IsoAid Advantage™ Iodine-125 Brachytherapy Source

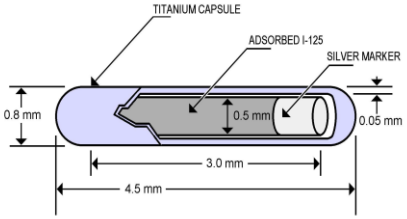
⚠ Instructions for Use – This leaflet contains important product use and safety information. Please read carefully and, retain these instructions for future reference.

Product Name:

ADVANTAGE™ I-125 Brachytherapy Source; Model IAI-125A

Description:

The ADVANTAGE™ I-125 source consists of a laser welded Titanium capsule, containing Iodine-125 chemically affixed (adsorbed), as silver iodide, onto a silver rod which acts as an x-ray detectable marker.



ADVANTAGE™ I-125

Physical Characteristics:

Iodine-125 has a half-life of 59.4 days and decays by electron capture with the emission of characteristic photons and electrons. The principal photon emissions are 27.2 KeV, 27.5 KeV, 31.0 KeV and 35.5 KeV with an average energy of 28.5 KeV. Table 1 shows the decay of I-125.

Table 1. Iodine-125 Decay

Day	Decay Factor	Day	Decay Factor	Day	Decay Factor	Day
0	1.00	20	0.79	40	0.63	60
1	0.99	21	0.78	41	0.62	61
2	0.98	22	0.77	42	0.61	62
3	0.97	23	0.76	43	0.61	63
4	0.95	24	0.76	44	0.60	64
5	0.94	25	0.75	45	0.59	65
6	0.93	26	0.74	46	0.58	66
7	0.92	27	0.73	47	0.58	67
8	0.91	28	0.72	48	0.57	68
9	0.90	29	0.71	49	0.56	69
10	0.89	30	0.70	50	0.56	70
11	0.88	31	0.70	51	0.55	71
12	0.87	32	0.69	52	0.55	72
13	0.86	33	0.68	53	0.54	73
14	0.85	34	0.67	54	0.53	74
15	0.84	35	0.66	55	0.53	75
16	0.83	36	0.66	56	0.52	76

Calibration: ADVANTAGE™ I-125 sources are calibrated by direct comparison against a standard source of the same model that has been calibrated by the National Institute of Standards and Technology for Air Kerma Strength. The resulting calibration is reported in Air Kerma Strength (μGy m^2/h) as well as Apparent Activity (mCi).

ADVANTAGE™ I-125 sources are calibrated to the NIST SK99std WAFAC standards for I-125 seeds.

Available Source Strength Range: The most commonly used source activity levels for prostate cancer treatment is between 0.2 mCi and 0.7 mCi. Other source strengths are available by special order.

In Vivo Characteristics: Clinical efficacy results from the interaction of the emitted ionizing radiation from ADVANTAGE™ I-125 source with the tissue being treated. Titanium encapsulation provides biocompatibility. Dose calculations should account for a moderate anisotropic dose distribution around each ADVANTAGE™ I-125 source. Appropriate parameters should be included in treatment planning.

Indications: The Advantage™ I-125 sources are indicated for use in the treatment of selected localized tumors. Tumors of the head, neck, breast, lung, pancreas, and prostate are commonly treated. The ADVANTAGE™ I-125 source is normally used as a permanent implant.

Contraindications: The use of Advantage™ I-125 sources are not recommended for the treatment of tumors in generally poor or ulcerated condition. Do not use non-sterile needles to implant sources. Do not use a damaged source or a source that may have become damaged when loading the applicator. Direct contact with I-125 sources should be avoided. Use vacuum or reverse action tweezers to handle I-125 sources.

Adverse Reactions: As brachytherapy sources achieve therapeutic results through radiation, any adverse event associated with tissue radiation damage may be associated with the use of I-125 sources. Adverse reactions associated with implant usage in the prostate have been reported to include irritative uropathy symptoms including increased urinary frequency, urgency and obstruction. Complications have also included cystitis, urethritis, superficial urethral necrosis, hematuria, stricture/contracture, incontinence, proctitis and impotence. Source migration to other parts of the body is possible. Although the risk from source migration is minimal it can be significantly reduced through the use of stranding systems that link I-125 sources together prior to implantation.

