London Medicines Evaluation Network Review

Collagenase Clostridium histolyticum (Xiapex™) for Peyronie's disease – July 2015

Summary

Background and licensed indication	Peyronie's disease (PD) is a local connective tissue disorder with a prevalence of 3-10%. It is characterised by fibrous collagen plaques which form in the penile shaft, causing the penis to curve painfully when erect. This can cause distress and can impact on sexual and emotional function. The pathophysiology is poorly understood but minor trauma, genetic predisposition and risk factors such as poor circulation may play a role. Xiapex™ (clostridium collagenase histolyticum or CCh) is a purified form of two collagenase enzymes which dissolve penile plaques. Xiapex™ was launched in February 2015 for palpable mature non calcified penile plaques of moderate (30-60°) penile curvature in PD.
Dosing	The dose of reconstituted Xiapex™ injection is 0.58mg (0.25ml) administered into the penile plaque by a trained physician over 4 treatment cycles (each cycle consists of 2 injections and penile modelling).
Alternatives	Various oral, topical, intralesional treatments and extracorporeal shockwave therapy (ESWT) have been tried but there is no convincing rationale or evidence of efficacy to support their use. Radiotherapy may be helpful but is limited by adverse effects and penile traction by impracticality. Surgery, though potentially risky, is the mainstay of treatment for men with PD with penile curvature of >60°.
Guidelines	NICE suggest that ESWT be used in audit/research but the lack of robust efficacy data are noted. The European Association of Urology (EAU) recommends a number of options for conservative management of PD, including intralesional Xiapex™, verapamil or interferon.
Clinical studies	In the two phase III pivotal IMPRESS studies (of 832 middle aged Caucasian men with mature PD plaques and moderate penile curvature of 50°) the co-primary efficacy endpoints were % improvement from baseline in penile curvature and change in the PDQSBDS score values from baseline values of 7.5 and 7.8 for CCh vs. placebo respectively. The PDQSBDS is rated from 0-16 and assesses sexual function and the degree to which patients are 'bothered' by the condition. In results for the pooled ITT population, mean penile curvature decreased by -17.0° and -9.3° in the Xiapex™ and placebo groups respectively ($p<0.0001$). The PDQSBDS decreased by a mean of 2.8 versus 1.8 points ($p<0.0037$) in the respective groups but the modified ITT group excluded men who were unable to engage in sexual activity, potentially overestimating efficacy of Xiapex™ on sexual function. Global response (proportion of men with > 20% improvement in a composite of the co-primary endpoints) was 60.8% and 29.5% in the respective groups ($p<0.0001$). Penile length and pain did not change significantly. Results from two other clinical studies (n=494) suggest modest improvement in penile curvature and sexual function for CCh vs. placebo respectively) in conjunction with penile modelling which plays a significant role.
Safety	Adverse effects are localised (penile bruising, swelling and pain), mild to moderate in severity and transient. In the IMPRESS studies, local adverse effects were reported by 84% and 36% of men in Xiapex™ and placebo groups respectively. Across all clinical studies (n=1330), serious adverse effects included corporeal rupture (n=4) and penile haematoma (n=5) which resolved with treatment. Longer term safety data (>24 weeks) would inform the long term safety and durability of Xiapex™ in PD.
Convenience	Compared with surgery, Xiapex™ is not as invasive, risky or resource intensive. However, Xiapex™ is intended to manage moderate penile curvature whilst surgery is for severe curvature. Xiapex™ must be used with penile modelling which requires a trained physician to administer it and some men might find modelling uncomfortable. Xiapex™ is stored in the fridge and reconstituted before use.
Risk assessment	Prior to approval of Xiapex™, the EMA required implementation of an educational programme about correct injection technique, dosing, recognising allergic reactions and contraindications (i.e. calcified or urethral penile plaques, bleeding risk or taking certain antibiotics).
Budget impact and funding	The acquisition cost of each cycle is £1,300. The number of men with moderate penile curvature is estimated at 423 per 100,000 of the population. The estimated cost of Xiapex™ per 100,000 people is £549,900 to £2,199,600 depending on the number of cycles required by each man. Additional costs to consider are physician time to administer Xiapex™ and perform penile modelling plus cost of local/regional anaesthesia and dressings. Xiapex™ is a specified high cost drug.
Suggested place in therapy	Xiapex™ is a modestly effective treatment for PD which is less invasive and time intensive than surgery or penile traction, making it an alternative option for PD in men with moderate penile curvature (30-60°). Ultimately, however, surgery may still be required due to the modest effect of Xiapex™.

