INSTRUCTIONS FOR USE

Bead Block™

STERILE • SINGLE USE ONLY • NON-PYROGENIC

Sterilised by steam. Do not use if the package is opened or damaged

■ DESCRIPTION:
Bead Block comprises a range of hydrogel microspheres that are biocompatible, hydrophilic, nonresorbable and precisely calibrated. Bead Block is produced from polyvinyl alcohol and is available in the following size ranges:

<table>
<thead>
<tr>
<th>Bead Size Range</th>
<th>Label Colour</th>
<th>Hypervascular Tumours/Arteriovenous Malformations</th>
<th>Uterine Fibroid</th>
<th>Benign Prostatic Hyperplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>100-300 µm</td>
<td>Yellow</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>300-500 µm</td>
<td>Blue</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>500-700 µm</td>
<td>Red</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>700-900 µm</td>
<td>Green</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>900-1200 µm</td>
<td>Purple</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

■ PRESENTATION:
• Syringe of 20 ml presented in a sterile, sealed pre-formed polycarbonate tray with a peel-off Tyvek® lid
• Each syringe contains approximately 1 ml or 2 ml of Bead Block in non-pyrogenic, sterile, phosphate buffered saline
• Each syringe is intended for single patient use only. Do not resterilise. Discard any unused material.

■ INDICATIONS:
Bead Block is intended to be used for the embolisation of hypervascular tumours, including uterine fibroids and arteriovenous malformations (AVMs). Bead Block is also intended to be used for the treatment of symptomatic benign prostatic hyperplasia (BPH).

■ CLINICAL APPLICATIONS:
The scientific literature provides extensive documentation of embolisation procedures using a wide variety of artificial agents in peripheral vascular systems, including the head, neck, spine, liver, genitourinary tract, uterus, gastrointestinal system and limbs. A representative bibliography is provided following these instructions for use.

WARNING: Studies have shown that Bead Block does not form aggregates and, as a result, penetrate deeper into the vasculature as compared to similarly sized PVA particles. Care must be taken to choose a larger sized Bead Block when embolising arteriovenous malformations with large shunts to avoid passage of the product into the pulmonary or coronary circulation.

The colour of Bead Block could be visible through the skin if injected into arteries feeding superficial tissues.
CAUTIONS:
- Do not use if the syringe or packaging appear damaged
- Select the size and quantity of Bead Block appropriate for the pathology to be treated
- Embolisation with Bead Block should only be performed by physicians who have received appropriate interventional occlusion training in the region intended to be embolised

CONTRAINDICATIONS:
1. Patients intolerant to occlusion procedures
2. Vascular anatomy or blood flow that precludes catheter placement or injection of embolics
3. Presence or likely onset of vasospasm
4. Presence or likely onset of haemorrhage
5. Presence of severe athromatous disease
6. Presence of feeding arteries smaller than the succeeding distal branches
7. Presence of patent extra-to-intracranial anastomoses or shunts
8. Presence of collateral vessel pathways potentially endangering normal territories during embolisation
9. Presence of end arteries leading directly to cranial nerves
10. Presence of arteries supplying the lesion/tumour not large enough to accept Bead Block
11. Vascular resistance peripheral to the feeding arteries precluding passage of Bead Block into the lesion/tumour
12. Do not use Bead Block in the following applications:
   i. Embolisation of large diameter arteriovenous shunts (i.e. where the blood does not pass through the arterial/capillary/venous transition but directly from artery to vein)
   ii. The pulmonary arterial vasculature
   iii. Any vasculature where Bead Block could pass directly into the internal carotid artery, the central circulatory system or other non-target territories
   iv. Any neurovascular location

POTENTIAL COMPLICATIONS:
1. Undesirable reflux or passage of Bead Block into normal arteries adjacent to the targeted lesion/tumour or through the lesion/tumour into other arteries or arterial beds
2. Non-target embolisation
   - Pulmonary embolism
   - Pancreatitis
3. Ischaemia at an undesirable location
4. Post embolisation syndrome
5. Capillary bed saturation and tissue damage
6. Ischaemic stroke or ischaemic infarction
7. Vessel or lesion/tumour rupture and haemorrhage
8. Neurological deficits including cranial nerve palsy
9. Liver abscess
10. Vasospasm
11. Death
12. Recanalisation
13. Foreign body reactions necessitating medical intervention
14. Infection necessitating medical intervention
15. Clot formation at the tip of the catheter and its subsequent dislodgement
UTERINE FIBROID EMBOLISATION (UFE) SPECIFIC CONTRAINDICATIONS, WARNINGS, PRECAUTIONS & POTENTIAL COMPLICATIONS

■ UFE SPECIFIC CONTRAINDICATIONS:
- Pregnant women
- Active or suspected pelvic inflammatory disease
- Malignancy of the pelvic region
- Endometrial neoplasia or hyperplasia
- Presence of submucosal fibroids with greater than 50% growth into the uterine cavity
- Presence of pedunculated serosal fibroid as the dominant fibroid(s)
- Fibroids with significant collateral feeding by vessels other than the uterine arteries