Patient Education: Patients and people who come into contact with the patient must be informed of the nature of the I-125 implants and follow radiation precautions as outlined by the National Council on Radiation Protection and Measurements, federal (US), state, and/or other government regulations. In the event an implanted source has dislodged and become separated from the patient, instruction should be given in proper handling of the loose implant. The implant should not be picked up by hand. A spoon or tweezers can be used to place it into a container such as a glass jar with lid. The jar should then be placed in an isolated area in the home until a local regulatory center or hospital radiation department can be contacted.

Sterilization:

⚠WARNING: If Advantage™ I-125 sources are supplied non-sterile, sterilization must be performed prior to implant. Always refer to the sterilizer manufacturer's instructions or those provided by the health care institution.

YWARNING: Temperature should not exceed 280˚F / 138˚C

CAUTION: DO NOT autoclave ADVANTAGE™ I-125 Sources in plastic tubing or containers which have a low melting point as it may prevent source recovery.

IsoAid recommends steam autoclaving using the following parameters:

Method	Cycle	Temp	Minimum Exposure Time
Steam	Gravity Displacement	250°F / 121°C	30 minutes

The recommended parameters for sterilization by steam are based on the following sterility information:

Validation Method	***-ANSI/AAMI/ISO 17665-1*** *Sterilization of health care products – Moist Heat – Part 1: Requirements for the development, validation, and routine control of a sterilization process for medical devices* ***-ISO 17664*** *Sterilization of medical devices – Information to be provided by the manufacturer for the processing of resterilizable medical devices.*
SAL	10^{-6}

When ADVANTAGE™ I-125 Sources are supplied sterile; product is sterilized by Ethylene Oxide with a Sterility Assurance Level [SAL] of 10^{-6}

Radiation Protection & Handling: The 27- 35.5 KeV photons of I-125 are substantially absorbed by any high Z material but exhibit desirable penetration in tissue.

Half Value Layer Lead = 0.025 mm
Half Value Layer Tissue = 20.0 mm

Exposure can be reduced by 99.9% with a thin sheet of lead (0.25 mm or 0.01 inch). The shielding of I-125 results in a reduction of exposure to attending medical personnel and visitors. I-125 sources should be handled only by those individuals trained by an

authorizing governmental agency in the safe use & handling of radioisotopes. Direct contact with I-125 sources should be avoided. The use of vacuum or reverse action tweezers is recommended. Proper precautions must be taken when handling the sources. Personnel monitoring is required. Dosimetry monitors, such as TLD devices, should be used to monitor hand and whole-body exposure. During preparation and source implantation procedures, all practical steps should be taken to keep exposure as low as reasonably achievable. Limited exposure time, increasing distance, careful planning of the administration procedure and use of shielded barriers should be considered in meeting this goal.

Implant Integrity: ADVANTAGE™ I-125 sources have been visually inspected, clean/leak tested, and assayed. They have been designated as ISO/11/C53211 according to the standards for ISO 2919 "Radiological protection - Sealed radioactive sources – General requirements and classification" and have been evaluated by the State of Florida Department of Health for sealed brachytherapy sources.

Accidental Damage: It is possible through rough handling (abrasion, incision, etc.), high temperatures or crushing that an implant could rupture and leak. The internal components of the implant are non-toxic, but the area should be closed off immediately and personnel limited to avoid radioactive contamination. The damaged implants should be placed in a sealed container and the area should be decontaminated.

Dosage and Administration: The amount of radioactivity from Advantage™ I-125 sources required for a particular treatment depends on the tumor volume, the previous radiation history of the tumor site, and whether external beam radiation will be used in conjunction with the brachytherapy treatment. Established practice should be used for the calculation of the amount of radioactivity to be implanted, the placement of sources within the tissue, and the evaluation of radiation dose distribution achieved.