1. Background and introduction

Peyronie's disease (PD) is a local connective tissue disorder, characterised by the formation of a fibrous plaque in the shaft of the penis. During the chronic phase of PD, the fibrous plaque can eventually matures into a stable calcified collagen plaque causing the penis to become inflexible and to curve painfully when erect. The precise aetiology and pathophysiology of PD is not fully understood but it may be triggered by minor trauma in men with a genetic predisposition to abnormal wound healing.(1) PD is distressing, painful and can cause difficulty during sexual intercourse which may affect a couple's emotional well-being, fertility and quality of life.(1) Untreated PD might lead to the prescription of other medicines to manage these issues, such as antidepressants. PD is most common in men aged over 40 years, particularly those with diabetes, high cholesterol, heart and/or vascular disease and those taking beta-blockers, anti-ulcer agents, antidepressants or antihistamines. The prevalence of PD is estimated to be between 3% and 10% which may be an underestimate because of the embarrassing nature of PD. In some cases, PD is self-limiting over 12-18 months and treatment may not be required but PD may progress if left untreated.(1-4) Xiapex™ (clostridium collagenase histolyticum) is derived from the *Clostridium histolyticum* enzyme and purified and formulated for use in PD as an intralesional injection in conjunction with penile modelling therapy. Xiapex™ consists of two collagenase enzymes, which dissolve collagen, the major component of fibrous tissue in PD plaques.(5-7) It is already approved by the European Medicines Agency (EMA) for use in adults with Dupuytren's contracture of the finger and there has been some off-label use in PD. A license extension for Xiapex™ for use in PD was approved and it was launched in the UK for this indication in February 2015.

Proposed place in therapy

Various oral and topical treatment options have been used despite the lack of evidence to support their efficacy (e.g. oral potassium para-aminobenzoate, vitamin E, tamoxifen, colchicine, corticosteroids, NSAID's, phosphodiesterase-5 inhibitors and topical lidocaine).(1-5;7;8) Extracorporeal shockwave therapy is another potential option.(9) Before the launch of Xiapex™, the only currently licensed pharmacological treatment option for PD was oral Potaba® (Potassium para-aminobenzoate), which is a type of vitamin B. Potaba® may reduce penile plaque size and pain but not penile curvature.(7;10;11) Intralesional injections of dimethyl sulfoxide (DMSO), illoprost, interferons, steroids or verapamil have also been tried in PD but none are licensed or supported by convincing evidence of efficacy. Intralesional steroids are even thought to worsen PD by destroying healthy tissues. Radiotherapy offers pain relief but can cause intolerable adverse effects. Penile traction devices are potentially effective but need to be used for several hours each day over 3-6 months.(1-5;8) Surgery, therefore, remains the mainstay of treatment for PD and aims to reduce the degree of penile curvature and restore sexual function. Surgery is indicated in men whose penile curvature is stable but exceeds 60° when erect and for whom sexual activity is impeded. Surgery is carried out under full general or spinal anaesthetic and involves either lengthening the shorter side of the penis (e.g. the Lue's procedure) or shortening the longer side (the Nesbit procedure which may be a day case procedure). Success rates are relatively high but recovery time is needed after surgery and there is a risk of complications such as persistent/recurrent curvature, loss of length, diminished sensation and post-operative Erectile Dysfunction (ED).(7)

NICE recommend extracorporeal shockwave therapy (ESWT) for PD although the lack of evidence of efficacy data are noted; "*Current evidence on the safety of ESWT for PD appears adequate. However, the evidence on the efficacy does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research.*" (2;8;9) The European Association of Urology (EAU) Guidance recommends intralesional Clostridium Collagenase histolyticum (CCh) (best evidence, grade B), verapamil, interferon, oral potassium para-aminobenzoate, topical verapamil gel 15% or iontophoresis with verapamil 5mg/dexamethasone 8mg for conservative management of PD (all grade C evidence).(11) Xiapex™ is indicated for the treatment of PD with a palpable plaque and curvature of 30-60° at the start of therapy.(6) Men most suited to treatment with Xiapex™ are likely to be those for whom surgery is not a feasible option.(7)

