single injection is enough for your doctor to conduct the test and make a diagnosis; and
- You will be asked to urinate just before the test. After injection, you will be offered something to drink and you will be asked to urinate as often as possible.

After gallium (^{68}Ga) oxodotreotide administration, you should:

- Avoid any close contact with young children and pregnant women for 12 hours after the injection; and
- Urinate frequently in order to eliminate the medicine from the body.

The nuclear medicine doctor will tell you if you need to take any special precautions after receiving this medicine. Contact your nuclear medicine doctor if you have any questions.

Duration of the procedure:

Your nuclear medicine doctor will inform you about the usual amount of time the procedure requires.

Overdose:

An overdose is unlikely because you will only receive a single dose in a controlled clinical setting. However, in the case of an overdose, you will receive the appropriate treatment. Drinking water and emptying your bladder frequently will help remove the medicine from your body more quickly.

Should you have any further questions on the use of this medicine, please ask your doctor who supervises the procedure.

What are possible side effects from using Netspot?

These are not all the possible side effects you may have when taking Netspot. If you experience any side effects not listed here, tell your healthcare professional. In a literature report of a clinical study with gallium (^{68}Ga) oxodotreotide, there were no serious adverse events reported and no participants had a trial related event requiring additional medical care, however, there were rare reports of mild changes in heart rate, increased liver protein (aspartate amino transferase) and increased blood sugar.

Short-term non-serious nausea, vomiting, injection site reactions (pain, burning sensation), hives, rash, redness and itching have been reported following Netspot prepared gallium (^{68}Ga) oxodotreotide administration.

Serious side effects and what to do about them		
Symptom / effect	**Talk to your healthcare professional**	
	Only if severe	**In all cases**
Injection site reactions (itching, swelling, redness, warm feeling at the injection site)		X
Nausea and vomiting		X

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

You will not have to store this medicine. This medicine is stored under the responsibility of your healthcare specialist.

If you want more information about Netspot:

- Talk to your healthcare professional; and/or
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); or the manufacturer's website (https://www.novartis.ca).

This leaflet was prepared by Novartis Pharmaceuticals Canada Inc.

Last Revised Feb 28, 2024

NETSPOT is a registered trademark