THERAGENICS CORPORATION®

Model AgX100®
I-125 Device

Instructions for Use

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1 INTRODUCTION

This document contains instructions for use of Theragenics®AgX100 Iodine-125 devices.

The product labels for all AgX100 configurations use symbols to convey essential product information. Each symbol is defined in Table 1.

Table 1: Definition Of Symbols

SYMBOL	MEANING
	Caution, consult accompanying documents
	Do not reuse
	Use by
LOT	Batch code / Production identifier
REF	Catalog number
SN	Serial Number
STERILE R	Sterilized using irradiation
STERILE EO	Sterilized using ethylene oxide
STERILE	Sterilized using steam
	Do not resterilize
	Do not use if package damaged
	Device Manufacturer
EC REP	Authorized Representative in the European Community
CE 2797	CE Mark of the Notified Body, authorized since February 2019
R_xOnly	Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.
	Caution: Radioactive material

2 WARNINGS AND PRECAUTIONS

A WARNING indicates the potential for death, serious injury, or other serious adverse event due to use or misuse of the device.

AgX100 Seed Products

- AgX100 seeds contain radioactive material.
- DO NOT reuse – Single use only.
- DO NOT re-sterilize.
- DO NOT use if sterile package is damaged.
- DO NOT use a damaged source. If a seed is damaged or broken contact your Radiation Safety Office and initiate containment and decontamination in accordance with your facility's radiation safety procedures.
- DO NOT expose implanted sources to therapeutic levels of ultrasound energy as the device may inadvertently concentrate the ultrasound field and cause harm.
- AgX100 seeds should never be handled roughly or forced into any implant accessory e.g. cartridge or needle. Such force may damage the wall of the brachytherapy source, potentially causing release of I-125 into the environment or tissues surrounding an implanted brachytherapy source.

C20™, VSM and Mick® Cartridges

- DO NOT handle cartridges by the spring loaded plunger.
- DO NOT overtighten the cartridge shield cover.
- DO NOT use force on seeds or cartridges.
- DO NOT force cartridges into applicator.
- DO NOT forcibly remove cartridges from applicator.

Customized preloaded needle kits

A customized preloaded needle kit is a prescription device and must not be used or substituted for use by anyone other than the patient for whom it has been prescribed.

3 RESTRICTIONS ON USE / CAUTIONS

General

AgX100 seeds and accessories should be used by physicians who are qualified by training and experience in the safe use and handling of radionuclide brachytherapy sources and whose experience and training has been approved by the appropriate government authorities authorized to license the use of radioactive materials.

AgX100 seeds and accessories should be used in those facilities that have been approved by the appropriate government authorities authorized to license the use of radioactive materials.

CAUTION: Only individuals trained by an authorized user at the licensed facility should handle the sources. Direct contact with the AgX100 device should be avoided; the use of forceps or tweezers is recommended.

DO NOT re-sterilize or reprocess the AgX100 device.

CAUTION: Implant Needles - Using the stylet with excessive force to manipulate a lodged seed may damage the seed. Needles are not intended to penetrate bone. If resistance is encountered, verify needle position. Do not push into bone as this may cause the needle to bend or break. Replace needle if cannula or tip is damaged.

4 RADIATION

The 27-35 keV photons of I-125 are substantially absorbed by any high Z material but exhibit desirable penetration in tissue. The half-value layer (HVL) of lead for I-125 is 0.025 mm; the HVL of tissue is 20.0 mm. Exposure can be reduced by 99.9% with a thin sheet of lead (0.25 mm). AgX100 seeds should be handled only by those individuals trained by an authorized user at the licensed facility. Proper precautions should be taken when handling the sources. Direct contact with the AgX100 device should be avoided; the use of forceps or tweezers is recommended.

Personnel monitoring is required. Dosimetry monitors, such as TLD devices, should be used to monitor hand and whole-body exposure. During preparation of the source device and implantation procedures, all practical steps should be taken to keep exposure as low as (is) reasonably achievable (ALARA). Limiting exposure time, increasing distance, careful planning of the administration procedure, and use of shielded barriers should be considered in meeting this goal.[1-3] The Site Radiation Safety Officer should be consulted regarding specific local requirements. Perform a radiation survey on all components upon completion of the seed implant.