2. Evidence selected for inclusion

Two phase III studies, IMPRESS-1 (n=417) and IMPRESS 2 (n=415), are the pivotal licensing studies used to evaluate efficacy and safety of Xiapex™ plus penile modelling compared to placebo in men with PD.(5) Two further studies evaluate safety and efficacy of Xiapex™ in PD. One is a PIII open label study comparing Xiapex™ plus penile modelling against baseline response (n=347) (12) and the other is a PIIb study (n=147) comparing Xiapex™ with placebo with or without penile modelling.(13)

Pivotal PIII studies

IMPRESS-1 (NCT01221597) and IMPRESS-2 (NCT01221623), the two pivotal licensing studies for Xiapex™ in Peyronie's disease, were phase III multicentre, randomised, double-blind, and placebo controlled trials. The 52 week trials were of identical design and were carried out in parallel to examine efficacy and tolerability of Xiapex™ in men with PD. (5) A total of 836 men were initially randomised and 612 men (73%) completed the study.

Inclusion criteria were as follows; the men had to be in a stable heterosexual relationship and they had to have had diagnosis of Peyronie's disease for at least 12 months (as opposed to 6 months in the PIIb study). Penile curvature, from the corona to the maximum point of curvature measured during an induced erection in any direction except ventral, was required to be between 30° and 90° without a calcified plaque. At baseline, the mean penile curvature was moderate at 50.1° (+/- 14.4°) and 49.3° (+/- 14°) in the Xiapex™ and placebo groups respectively. None of the men included had uncontrolled ED and none had received prior surgery for PD. Men were stratified according to their degree of penile curvature and randomised 2:1 to the Xiapex™ or placebo groups using a web based stratification and randomisation tool. To support blinding, the treatment and placebo were packaged identically with a cycle of treatment, each containing two injections of Xiapex™ 0.58mg or matched placebo. The two doses of Xiapex™ were injected into the penis at the point of maximal curvature using a standardised technique with 24-72 hours between the two injections. Penile plaque modelling was administered manually by the investigators 24-72 hours after the second injection. Modelling involved the application of firm, steady pressure for 30 seconds to elongate and stretch the penis using the plaque as a fulcrum point. Men were given instructions to administer self-modelling at home in between the four treatment cycles (8 injections) that they were each eligible to receive, 6

weeks apart, over 52 weeks. Procedures were terminated if penile curvature was reduced to less than a 15° angle.

The co-primary efficacy endpoints were identical for the two IMPRESS studies and were, percentage improvement in penile curvature and change in the PDQ Symptom Bother Domain score (PDQSBDS)* from baseline values to values at 52 weeks. Seven different secondary efficacy endpoints were examined, including change in penile length, plaque consistency and penile pain. Other secondary efficacy endpoints evaluated the physical and psychological effects of the treatment using validated questionnaires such as the International Index of Erectile Function (IIEF) questionnaire which assesses Erectile Function. The results data presented here are pooled from the IMPRESS-1 and IMPRESS-2 studies. The predefined ITT population included men who had received at least one injection of Xiapex™ and who were sexually active within 3 months of randomisation (as only they were eligible to complete the PDQ questionnaire). There was a statistically significant decrease in mean penile curvature, measured using standard goniometer measurements of the erect penis, in the Xiapex™ group (n=555) compared to the placebo group (n=281); 34% versus 18.2% (p< 0.0001). Curvature decreased by a mean of -17.0° (+/- 14.8°) and -9.3° (+/- 13.6°) in the Xiapex™ and placebo groups respectively (p<0.0001). The mean change in PDQSBDS* in the Xiapex™ group versus the placebo group was by 2.8 versus 1.8 points (p < 0.0037) from baseline scores of 7.5 and 7.8 respectively (a co-primary endpoint). Composite responders were defined as those men who had at least a 20% improvement in penile curvature plus an improvement in the (PDQSBDS)* of more than 1 or improvement in reported sexual activity (i.e. a composite of the co-primary endpoints). The proportion of men who were considered to be global responders was higher in the Xiapex™ group (60.8%) compared to the placebo group (29.5%), p<0.0001). The difference in the percentage of composite responders was statistically significant across the individual IMPRESS studies and in the pooled dataset. There were statistically significant improvements in erectile function and in physical and psychological effects between the Xiapex™ versus the placebo groups. Penile length remained similar to baseline throughout, regardless of treatment allocation, whilst penile pain decreased similarly by 4.4 and 4.3 points on a subjective pain scale from 0-30, p=0.9672) in both Xiapex™ and placebo groups respectively.

