

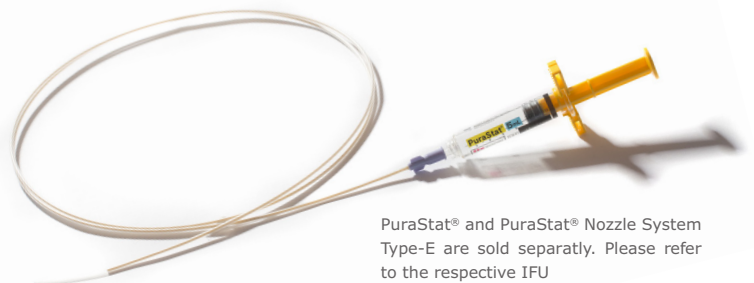
PuraStat®



the first haemostat approved to reduce
delayed bleeding following ESD in the colon

For application within gastro-enterology, PuraStat® is indicated¹ for

- Achieving haemostasis in bleeding from small blood vessels and oozing from capillaries of the GI tract following surgical procedures [when haemostasis by ligation or standard means is insufficient or impractical]
- Reduction of delayed bleeding following gastrointestinal endoscopic submucosal dissection (ESD) procedures in the colon



PuraStat® and PuraStat® Nozzle System Type-E are sold separately. Please refer to the respective IFU

It is widely accepted that delayed bleeding is a possible complication when performing ESD

► “Endoscopic submucosal dissection (ESD) is now an established technique to treat precancerous and early cancerous lesions in the colon. Delayed bleeding is a well recognised complication following colonic ESD that can occur in up to 5% of patients. The risk of bleeding may be increased depending on the lesion size, location, anticoagulant use, age and co-morbidities. The endoscopic management of delayed bleeding conventionally includes electrocautery of visible vessels although there has been growing interest in topical haemostatic products that can be applied over the ESD resection site.” ^{II}

► “Bleeding is a recognized complication of endoscopic resection (e.g. in endoscopic submucosal dissection/ESD). Conventional methods

of haemostatic control include electrocautery that may increase the risk of perforation” ^{III}

► “Delayed bleeding after ESD has been reported to range from 0% to 15.6%.” ^{IV}

► “High-risk endoscopic procedures, such as endoscopic mucosal resection (EMR) and submucosal dissection (ESD) are associated with a potential risk of bleeding requiring further interventions, like hospitalization, transfusion, endoscopic treatment or surgery. The incidence after polypectomy ranges up to 10% and can be displayed until 1 month after the procedure.” ^V

There are multiple patient-related factors that increase the risk for complications

► “Delayed bleeding has been reported in approximately 1–15% of cases, increasing with antiplatelet/anticoagulant therapy or portal hypertension.” ^{VI}

► “Continuous aspirin therapy is responsible for an increase in delayed bleedings from 3.2% to 16.1% after colorectal resections compared to patients with interrupted aspirin treatment.” ^{VI}

► “For patients with liver cirrhosis, the bleeding risk after gastric ESD is increased from 5% to 13.1% or 20%.” ^{VI}



PuraStat proven to reduce the rate of delayed bleeding following colonic ESD

“This study has demonstrated that the rate of bleeding in colonic ESD was reduced by >50% in the group of patients receiving PuraStat®.” ^{II}

