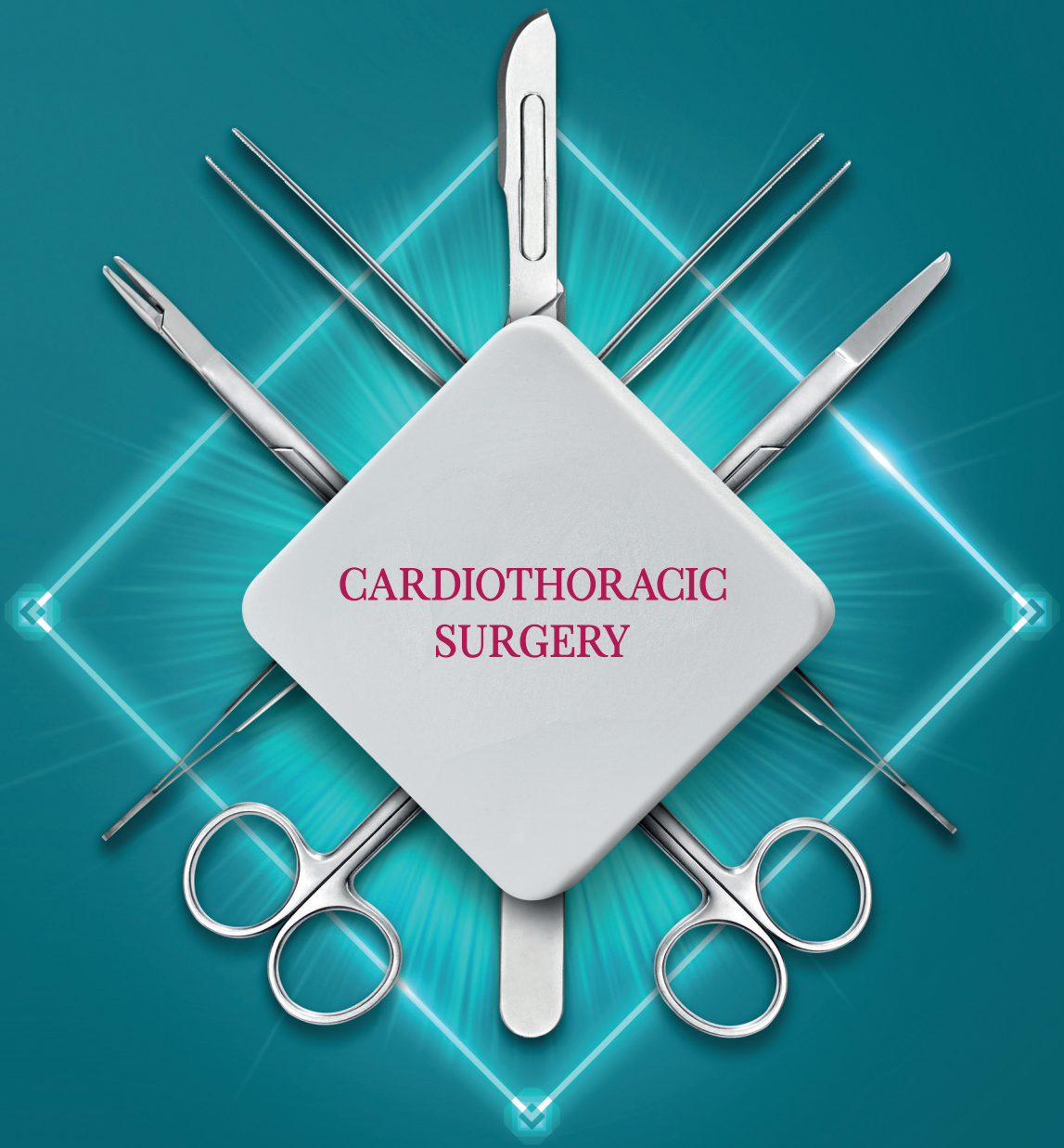
COLLATAMP®G

Collagen gentamicin implant

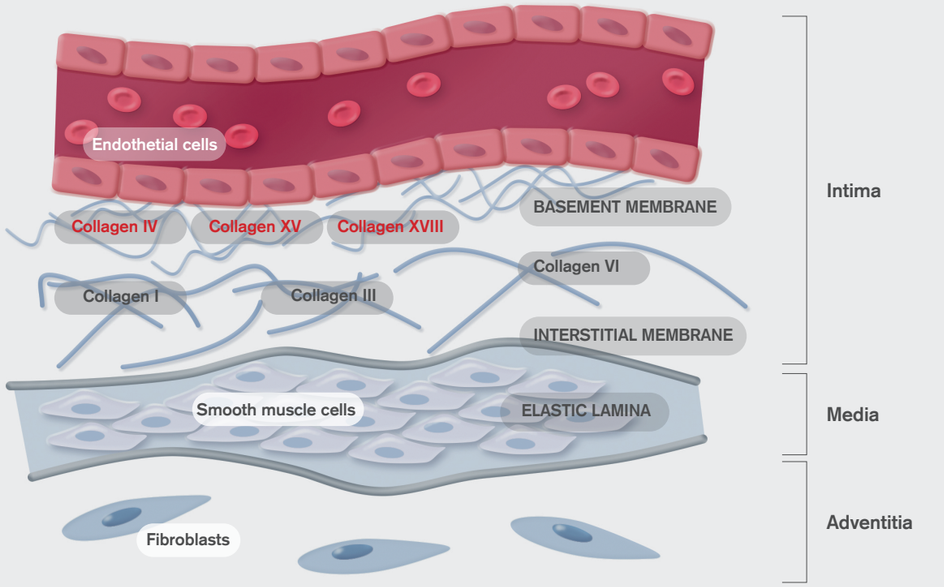


21/07/UK/COLG/014

SERB SURGERY

Local haemostasis

- Collagens are the most abundant proteins in the extracellular matrix (ECM) and provide mechanical strength to the vascular wall.[1]
- Their structural properties help to maintain vascular membrane mechanical stability, and their adhesive properties help to counteract blood extravasations upon vascular injury.[1]



Schematic representation of basement membrane & interstitial matrix localization to the vascular wall.[1]

Adapted by SERB from Manon-Jensen T. *et al.,* 2016

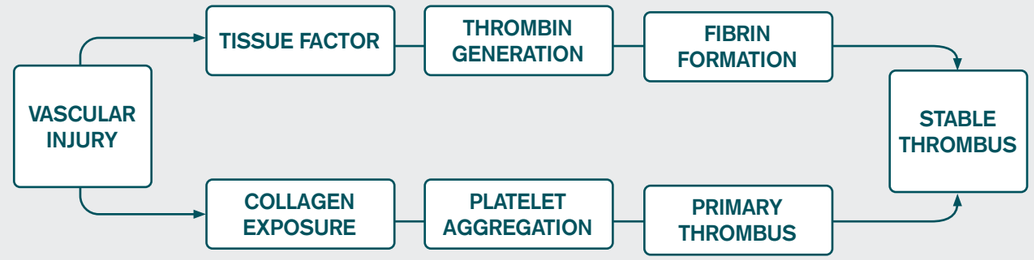
The extracellular matrix surrounding the vascular vessel consists first of a basement membrane and then an interstitial matrix.
Collagens of the basement membrane include collagen types IV, XV and XVIII.
Collagen of the interstitial matrix include collagen types I, III and VI.
The collagens provide tensile strength, adhesiveness, and structural integrity.[1]

References:
1. Manon-Jensen T. et al., Collagen-mediated hemostasis. J Thromb Haemost. 2016 Mar;14(3):438-48. 2. Stemberger A. et al., Local treatment of bone and soft tissue infections with the collagen-gentamicin sponge. Eur J Surg Suppl. 1997;(578):17-26. 3. Seré KM. et al., Basic mechanisms of hemostasis. Semin Vasc Med. 2003 Feb;3(1):3-12. 4. Instruction for use, Collatamp G, May 2021. 