ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Axumin 1,600 MBq/mL solution for injection
Axumin 3,200 MBq/mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Axumin 1,600 MBq/mL solution for injection

Each mL of solution contains 1,600 MBq of fluciclovine (^{18}F) at the date and time of calibration (ToC).

The activity per vial ranges from 1,600 MBq to 16,000 MBq at the date and ToC.

Axumin 3,200 MBq/mL solution for injection

Each mL of solution contains 3,200 MBq of fluciclovine (^{18}F) at the date and ToC.

The activity per vial ranges from 3,200 MBq to 32,000 MBq at the date and ToC.

Fluorine (^{18}F) decays to stable oxygen (^{18}O) with a half-life of 110 minutes by emitting a positronic radiation of maximum energy of 634 keV, followed by photonic annihilation radiations of 511 keV.

Excipients with known effect

Each mL of solution contains 7.7 mg of sodium.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Axumin is indicated for positron emission tomography (PET) imaging to detect recurrence of prostate cancer in adult men with a suspected recurrence based on elevated blood prostate specific antigen (PSA) levels after primary curative treatment.

For the limitations in the interpretation of a positive scan, see section 4.4 and 5.1.

4.2 Posology and method of administration

A PET scan with fluciclovine (^{18}F) should be administered by appropriately qualified healthcare professionals.

Images should only be interpreted by readers trained in the interpretation of PET images with fluciclovine (^{18}F).

Posology

The recommended activity for an adult is 370 MBq fluciclovine (^{18}F).

Special populations

Elderly
No dose adjustment required.

Renal and hepatic impairment
Axumin has not been studied in patients with renal or hepatic impairment.
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

Paediatric population
There is no relevant use of fluciclovine (^{18}F) in the paediatric population.

Method of administration

Axumin is for intravenous use.

The activity of fluciclovine (^{18}F) has to be measured with an activimeter immediately prior to injection.

Axumin should be administered as a bolus intravenous injection. The recommended maximum volume of injection of undiluted Axumin is 5 mL. Axumin may be diluted with sodium chloride 9 mg/ml (0.9%) solution for injection by a factor of 8. The injection should be followed by an intravenous flush of sterile sodium chloride 9 mg/ml (0.9%) solution for injection to ensure full delivery of the dose.

Axumin is for multidose use.

For instructions on dilution of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

Image acquisition
The patient should be positioned supine with arms above the head. A computed tomography (CT) scan should be obtained for attenuation correction and anatomic correlation. PET scanning should begin from 3-5 minutes (target 4 minutes) after completion of the injection; an acquisition time of 3 minutes per bed position is recommended. Increasing the duration of acquisition over the pelvis may increase the sensitivity of detection of disease. It is recommended that image acquisition should start from mid-thigh and proceed to the base of the skull. Typical total scan time is between 20-30 minutes.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

4.4 Special warnings and precautions for use

Individual benefit/risk justification

For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should, in every case, be as low as reasonably achievable to obtain the required diagnostic information.

The PSA value may affect the diagnostic performance of fluciclovine (^{18}F) PET (see section 5.1, Pharmacodynamic properties).

Renal impairment

Careful consideration of the benefit/risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population

For information on use in the paediatric population, see section 4.2.

Patient preparation

It should be recommended to the patient that they do not undertake any significant exercise for at least a day before the fluciclovine (^{18}F) scan.

Prior to administration of fluciclovine (^{18}F), patients should not eat or drink for at least 4 hours (other than small amounts of water for taking medicinal products).

In order to mitigate the quantity and intensity of early excretion into the bladder, which may mask or mimic local prostate cancer recurrence, patients should be informed that they may void at the latest 60 minutes before injection of fluciclovine (^{18}F), and should then refrain from voiding until after the scan has been completed.

Interpretation of fluciclovine (^{18}F) images and limitations of use

Fluciclovine (^{18}F) images should be interpreted by appropriately trained personnel.

PET images with fluciclovine (^{18}F) should be interpreted visually. Suspicion of cancer in sites typical for prostate cancer recurrence is based on fluciclovine (^{18}F) uptake in comparison with tissue background. For small lesions (<1 cm diameter) focal uptake greater than blood pool should be considered suspicious for cancer. For larger lesions, uptake equal to or greater than bone marrow is considered suspicious for cancer.