Activity Verification: Customer verification of reported ADVANTAGE™ I-125 source output can be accomplished using an ionization chamber calibrated for ADVANTAGE™ I-125 sources. A calibrated ADVANTAGE™ I-125 source can be obtained from IsoAid upon request.

Directions for Use: If ADVANTAGE™ I-125 sources are supplied non-sterile; they must be sterilized prior to use. During the treatment procedure, the patient must be properly anesthetized. A qualified practitioner trained in brachytherapy should place the sources within the tumor according to the treatment plan to achieve the desired tissue dose distribution. The sources will fit in a standard 18-gauge (1.2 mm) implant needle. When using commercially available applicators refer to the instructions for use to determine compatibility with the I-125 implant.

⚠WARNING: Do not use a damaged source or a source that may have become damaged when loading the applicator.

Accountability & Disposal: Records of receipt, storage and disposal of Advantage™ I-125 sources should be maintained in accordance with government regulatory policies. I-125 sources should be strictly controlled and stored in a secured area. When disposal is indicated, the Advantage™ I-125 sources should be transferred to an authorized radioactive waste disposal agency or returned to IsoAid for disposal. Advantage™ I-125 sources should not be disposed of in normal waste. Any discrepancies must be reported immediately to IsoAid Customer Service.

Licensing: The Florida Department of Health (FDOH), Bureau of Radiation Control has approved this sealed source for distribution to persons licensed pursuant to Florida Administrative Code Chapter 64E-5, "Control of Radiation Hazard Regulations," Part VI or under equivalent licenses of the USNRC or issued by an Agreement State. IsoAid requires proof of USNRC radioactive materials license or respective government license as well as agreement state and licensing state information. Orders cannot be processed without license verification. Compliance with the applicable local, state, federal, and/or government regulations concerning procurement, possession, use and disposal of radioactive materials is the responsibility of the customer.

⚠CAUTION: Federal (USA) and State law(s) restrict this device to sale by or on the order of a physician.

Leak Testing: ADVANTAGE™ I-125 sources are leak tested prior to shipment and have passed a leak test showing less than 185 Bq (5 nCi) of removable I-125 as required by ISO 9978 "Radiation protection - Sealed radioactive sources. Advantage™ I-125 seeds do not require any additional leak testing; provided the seeds are used within the Use By date (Sterile product) and/or Implant/Reference Date (Non-Sterile product).

Accidental Damage:
Do not use the product if there is suspicion that the product is damaged or if the sterile barrier has been breached. It is possible through rough handling (abrasion, incision, etc.), high temperatures or crushing that a seed could rupture and leak. The internal components of the seed are non-toxic, but the area should be closed off immediately and personnel limited to avoid radioactive contamination. The damaged seeds should be placed in a sealed container and the area should be decontaminated. In accordance with radiation regulations only authorized, specialized staff trained in handling radioactive substances may handle the ADVANTAGE™ ® I-125 seeds.

Canada- Canadian Nuclear Safety Commission

Application of REGDOC-2.12.3, Security of Nuclear Substances: Sealed Sources for typical uses of sealed sources, Brachytherapy - low dose rate is a category 4 source. Category 4 Sources that are very unlikely to permanently injure anyone. However, this amount of unshielded radioactive material, if not safely managed or securely protected, could possibly – although it is unlikely – temporarily injure someone who handled it or was otherwise in contact with it, or who was close to it for a period of many weeks. This Code of Conduct on the Safety and Security of Radioactive Sources was approved by the Board of Governors of the International Atomic Energy Agency (IAEA) on 8 September 2003. It replaces the version published (with the symbol IAEA/CODEOC/2001) by the IAEA in March 2001. It reflects the important findings produced by the International Conference on Security of Radioactive Sources held in Vienna in March 2003 (the Hofburg Conference). Member States to be encouraged to join and effectively implement these Conventions. Canada is already a signatory to these conventions, together with codes of conduct on nonproliferation, research reactors and the safety and security of radioactive sealed sources, along with the Comprehensive Nuclear Test-Ban Treaty.