5. Ruszczak Z. et al., Collagen as a carrier for on-site delivery of antibacterial drugs. Adv Drug Deliv Rev. 2003 Nov 28;55(12):1679-98. 6. Jørgensen LG. et al., Clinical and pharmacokinetic evaluation of gentamycin containing collagen in groin wound infections after vascular reconstruction. Eur J Vasc Surg. 1991 Feb;5(1):87-91. 7. ECDC Surveillance Report, Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals. 2011–2012. 8. Mangram AJ. et al., Guidelines for prevention of surgical site infection. Infect Control Hosp Epidemiol.1999;20:247–280. 9. Tang R. et al., Risk factors for surgical site infection after elective resection of the colon and rectum: A single-center prospective study of 2,809 consecutive patients. Ann Surg 2001;234:181–189. 10. Scottish Intercollegiate Guidelines Network, Antibiotic prophylaxis in surgery. SIGN 104. July 2008 accessed at: http://www.sign.ac.uk/pdf/sign104.pdf. 11. Friberg O. et al., Local gentamicin reduces sternal wound infections after cardiac surgery: a randomized controlled trial. Ann Thorac Surg. 2005 Jan;79(1):153-61. 12. Friberg O. et al., Collagen-gentamicin implant for prevention of sternal wound infection; long-term follow-up of effectiveness. Interactive Cardiovascular and Thoracic Surgery. 2009 Sep;9(3):454-458. 13. Benedetto U. et al., Cardiac Outcomes Research Group. Scoring system to guide decision making for the use of gentamicin-impregnated collagen sponge to prevent deep sternal wound infection. J Thorac Cardiovasc Surg. 2014 Nov;148(5):2390-2396.e1.