Overall the pivotal IMPRESS-1 and IMPRESS-2 studies support the efficacy and safety of Xiapex™ for the physical, functional and psychological aspects of PD. (5;14)

PIII open label study

A phase III open label study (NCT01243411) enrolled 347 men with PD who had been previously enrolled in the placebo groups of phase 2 pharmacokinetic studies.(12) The men included had similar baseline characteristics to those included in the IMPRESS trials with moderate penile curvature of 30° to 60° (mean 53°) and a mean symptom bother score* of 7.3. The men were treated with two intralesional injections of Xiapex™ 0.58mg given 24-72 hours apart in conjunction with penile plaque modelling administered by investigators. This regimen was repeated in up to 4 cycles administered 6 weeks apart during which penile modelling was carried out at home by men themselves. The co-primary endpoints were the mean percent change in penile curvature and improvement in PD symptom bother score* from baseline to week 36. The mean penile curvature decreased by 18.3° (+/- 14.02°), a statistically significant improvement from baseline. The symptom bother score* had reduced by 3.3 points (from 7.3 to 4.1 points) at week 36 which was also considered a statistically significant difference. Penile length increased by 0.4cm over 36 weeks, which was considered statistically significant. The majority of men (77%) received all 8 injections as well as penile modelling (68%).(12)

Phase IIb study

A randomised, double-blind, placebo controlled PIIb study was carried out in 147 men with PD.(13) The men included in this PIIb study has similar baseline characteristics to those included in the IMPRESS trials; with mature Peyronie's plaques and moderate (non ventral) penile curvature of 48.9 (+/- 14.3°) to 54.7° (+/- 15.2°) at baseline. The men were randomised using an interactive internet based system (3:1) to one of four possible groups; penile modelling plus either intralesional Xiapex™ (n=54), placebo (n=20), intralesional Xiapex™ (n=57) or placebo without penile modelling (n=16). Up to six injections of Xiapex™ 0.58mg or placebo (as 3 cycles of 2 injections given 6 weeks apart) were injected. Primary outcomes were change in penile curvature (evaluated using a goniometer) and patient reported symptom bother assessed using PD PRO** scores. In the non-modelled group, mean penile curvature was reduced at 36 weeks by -15° (+/- 14.0°) in the Xiapex™ group vs. -13.0° (+/- 10.7°) in the placebo group (p=0.9). In the modelled group, mean penile curvature was reduced at 36 weeks by -17.5° (+/- 15.3°) in the Xiapex™ group vs. + 0.6° (+/- 13.2°) in the placebo group (p<0.001). Therefore, only Xiapex™ plus modelling significantly reduced mean penile curvature compared to placebo at 36 weeks. The men completed a PD PRO** questionnaire at baseline and after treatment. In the non-modelled group, the PD PRO score decreased by -1.5 points in both Xiapex™ and placebo groups and there was no numerical or statistically significant difference between the groups. However, in the modelled group, the PD PRO score decreased by -3.6 and -0.1 points in the Xiapex™ and placebo groups respectively, p=0.001. Those on Xiapex™ were found to score significantly better than those on placebo for the symptom bother domain (p=0.05). Interestingly, of the 5 men who reported painful erections, 4 reported no improvement by 36 weeks.(13)

**PDQ Symptom Bother Domain score and **PD PRO.*(5)

Validated scales (by Hellstrom et al. 2013) based on patient's self-assessment of how much he is bothered by pain on erection, appearance of his penis on erection, impact of PD on, and frequency of, sexual intercourse. For 4 questions, the score ranged from 0–15.