5 In-VIVO CHARACTERISTICS

Clinical efficacy results from the interaction between the emitted ionizing radiation of the I-125 source and the tissue being treated. Titanium encapsulation provides good biocompatibility. Total photon transmission after accounting for attenuation resulting from the titanium capsule and the internal components is approximately 50%.

6 SOURCE RECEIPT AND STORAGE

Records of receipt, storage, and disposal of AgX100 I-125 devices should be maintained in accordance with government regulatory policies. Products should be strictly controlled and stored in a secured area. Any discrepancies in seed count must be reported immediately to Theragenics® Customer Service. See Section 15 for contact information.

- AgX100 products should remain in the sterile package until ready to use.
- Sterile needles should remain sealed in the sterile package until ready to use.
- Refer to the product label for expiration date.

7 DISPOSAL

7.1 Seeds

When disposal is indicated, AgX100 sources should be transferred to an authorized radioactive waste disposal agency. AgX100 should not be disposed of in normal waste. AgX100 should be disposed of in accordance with applicable laws and regulations.

7.2 Packaging

CAUTION: Handle and dispose of radioactive material, needles, accessories, shielding and packaging, in accordance with applicable laws and regulations.

8 PRODUCT DESCRIPTIONS

8.1 AgX100

The AgX100 device consists of a laser welded titanium capsule containing I-125 adsorbed onto a silver rod. (Figure 1.)

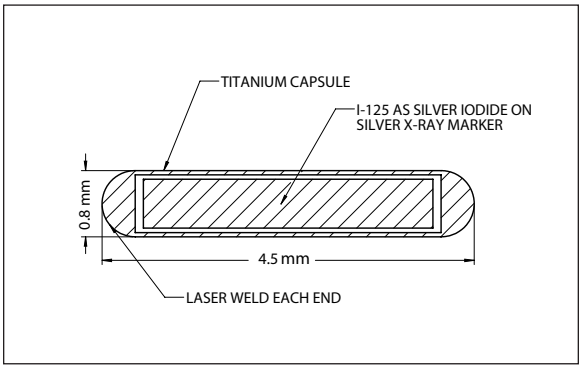

Figure 1: AgX100®

8.2 Seeds in Magazines

Theragenics offers three seed magazines compatible with the Mick® applicator as listed below. The seeds/magazines are sterilized using moist heat at the Theragenics manufacturing facility.

8.2.1 Theragenics Vertical Seed Magazine and C20™ magazine has a 20-seed capacity with integrated radiation shielding and seed counter.

8.2.2 Mick® Shielded Magazine has a 15-seed capacity.

8.3 Stranded and Custom Loaded Products

8.3.1 TheraLoad® consists of a variable number of seeds and spacers custom loaded into an 18-gauge brachytherapy needle. The maximum length of configured components may not exceed 7.0 cm.

8.3.2 TheraSleeve® consists of a variable number of seeds and spacers contained in a bioabsorbable sleeve and custom loaded into an 18-gauge brachytherapy needle. The maximum length of configured components may not exceed 7.0 cm.

8.3.3 TheraStrand® consists of a variable number of seeds and spacers contained in bioabsorbable suture and custom loaded into an 18-gauge brachytherapy needle. All TheraStrand® configurations begin and end with a 2.75 mm spacer. The maximum length of configured components is 6.5 cm.

8.3.4 TheraStrand® RT - Loose TheraStrand® may be packaged in a 20-strand capacity shielded container or a 4-strand capacity shielded container suitable for sterile strand well-chamber assay.

The stiffened suture material used for TheraStrand® and the bioabsorbable sleeve used for TheraSleeve® stabilize the seeds in the treated tissue to provide desired dosimetry and minimize seed movement during delivery/insertion, and help to prevent seed migration[4-5]. Both materials are biocompatible and are commonly used in medical devices. The spacers used in custom loaded product configurations are made from the same material as the suture.

8.4 Needle/Strand Specifications

- The components are supplied in a standard 18-gauge brachytherapy needle.
- The needles contain a bone wax plug that is 5 mm long.
- The bioabsorbable suture and spacers are made of 90/10 (glycolide/L-lactide), for which absorption occurs in 56-70 days.
- The bioabsorbable sleeve is made of 20/80 (glycolide/L-lactide), for which absorption occurs in 140-180 days.