Local haemostasis

- After surgical operations or injuries, the exposure of collagen fibrils triggers the adhesion of platelets and the activation of plasma coagulation factors leading to wound closure.[2]
- Haemostasis is triggered when blood comes into contact with released tissue factors and exposed endogenous collagen fibrils or renatured collagen fibrils like those in Collatamp®G.[4]

Procoagulant response to vascular injury[3]



- Collatamp®G is intended to achieve haemostasis when blood comes into contact with the released tissue factors and exposed collagen fibrils.[4]
- The adhesion and aggregation of platelets is induced on the renatured collagen fibrils of Collatamp®G and the plasmatic coagulation process is accelerated.[4]
- The sponge-like structure of Collatamp®G stabilises the wound clot, and takes up a certain amount of blood. Collagen also promotes granulation and epithelialization.[4]

14. Kowalewski M. et al., Gentamicin-collagen sponge reduces the risk of sternal wound infections after heart surgery: Meta-analysis. J Thorac Cardiovasc Surg. 2015 Jun;149(6):1631-40.e1-6. 15. Lazar HL.et al., Prevention and management of sternal wound infections. J Thorac Cardiovasc Surg. 2016 Oct;152(4):962-72. 16. Sousa-Uva M. et al., 2017 EACTS Guidelines on perioperative medication in adult cardiac surgery. Eur J Cardiothorac Surg. 2018 Jan 1;53(1):5-33. 17. World Union of Wound Healing Societies (WUWHS) Consensus Document. Surgical wound dehiscence: improving prevention and outcomes. Wounds International, 2018. 18. NICE guideline NG125 Evidence reviews April 2019. 19. Friberg O. et al., Cost effectiveness of local collagen-gentamicin as prophylaxis for sternal wound infections in different risk groups. Scand Cardiovasc J SCJ, 2006; 40(2): 117-125. 20. Jenks P.J. et al., Clinical and economic burden of surgical site infection (SSI) and predicted financial consequences of elimination of SSI from an English hospital. Journal of Hospital Infection, 2014; 86: 24-33 21. Costa A. et al., Collagen implant with gentamicin sulphate reduces surgical site infection in vascular surgery: a prospective cohort study. Int J Surg. 2014 Oct;12(10):1100-4. 22. Maczynska B. et al. (2019) In vitro efficacy of gentamicin released from collagen sponge in eradication of bacterial biofilm preformed on hydroxyapatite surface. PLoS ONE 14(6): e0217769. 23. Brehant O. et al., The gentamicin-collagen sponge for surgical site infection prophylaxis in colorectal surgery: a prospective case-matched study of 606 cases. Int J Colorectal Dis. 2013 Jan;28(1):119-25. 24. Rutkowski A. et al., The gentamicin-collagen implant and the risk of distant metastases of rectal cancer following short-course radiotherapy and curative resection: the long-term outcomes of a randomized study. Int J Colorectal Dis. 2018 Aug;33(8):1087-1096.