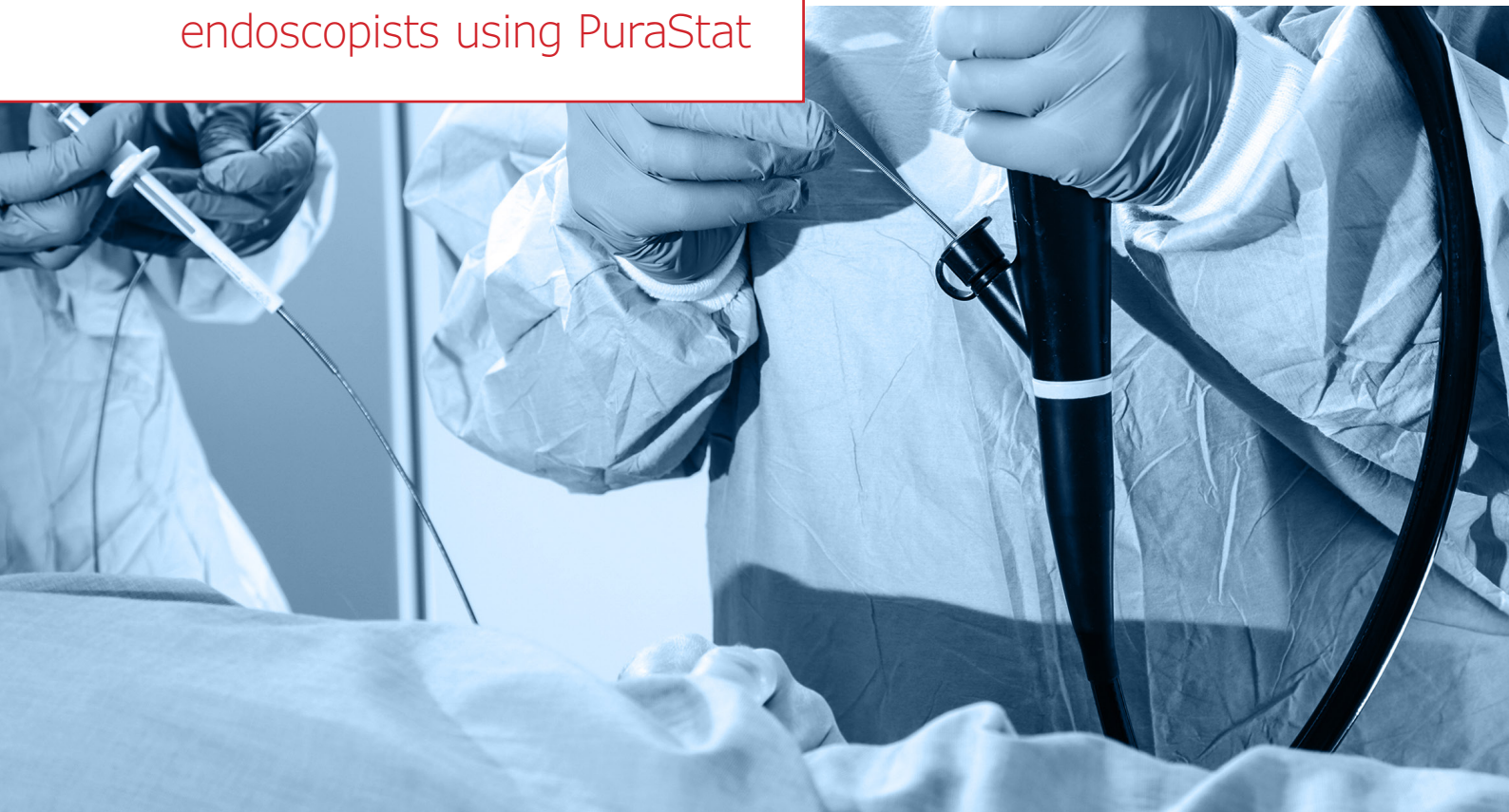
		PuraStat® (n=76)	Control* (n=202)
Age (years)		69.9	72.3
Gender (M:F)		44:32	123:79
Location of lesions	Rectum	25/76 (32.9%)	69/202 (34.2%)
	Sigmoid/descending	16/76 (21.1%)	72/202 (35.6%)
	Transverse/ascending	26/76 (34.2%)	40/202 (19.8%)
	Caecal	9/76 (12%)	20/202 (9.9%)
Median lesion size (mm)		32	40
Number of bleeds (n,%)		1/76 (1.3%)	6/202 (3.0%)

*In the control group neither PuraStat nor other techniques were used.

An animal study suggests the lasting presence of PuraStat at GI mucosal resection defect sites:

“Purastat® Gel appears safe and remains visible on many excision sites 6 days after endoscopic resection.” ^{VII}

Feedback from expert endoscopists using PuraStat



"PuraStat is very easy to deliver and to handle. PuraStat stops oozing and slows down brisk bleeds.