8.5 Loose Seeds for Temporary Ocular Implants

Loose seeds intended for temporary ocular implants are shipped in a shielded sterile glass vial.

9 INDICATION FOR USE AND CONTRAINDICATIONS

AgX100 seeds with an activity range of 0.198 mCi to 0.898 mCi are indicated for permanent interstitial treatment of localized prostate cancer. The seeds may be used as primary treatment as monotherapy, or combined with other modalities such as external beam radiation therapy and/or androgen deprivation therapy.

AgX100 seeds with an activity range of 1mCi – 10mCi or more are indicated for temporary interstitial treatment of ocular tumours. They may be used as a primary treatment, or in recurrent or residual tumours following excision of the primary tumour, or concurrent with other modalities such as external beam radiation therapy or chemotherapy

Contraindications for permanent prostate brachytherapy stipulated by the American College of Radiology and the American Brachytherapy Society[6] are:

- Life expectancy of less than 10 years in the setting of low-risk prostate cancer.
- Unacceptable operative risk
- Poor anatomy which, in the opinion of the radiation oncologist, could lead to a suboptimal implant (e.g., large or poorly healed transurethral resection of the prostate (TURP) defect, large median lobe, large gland size).
- Pathologically positive lymph nodes
- Significant obstructive uropathy
- Distant metastases

Contraindications for ocular plaque brachytherapy stipulated in the American Brachytherapy Society consensus guidelines[7] are:

- Tumours with T4e extraocular extension, basal diameters that exceed the limits of brachytherapy, blind painful eyes, and those with no light perception vision are not suitable for plaque therapy.
- Ocular brachytherapy is not recommended for patients whose death is imminent or those who cannot tolerate surgery.

10 PRODUCT SPECIFICATIONS

10.1 Source Limitations

It is possible through rough handling (abrasion, incision, etc.), or crushing that an AgX100 device could rupture and leak. If this happens, contact your facility Radiation Safety Officer.

10.2 Source Characteristics/Dosimetry

I-125 has a half-life of 59.43 days and decays by electron capture with the emission of characteristic photons and electrons. The titanium walls of the AgX100 device absorb the electrons. The principal photon emissions are 35.49, 31.71, 30.98, 27.472, and 27.202 keV. The I-125 is adsorbed onto a silver rod as silver iodide. Table 2 shows the decay of I-125. The sources remain therapeutic through about 10 half-lives, or about 180 days. A dosimetric characterization of AgX100 including Monte Carlo[8] and experimental[9] studies was conducted in accordance with AAPM Task Group 43 update (TG43U1)[10].

Table 2: Decay of Iodine-125

Day	Decay Factor	Day	Decay Factor	Day	Decay Factor	Day	Decay Factor	Day	Decay Factor
0	1.000	16	0.830	32	0.689	48	0.571	64	0.474
1	0.988	17	0.820	33	0.681	49	0.565	65	0.469
2	0.977	18	0.811	34	0.673	50	0.558	66	0.463
3	0.966	19	0.801	35	0.665	51	0.552	67	0.458
4	0.954	20	0.792	36	0.657	52	0.545	68	0.452
5	0.943	21	0.783	37	0.650	53	0.539	69	0.447
6	0.932	22	0.774	38	0.642	54	0.533	70	0.442
7	0.922	23	0.765	39	0.635	55	0.527	71	0.437
8	0.911	24	0.756	40	0.627	56	0.520	72	0.432
9	0.900	25	0.747	41	0.620	57	0.514	73	0.427
10	0.890	26	0.738	42	0.613	58	0.508	74	0.422
11	0.880	27	0.730	43	0.606	59	0.503	75	0.417
12	0.869	28	0.721	44	0.599	60	0.497	76	0.412
13	0.859	29	0.713	45	0.592	61	0.491	77	0.407
14	0.849	30	0.705	46	0.585	62	0.485	78	0.403
15	0.839	31	0.697	47	0.578	63	0.480	79	0.398

10.3 Calibration

The AgX100 I-125 device is calibrated by direct comparison against a standard source of the same model that has been calibrated by the National Institute of Standards and Technology (NIST) for air kerma strength. The resulting calibration is reported in air kerma strength (μGy m^2 h^{-1}, also defined as U) as well as Apparent Activity (mCi).