COLLATAMP®G

Indications

- Collatamp®G is used for local haemostasis of capillary, parenchymatous and seeping haemorrhages in areas with a high risk of infection (determined by the surgeon on a case-by-case basis, including patient-related, surgery-related, and physiological factors).[4]
- After implantation of Collatamp®G, systemic gentamicin plasma amounts may temporarily reach therapeutic levels.[4]

Composition

- Collatamp®G is composed of bovine collagen incorporating gentamicin sulfate at a locally effective dose.[4]
- Available in 3 sizes.[4]

Size (cm)	Dimension & Composition of Collatamp®G			
	Bovine collagen		Gentamicin sulfate (base)	
	mg/implant	mg/cm²	mg/implant	mg/cm²
5 x 5 x 0.5	70	2.8	50 (32.5)	2.0 (1.3)
10 x 10 x 0.5 5 x 20 x 0.5	280		200 (130)	

Dosage & method of administration

- The implant procedure should be performed by an appropriately trained surgeon under aseptic conditions. Avoid any unsterile handling of the product before or during application to avoid contamination.[4]
- Collatamp®G is administrated as follows:[4]

✓ **Before surgery:**

- Read the instruction for use carefully.
- Check the integrity of packaging.
- The product must be used as soon as the sterile package component has been opened.
- Do not used if the packaging is damaged.

✓ **During surgery:**

- Gloves and instruments should be wetted to prevent Collatamp®G from adhering to them. Collatamp®G can be cut to size to fit the area to be treated.
- Place a dry Collatamp®G on the area to be treated, which should be as dry as possible, and light pressure applied for about a few minutes to achieve better adhesion.
- Up to 3 large Collatamp®G sponges (10 × 10 × 0.5 or 5 × 20 × 0.5 cm) can be used, depending on the size of the area requiring haemostasis. However, the patient's body weight should be taken into account. The number and size of the implants should be selected so that a total dose of 9 mg gentamicin sulfate per kg body weight is not exceeded.

✓ **After surgery:**

- Collatamp®G is completely absorbed.
- Timelines for complete absorption depend on the site of surgical implantation.

Undesirable effects

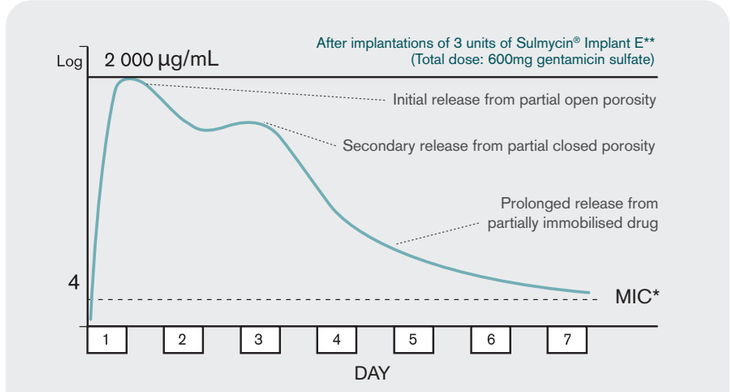
- Undesirable effects related to the use of this product are possible - refer to the IFU at the end of the document.

Properties

- The gentamicin included in Collatamp®G helps to prevent infections that might occur at the site of implantation caused by gentamicin-sensitive bacteria.[4]

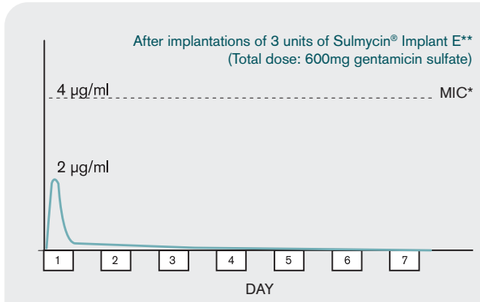
  The administration of Collatamp®G might not prevent an infection with gentamicin-resistant bacteria. The risk of infection is based on individual/combination of factors.[4]

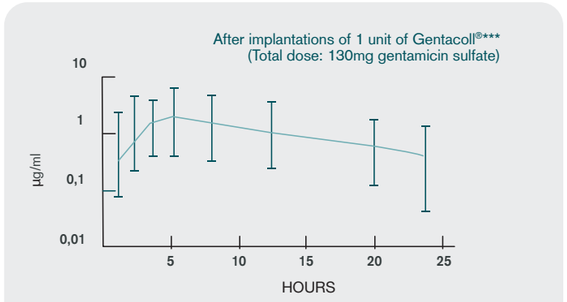
Local concentration of gentamicin in soft tissue[5]



- After implantation of Collatamp®G, systemic gentamicin plasma amounts may temporarily reach therapeutic levels.[4]

Low and short-lasting systemic exposure reported below toxicity thresholds[5,6]