The impact of quantitative/semiquantitative measurement of fluciclovine (^{18}F) uptake as an aid to image interpretation has not been assessed.

Image interpretation errors can occur with PET with fluciclovine (^{18}F) (see section 5.1).

Fluciclovine (^{18}F) uptake is not specific for prostate cancer and may occur with other types of cancer, prostatitis and benign prostatic hyperplasia. False-positive cases have been also described in association with an inflammatory response after cryotherapy and radiation artefacts in patients previously treated with radiotherapy. Clinical correlation, which may include histopathological evaluation of the suspected recurrence site, should be considered where appropriate.

The use of either intravenous iodinated CT contrast or oral contrast media is not required to interpret fluciclovine (^{18}F) PET images.

The detection of prostate cancer recurrence in prostate/prostate bed, regional lymph nodes, bone, soft tissue and non-regional lymph nodes by fluciclovine (^{18}F) PET has been reported.

Diagnostic performance of fluciclovine (^{18}F) to detect recurrences has not been investigated in patients with a suspected recurrence based on elevated blood PSA levels after primary radical treatment with a recent positive whole-body bone scintigraphy.

After the procedure

The patient should be encouraged to drink sufficient amounts and void as often as possible during the first hours after the scan in order to reduce radiation exposure of the bladder.

Close contact with infants and pregnant women should be restricted during the initial 12 hours following the injection.

Specific warnings

This medicinal product contains up to 39 mg sodium in each injected dose, equivalent to 2% of the WHO recommended maximum daily intake of 2g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

The impact of anti-mitotic agents and colony stimulating factors on uptake of fluciclovine in patients with prostate cancer has not been studied.

4.6 Fertility, pregnancy and lactation

Fluciclovine (^{18}F) is not indicated for use in women.

Fertility

No studies on fertility have been performed.

4.7 Effects on ability to drive and use machines

Axumin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 8.2 mSv when the maximal recommended activity of 370 MBq is administered these adverse reactions are expected to occur with a low probability.

Tabulated list of adverse reactions

Adverse reactions were reported commonly (≥ 1/100 to < 1/10) during clinical studies.
They are listed below by MedDRA body system organ class.

MedDRA system organ class	**Adverse reactions**
Nervous system disorders	Dysgeusia
Respiratory thoracic and mediastinal disorders	Parosmia
General disorders and administration site conditions	Injection site reactions

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In the event of administration of a radiation overdose with fluciclovine (^{18}F) the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis, frequent micturition and defecation. It might be helpful to estimate the effective dose that was applied.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceuticals, other diagnostic radiopharmaceuticals for tumour detection, ATC code: V09IX12.

Mechanism of action

Fluciclovine (^{18}F) is a synthetic amino acid which is transported across mammalian cell membranes by amino acid transporters such as LAT-1 and ASCT2. The activities of LAT-1 and ASCT2 are known to be upregulated in prostate cancer, providing a mechanism for the enhanced accumulation of fluciclovine (^{18}F) in prostate cancer.

A quantitative correlation between fluciclovine uptake and enhanced fluciclovine influx into cells was not assessed *in vivo* in healthy volunteers or prostate cancer patients.

Pharmacodynamic effects

At the chemical concentrations used for diagnostic examinations, fluciclovine (^{18}F) does not appear to have any pharmacodynamic activity.

Clinical efficacy and safety

The pivotal efficacy data derives from 115 patients recruited into the BED-001 study at Emory University. Patients were adult and elderly men presenting with suspected recurrence, based on elevated blood PSA levels after primary curative treatment of localised prostate cancer and with negative bone scintigraphy. Patients with non-surgical therapy were treated at least 2 years before. Fluciclovine (^{18}F) PET-CT was restricted to the abdomino-pelvic region.

Histopathology standard of truth data was available for 99 of the 115 subjects. Histological assessment of extraprostatic sites (either regional lymph nodes or distant sites) was only conducted for sites with positive image findings.

