Read all of this leaflet, before you start having this medicine.

- Please keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or nurse.
- If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

In this leaflet:

1 WHAT SEPTOPAL CHAINS ARE AND WHAT THEY ARE USED FOR
2 READ THIS, BEFORE YOU HAVE SEPTOPAL CHAINS
3 HOW SEPTOPAL CHAINS WILL BE GIVEN TO YOU
4 POSSIBLE SIDE EFFECTS
5 HOW SEPTOPAL CHAINS ARE STORED
6 FURTHER INFORMATION

1 WHAT SEPTOPAL CHAINS ARE AND WHAT THEY ARE USED FOR

What Septopal Chains are
Septopal Chains are an antibiotic implant. It is made up of tiny beads strung together on stainless steel wire.

Each chain consists of 10, 30 or 60 beads. Each bead contains the active ingredient gentamicin sulphate. This is the antibiotic. The gentamicin is slowly released from the beads at the place of a possible or existing infection, so that it can provide protection against future infection or treat an existing one.

What Septopal Chains are used for
They are used for:
- the short and longer term treatment of bone infections, such as:
  - infection of the bone marrow and the surrounding bone (osteomyelitis);

- infection of a break in a bone that has not knitted together properly (infected pseudoarthroses);
- infection where a broken bone has been fixed together by something like a metal plate (infected osteosynthesis);
- the short term prevention of infection in bone injuries;
- the short term prevention and treatment of infections that can occur after operations on the bowels;
- other conditions, such as: infection of the lining of the abdominal wall (bacterial peritonitis), gall bladder removal (cholecystectomies), abnormal channels between surfaces of the body, such as between the bowel and the skin (infected fistulae), replacements for damaged blood vessels (infected vascular grafts) and abscesses in the soft tissues of the body.

2 READ THIS, BEFORE YOU HAVE SEPTOPAL CHAINS

You will not have Septopal Chains if:
- you are known to have a bad reaction to any of the ingredients in Septopal Chains (see Section 6 for a list of these).

Special care will be taken in giving you Septopal Chains
If tests have identified bacteria which may not respond when Septopal Chains are used on their own, you will have treatment with another antibiotic, as well as with these chains.

In the young (under 18) and elderly (65+), there is no evidence that Septopal Chains can cause damage to the kidneys or to the hearing. But, if you receive these chains and you have moderate or severe kidney disease, then the state of your kidneys and the level of gentamicin in your blood will be checked during your treatment.
Septopal Chains and medical devices

- Tell your doctor if you have any implants containing metal. This is because of the possibility that the stainless steel wire and the implant might become corroded.
- If you already have any implants which contain metal, Septopal Chains will not be placed next to them.
- If, during your treatment, it is decided that you will need a metallic implant, the chains will be removed beforehand.

Taking other medicines

Please tell your doctor or nurse if you are taking, or have recently taken, any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

Septopal Chains are not recommended for use if you are pregnant, because there is a faint possibility that gentamicin might damage the hearing of an unborn child.
If you are breast-feeding, talk to your doctor before receiving Septopal Chains.

3 HOW SEPTOPAL CHAINS WILL BE GIVEN TO YOU

Where the chains will be placed

The chains are placed, during your operation, in the space left after the surgeon has thoroughly removed damaged or infected bone or tissue.

How many chains you will have

- The number of chains you receive will depend on the size of the space left after the damaged or infected bone or tissue has been removed.
- The surgeon usually places from one to three chains in the cavity, but may use up to five.

How the chains will be inserted

This will depend on whether you are going to have the chains for a short or longer period of time. Your doctor will let you know.

Short term – for bone and soft tissue infection

If you will be having the chains for a short time, they will be inserted as follows:
- The surgeon will leave the last bead in each chain sticking out above skin level, and held in position by a loose stitch, so that, later on, a few beads at a time can be withdrawn, each day, from the wound.

Longer term – for bone infection

If you will be having the chains for a longer time, they will be implanted:
- either with the last bead sticking out, (as described in ‘Short term’ above),
- or they will be completely enclosed in the wound, perhaps with a drain in place to let fluid out.

When and how the chains will be removed

Short term – for bone infection

If you received the chains for a short time and for a bone infection, then:
- All the chains should normally be completely removed 10 – 14 days after the surgeon inserted them.
- The number of beads removed each day will be counted carefully.
- When a chain is being removed, there is a small chance that either some of the beads are left behind or, very unusually, the wire may break. If this happens, your doctor will try to remove the remaining beads and/or wire. If an operation is required to do this, the doctor may decide that it is safer to leave them where they are.
- If your doctor finds that an infection continues for more than five days after the operation, the chains may be removed, and the cause of the infection identified, before treatment with further antibiotics.

Longer term – for bone infection

If you received the chains for a longer time, then:
- If the chains were completely enclosed in the wound, they will be removed through another operation, up to 3 months later, depending on the original operation.