Apparent activity refers to the radiation output and not the contained activity. This output quantity is calculated to 12:00 noon Eastern Time (GMT-05:00) on the given reference date.

10.4 Source Output Verification

A Sealed Source Calibration Certificate is provided with every order. The seeds are 100% assayed and assigned to inventory ranges. The Sealed Source Calibration Certificate identifies the calibration information for each order based on the original assay/inventory range. If you request either 10% or 100% independent assay, an additional Sealed Source Calibration Certificate, including assay results, is provided. For further verification, a radiograph and digital image are provided for stranded orders. Extra loose seeds or calibrated seeds can be provided for independent measurement.

11 AVAILABLE SOURCE STRENGTH RANGE

Source strength is based on the corrected NIST 1999 WAFAC standard, implemented August 16, 2010. Because of the inherent uncertainty in I-125 seed calibration, some seeds within a given lot may fall outside a specific range. The uncertainty of the Air Kerma Strength for Model AgX100 is approximately ± 7%.

The amount of radioactivity from 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.[9-12]

Dose calculations should account for the anisotropic dose distribution around each I-125 source as with other brachytherapy sources.[10,11] Appropriate parameters should be included for planning.

12 DIRECTIONS FOR USE

12.1 TheraStrand RT

12.1.1 Open the shipping container and review documentation to verify order contents.

12.1.2 Remove the sterile container from the lead pig.

12.1.3 Carefully inspect the sterile container – Do not use if container or Tyvek lid are damaged.

12.1.3.1 If using the Realtime (RT) individual container, perform assay per your established protocol.

12.1.3.2 Contact Theragenics® Radiation Physics department if assistance is needed with the assay protocol.

12.1.4 Peel back the lid and remove the shielded container to the sterile field, utilizing ALARA practices.

12.1.5 Using sterile tweezers to grasp the protruding end of a strand.

12.1.6 Remove the strand and transfer directly to a sterile brachytherapy needle or to a sterile cutting surface for further handling.

12.1.7 Repeat steps 12.1.5 – 12.1.6 until all strands have been removed from the container.

Note: In accordance with ALARA principles, it is recommended that strands remain in the shielded insert until ready to use.

12.2 Custom Loaded Needles

12.2.1 Open the shipping container and review documentation to verify order contents.

12.2.2 Ensure that the Needle Configuration Plan (Form F1007) provided is consistent with the treatment plan. Contact Customer Service if there are discrepancies.

12.2.3 Open the inner shipper and remove the sterile package(s).

12.2.4 Carefully inspect the sterile packages – Do not use if package or Tyvek lid are damaged.

12.2.5 Peel to open the sterile package. Remove the foam liner and remove the inner tray to the sterile field.

NOTE: If you need to radiograph your order, remove the bottom cover by separating the snap locks and replace upon completion.

12.2.6 During placement of a pre-loaded needle product, ensure the needle hub is pulled fully against the stylet prior to removal from the gland. Pre-loaded products should remain in the sterile container until ready for use.

12.2.7 Take care to avoid contamination when opening the sterile package. TheraLoad®, TheraSleeve®, and TheraStrand® devices may not be resterilized.

12.2.8 The needle tray is shielded and can be used in either a horizontal or vertical position.

NOTE: Refer also to the Tray Set-Up Guide for visual set up instructions.

12.2.9 To use horizontally:

- Remove the top cover (unshielded portion, covering the needle stylets) by separating the snap locks.
- Fold the upper half of the tray underneath the needles and lay flat on the sterile work surface to dispense.

12.2.10 To use vertically, the top cover is used as a tray base:

- Repeat the steps above, and place the folded needle tray into the tray base. The tray base should be oriented with the three circular stops forward, and the two triangular stops to the rear.
- Using your thumb and forefinger, engage the butterfly clips on both sides.
- *Note – Use of the butterfly clips provides extra stability to the upright needles, but is not required.*

12.2.11 Upon removing needles for use, ensure the stylet lock is secure and carry needles in a horizontal or "tip up" position to avoid loss of seeds in the event that the needle plug has become displaced during shipment.