- Collatamp®G is completely absorbed (estimated that in the overwhelming majority of cases, Collatamp®G is completely or predominantly degraded within 4-8 weeks, regardless of the site of implantation).[4]
- Prolonged use may lead to the emergence of resistant organisms. There is no evidence that single use Collatamp®G administration in patients promotes or induces the formation of resistance against gentamicin.[4]

*MIC: Minimal Inhibitory Concentration **Sulmycin® Implant E: Tradename of the registered medicinal product in Germany with collagen and gentamicin sulfate equivalent to Collatamp®G, the only difference is the origin of the collagen (equine and not bovine) ***Gentacoll®: Tradename of the registered product in Danemark with collagen and gentamicin sulfate equivalent to Collatamp®G.

Surgical site infections (SSI*)

- Surgical site infections represent 19,6% of hospital associated infections.[7]
- Some patients may be at high risk of infections:[8,9,10]
  - Obesity (>20% ideal body weight)
  - Diabetes
  - Smoker
  - Altered immune response (steroids or others)
  - Extremes of age
  - ASA** score 2 or 3

Reduction of SSI* in randomized studies in cardiac surgery

FRIBERG 2005[11] (including 1 950 patients) → 53% relative reduction (4.7% absolute reduction) in the incidence of SWI*** after sternotomy on an unselected cardiac surgery patient population

FRIBERG 2009[12] (including 2 326 patients) → Persistent significant reduction in superficial and deep SWI*** (OR^{α} = 0.34)

BENEDETTO 2014[13] (including 8 750 adult patients with 329 patients (3.8%) receiving GICS$^{\beta}$ implant) → Overall incidence of deep SWI*** was lower among patients who received GICS$^{\beta}$ implant (0.6%) than patients who did not (2.01%) *(p = 0.02)*

KOWALEWSKI 2015[14] (including 22 135 patients) → 40% significant risk reduction of superficial SWI*** compared with the control group *(p = 0.002)*
38% risk reduction of deep SWI*** compared with the control group *(p = 0.006)*

Supported by guidelines & consensus

AATS 2016[15] (American Association of Thoracic Surgery) → "Topical antibiotics applied to the cut edges of the sternum have been found to significantly reduce the incidence of SWI***."

EACTS 2017[16] (European Association of Cardio-Thoracic Surgery) → "The results from a recent metaanalysis showed significant reduction of the risk for SWI*** after implantation of gentamicin–collagen sponges."[14]

WUWHS 2018[17] (World Union of Wound Healing Societies) → Interventions for reduction of risk of surgical site complications such as SWD^{γ} and SSI*
"Use of gentamicin-impregnated collagen sponges reduce rates of SSI* in cardiac surgery."

NICE 2019[18] (National Institute for Health & Care Excellence) → "Based on the evidence, the committee recommended gentamicin collagen implants to be considered in cardiac surgery."

Leading to a favorable healthcare outcome

	In Sweden[19]	In United Kingdom[20]
Mean SSI* cost	14 481 €	£ 11 003

NICE 2019[18]
(National Institute for Health & Care Excellence)

"The committee was satisfied that a recommendation to consider the **use of gentamicin-collagen sponges** in **cardiac surgery,** where its **clinical evidence** is the **most supportive,** is likely **to be a cost-effective used of NHS resources."**[18]

*SSI: Surgical Site Infection **ASA : American Society of Anesthesiology ***SWI : Surgical Wound Infection
$^{\alpha}$OR: Odds Ratio $^{\beta}$GICS: Gentamicin-Impregnated Collagen Sponge $^{\gamma}$SWD : Sternal Wound Dehiscence

21/07/UK/COLG/014

In summary

COLLATAMP®G

- ✓ Class III medical device.[4]
- ✓ Gentamicin collagen implant is used for **local haemostasis** of capillary, parenchymatous and seeping haemorrhages **in areas with a high risk of infection.**[1,2,3,4]
- ✓ Used in various procedures as **cardiac**[11,12,13,14], **vascular**[21], **orthopedic**[22], **gastro-intestinal**[23,24] surgeries.
- ✓ Supported by **scientific based evidence.**[11,14,21,23]
- ✓ Recommended in **international guidelines.**[15,16,17,18]
- ✓ Leading to a **positive economic impact.**[18]
- ✓ **Sterile fully absorbable** haemostatic device for implantation.[4]
- ✓ Available in **3 different sizes.**[4]