The diagnostic performance of fluciclovine (^{18}F) PET-CT for the detection of recurrence overall (at any location), and in 3 different locations (prostate/bed, pelvic lymph nodes, and distant metastases) is shown in Table 1. Distant metastases involved distal lymph nodes, soft tissue and bone.

Table 1. Patient and region based diagnostic performance of fluciclovine ^{18}F PET *vs* histopathology

	Patient based	Location		
		Prostate & prostate bed	Pelvic lymph nodes	Extraprostatic (pelvic and distal recurrence)
N	105	97	24	29
True positive n (%)	73 (69.5)	57 (58.8)	23 (95.8)	27 (93.1)
False positive n (%)	19 (18.1)	27 (27.8)	1 (4.2)	2 (6.9)
True negative n (%)	12 (11.4)	12 (12.4)	0 (0.0)	0 (0.0)
False negative n (%)	1 (1.0)	1(1.0)	0 (0.0)	0 (0.0)
Sensitivity [95% CI]	98.6% (73/74) [92.7 - 100%]	98.3% (57/58) [90.8 - 100%]	100% (23/23) [85.2 - 100%]	100% (27/27) [87.2 - 100%]
Specificity [95% CI]	38.7% (12/31) [21.8 - 57.8%]	30.8% (12/39) [17.0 - 47.6%]		
Positive likelihood ratio [95% CI]	1.61 [1.22 - 2.13]	1.42 [1.15 - 1.75]		
Negative likelihood ratio [95% CI]	0.03 [0 - 0.26]	0.06 [0.01 - 0.41]		

Using the findings of other relevant imaging modalities and clinical follow-up as reference standard in the recruited population, patient-based sensitivity and specificity of fluciclovine (^{18}F) PET-CT for detection of prostate/prostate bed recurrences were 94.7% (89/94) (95%CI: 88.0-98.3%) and 54.8% (17/31) (95%CI:36-72.7%), respectively. For detection of extraprostatic recurrences (regional lymph node and/or distal metastases) sensitivity was 84.2% (32/38) (95%CI: 68.7-94%) and specificity was 89.7% (78/87) (95%CI: 81.3-95.2%), respectively.

The patient-based diagnostic performance of fluciclovine (^{18}F) PET-CT by blood PSA level is shown in Table 2.

Table 2. Effect of blood PSA level on the patient-based diagnostic performance of fluciclovine (^{18}F) PET-CT at BED-001 Emory

	PSA (ng/mL)			
	≤1.05	>1.05 - ≤3.98	>3.98 - ≤8.90	>8.90
No. subjects in analysis	16	31	25	27
True positive (%)	3 (18.8)	23 (74.2)	20 (80)	23 (85.2)
False positive (%)	4 (25)	5 (16.1)	4 (16)	4 (14.8)
True negative (%)	8 (50)	3 (9.7)	1 (4)	
False negative (%)	1 (6.3)	0 (0)	0 (0)	
Sensitivity [95% CI]	75% (3/4) [19.4 - 99.4%]	100% (23/23) [85.2 - 100%]	100% (20/20) [83.2 – 100%]	100% (23/23) [85.2 – 100%]
Specificity [95% CI]	66.7% (8/12) [34.9 - 90.1%]	37.5% (3/8) [8.5 - 75.5%]	20% (1/5) [0.5 - 71.6%]	

An additional study BED002 conducted a blinded read of fluciclovine (^{18}F) PET-CT images from the Emory subset data in BED-001 study by 3 readers. Blinded reads were compared with the histopathological standard of truth. The patient-based sensitivity of fluciclovine (^{18}F) was higher than 88.6% for all three readers while specificity ranged from 17.2-53.6%.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Axumin in one or more subsets of the paediatric population in diagnosis of amino acid metabolism in solid tumours (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Distribution

Fluciclovine (^{18}F) distributes immediately following administration to the liver (14% of administered activity), pancreas (3%), lung (7%), red bone marrow (12%) and heart wall (4%).
Fluciclovine is not incorporated into proteins. Fluciclovine is not metabolised *in vivo*.