It is a transparent gel which does not compromise endoscopic views after application as compared to other spray powders. This allows endoscopist to apply additional haemostatic therapy if necessary. The standard therapy for haemostasis control such as electrocautery introduces a thermal injury to the bowel wall and carries the risk of causing perforation. Furthermore, it requires precise targeting of the bleeding vessel which can be very difficult during active bleeds.

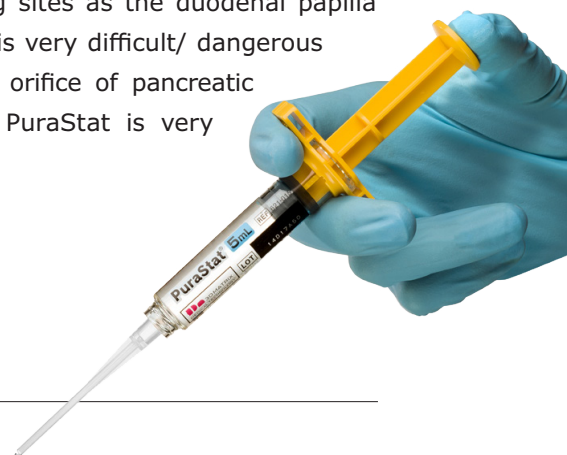
PuraStat can be applied in the general area of bleeding and does not require precise application to the exact point of bleeding. It was really surprising to see enhanced healing and formation of soft scar at the EMR site, 15 days post procedure." ^{viii}

"Scarred polyps can be very difficult to resect with significant risk of bleed and perforation. PuraStat is helping reduced the immediate risk." ^{ix}

"Due to the transparency and the fact that it is easy-to-use, PuraStat is well applicable to treat and *prevent bleedings in the sub-mucosa due to possible residual lesions" ^x

*see for GI indication page 1 or 8

"PuraStat is very helpful new tool in hemostasis that allows successful application also in such special bleeding sites as the duodenal papilla where clipping is very difficult/ dangerous because of the orifice of pancreatic and bile duct. PuraStat is very easy to use." ^{xi}





If PuraStat is able to reduce the prevalence of delayed bleeding following colonic ESD with > 50%, you may be able to reduce the costs associated with this type of delayed bleeding with >50%.

Reduction of post ESD events is cost-efficient

“As options evolve to prevent delayed adverse events after ESD and any other large mucosal defect, it is important to consider the economics, the upfront cost for the added prophylactic intervention, and the downstream cost savings for an avoided hospitalization.”^{IV}

“If the overall rate of post-ESD adverse events is assessed as 5% and the cost for additional therapy including admission for a treatment of

the adverse event is estimated at \$5000 per patient, we can distribute a \$250 cushion for an economical prophylactic measure for each patient without adding to the overall financial cost.

If the rate for delayed bleeding alone in high-risk patients with large defects and need for anti-thrombotics is estimated at 22%, then there is more room to accommodate more expensive added prophylactic steps.”^{IV}



► **5000**

Assumed cost for additional therapy including admission for a treatment of the adverse event



► **250**

Available financial cushion for prophylaxis with 5% post-ESD adverse events



► **1100**

Available financial cushion for prophylaxis with 22% post-ESD adverse events



► **100-150**

Price range of 1 mL PuraStat (not included in the publication)

Data in figure derived from Dobashi A, Sumiyama K, Gostout C. Simplified prophylaxis of mucosal resection site defects. Gastrointestinal Endoscopy Volume 83, No. 6 : 2016; 1265-1266. Please note that PuraStat was not part of the publication

PuraStat fits requirements for a hemostat in endoscopy

- ▶ PuraStat fits requirements for a hemostat in endoscopy and enables precise work in a narrow space. It is inert, transparent, deliverable through endoscopic applicator, non-cohesive and not clogging.
- ▶ "In addition to its efficacy in stopping bleeding, we found more advantageous properties of PuraMatrix*, especially during endoscopic surgery. First, PuraMatrix* is a clear material. It does not block the field of view, which is particularly important during endoscopic surgery. Second, PuraMatrix* is applied as a solution and only gels when in contact with body fluids, making it easy to apply." ^{XII} *In this study the name PuraMatrix is erroneously used instead of PuraStat