■ UFE SPECIFIC WARNINGS: Warnings about UFE and Pregnancy:
- There are no long term data on the effects of UFE on the ability to become pregnant and carry a foetus to term, and on the development of the foetus
- This procedure should only be performed on women who do not intend future pregnancy
- Women who become pregnant following UFE may be at increased risk for the following:
  - Postpartum haemorrhage
  - Preterm delivery
  - Caesarean delivery
  - Abnormal presentation at birth
- Devascularisation of the uterine myometrium resulting from UFE may increase the risk of uterine rupture of women who subsequently become pregnant following UFE

■ OTHER UFE WARNINGS:
- When using Bead Block for uterine fibroid embolisation, do not use beads smaller than 500 microns
- An appropriate gynaecologic work-up should be performed on all patients presenting for embolisation of uterine fibroids (e.g. gynaecologic history, fibroid imaging, endometrial sampling to rule out carcinoma in patients with abnormal menstrual bleeding)
- The diagnosis of uterine sarcoma could be delayed by taking a non-surgical approach (such as UFE) to treating fibroids. It is important to pay close attention to warning signs for sarcoma (e.g., rapid tumour growth, postmenopausal with new uterine enlargement, MRI findings) and to conduct a more thorough work-up of such patients prior to recommending UFE. Recurrent or continued tumour growth following UFE should be considered a potential warning sign for sarcoma and surgery should be considered.

■ UFE SPECIFIC PRECAUTIONS:
- There is an increased chance of reflux of Bead Block into unintended blood vessels as uterine artery flow diminishes. Comparison of angiographic endpoint & infarction rate in individual patients indicates that best results were obtained with an endpoint close to stasis.
- The long-term outcome of UFE is at present unknown
UFE SPECIFIC POTENTIAL COMPLICATIONS: Potential post procedure complications include:
1. Abdominal pain
2. Discomfort
3. Fever
4. Nausea
5. Constipation
6. Premature ovarian failure (i.e. menopause)
7. Amenorrhoea
8. Infection of the pelvic region
9. Uterine/ovarian necrosis
10. Local vascular inflammation
11. Deep vein thrombosis with or without pulmonary embolism
12. Vaginal discharge
13. Tissue passage, fibroid sloughing, or fibroid expulsion post UFE
14. Post-UFE intervention to remove necrotic fibroid tissue
15. Vasovagal reaction
16. Transient hypertensive episode
17. Hysterectomy

PROSTATE ARTERY EMBOLISATION (PAE) FOR BPH SPECIFIC CONTRAINDICATIONS, WARNINGS, PRECAUTIONS & POTENTIAL COMPLICATIONS

PAE SPECIFIC CONTRAINDICATIONS:
• Presence of prostate cancer
• Presence of prostatic or lower urinary tract infection
• Prior prostatitis

PAE SPECIFIC WARNINGS:
• PAE does not reduce symptoms in all cases despite decreased prostate volume
• The prostate may continue to grow (with or without a reduction in symptoms)

PAE SPECIFIC PRECAUTIONS:
• Patients with tortuous arterial supply or atherosclerotic arteries should be excluded from treatment
• The long-term outcome of PAE is at present unknown

PAE SPECIFIC POTENTIAL COMPLICATIONS:
1. Post procedural abdominal pain
2. Transient pollakiuria (frequent urge to urinate)
3. Transient haematuria
4. Transient urinary retention
5. Transient haematospermia
6. Genitourinary tract infection
INSTRUCTIONS FOR USE:

- Carefully evaluate the vascular network associated with the lesion/tumour using high resolution imaging prior to beginning the embolisation procedure.
- Bead Block is available in a range of sizes. Care should be taken to choose the appropriate size Bead Block that best matches the pathology (i.e., vascular target/vessel size) and provides the desired clinical outcome.
- When embolising arteriovenous malformations, choose a bead size that will occlude the nidus without passing through the AVM.
- Choose a delivery catheter based on the size of the target vessel. Bead Block can tolerate temporary compression of 20% to 30% in order to facilitate passage through the delivery catheter.
- Introduce the delivery catheter into the target vessel according to standard techniques. Position the catheter tip as close as possible to the treatment site to avoid inadvertent occlusion of normal vessels.
- Bead Block is not radio-opaque. It is recommended to monitor the embolisation under fluoroscopic visualisation by adding the desired amount of contrast medium to the phosphate buffered saline.

