BioXmark®

EN

Liquid fiducial marker

Read all sections of this instruction for use before using BioXmark® for the first time.

FOR PROFESSIONAL USE ONLY
BioXmark® must be handled only by qualified healthcare professionals. Injection of BioXmark® requires experience with implantation of fiducial markers or with taking biopsies from the tissue intended for injection of BioXmark®.

MANDATORY LOT NUMBER REGISTRATION
The healthcare professional injecting BioXmark® must ensure that a procedure is in place for registration of the lot number assigned to the BioXmark® liquid administered to each patient. This is a requirement under EU law and ensures that patients can be identified expediently in the case of e.g. product recalls.

1. DEVICE INFORMATION

1.1 DEVICE DESCRIPTION

- BioXmark® is a single use, implantable medical device consisting of a sterile transparent liquid in a one-point-cut (OPC) glass ampoule.
- Each ampoule contains 1 ml.
- Sterilized using steam.
- Magnetic Resonance (MR) safe.
- Upon injection of the BioXmark® liquid into soft tissue, efflux of ethanol leads to the formation of a radiopaque, sticky and gel-like fiducial marker in-vivo.

1.2 DEVICE COMPONENTS

- The liquid is a mixture of ethanol, sucrose acetate isobutyrate (SAIB) and an iodinated and acylated derivative of sucrose (x-SAIB).
- The OPC glass ampoule consists of borosilicate.

1.3 STORAGE

- Store at 2–25 °C.
- Keep away from sunlight.

1.4 INJECTION VOLUME

The optimal injection volume depends on the intended target site, the planned treatment and the applied image modality as well as the desired visibility and artefact level. In general, both visibility and artefacts increase with higher injection volumes.

A simplified overview of injection volumes and corresponding marker visibility in different imaging modalities is displayed in the table below.

	0.025 ml	0.040 ml	0.050 ml	0.100 ml	0.200 ml
CT and CBCT [A]		Visible	Visible	Visible	Visible
2D X-ray [B]				Visible	Visible
Automated detection on kV X-ray [B]	Visible	Visible	Visible	Visible	Visible
MRI (hyperintense background) [C]			Visible	Visible	Visible
US [D]	(Visible)	(Visible)	(Visible)	Visible	Visible
MV X-ray	Not visible on megavoltage imaging				

[A] **CT and CBCT:** Injection volumes ≥ 0.040 ml usually form markers visible on computed tomography (CT) and cone beam computed tomography (CBCT).

[B] **2D X-ray:** Injection volumes ≥ 0.100 ml form markers visible on 2D X-ray depending on the anatomical site. Injection volumes between 0.025 ml and 0.200 ml can be automatically detected on kV X-ray images.

[C] **MR:** BioXmark® markers appear as hypointense spots on magnetic resonance (MR) and are visible if the anatomical site provides a hyperintense background (on either T1 or T2). Injection volumes ≥ 0.050 ml form markers usually visible on MRI depending on the anatomical site and the applied voxel sizes.

[D] **US:** Injection volumes ≥ 0.100 ml form markers usually visible on ultrasound (US). Injection volumes ≥ 0.025 ml form markers visible in a breast phantom study (3 MHz).

Recommendations on maximum volumes

- The accumulated injection volume of multiple markers must be ≤ 0.700 ml for each patient.
- The injection volume of each single marker must be ≤ 0.300 ml.

Higher single or higher accumulated injection volumes have not been investigated in clinical settings.

Dimension and shape of a formed marker will vary depending on the injection volume and the anatomical implantation site.

2. INDICATIONS

- BioXmark® is indicated for use to radiographically mark soft tissue.
- BioXmark® is intended to mark tissue for at least 2 months after implantation.

3. CONTRAINDICATIONS

- Do not use in patients with known hypersensitivity to iodine or any other component in BioXmark®.
- Do not use in pregnant women and paediatric patients. Use of BioXmark® in these patient groups has not been investigated and teratogenicity tests have not been performed.

4. WARNINGS

NOT FOR INTRAVASCULAR USE

- The BioXmark® liquid may cause emboli if injected directly into the blood stream; Do not inject the BioXmark® liquid if excessive bleeding is observed. Do not inject near a lung vein as misplacement may result in emboli.

5. PRECAUTIONS

5.1 BEFORE USE

For percutaneous and endoscopic assisted injection

- The BioXmark® liquid is **sticky and viscous**. It is recommended to allow sufficient time to get acquainted with BioXmark® before first implantation in patients.
- Do not re-sterilize.
- Perform visual inspection of BioXmark® before use. Do not use if the ampoule is damaged. Do not use if the liquid is non-transparent.
- Use immediately after opening. Do not re-use.
- Cautions should be taken if the patient takes anti-coagulants, non-steroid anti-inflammatory drugs (NSAIDs) or other medication that can affect bleeding.
- It is recommended to perform implantation of BioXmark® ~1 day prior to the medical imaging for treatment planning in order to allow the marker to settle in the tissue.

For endoscopic assisted injection only

- Dependent on the intended number of markers to be implanted, the intended injection volume per marker, and the amount of dead volume in the endoscopic needle, it may be required to use more than one ampoule of BioXmark® per patient.
  The larger the inner endoscopic needle diameter and the longer the needle, the larger the amount of dead volume.
- The force required to fill the endoscopic needle and inject the BioXmark® liquid depends on the choice of endoscopic needle.
  The smaller the inner endoscopic needle diameter and the longer the needle, the more force is required to fill the needle and inject BioXmark®.
- Endoscopic needles with side holes shall not be used.