Short term – for soft tissue infection

If you received the chains for a short time and for a soft tissue infection, then:
- The chains are best removed by day six or, at the latest, by day 10 after the operation. They will usually be withdrawn gradually, each day, a few beads at a time, beginning on the second day after insertion.
If you receive more Septopal Chains than you should
These chains are given to you by healthcare professionals. It is extremely unlikely that you will receive more chains than you should.

If you have any further questions about taking Septopal Chains, please ask your doctor or nurse.

4 POSSIBLE SIDE EFFECTS

Like all medicines, Septopal Chains can cause side effects, although not everybody gets them. If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse as soon as possible.

The beads in the chains are strung on stainless steel wire. If you find you experience an allergic reaction, please tell your doctor or nurse as soon as possible.

Please remember: the benefits you get from having these Septopal Chains will usually be greater than the risk of suffering any harmful side effects.

5 HOW SEPTOPAL CHAINS ARE STORED

The hospital staff will ensure that the following instructions for the storage of Septopal Chains are observed:

- Store at room temperature.
- Do not freeze.
- Keep out of the reach and sight of children.
- Once the inner pouch is opened, any unused chains will be discarded.
- The chains will not be used after the expiry date stated on the carton and the aluminium pouch. The expiry date refers to the last day of that month.

6 FURTHER INFORMATION

What Septopal Chains contain
Each bead contains the active ingredient gentamicin sulphate 7.5 mg (equivalent to 4.5 mg gentamicin base).

Other, non-active, ingredients in Septopal Chains are: glycine, methylmethacrylate-methylacrylate copolymer, zirconium dioxide, stainless steel.

What Septopal Chains look like and contents of the pack
Each Septopal Chain is contained in an inner sachet, which is then contained in a transparent peel-pouch, which is then contained in a protective aluminium pouch, which is then packaged in an outer carton.

These chains are supplied in packs of 1 or 5 sachets. Each sachet contains one chain of 10, 30 or 60 impregnated methylmethacrylate-methylacrylate copolymer (PMMA) beads threaded on a stainless steel wire.

Not all pack sizes and chain lengths are marketed.

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1 NAME OF THE MEDICINAL PRODUCT
Septopal Chains.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Chain of 10, 30 or 60 beads. Each contains 7.5 mg Gentamicin Sulphate EP (equivalent to 4.5 mg gentamicin base).

3 PHARMACEUTICAL FORM
Impregnated methylmethacrylate-methylacrylate copolymer (PMMA) beads for surgical use. Each chain consists of 10, 30 or 60 beads threaded on multiple stranded surgical wire.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Short term and longer term therapy in bone infection, e.g. osteomyelitis, infected pseudoarthroses, infected osteosynthesis.

Short term preventative treatment of potentially infected bone injuries.

Short term prevention and therapy of soft tissue infections associated with abdominoperineal resections; operations on the small or large bowel. Other therapeutic indications for use include bacterial peritonitis, cholecystectomy, infective fistulae, infected vascular grafts, soft tissue abscesses.

4.2 Posology and method of administration
For implanting in the cavity resulting from thorough surgical removal of sequestrated bone or infected tissue.

The number of chains used will depend upon the size of the cavity which results after thorough surgical removal of infected tissue or that remaining after operation in the sacral cavity. Usually 1 – 3 chains are inserted but up to 5 chains have been used. The chains are laid in the cavity in such a way as to facilitate easy removal. It is recommended that the 10 bead chain is used for smaller cavities.

1 BONE INFECTIONS
a) Short term application
When implanting the chains, it is recommended to take into account the direction in which the chain will later be pulled out and to let the last bead project above the skin level, through a separate stab incision anchored by a loose suture, in order that the chain may be removed by careful steady traction, a few beads at a time daily. The chains should normally be completely removed by 10-14 days following insertion and preferably no more than 10 days after the operation. Where there is evidence of persisting local infection beyond 5 days post-operatively, it is recommended that the chain is removed and the cause of infection determined prior to recommending further antibacterial therapy.

The less the chains are fixed to connective tissue, the easier it is to remove them, thus making the procedure more comfortable for the patient.

If the beads become fixed to connective tissue to a great extent, or if the traction of the beads is not adapted to the tissue conditions, then there is a small possibility that one or several may become detached from the wire or, in exceptional circumstances, the wire may break on removal of the chain. In such an event, attempt should be made to remove the individual beads and the remaining wire. Should, however, extensive surgery be necessary then the risk of reoperation should be considered carefully. In high-risk patients, it may be preferable to leave the beads in situ permanently. For the above reasons the beads should always be counted on their removal.

b) Longer term application
This may be as above or if circumstances require it, the chains may be implanted completely, and removed by reoperation up to 3 months later. The length of time the chains are left in situ prior to secondary intervention will depend on the orthopaedic procedure. Inserted chains will be completely enclosed by primary wound closure. Control of local infection allows subsequent surgical procedures e.g. cancellous bone grafting.
2 SOFT TISSUE INFECTIONS
(SHORT TERM APPLICATIONS ONLY)
The insertion of chains is carried out as described under 1a above. In this indication the chains are best removed by the sixth and at the latest the tenth day after operation. In most cases it is advised that the chains are withdrawn gradually, a few beads at a time daily from about the second past insertion day.