Canadian Nuclear Safety Commission

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Tel.: 613-995-5894 or 1-800-668-5284 (in Canada only) Facsimile: 613-995-5086 Email: info@cnsc-ccsn.gc.ca

Web site: nuclearsafety.gc.ca

Australia- Australian Radiation Protection and Nuclear Safety Agency

The establishment of a NRWMF is governed by the National Radioactive Waste Management Act 2012. A NRWMF also needs to adhere to the Environment Protection and Biodiversity Conservation Act 1999, the Nuclear Non-Proliferation (Safeguards) Act 1987 and the Australian Radiation Protection and Nuclear Safety Act 1998.

The proposed National Radioactive Waste Management Facility would be a controlled facility under the Australian Radiation Protection and Nuclear Safety Act 1998 (the Act). Under the Act, licences are required to prepare a site for, construct, or operate a controlled facility. The decision to submit a licence application is a matter for the applicant. Before an application is made to the CEO of ARPANSA for a licence to prepare a site for the National Radioactive Waste Management Facility, the applicant will have to obtain approval from the Minister for the Environment under the Environment Protection and Biodiversity Conservation Act 1999. Before any radioactive material is allowed to be transported it must be packed, shielded, labelled and marked as set out in the ARPANSA Code: Safe Transport of Radioactive Materials. This code is based on the International Atomic Energy Agency's (IAEA) Regulations for Safe Transport of Radioactive Material. nrwmfsupport@arpansa.gov.au; www.arpansa.gov.au

A radioisotope is considered to be for medical use when it is intended to be:

1. administered to humans or used for any therapeutic procedure or purpose in any planned exposure of humans to ionising radiation
2. used in any in vitro medical diagnosis or test
3. used in research which is either directly or indirectly related towards medical diagnosis or therapy in humans.

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Note: Sealed and unsealed radioactive sources that are used to calibrate instruments in medical practices and pathology laboratories are also included as medical radioisotopes for permit purposes. The applicant/ “end user” declares that he/she holds an appropriate licence issued by the relevant Commonwealth, State or Territory radiation regulatory authority to deal with the above radioisotopes. The applicant/ “end user” also undertakes not to supply any of the above radioisotopes to an unapproved user. The applicant/ “end user” should contact the relevant Commonwealth, State or Territory radiation regulatory authority for advice on legislative requirements. medicalpermits@arpansa.gov.au; www.arpansa.gov.au

ARPANSA, like other regulatory bodies in Australia and abroad, has been working on developing capability in holistic safety. Charged with the function of protecting the health and safety of people under the Australian Radiation Protection and Nuclear Safety Act 1998 (the Act), ARPANSA proposes to use a holistic approach to assess and monitor the safety of licence holders and applicants. These guidelines outline ARPANSA’s vision and expectations for holistic safety.

Leak Testing:

ADVANTAGE™ I-125 Brachytherapy sources are 100% leak tested prior to shipment and have passed a leak test showing less than 185 Bq (5 nCi) of removable I-125 surface contamination as required by ISO 9978 “Radiation protection – Sealed radioactive sources.” ADVANTAGE™ I-125 seeds do not require any additional leak testing provided the seeds are used within the use-by-date.

⚠ **Adverse Reactions:**

- Any adverse reaction associated with tissue radiation damage may be associated with use of ADVANTAGE ® I-125 sources. Proper precautions must be taken when handling the sources.
- As with any surgical procedure, complications may occur including: bruising, discomfort, prolonged bleeding, inflammation or infection near the implant site.
- Although the risk of source migration is minimal it can be significantly reduced through the use of stranding that links the seed and spacer together prior to implantation.
- As brachytherapy sources achieve therapeutic results through radiation, any adverse event associated with tissue radiation damage may be associated with use of ADVANTAGE™ ® I-125.
- Adverse reactions associated with implant usage in the prostate. Bladder, uterus, anal and colon implant usage have been reported to include irritative uropathy symptoms including increased urinary frequency, urgency, incontinence, and obstruction.
- Complications have also included cystitis, urethritis, superficial urethral necrosis, hematuria, stricture/contracture, incontinence, proctitis, and impotence, bleeding and discharge, fibrosis and necrosis.
- Seed migration to other parts of the body is possible.
- Allergic reaction to Iodine.