Organ uptake

Fluciclovine (^{18}F) accumulates in prostate cancer and other types of cancer but also in normal tissues and some other prostate pathologies (such as benign prostatic hyperplasia, chronic prostatitis, high grade prostatic intraepithelial hyperplasia). In addition, fluciclovine uptake may be increased by an inflammatory reaction to recent radiotherapy or cryotherapy.

Fluciclovine (^{18}F) is preferentially taken up into prostate cancer cells compared with surrounding normal tissues. Uptake by tumours is rapid, with the highest tumour-to-normal tissue contrast between 4 and 10 minutes after injection and continuing for around 30 minutes, with a 61% reduction in mean tumour uptake at 90 minutes after injection.

Washout of activity from most organs and tissues (with the exception of the pancreas) is slow. Activity in the brain is low. With increasing time post injection, distributed uptake is apparent and is mostly associated with skeletal muscle. Washout of ^{18}F activity from the blood is such that about half of the maximum ^{18}F concentration in blood is reached by about 1 hour after administration.

Elimination

The major route of elimination is via the renal pathway. Urinary excretion is slow, reaching approximately 3% of administered radioactivity within 4 hours and 5% within 24 hours.

Half-life

The effective half-life of fluciclovine (^{18}F) equates to the radioactive half-life of fluorine (^{18}F), which is approximately 110 minutes.

Renal/Hepatic impairment

The pharmacokinetics in patients with renal or hepatic impairment have not been characterised.

In *in vitro* studies, fluciclovine (^{18}F) was not taken up by common drug transporters indicating a negligible potential for medicinal product interactions.

5.3 Preclinical safety data

Toxicological studies with rats and dogs have demonstrated that with a single intravenous injection no deaths were observed. Toxicity with repeated administration of up to 1000 mcg/kg/day over 14 days in rats and dogs was not observed. This medicinal product is not intended for regular or continuous administration. Long-term carcinogenicity studies have not been carried out.

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate
Concentrated hydrochloric acid
Sodium hydroxide
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in sections 6.6 and 12.

6.3 Shelf life

Axumin 1,600 MBq/mL solution for injection

8 hours from the ToC.

Axumin 3,200 MBq/mL solution for injection

10 hours from the ToC.

In-use

Chemical and physical in-use stability has been demonstrated for Axumin 1,600 MBq/mL for 8 hours and for Axumin 3,200 MBq/mL for 10 hours.

From a microbiological point of view, unless the method of opening/ dose withdrawal/dilution precludes the risk of microbiological contamination, the medicinal product should be used immediately.

If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

Axumin is supplied in a 10 mL or 15 mL type 1 glass vial sealed with a fluoro-coated chlorobutyl, chlorobutyl or bromobutyl rubber closure and aluminium overseal.

Axumin 1,600 MBq/mL solution for injection

One vial contains 1 to 10 mL of solution, corresponding to 1,600 to 16,000 MBq at calibration time.

Axumin 3,200 MBq/mL solution for injection

One vial contains 1 to 10 mL of solution, corresponding to 3,200 to 32,000 MBq at calibration time.

Not all pack sizes may be marketed.

As a result of the manufacturing process some vials are distributed with punctured rubber stoppers.

6.6 Special precautions for disposal and other handling

General warning

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

For instructions on dilution of the medicinal product before administration, see section 12.

If at any time in the preparation of this medicinal product the integrity of the vial is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Blue Earth Diagnostics Ireland Ltd
6th Floor, 2 Grand Canal Square
Dublin 2
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/17/1186/001
EU/1/17/1186/002
EU/1/17/1186/003
EU/1/17/1186/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 May 2017
Date of latest renewal: 10 February 2022

10. DATE OF REVISION OF THE TEXT

11. DOSIMETRY

The estimated absorbed radiation doses for adult patients following intravenous injection of fluciclovine (^{18}F) are shown in Table 3. Values were calculated from human biodistribution data using OLINDA/EXM (Organ Level Internal Dose Assessment/Exponential Modeling) software.