In considering wound closure/drainage, it should be remembered that excess drainage will dilute the gentamicin concentration at the site of infection so, if possible, primary wound closure should always be employed. Local circumstances and degree of inflammation should, however, be taken into consideration. An overflow drain may be employed only when considered necessary. Suction drainage should not be employed but may be temporarily used in cases of obstructed wound secretion flow.

Toxic effects due to the antibiotic are not anticipated since, after use of Septopal Chains, barely detectable gentamicin concentrations (no more than 0.5 µg/ml) are found in the systemic circulation for up to 4 days post-operatively.

There is no distinguishing factor between doses for the young, adults and elderly since the number of chains used depends on the size of the cavity in individual cases and the clinical conditions at the site of infection.

4.3 Contraindications
Established intolerance to Gentamicin.

4.4 Special warnings and precautions for use
Septopal Chains should not be used alone in those situations where culture of wound secretion reveals the presence of anaerobic bacteria, or organisms which could be insensitive to gentamicin therapy. In these instances, additional systemic therapy with an appropriate antibiotic should be used.

Septopal may be used in all orthopaedic surgical procedures where gentamicin sensitive organisms are found to be present from routine bacteriological screening. Where resistant organisms are encountered to the standard 10 microgram disc test, an MIC determination is recommended. In view of the high bactericidal gentamicin concentration at the infection site, organisms found resistant to the standard 10 microgram sensitivity disc screen may in fact be sensitive and therefore results of such screening may not give a true reflection of clinical efficacy.

In soft tissue the chains should not be planted intraperitoneally.

In the young and elderly there is no evidence to suggest that use of Septopal Chains has caused either nephrotoxic or ototoxic effects. Nevertheless, if Septopal therapy is desirable in patients who have moderate to severe impairment of renal function, monitoring of renal state and plasma gentamicin levels is advised.

4.5 Interaction with other medicinal products and other forms of interaction
Septopal Chains should not be used concurrently in apposition to metal-containing implants because of the theoretical possibility of surgical wire and implant corrosion. Septopal Chains should be removed prior to implant of a metal prosthesis.

4.6 Pregnancy and Lactation
Gentamicin crosses the placenta and may cause oto-toxicity in the foetus although no problems in clinical use have positively been identified. Implantation of Septopal Chain results in only a transient, barely detectable plasma concentration of Gentamicin (no more than 0.5 µg / ml). Therefore, no ototoxic effects on the foetus are to be expected. Nevertheless, it is recommended that the product should not be used in pregnancy.

4.7 Effects on ability to drive and use machines
No effect.

4.8 Undesirable effects
Because the beads are strung on surgical wire containing chrome and nickel, there is a potential for local sensitivity to these metals.

4.9 Overdose
Not applicable.
5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Gentamicin, an aminoglycoside antibiotic, possesses an “in vivo” and “in vitro” broad antibacterial spectrum of action. Its activity covers gram-positive bacteria and gram-negative micro-organisms such as E. coli, Klebsiella, Enterobacter, Pseudomonas and Proteus. It is effective against problem organisms which are resistant to other antibiotics.

Gentamicin has a bactericidal effect on proliferating and latent organisms.

Gentamicin is released gradually from the PMMA beads over a prolonged period and the high bactericidal concentrations of the antibiotic reached at the site of the infection enable the infection to be controlled, or provide protection against infection.

5.2 Pharmacokinetic properties
Low levels of Gentamicin are detectable in the serum for only a few days after implantation, (maximum found is 0.5 µg/ml).

Gentamicin is detectable in the urine for several months after implantation which is evidence of persistent release from implanted beads.

In wound secretions originating directly from the operation area, high gentamicin concentrations of between 14 and 215 µg/ml are found. These are in excess of the MICs required for the elimination of causative organisms at the site for infection.

5.3 Preclinical safety data
N/A

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Glycine, methylmethacrylate-methylacrylate copolymer, zirconium dioxide, polyfilic stainless steel.

6.2 Incompatibilities
None.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Store at room temperature. Do not freeze. Resterilisation should not be attempted under any circumstances.

6.5 Nature and contents of container
Container: Sterile inner sachet within a secondary peel-open sachet in an aluminium sachet containing drying agent. The aluminium sachet is packed in a cardboard box. Contents: Packs of 1 or 5 sachets each containing 1 chain of 10, 30 or 60 beads.

6.6 Special precautions for disposal
None.

7 MARKETING AUTHORISATION HOLDER
Biomet UK Ltd.
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PL 13442/0003

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11 DOSIMETRY (IF APPLICABLE)

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)