



**PAN MERSEY AREA PRESCRIBING COMMITTEE**  
**PRESCRIBING POLICY STATEMENT**  
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**Pan Mersey**  
Area Prescribing Committee

## **COLLAGENASE CLOSTRIDIUM HISTOLYTICUM injection (Xiapex<sup>®</sup>) for Peyronie's disease**

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**The Pan Mersey Area Prescribing Committee does not recommend the prescribing of COLLAGENASE CLOSTRIDIUM HISTOLYTICUM injection (Xiapex<sup>®</sup>) for Peyronie's disease**

The Pan Mersey Area Prescribing Committee does not recommend this drug for the treatment of Peyronie's disease for the following reasons:

- Although collagenase has shown a mean percent improvement in penile curvature abnormality of 34.0% vs a mean 18.2% improvement in placebo recipients ( $p < 0.0001$ ), and the mean change in the symptom bother domain score was significantly improved in the collagenase group compared with the placebo group ( $-2.8 \pm 3.8$  vs  $-1.8 \pm 3.5$ ;  $p = 0.0037$ ), there has been no comparison with surgery which is the current gold standard for correcting erectile penile deformity in stable disease.<sup>1,2</sup>
- There are no cost effectiveness data available; however, the treatment course requires significant resource. For 8 injections, the drug costs are £4,576, and there will be additional costs as the injection will be delivered as outpatient episodes – up to 8 visits and 4 follow-up visits (in trials approximately 78.8% received the maximum of 8 collagenase injections, 4 cycles). At the follow-up visits, 1 to 3 days after the second injection of each treatment cycle, a trained physician has to perform a penile modelling procedure. Patients are then provided with instructions to self-perform penile modelling activities at home each day for the following 6 weeks. The cost of tunical shortening (typically carried out as a day case) is approximately £1,075-£1,320 and the annual cost of Potassium aminobenzoate capsules 500mg (Potaba<sup>®</sup>), 12g daily is £1633. Note: Collagenase injection is a PBR excluded high cost drug only when used in outpatients.
- The potential drug costs for the local health economy are unknown as local specialists have not been able to describe a cohort of patients who may benefit from this treatment. The original manufacturer's estimate was much larger than that identified through the NICE scoping exercise\*.

\* Following a consultation exercise and the scoping workshop, NICE decided that an appraisal of collagenase clostridium histolyticum and potassium para-aminobenzoate for treating Peyronie's disease was not appropriate. This was due to the small population size (no more than 500 patients likely to be eligible) and individualised approach to patient care (because of the heterogeneous nature of the condition).<sup>3</sup>

**Note:** Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

## COLLAGENASE CLOSTRIDIUM HISTOLYTICUM injection (Xiapex<sup>®</sup>) for Peyronie's disease

<p><b>EFFECTIVENESS</b></p> <p>Collagenases are proteinases that hydrolyse collagen under physiological conditions.<sup>4</sup> The results of two multi-institutional phase 3, double-blind, randomized, placebo controlled studies (IMPRESS I and II) conducted in the USA and Australia over 52 weeks were combined (n=836). Collagenase treatment showed a mean percent improvement in penile curvature abnormality of 34.0% vs a mean 18.2% improvement in placebo recipients (p&lt;0.0001). The mean change in the Peyronie's disease symptom bother domain score was significantly improved in the collagenase group compared with the placebo group (-2.8 ± 3.8 vs -1.8 ± 3.5; p=0.0037).<sup>1</sup></p> <p>There have been no trials comparing collagenase with other treatments for Peyronie's disease.</p>	<p><b>SAFETY</b></p> <p>In IMPRESS I and II, the most frequently reported adverse event (45.0% or greater) in collagenase treated men included penile ecchymosis, penile swelling and penile pain. Six men experienced collagenase treatment related serious adverse events, including corporeal rupture in three and penile hematoma in three.<sup>1</sup></p> <p>Following injection, severe allergic reaction could occur, and patients should be observed for 30 minutes before leaving the clinic. Collagenase injection must be used with caution in patients with coagulation disorders or those taking anticoagulants. Use in patients who have received tetracycline antibiotics (e.g. doxycycline) within 14 days prior to collagenase is not recommended.<sup>4</sup></p> <p>For full details of side-effects and contraindications, see the <a href="#">SPC</a>.<sup>4</sup></p>
<p><b>COST<sup>5</sup></b></p> <p><u>Collagenase injection</u>: At maximum of 4 cycles (8 injections) drug costs are £4,576, plus 8 outpatient episode costs plus 8 follow up visit costs. Note: 78.8% of patients received 8 injections in the licensing trial.<sup>1</sup></p> <p><u>Potassium aminobenzoate capsules 500mg (Potaba<sup>®</sup>)</u> 12g daily: £1,633 per annum.</p> <p><u>Tunical shortening</u> (typically carried out as a day case): £1,075-£1,320 (manufacturer's estimate).</p> <p>NICE estimate: No more than 500 patients likely to be eligible in the NHS.<sup>3</sup></p>	<p><b>PATIENT FACTORS<sup>4</sup></b></p> <p>Patients with penile curvature &gt;90° were not included in the clinical studies. Treatment in this group can therefore not be recommended.</p> <p>If more than one plaque is present, only the plaque causing the curvature deformity should be injected.</p> <p>No dose adjustment is necessary in any special subject groups.</p>

### ADDITIONAL INFORMATION

Collagenase clostridium histolyticum injection must be administered by a physician appropriately trained in the correct administration of the product, and experienced in the diagnosis and treatment of male urological diseases. Administration of regional anaesthesia (penile block) or topical anaesthesia can be applied prior to injection; in the clinical studies about 30% of the patients received penile block before injection. The injection is delivered as an outpatient episode – up to 8 visits (4 treatment cycles). At the follow-up visit, 1 to 3 days after the second injection of each treatment cycle, a trained physician should perform a penile modelling procedure. Patients should be provided with instructions on the appropriate technique to self-perform penile modelling activities at home each day for the 6-week period following the physician penile plaque modelling visit of each treatment cycle. The safety of more than one treatment course is not known.

### PRESCRIBING INFORMATION

Collagenase clostridium histolyticum injection is not recommended for the treatment of Peyronie's disease within the Pan Mersey Health Economy.

### REFERENCES

1. Gelbard M., et al. Clinical efficacy, safety and tolerability of collagenase clostridium histolyticum for the treatment of Peyronie disease in 2 large double-blind, randomized, placebo controlled phase 3 studies. J Urol 2013; 190(1): 199-207
2. European Medicines Agency. Xiapex – European Public Assessment Report; December 2014. Accessed 29.12.17 at: [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Assessment\\_Report\\_-\\_Variation/human/002048/WC500187327.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Assessment_Report_-_Variation/human/002048/WC500187327.pdf).
3. National Institute for Health and Care Excellence. Accessed 23.10.17 at: <https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/Block-scoping-reports/Batch-43-block-scoping-report-noCIC.pdf>
4. Swedish Orphan Biovitrum Ltd. Summary of Product Characteristics - Xiapex 0.9 mg powder and solvent for solution for injection July 2016. Accessed 29.9.17 at: <http://www.medicines.org.uk/emc/medicine/28953>
5. NHSBSA dm+d browser, Accessed 29.9.17 at: <https://apps.nhsbsa.nhs.uk/DMDBrowser/DMDBrowser.do>