Table 3: Estimated radiation absorbed doses for adults receiving Axumin

Organ/Tissue	Mean absorbed dose per unit administered activity (µGy/MBq)
Adrenal glands	16
Brain	9
Breasts	14
Gallbladder wall	17
Lower large intestine wall	12
Small intestine wall	13
Stomach wall	14
Upper large intestine wall	13
Heart wall	52
Kidneys	14
Liver	33
Lungs	34
Muscle	11
Ovaries	13
Pancreas	102
Red bone marrow	25
Osteogenic cells	23
Skin	8
Spleen	24
Testes	17
Thymus gland	12
Thyroid	10
Urinary bladder wall	25
Uterus	45
Total body	13
Effective dose	**22 (µSv/MBq)**

The adult effective dose resulting from the administration of the recommended activity of 370 MBq of fluciclovine (^{18}F) is 8.2 mSv. For an administered activity of 370 MBq the typical radiation doses to the critical organs, pancreas, the cardiac wall and uterine wall are 37.8 mGy, 19.1 mGy and 16.5 mGy, respectively.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Method of preparation

The medicinal product may be diluted with sodium chloride 9 mg/mL (0.9%) solution for injection by up to a factor of 8.

Withdrawals should be performed under aseptic conditions. The vial must not be opened before disinfecting the stopper, the solution should be withdrawn via the stopper using a single dose syringe fitted with suitable protective shielding and a disposable sterile needle or using an authorised automated application system.

If the integrity of this vial is compromised, the medicinal product should not be used.

Axumin should only be used when the injection volume is greater than 0.5 mL (approximately 2 hours after time of calibration for Axumin 1,600 MBq/mL and 4 hours after time of calibration for Axumin 3,200 MBq/mL).

If the injection volume is between 0.5 and 1 mL, only syringes of an appropriate size (1 mL) should be used.

Quality control

The solution should be inspected visually prior to use. Only clear solutions, free of visible particles should be used.

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Norsk medisinsk syklotronsenter AS
Rikshospitalet
Sognsvannsveien 20
OSLO
NO-0372
Norway

Seibersdorf Labor GmbH
Grundstück Nr. 482/2 EZ 98 KG
2444 Seibersdorf
AUSTRIA

Curium PET Liège
Allée du 6 Août, 8
Bâtiment 30
Liège 4000
Belgium

Advanced Accelerator Applications Molecular Imaging Italy S.r.l.
Via Piero Maroncelli 40
47014
Meldola (FC)
Italy

Synektik Pharma Sp. z o.o.
ul. Keramzytowa 16
96-320 Mszczonów
Poland

Pharmazac S.A.
3 & 3a Str Building Block Ot4b
Industrial Zone
Lamia
351 50
Greece

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Prior to launch of Axumin in each Member State the Marketing Authorisation Holder (MAH) must agree about the content and format of the educational programme with the National Competent Authority.
The MAH shall ensure that in each Member State where Axumin is marketed, all Healthcare professionals who are expected to use Axumin have access to self-training educational material in order to reduce the risk of PET imaging interpretation errors.

The Healthcare professionals self-training material shall contain the following key elements:

- Physiological distribution of fluciclovine
- Image interpretation guidelines
- Examples of incidental findings on PET-CT with fluciclovine
- Examples of positive and negative findings on PET-CT with fluciclovine
- Demonstration cases with image interpretation provided by an expert

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

SHIELD LABEL:

1. NAME OF THE MEDICINAL PRODUCT

Axumin 1,600 MBq/mL solution for injection
fluciclovine (^{18}F)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL of solution for injection contains 1,600 MBq of fluciclovine (^{18}F) at date and time of calibration (ToC).

3. LIST OF EXCIPIENTS

Excipients: sodium citrate, concentrated hydrochloric acid, sodium hydroxide, and water for injections. For sodium, see leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 vial
Volume: {xx.x} mL
Activity: {YYYY} MBq in {xx.x} mL at {hh:mm}{Time Zone} {DD/MM/YYYY}

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

radioactive

8. EXPIRY DATE

EXP{hh:mm}{Time Zone}{DD/MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Any unused material should be disposed of in accordance with local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Blue Earth Diagnostics Ireland Ltd, 6th Floor, 2 Grand Canal Square, Dublin 2, Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/17/1186/001
EU/1/17/1186/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Axumin 1,600 MBq/mL solution for injection
fluciclovine (^{18}F)
Intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP ToC + 8h