⚠ **Precautions:**

- ⚠ Use caution when patients are diagnosed with non-cancerous tumors/lesions.
- ⚠ Product should remain in leaded pouch until ready for use. Handle lead pouch and contents with care to prevent damage to product.

⚠ **Contraindications:**

- ⚠ Do not use ADVANTAGE™ I-125 in neurological or cardiovascular tissues.
- ⚠ The is sold sterile. Use of a non-sterile device may compromise patient care. Do not re-sterilize.
- ⚠ Caution should be taken when using an MRI to aid in delivery of the seeds. The needles used to deliver the seeds are stainless steel and may affect the quality of the diagnostic information.
- ⚠ No not use needle, Advantage Magazine Cartridge, and Advantage Magazine in an MRI Environment.
- ⚠ Do not use a damaged seed or a seed that may have become damaged when using the device.
- ⚠ Do not use bent or broken needle.
- ⚠ Do not come in direct contact with the ADVANTAGE™ I-125 source. Use vacuum or reverse action tweezers to handle the ADVANTAGE™ I-125 sources.
- ⚠ Do not use if allergic to iodine

⚠ **Warnings:**

- ⚠ Dispose of radioactive material per nuclear regulatory guidelines (for USA, 10 CFR 35.1000; for EU per EURATOM 1493/93)
- ⚠ Loss of a radioactive seed must be avoided. Protocols must be in place to ensure tracking of the seed throughout the process.
- ⚠ Any attempt to cut or segment stranded product may adversely result in radioactive contamination. Use product as intended.
- ⚠ Do not use if damaged. Discard if damaged during use or after use in accordance with waste disposal procedures.
- ⚠ Do not use when patients are pregnant or breastfeeding. An alternative non-radioactive device should be used to avoid radiation exposure.

MR-Conditional:

The ADVANTAGE ® I-125 seeds have been evaluated for safety in the MRI environment. It is MRI-conditional and tested for heating, migration, and image artifact in the MRI environment. IsoAid seeds are made with titanium shell with non-magnetic internal materials. Patients with the seeds may safely undergo MRI under the following conditions: 1) Static field of 3 T or less 2)Whole body SAR of 4 W/kg or less and head SAR of 3.2 W/kg or less 3) Normal or first level controlled mode of the MRI system for both RF and gradients 4) Maximum spatial gradient in the static field of 30 T/m (3000 Gauss/cm) 5) Maximum slew rate of the time-varying magnetic gradient for the seed is 200 [T/m/s], which is the high-end gradient slew rate and is worst-case for the seed that does not have any magnetic or transistors in the seed components, no conceivable negative impact. However, the stainless-steel needle may produce image artifact if an MRI is performed during the ADVANTAGE ® I-125 procedure.

⚠ The stainless-steel needle may produce image artifact and may affect the quality of the image, it is recommended that the needle is not used during the MRI procedure performed during the Brachytherapy procedure.

⚠ **CAUTION: No not use needle, applicator needle, Advantage Magazine Cartridge, and Advantage Magazine in an MRI Environment.**

⚠ **CAUTION: Federal (USA) and State law(s) restrict this device to sale by or on the order of a physician.**

⚠ **CAUTION: Use and Distribution in the EU is governed by EURATOM 2013/59 and 1493/93.**

⚠ **CAUTION: Canadian National and regional/State law(s) restrict this device to sale by or on the order of a physician.**

⚠ **CAUTION: Australian National and Regional/State law(s) restrict this device to sale by or on the order of a physician.**

Seeds that have become separated from their host are considered biohazardous and must be contained and disposed of in accordance with standard precautions.

⚠	Caution: Consult Accompanying Documents
2	Do Not Reuse
	Consult Instructions for Use

IsoAid Advantage™ Iodine-125 Brachytherapy Source

STERILE EO	Ethylene Oxide Sterilization
STERILE	Steam Sterilization
	Use by Date
REF	Catalog Number
	Do not Resterilize
	Date of Manufacture
	Biohazard
	Radioactive
MR	MR Conditional
	Do not use if package is damaged

Manufacturer:
IsoAid LLC
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