Oxford Pharmacy Store (OPS)
Contact Details
Tel: 01865 904141
Fax: 01865 337550
Email: ops.orders@oxfordhealth.nhs.uk

21/07/UK/COLG/014

INSTRUCTION FOR USE

1 Introduction Collatamp G is a sterile fully absorbable haemostatic device for implantation. It is composed of bovine collagen incorporating gentamicin sulfate at a locally effective dose. The product is available in three different sizes. Dimensions and composition of Collatamp G Size (cm) Bovine collagen Gentamicin sulfate (base) mg/implant mg/cm^2 mg/implant mg/cm^2 5 × 5 × 0.5 70 2.8 50 (32.5) 10 × 10 × 0.5 2.0 (1.3) 5 × 20 × 0.5 280 200 (130) **2 Intended use** Collatamp G is intended to achieve haemostasis when blood comes into contact with the released tissue factors and exposed collagen fibrils. The adhesion and aggregation of platelets is induced on the collagen fibrils at the surface of Collatamp G. **3 Indications** Collatamp G is used for local haemostasis of capillary, parenchymatous and seeping haemorrhages in areas with a high risk of infection (determined by the surgeon on a case-by-case basis, including patient-related, surgery-related, and physiological factors). After implantation of Collatamp G, systemic gentamicin plasma amounts may temporarily reach therapeutic levels. **4 Contraindications** Do not use Collatamp G if: - a protein allergy is known; - any signs of hypersensitivity (severe allergy) to gentamicin has been observed or the patient is allergic to other aminoglycosides; - the patient is suffering from myasthenia gravis. Collatamp G should not be used in the paediatric population due to a lack of data on safety. **4.1 Pregnancy and lactation** There is no adequate data from the use of gentamicin in pregnant women. Studies in animals have shown reproductive toxicity. Because of the potential risk of inner ear and renal damage to the foetus, gentamicin should not be used in pregnancy unless in case of a life-threatening indication and if no other therapeutics option is available. Gentamicin is excreted in breastmilk and was detected in low concentrations in serum of breastfed children. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from gentamicin therapy. **5 Precautions for use** Use Collatamp G with caution in case of: - Impaired renal function - Vestibular or hearing disorders - Neuromuscular disease - Immune disease - Connective tissue disease - Advanced age - Dehydration - Electrolyte imbalance Collatamp G should be used with extreme caution if used in combination with other gentamicin-containing products. In case of combined therapy, gentamicin serum levels should be measured, and should not exceed 12 mg/L. If required, serum aminoglycoside levels may be determined during implant treatment and renal function monitored by measuring serum creatinine concentrations (particularly in patients who are elderly, diabetic, have renal/hepatic impairment, or have a history of ear infections or hearing impaired). Special caution is advised in patients with reduced renal function and patients taking other medication such as: - antibiotics that also affect kidneys or hearing (such as aminoglycosides, cephalosporins, methicillin) - anticoagulants (e.g. warfarin and phenindione) - antifungal medication (e.g. amphotericin B) - medicines used to treat muscle weakness conditions (e.g. neostigmine, pyridostigmine, botulinum toxin) - immunosuppressants (e.g. cyclosporin) - anti-cancer medicines (e.g. cisplatin) - some diuretics, such as ethacrynic acid and furosemide - non-steroidal anti-inflammatory agents to treat pain and inflammation (e.g. indomethacin) - medicines used to treat osteoporosis (e.g. bisphosphonates) If several implants are used, use of an overflow drain is recommended. Long-term continuous therapy with gentamicin should be avoided. Prolonged use may lead to the emergence of resistant organisms. There is no evidence that single use Collatamp G administration in patients promotes or induces the formation of resistance against gentamicin. Do not use the implant alone to treat a suspected or confirmed infection, appropriate systemic antibiotics must be administered. **6 Interaction with other substances** No interactions have been reported to date. If adjuvant systemic treatment with gentamicin, other aminoglycoside antibiotics or other ototoxic or nephrotoxic drugs is necessary, the cumulative effects should be taken into account. **7 Properties** Haemostasis is triggered when blood comes into contact with released tissue factors and exposed endogenous collagen fibrils or renatured collagen fibrils like those in Collatamp G. The adhesion and aggregation of platelets is induced on the renatured collagen fibrils of Collatamp G and the plasmatic coagulation process is accelerated. The sponge-like structure of Collatamp G stabilises the wound clot, and takes up a certain amount of blood. Collagen also promotes granulation and epithelialisation. Collatamp G is completely absorbed (estimated that