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Activity: {YYYY} MBq
Volume: {xx.x] mL

6. OTHER

Seibersdorf Labor GmbH, 2444 Seibersdorf, Austria

Norsk medisinsk syklotronsenter AS, 0372 Oslo, Norway

Curium PET Liège, 4000 Liège, Belgium

Advanced Accelerator Applications Molecular Imaging Italy S.r.l., 47014, Meldola (FC), Italy

Synektik Pharma Sp. z o.o., 96-320 Mszczonów, Poland

Pharmazac S.A., 351 50, Lamia, Greece

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

SHIELD LABEL

1. NAME OF THE MEDICINAL PRODUCT

Axumin 3,200 MBq/mL solution for injection
fluciclovine (^{18}F)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL of solution for injection contains 3,200 MBq of fluciclovine (^{18}F) at date and time of calibration (ToC).

3. LIST OF EXCIPIENTS

Excipients: sodium citrate, concentrated hydrochloric acid, sodium hydroxide, and water for injections. For sodium, see leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 vial
Volume: {xx.x} mL
Activity: {YYYY} MBq in {xx.x}mL at {hh:mm}{Time Zone} {DD/MM/YYYY}

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Intravenous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

radioactive

8. EXPIRY DATE

EXP{hh:mm}{Time Zone}{DD/MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Any unused material should be disposed of in accordance with local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Blue Earth Diagnostics Ireland Ltd, 6th Floor, 2 Grand Canal Square, Dublin 2, Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/17/1186/002
EU/1/17/1186/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Axumin 3,200 MBq/mL solution for injection
fluciclovine (^{18}F)
Intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP ToC + 10h

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Activity: {YYYY} MBq
Volume: {xx.x] mL

6. OTHER

Seibersdorf Labor GmbH, 2444 Seibersdorf, Austria

Norsk medisinsk syklotronsenter AS, 0372 Oslo, Norway

Curium PET Liège, 4000 Liège, Belgium

Advanced Accelerator Applications Molecular Imaging Italy S.r.l., 47014, Meldola (FC), Italy

Synektik Pharma Sp. z o.o., 96-320 Mszczonów, Poland

Pharmazac S.A., 351 50, Lamia, Greece

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Axumin 1,600 MBq/mL solution for injection
Axumin 3,200 MBq/mL solution for injection
fluciclovine (^{18}F)

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Axumin is and what it is used for

This medicine is a radiopharmaceutical product for diagnostic use only.

Axumin contains the active substance fluciclovine (^{18}F) and is given so that doctors can perform a special type of scan called a positron emission tomography (PET) scan. If you have previously had treatment for prostate cancer and information from other tests (e.g. prostate specific antigen, PSA) indicates that the cancer may have returned, an Axumin PET scan can help your doctor find the locations where the cancer has come back.

You should discuss the results of the test with the doctor that requested the scan.

The use of Axumin does involve exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the benefit of this procedure with the radiopharmaceutical outweighs the risk of being exposed to radiation.

2. What you need to know before you use Axumin

Axumin must not be used
- if you are allergic to fluciclovine (^{18}F) or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your nuclear medicine doctor before you are given Axumin if you:
- have **kidney problems**
- are on a **low sodium diet** (see section "Axumin contains sodium").

Before administration of Axumin you:
- should avoid exercise for at least a day before the Axumin scan.
- should not eat or drink for **at least 4 hours** before the scan (you can take your usual medicines with small amounts of water).

- may urinate at the latest 60 minutes before the Axumin injection and you should avoid urination until after the scan has been completed.

Children and adolescents
Talk to your nuclear medicine doctor if you are under 18 years old. Axumin is not intended for use in children and adolescents aged under 18 years.

Other medicines and Axumin
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images.

Pregnancy and breast-feeding
This medicine is not indicated for use in women.

Driving and using machines
It is considered unlikely that Axumin will affect your ability to drive or to use machines.