5.2 DURING INJECTION

- Avoid injections in necrotic tissue, highly vascularized tumour tissue and air-filled cavities e.g. tumour cavity or lung emphysema as it may result in loss of markers and/or in the tissue not being marked properly.
- Do not add other liquids in the needle before, during or after filling it with BioXmark® liquid. It may impact the performance of BioXmark®.
- It is recommended to use the least invasive implantation procedure for the given indication.
- It is recommended to use medical image guidance to ensure markers are placed at the intended site.
- Percutaneous/endoscopic assisted injections may result in infection or trauma, such as bleeding. Use relevant concomitant treatments as needed.

6. ADVERSE EVENTS

The patient shall be informed about the following possible adverse events related to the implantation of BioXmark®:

- Allergic reaction
- Bleeding
- Emboli
- Infection
- Local inflammatory response
- For implantation in thorax: pneumothorax

7. PROCEDURE

- For endoscopic assisted injection, including preparation, injection and flushing steps, see section 7.1.
- For percutaneous injection, including preparation and injection steps, see section 7.2.
- For disposal, see section 7.3.
- For follow-up, see section 7.4.

7.1 ENDOSCOPIC ASSISTED INJECTION

Preparation

A. See section 5.1 for a carefully considered choice of endoscopic needle and the required number of ampoules.
B. Prepare a syringe with a pressure resistant connection (e.g. Luer lock) and a loading needle (18-20G).
   Thinner needles may require longer time to fill the syringe.
C. Open the BioXmark® ampoule and fill the syringe using the loading needle. BioXmark® liquid is **sticky and viscous**.
D. Change the loading needle to an endoscopic needle (without side-holes, 19-25G):
   - Remove the loading needle.
   - Remove the stylet, if any, from the endoscopic needle and attach the syringe containing the BioXmark® liquid to the endoscopic needle.
E. Push the needle tip out of the protection sheath.
F. Completely fill the endoscopic needle with the BioXmark® liquid.
G. Important: Wipe off the endoscopic needle tip with an ethanol wipe to remove any excess liquid and avoid damage when installing the endoscopic needle into the endoscope. If BioXmark® liquid is spilled on equipment, the spill on surfaces can be removed with ethanol wipes and endoscopic work channels can be flushed as described under 7.1 L.
H. Retract the needle tip into the protection sheath before installing the endoscopic needle into the endoscope.
   The needle tip shall always be retracted when moving the endoscopic needle in or out of the endoscope.
   If there is any unexpected resistance when installing the endoscopic needle into the endoscope, do not push harder than usual. Instead flush the endoscopic work channels as described under 7.1 L. to remove potential spill of BioXmark® liquid.

Injection under medical image guidance

I. Place the endoscopic needle at the target site. Push the needle tip out of the protection sheath and inject the desired volume of the BioXmark® liquid in the intended position for tissue marking.
J. Retract needle tip into protection sheath.
K. When placing next marker, repeat I. and J.

Flushing of the reusable endoscope with ethanol

L. Immediately after use, the endoscopic channel shall be flushed 3 times with a minimum of 10 ml ethanol (≥99.0 v/v%) per flush to remove potential spill of BioXmark®. Flushing can be done from either end of the endoscopic channel depending on the recommendations by the manufacturer of the reusable endoscope. This flushing with ethanol does not substitute any regular cleaning process recommended by the manufacturer of the reusable endoscope.

7.2 PERCUTANEOUS INJECTION

Preparation

A. Prepare a syringe with a pressure resistant connection (e.g. Luer lock) and a loading needle (18-20G).
   Thinner needles may require longer time to fill the syringe.
B. Open the BioXmark® ampoule and fill the syringe using the loading needle. The BioXmark® liquid is **sticky and viscous**.
C. Change the loading needle to an injection needle (19-25G):
   - Remove the loading needle.
   - Remove the stylet, if any, from the injection needle and attach the syringe containing the BioXmark® liquid to the injection needle.
D. Completely fill the injection needle with the BioXmark® liquid.
E. Wipe off the injection needle tip with an ethanol wipe to remove excess liquid.
   If BioXmark® liquid is spilled, the spill on surfaces can be removed with ethanol wipes.

Injection under medical image guidance

F. Place the injection needle in the intended position for tissue marking and inject the desired volume of the BioXmark® liquid.
G. When placing the next marker, move to the intended position for this next marker and inject the desired volume of the BioXmark® liquid.

7.3 DISPOSAL

- After use, syringes and needles may be potential biohazards. Dispose according to local procedures in line with applicable requirements.
- The ampoule and possible residual BioXmark® liquid shall be disposed according to local procedures, e.g. as normal waste and glass.

7.4 FOLLOW-UP

- Monitor patient for adverse reactions according to local procedures and national guidelines.

8. SYMBOL EXPLANATIONS


Do not use if product sterile barrier system or its packaging (ampoule) is compromised

MR safe

9. CONTACT INFORMATION

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Product malfunction and adverse events must be reported by e-mail to urgent@nanovi.com. Please include your phone number in the subject line.