12.2.12 Remove stylet lock from needle hub and begin seed placement.

12.3 Loose Seeds and Seeds in Magazines

12.3.1 For seeds in magazines, always remove the magazine cover gently to prevent the shifting of seeds. Hold the magazine upright when opening/removing the cover so that seeds do not fall out.

12.3.2 If you have purchased sterile AgX100 in vials or magazines, aseptic practices should be followed when loading the seeds into standard 18-gauge brachytherapy needle or an ocular plaque. Take care not to damage seeds during loading.

12.3.3 Insert a sterile magazine into your MICK® applicator and proceed with the implant procedure.

12.3.4 To open a C20™ or MICK® magazine, grasp the magazine body and hold in an upright position.

12.3.4.1 To open a C20™ or MICK® magazine, unscrew the magazine cover and lift off.

12.3.4.2 Remove seeds with fine point tweezers using ALARA practices.

12.3.5 To open the vertical seed magazine (VSM), rotate the cover counterclockwise past the notch until the tab is in the open position (See Figure 2). Remove the cover using gentle upward pressure.

12.3.5.1 Remove seeds with fine point tweezers using ALARA practices.

12.3.6.2 To replace the VSM cover: position the plunger paddle into the magazine body.

12.3.6.3 Align the open position of the magazine cover with the tab on the magazine body and press the cover into place. Rotate the cover clockwise past the notch until it locks.

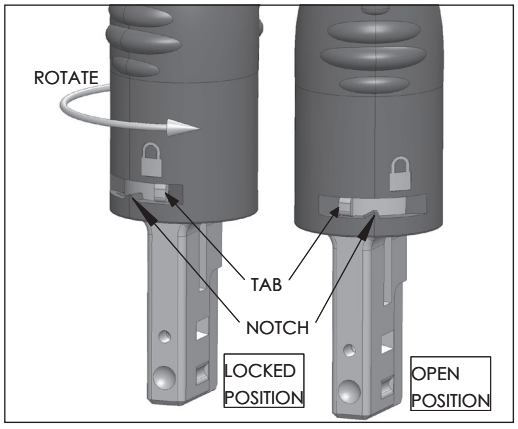

Figure 2: Removing the Magazine Cover

13 ADVERSE EFFECTS

Adverse effects associated with low dose rate prostate brachytherapy implants are:

- *Urinary toxicity*: haematuria, perineal bruising and pain, lower urinary tract symptoms (LUTS – such as dysuria, urinary urgency, frequency and nocturia), cystitis, urethritis, superficial urethral necrosis, urinary retention, urinary stricture, bladder neck contracture, urinary incontinence.[13-16]
- *Rectal toxicity:* Diarrhoea, constipation, anal incontinence/urgency, proctitis, rectal bleeding, rectal stricture, rectal ulcer/rectal fistula.[16] Fistula formation has been described following anterior wall biopsy of the rectum in patients who have been treated with low dose rate brachytherapy.[17-19] Therefore anterior wall biopsy of the rectum should be avoided in these patients.
- Erectile and sexual function toxicity: Haematospermia, a decline in erectile function is common after brachytherapy with recovery to baseline function returning from 3 months to 5 years after therapy.[20] There are sporadic reports in the literature of paternity after brachytherapy with no evidence of birth anomalies, however usual practice is to recommend sperm banking prior to the procedure if subsequent fertility is a concern.[21]

Adverse effects associated with temporary ocular plaque brachytherapy reported by the American Brachytherapy Society task force[7] are:

- Decrease in visual acuity
- Radiation cataract
- Intraocular radiation vasculopathy that may involve retina, optic disc and/or iris
- Brachytherapy may affect the eyelids, eye-lashes, conjunctiva, tear production, corneal surface integrity, sclera, and ocular muscles.
- Within the eye, radiation can cause iritis, uveitis, synechiae, neo- vascular glaucoma, cataract, posterior neovascularization, haemorrhage, 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:

14 CUSTOMER SERVICE

To place an order, obtain return authorization, or obtain product information, please contact Theragenics® Customer Service or your distributor.

15 REPORTING REQUIREMENTS

All serious incidents are required to be reported as soon as possible to Theragenics Corporation® or the distributor. US phone number 1-770-831-5225 or email: customerservice@theragenics.com.

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