Axumin contains sodium
This medicine contains up to 39 mg sodium (main component of cooking/table salt) in each dose. This is equivalent to 2% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Axumin

There are strict laws on the use, handling and disposal of radiopharmaceutical products.
Axumin will only be used in specially controlled areas. This medicine will only be handled and given to you by people who are trained and qualified to use it safely. These persons will take special care for the safe use of this medicine and will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the quantity of Axumin to be used in your case. It will be the smallest quantity necessary to get the desired information. The quantity to be administered usually recommended for an adult is 370 MBq (megabecquerel, the unit used to express radioactivity).

Administration of Axumin and conduct of the procedure
Axumin is administered intravenously as an injection into your vein followed by a flush of sodium chloride solution to ensure that you receive the full dose.

One injection is usually sufficient to conduct the test that your doctor needs.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure. The scan will usually start approximately 5 minutes after the Axumin injection is given.

After administration of Axumin you should:
- **avoid any close contact** with **young children** and **pregnant women** for the 12 hours following the injection
- **urinate** frequently in order to eliminate the product from your body.

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

If you have been given more Axumin than you should
An overdose is unlikely because you will only receive a single dose of Axumin precisely controlled by the nuclear medicine doctor supervising the procedure. However, in the case of an overdose, you will receive the appropriate treatment. In particular, the nuclear medicine doctor in charge of the procedure may provide ways to increase the passing of urine and stools in order to facilitate the removal of radioactivity from your body.

Should you have any further question on the use of Axumin, please ask your nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. In clinical studies side effects were reported by less than 1 in 100 patients given the medicine.

The following side effects of Axumin are **uncommon** (may affect up to 1 in 100 people).
- Altered taste in the mouth, altered sense of smell, pain or rash at the site of injection.

This radiopharmaceutical will deliver low amounts of ionising radiation associated with the least risk of cancer and hereditary abnormalities.

Reporting of side effects
If you get any side effects talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Axumin

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

The following information is intended for the specialist only.

Axumin must not be used after the expiry date which is stated on the shield label after EXP.

6. Contents of the pack and other information

What Axumin contains
- The active substance is fluciclovine (^{18}F).
  Axumin 1,600 MBq/mL solution for injection
  Each mL of solution contains 1,600 MBq fluciclovine (^{18}F) at date and time of calibration (ToC).
  The activity per vial ranges from 1,600 MBq to 16,000 MBq at the date and ToC.
  Axumin 3,200 MBq/mL solution for injection
  Each mL of solution contains 3,200 MBq fluciclovine (^{18}F) at date and ToC.The activity per vial ranges from 3,200 MBq to 32,000 MBq at the date and ToC.
- The other ingredients are sodium citrate, concentrated hydrochloric acid, sodium hydroxide, water for injections (see section 2 "Axumin contains sodium")

What Axumin looks like and contents of the pack
Axumin is a clear, colourless solution stored in a 10 mL or 15 mL glass vial.

Axumin 1,600 MBq/mL solution for injection
Each multidose vial contains 1 to 10 mL of solution, corresponding to 1,600 to 16,000 MBq at the date and ToC.

Axumin 3,200 MBq/mL solution for injection
Each multidose vial contains 1 to 10 mL of solution, corresponding to 3,200 to 32,000 MBq at the date and ToC.

Pack size: 1 vial.

Marketing Authorisation Holder
Blue Earth Diagnostics Ireland Ltd, 6th Floor, 2 Grand Canal Square, Dublin 2, Ireland

Manufacturer
Seibersdorf Labor GmbH, 2444 Seibersdorf, Austria.

Norsk medisinsk syklotronsenter AS, 0372 Oslo, Norway.

Curium PET Liège, 4000 Liège, Belgium

Advanced Accelerator Applications Molecular Imaging Italy S.r.l., 47014, Meldola (FC), Italy

Synektik Pharma Sp. z o.o., 96-320 Mszczonów, Poland

Pharmazac S.A., 351 50, Lamia, Greece

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

The following information is intended for healthcare professionals only:

The complete SmPC of Axumin is provided as a separate document in the package of the medicinal product, with the objective to provide healthcare professionals with other additional scientific and practical information about the administration and use of this radiopharmaceutical.
Please refer to the SmPC [SmPC should be included in the box]