ADDITIONAL UFE SPECIFIC INSTRUCTIONS:

- An endpoint of stasis or near stasis is recommended with the main uterine artery remaining patent but with negligible residual flow toward the uterus. Based on published data, Bead Block sizes from 500-700µm and greater are shown to be effective in the treatment of uterine fibroids; however, 700-900µm Bead Block is recommended, with upsizing to 900-1200µm if required.
- This endpoint corresponds to an angiographic image of a patent horizontal segment with absent flow in the ascending segment of the uterine artery.
- At the discretion of the physician, pneumatic compression devices may be used for patients currently taking hormone therapy, uterine volume >1000cc, and patients that are overweight to lower the risk of deep vein thrombosis.

ADDITIONAL PAE SPECIFIC INSTRUCTIONS:

- There is some clinical evidence to date for the use of smaller bead or particle sizes, however, the majority has documented the use of 300-500µm microspheres for PAE.

UFE and PAE PATIENT COUNSELLING INFORMATION:

- Patients should have a clear understanding prior to embolisation of who will provide their post procedure care and whom to contact in case of an emergency after embolisation.
- UFE and PAE candidates should have an understanding of the potential benefits, risks, and adverse events associated with the embolisation procedure. In particular, patients should understand that there is a chance their fibroid or prostatic symptoms will not improve following embolisation.

Recommended catheters and contrast agents:

<table>
<thead>
<tr>
<th>Product size range of Bead Block™</th>
<th>Recommended catheter (internal diameter)</th>
<th>Recommended contrast agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 – 300 µm</td>
<td>≥ 2.4 Fr (0.016 in/0.42 mm)</td>
<td>Omnipaque 300 (Iohexol 300)</td>
</tr>
<tr>
<td>300 – 500 µm</td>
<td></td>
<td>Omnipaque 350 (Iohexol 350)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Visipaque 320 (Iodixanol 320)</td>
</tr>
<tr>
<td>500 – 700 µm</td>
<td>≥ 4.0 Fr (0.041 in/1.03 mm)</td>
<td>Iomeron 350 (Iomepral 350)</td>
</tr>
<tr>
<td>700 – 900 µm</td>
<td></td>
<td>Niopam/Optiray 300 (Ioversol 300)</td>
</tr>
<tr>
<td>900 – 1200 µm</td>
<td>≥ 4.0 Fr (0.041 in/1.03 mm)</td>
<td>Isovue 300 (Solutrust 300)</td>
</tr>
</tbody>
</table>

Note: Other contrast agents have not been tested in conjunction with Bead Block™.
DELIVERY INSTRUCTIONS:

Preparation
1. To obtain a homogeneous suspension, directly aspirate the contrast medium into the syringe containing the beads in phosphate buffered saline and remove all air from the syringe. The volume of contrast medium to be added varies depending on the contrast medium viscosity and the bead size. As an indication, the typical volume of contrast medium required for addition to the syringe content will range from 3 to 6mL to achieve a contrast medium to product volume ratio ranging from approximately 40:60 (e.g. with Omnipaque 350) to 60:40 (e.g. with Niopam 300).
2. To evenly suspend the Bead Block/contrast medium, gently invert the 20ml syringe several times. Attach the 20ml syringe to one port of the luer-lock 3-way stopcock; and, if desired, a delivery catheter may be attached to the remaining port on the stopcock. Wait several minutes to allow the Bead Block to suspend properly.
3. Draw the Bead Block/contrast medium into the injection syringe slowly and gently to minimise the potential of introducing air into the system. Purge all air from the system prior to injection.

Delivery
1. Inject the Bead Block/contrast medium from the injection syringe under fluoroscopic visualisation using a slow pulsatile action, while observing the contrast medium flow rate. If there is no effect on the flow rate, repeat the delivery process with additional injections of Bead Block/contrast medium or larger sized Bead Block may be considered. If the Bead Block/contrast medium requires re-suspension, gently invert the 20ml syringe several times.
2. Exercise conservative judgement in determining the embolisation endpoint

Post Procedure
1. Upon completion of the treatment, remove the catheter while maintaining gentle suction so as not to dislodge Bead Block still within the catheter lumen.
2. Discard any open, unused Bead Block as well as any other ancillary equipment used in the procedure such as syringes, needles and catheters etc.

PACKAGE LABEL:

<table>
<thead>
<tr>
<th>REF</th>
<th>Catalogue number</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOT</td>
<td>Batch number/Lot number</td>
</tr>
<tr>
<td></td>
<td>Steam Sterilised</td>
</tr>
<tr>
<td></td>
<td>Use before/Expiry</td>
</tr>
<tr>
<td></td>
<td>Protect from light</td>
</tr>
<tr>
<td></td>
<td>Attention see instructions for use</td>
</tr>
<tr>
<td></td>
<td>Protect from moisture</td>
</tr>
<tr>
<td></td>
<td>Do not freeze</td>
</tr>
<tr>
<td></td>
<td>Do not reuse</td>
</tr>
</tbody>
</table>

CONSERVATION AND STORAGE:
- Bead Block must be stored in a cool, dry and dark place in its original packaging.
- Use by the date indicated on the syringe label.
- Do not freeze.