The added value of PuraStat in GI procedures

- ▶ Ready-to-use, no preparation required
- ▶ PuraStat is easy to apply during endoscopic procedures and it does not clog the lumen of the applicator or endoscope
- ▶ It is suited for use in delicate/hard to reach areas since it is fluid and can flow into tiny niches, even between placed clips
- ▶ PuraStat covers uneven surfaces well
- ▶ It can be used in combination with electro-surgical coagulation forceps and clips. Both can be used even after application of PuraStat
- ▶ Transparency of PuraStat maintains a clear view, increasing accuracy which is important during endoscopic surgery
- ▶ Can be used repetitively during the same procedure at the beginning, middle and end of the procedure
- ▶ Second application of PuraStat is possible and easy

Further relevant characteristics

- ▶ PuraStat is inert and it is broken down to its constituent amino acids that will be absorbed
- ▶ In the clinical study reported by Masuhara H. et al. (2012), "no differences in the efficacy of TDM-621* in heparin- and protamine- treated individuals were observed."^(XIII)

*TDM-621 is the research codification for PuraStat®



PuraStat is easy to deliver and to handle

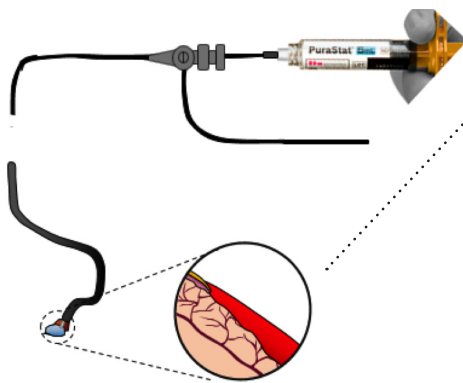
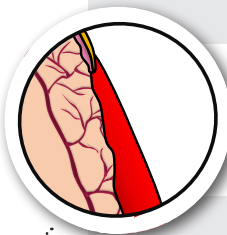
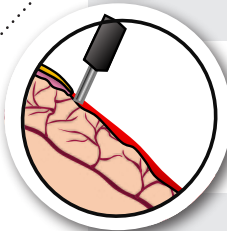


Illustration of endoscopic application of PuraStat

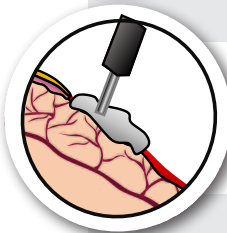
PuraStat is also indicated for the reduction of delayed bleeding following gastrointestinal endoscopic submucosal dissection (ESD) procedures in the colon.



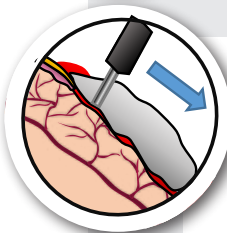
Bleeding from small blood vessels and oozing from capillaries of the GI tract following surgical procedures.



Step 1: Remove as much blood as possible from hemorrhagic site

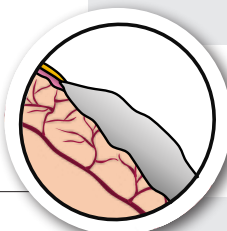


Step 2: Apply PuraStat as close as possible to the bleeding point



Step 3: Continue to apply PuraStat by moving the endoscopic applicator until the product exceeds the margins of the lesion. Practical experience suggests to work from distal to proximal (Prof. Bhandari).

When potentially re-applying; go through the already present material and apply PuraStat as close as possible to the bleeding point.
Note: PuraStat in the lumen of the catheter ('dead volume') can be pushed out by e.g. air.



Haemostasis achieved

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PuraStat:



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PuraStat is a class III medical device, CE marked according to European council directive 93/42/EEC on medical devices and its relatives

Catheter:



TOP Corporation
19-10 Senjunakai-cho
Adachi-ku, Tokyo
120-0035 Japan



MPS Medical Product Service GmbH
Borngasse 20
35619 Braunfels
Germany



PuraStat Nozzle System Type-E is a class IIa medical device, CE marked according to European council directive 93/42/EEC on medical devices and its relatives.

Availability of this product may vary from country or region to another, as a result of specific local regulatory approval or clearance requirements for sales in such country or region.

PuraStat Nozzle System type E Distributed by 3-D Matrix Europe SAS

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