in the overwhelming majority of cases, Collatamp G is completely or predominantly degraded within 4-8 weeks, regardless of the site of implantation). The gentamicin included in Collatamp G helps to prevent infections that might occur at the site of implantation caused by gentamicin-sensitive bacteria. The administration of Collatamp G might not prevent an infection with gentamicin-resistant bacteria. The risk of infection is based on individual/combination of factors. **8 Dosage and method of administration** The implant procedure should be performed by an appropriately trained surgeon under aseptic conditions. Avoid any unsterile handling of the product before or during application to avoid contamination. Collatamp G is administrated as follows: a) Before surgery - Read the instruction for use carefully. - Check the integrity of packaging. - The product must be used as soon as the sterile package component has been opened. - Do not use if the packaging is damaged. b) During surgery - Gloves and instruments should be wetted to prevent Collatamp G from adhering to them. Collatamp G can be cut to size to fit the area to be treated. - Place a dry Collatamp G on the area to be treated, which should be as dry as possible, and light pressure applied for about a few minutes to achieve better adhesion. - Up to 3 large Collatamp G sponges (10 × 10 × 0.5 or 5 × 20 × 0.5 cm) can be used, depending on the size of the area requiring haemostasis. However, the patient's body weight should be taken into account. The number and size of the implants should be selected so that a total dose of 9 mg gentamicin sulfate per kg body weight is not exceeded. c) After surgery - Collatamp G is completely absorbed. - Timelines for complete absorption depend on the site of surgical implantation. **9 Undesirable effects** Serious adverse reactions including neurotoxicity (vertigo, tinnitus), ototoxicity (potential hearing loss, deafness, balance loss) and nephrotoxicity have occurred primarily in patients receiving systemic gentamicin therapy. However, systemic absorption following implantation of Collatamp G is unlikely to constitute a comparable risk. Rare / very rare incidents (maximum 1 incident by sales volume of 10,000 qty.) potentially associated with Collatamp G use include delayed/impaired wound healing, local infection / secretion, haematoma, seroma, elevated creatinine levels, sensitisation/hypersensitivity reactions, and thrombosis. Categories and ranges have been calculated based on `probability of occurrence' estimates using the manufacturer's risk management rating system. As a reference parameter, the probability of occurrence of an ´event per patient´ is used, which is based on product sales numbers. **10 Information/warnings** Implants are for single use only and are delivered sterile. Implants are supplied in unit packages allowing sterile presentation. If any aspect of the packaging is damaged, sterility cannot be guaranteed. Use of the implant is then under the total responsibility of the user. Wetting Collatamp G prior to implantation may result in loss of efficacy through premature elution of the water-soluble gentamicin sulfate. Re-sterilisation of an implant by any method is prohibited. There is a risk of deterioration of the material during a second sterilisation and this risk is not controlled. Once the outer package is opened, the implant must be used or discarded. Once opened, single packs of Collatamp G may not be kept for later use. Any implant which has been implanted cannot be reused. In case of an error in use, the implant is not designed for cleaning without risk of deterioration. If Collatamp G requires surgical removal or replacement, the procedure should be performed under aseptic conditions. **11 Storage conditions** Store in original package. Store between +4°C and +25°C. Store in a clean, dry place. Verify the integrity of all aspects of the sterile packaging. DO NOT use if open or damaged. Do not use after the expiry date. **12 Disposal** Any unused or discarded product must be disposed of in accordance with local regulations in force. **Detailed prescribing information:** Information about this product including: adverse reactions, precautions, contraindications, and method of use can be obtained by contacting SERB SA at medinfo.uk1@serb.eu. **Legal category:** Class III Medical Device. **Distributor and legal manufacturer:** SERB SA, Avenue Louise 480, 1050 Brussels, Belgium.

Adverse reactions should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Adverse reactions should also be reported to SERB SA via email at medinfo.uk1@serb.eu

Date of last revision: September 2021
Job code: UK009

CE 0123

CE marking and identification number of the notified body. Product conforms to the essential requirements of the Council Directive 93/42/EEC concerning medical devices.

21/07/UK/COLG/014

SERB SA
Avenue Louise 480, 1050 Brussels, Belgium
Tel. : + 32 (0) 2 792 05 00
www.serb.eu