Advantage Eye Plaque System™ (AEPS™)

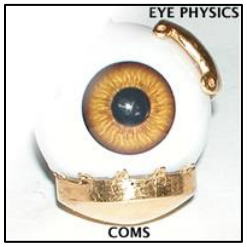
⚠ Instructions for Use – This leaflet contains important product use and safety information. Please read carefully and retain these instructions for future reference.

Product Name:
Advantage® Eye Plaque System ™ :

"Advantage Eye Plaque System COMS Eye Plaques"

"Advantage Eye Plaque System Eye Physics Eye Plaques"

Description: The Eye Plaque consists of a plaque pre-loaded with the requested activity of the brachytherapy seeds. The eye plaque itself is a concave device made of a gold alloy, which is shaped in such a way that the inside diameter follows the curvature of the eye. The seeds are affixed to the face of the plaque; this allows the target tissue to receive treatment while surrounding tissues are shielded by the device itself. During ordering, one must specify the brand, size, shape and/or style required. This allows for convenient customization of the plan, from the health care professional, per patient prescription, so that the appropriate plaque may be used for optimal treatment of the suspect tissue. The use of an Eye Plaque allows for the brachytherapy seeds to remain in the eye socket to treat the tumor; while reducing the radiation exposure to the brain and other organs.



Indications for Use: The Advantage Eye Plaque System is indicated for use in adults (18 years and older) for the treatment of eye cancer and benign tumors, may be used in conjunction with external beam radiation therapy or other therapeutic modalities.

Intended Use: The IsoAid Advantage Eye Plaque System (AEPS) is intended for the delivery and placement of radioactive seeds in the treatment of selected localized eye tumors. The seeds are temporarily implanted (3-7 days) as a source of nuclear radiation therapy for adults with ocular cancer.

Eye Physics: Either Advantage I-125® or Pd-103® Brachytherapy Seeds are placed into an EYE PHYSICS Gold Plaque and glued using biocompatible Loctite 4310 or 4311. A "dummy template ring" may be used for alignment and is to be removed prior to placement of the eye plaque.

COMS: Either Advantage I-125 or Pd-103 Brachytherapy Seeds are loaded into slots on the convex area of the Silastic® (biomedical grade medical elastomer) of which is the brachytherapy source carrier insert that fits in the concave aspect of the Eye Plaque. The Silastic® insert is provided in the COMS Gold Plaque and adhered using biocompatible Loctite 4310 or 4311. A "dummy acrylic template" may be used for alignment and is to be removed prior to placement of the eye plaque.

Steam Sterilization: The COMS and EYE PHYSICS Plaques are sterilized prior to shipment from IsoAid using moist heat validated in accordance with ANSI/AAMI/ISO 17665-1:2006 (R2013) "Sterilization of health care products—Moist heat—Part 1: Requirements for the development, validation, and routine control of a sterilization process for medical devices."

⚠**CAUTION:** Do not autoclave the COMS acrylic template "dummy plaque" – it may deform at the temperatures employed.

The Eye Physics template ring may be either Steam or EO sterilized.

Ethylene Oxide Sterilization:

COMS Acrylic Inserts and Eye Physics dummy template rings are sterilized prior to shipment from IsoAid using ethylene oxide; and The COMS and EYE PHYSICS Plaques may be sterilized prior to shipment from IsoAid using ethylene oxide. The ethylene oxide sterilization process is validated in accordance with ANSI/AAMI/ISO 11135:2014 "Sterilization of health care products—Ethylene Oxide—Part 1: Requirements for the development, validation, and routine control of a sterilization process for medical devices"

Instructions for Safe Use: The Eye Plaque is intended for temporary implant. The dummy templates may be used to align placement for accuracy and optimum results. The templates must be removed prior to placement of the eye plaque. Once the eye plaque is in place radiation is continually delivered, typically over a three to seven-day period. The eye plaque is then removed by the surgeon.

Contraindications:

- Do not use non-sterile product for implantation.
- Do not use a damaged seed, or a seed that may have become damaged in the preparation for use of this device.
- Use for brachytherapy of the eye only.

Accidental Damage: 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 entire device and/or the damaged seed/s (if they've been separated from the device) should be placed in a sealed container and the area should be decontaminated. Do not use the product if there is suspicion that the product is damaged; especially if the sterile barrier has been breached.

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

Adverse Reactions:
Ophthalmic brachytherapy complications relate to both radiation and patient specific factors like tumor size, location, dose rate, dose volume, and total dose. Possible adverse effects from the use of this device may result in optic neuropathy, cataracts, and retinopathy. Within the eye, radiation can cause iritis, uveitis, synechiae, neovascular glaucoma, cataract, posterior neovascularization, hemorrhage, retinal detachment, retinopathy, and optic neuropathy. The most common late sight limiting posterior segment complication is radiation maculopathy. Unusual complications include persistent strabismus and scleral thinning. All the aforementioned side effects can result in loss of vision and quality of life. The ABS-OOTF recognize that there exists no comprehensive staging system for the ophthalmic side effects of radiation therapy. Classification for radiation retinopathy for the following stages according to the American Brachytherapy Society – Ophthalmic Oncology Task Force/Brachytherapy (2013).

Stage 1: Cotton wool spots, Retinal hemorrhages, Retinal microaneurysms, Exudate, Uveal effusions, Chorioretinal atrophy, Choroidopathy, Retinal ischemia in less than 5 days within implant.

- Symptom: None
- Location: Extramacular
- Risk of vision loss: mild.

Stage 2: Above findings.
- Symptom: None.
- Location: Extramacular
- Risk of vision loss: Moderate.

Stage 3: Any combination of the above plus Retinal Neovascularization.

- Symptom: Vision Loss;
- Location: Extramacular
- Risk of Vision Loss: Severe

❖ Macular Edema- new onset

- Symptom: Vision Loss
- Location: Extramacular
- Risk of Vision Loss: Severe

Stage 4: Any combination of the above plus Vitreous Hemorrhage.
- Symptom: Vision loss
- Location: Vitreous
- Risk of Loss of Vision: Severe

❖ Retinal ischemia at or greater than 5 days
- Symptom: Vision loss
- Location: Vitreous
- Risk of Loss of Vision: Severe

Although many of these findings are fundamentally, albeit less specifically, classified by the United States National Cancer Institute (Cancer Therapy Evaluation Program, Common Terminology Criteria for Adverse Events, Version 4.0, DCTD, National Cancer Institute, National Institute of Health, Department of Health and Human Services (http://ctep.cancer.gov)), the ABS-OOTF recommends that a radiation-specific ophthalmic side effect staging system should be developed to improve communication for patient care, research, and publication. (ABS- The American Brachytherapy Society consensus guidelines for plaque brachytherapy of uveal melanoma and retinoblastoma The American Brachytherapy Society - Ophthalmic Oncology Task Force).

⚠ **Warnings:**

- Dispose of radioactive material per nuclear regulatory guidelines (for USA, 10 CFR 35.1000)
- Loss of a radioactive seed must be avoided. Protocols must be in place to ensure tracking of the seed throughout the process.
- Use of this product may compromise post-treatment vision. Calculated doses to critical structures are determined by the ophthalmologist and Radiotherapist

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Licensing:
USA – State/Federal:

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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, country, and/or government regulations concerning procurement, possession, use and disposal of radioactive materials is the responsibility of the customer.

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

Canada- Canadian Nuclear Safety Commission

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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
280 Slater Street P.O. Box 1046
Station B Ottawa, Ontario K1P 5S9 CANADA
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

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

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.

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Leak Testing: ADVANTAGE Brachytherapy 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. The Seed Models IAI-125A and IAPd-103A are licensed by the department for distribution to persons licensed pursuant to 64E-5, F.A.C., Part VI or under equivalent licenses of the United States Nuclear Regulatory Commission, an agreement state or a licensing state.

⚠ **Adverse Reactions:**

- Any adverse reaction associated with tissue radiation damage may be associated with use of ADVANTAGE ® 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 or dislodged seed is minimal, it can be significantly reduced through the use proper amount of adhesive on the source boding it to the surface of the eye plaque or the Silastic® insert 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™ ® Sources.
- Ophthalmic brachytherapy complications relate to both radiation and patient specific factors like tumor size, location, dose rate, dose volume, and total dose.
- Possible adverse effects from the use of this device may result in optic neuropathy, cataracts, and retinopathy.
- Within the eye, radiation can cause iritis, uveitis, synechiae, neovascular glaucoma, cataract, posterior neovascularization, hemorrhage, retinal detachment, retinopathy, and optic neuropathy.
- The most common late sight limiting posterior segment complication is radiation maculopathy.
- Unusual complications include persistent strabismus and scleral thinning.
- All the aforementioned side effects can result in loss of vision and quality of life. The ABS-OOTF recognize that there exists no comprehensive staging system for the ophthalmic side effects of radiation therapy. Although many of these findings are fundamentally, albeit less specifically, classified by the United States National Cancer Institute (Cancer Therapy Evaluation Program, Common Terminology Criteria for Adverse Events, Version 4.0, DCTD, National Cancer Institute, National Institute of Health, Department of Health and Human Services (http://ctep.cancer.gov)), the ABS-OOTF recommends that a radiation-specific ophthalmic side effect staging system should be developed to improve communication for patient care, research, and publication. (ABS- The American Brachytherapy Society consensus guidelines for plaque brachytherapy of uveal melanoma and retinoblastoma The American Brachytherapy Society - Ophthalmic Oncology Task Force).
- Seed migration to other parts of the body is possible.
- Allergic reaction to Iodine.
- Allergic reaction to Palladium

⚠ **Precautions:**

- ⚠ Use caution when patients are diagnosed with non-cancerous tumors/lesions of the eye.
- ⚠ 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™ Sources in neurological or cardiovascular tissues.
- ⚠ The Advantage Eye Plaque System 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.
- ⚠ Do not use a damaged seed or a seed that may have become damaged when using the device.
- ⚠ Do not use damaged eye Plaques, eye plaques that are bent or eye plaques that have broken eyelets.
- ⚠ Do not come in direct contact with the ADVANTAGE™ Sources. Use vacuum or reverse action tweezers to handle the ADVANTAGE™ Sources.

⚠ **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 source 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.
- ⚠ During handling of these devices, the user should handle the devices carefully as to not damage with pressure, torque, or used as a lever.
- ⚠ Do not use if eyelets are broken or damaged. Discard if damaged during use or after use in accordance with waste disposal procedures.
- ⚠**WARNING** Do not separate the COMS Eye Plaque Applicator Kit's Dummy Ring (Template) Acrylic from the COMS Eye Plaque Applicator Kit's Dummy Ring.

MR-Conditional:

The ADVANTAGE ® 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.

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	Do Not Reuse
	Caution: Consult Accompanying Documents
	Consult Instructions for Use
	Use By Date
	EtO Sterilization
	Steam Sterilization
	Do not Resterilize
	Biohazard
	Radioactive
	Do not use if package is damaged

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