3. Critical evaluation

Overall the pivotal IMPRESS-1 and IMPRESS-2 studies support the efficacy and safety of Xiapex™ against placebo for the physical, functional and psychological aspects of PD.(5) The studies were of reasonable size and adequately powered to detect a difference between co-primary outcome measures of efficacy and to measure its tolerability.(5;12;13) There was a modest absolute reduction in penile curvature of around 8° (mean reductions of -17° and -9.3° in the CCh and placebo groups respectively) which may not have been sufficient to avoid surgery according to one commenter who criticised the modest effect. (5,15) However, this depends on several factors such as the shape and the treatment lability of the collagen plaque and the efficacy and consistency with which the penile modelling was carried out by the investigator and by the patient at home.(5) The standard deviation of penile curvature outcomes was fairly wide with responses ranging from disappointing in some patients to excellent in others. Men with long narrow penile plaques

(compared to bulky plaques) seemed to achieve most benefit. Other factors such as the treatment lability of the collagen plaque and the efficacy and consistency with which the penile modelling was performed may also influence outcome. (14) The reported improvement in sexual function was 1 point on the PDQSBDS scale from 0-15 which may be an overestimate given that the ITT population excluded men who were not sexually active.(5)

Limitations of the PIII open label study were its design, lack of comparison group and relatively short duration which precludes longer term safety assessment of Xiapex™ in PD. As with the IMPRESS studies, men with calcified penile plaques had to be excluded and the relatively homogenous population means there is no evidence of benefit in patient who do not fit this description (see 3.1 Clinical application). Eligibility for the open label study required sexual activity within 3 months of enrolment but the composite endpoint in this study assessed all men regardless of sexual activity during subsequent months.(12) In the PIIb study, which assessed the effect of Xiapex™ compared with placebo with or without penile modelling, it was clear that the modelling plays a highly significant role in the efficacy of Xiapex™ and physicians must not omit this. The groups in this study were imbalanced at baseline in terms of disease duration which may have confounded results.(13) Results from the other two clinical studies (n=494) suggested less modest improvements in penile curvature and in sexual function scores.(12;13)

3.1.Clinical application

There are no comparative data of any other types of pharmacotherapy (including intralesional injections of steroids, verapamil or interferon) or against any surgical techniques against Xiapex™ in PD. Whereas Xiapex™ is intended to manage moderate penile curvature; surgery is indicated for more severe curvature. Xiapex™ has been studied only against placebo or baseline values in a relatively homogenous population of middle aged, Caucasian men with mature non calcified palpable Peyronie's plaques and moderate penile curvature (30-60°). Xiapex™ is only proven to be effective when administered by a trained physician in conjunction with penile modelling procedures as well as self-modelling performed by the patient at home. Xiapex™ is contraindicated in men whose penile plaques involve the urethra due to potential damage to the structure. In theory, tetracycline and anthracycline/anthraquinolone antibiotics can inhibit matrix metalloproteinase mediated collagen degradation and this potential drug interaction means that Xiapex™ should be avoided in men who have received these antibiotics within the last 14 days. Xiapex™ should be avoided in men who use anticoagulants due to increased risk of bleeding. Overall, Xiapex™ (with modelling) is a modestly effective treatment for PD which is less invasive and time intensive than surgery or penile traction, making it an alternative option for PD in men with moderate penile curvature (30-60°). Ultimately, however, surgery may still be required due to the modest effect of Xiapex™.

3.2.Safety

4.2.1. Key adverse events

Xiapex™ is already licensed for management of Dupuytren's contracture and its safety profile is established in this population. (6) Adverse effects in the PD population were generally localised to the penis and groin, mild to moderate in severity, self-limiting in most cases (79%) and transient, resolving within 14 days. The incidence of localised adverse effects was 84% in men treated with Xiapex™ compared with 36% of men who received placebo. Localised adverse effects were mild to moderate in intensity and included penile bruising, swelling and pain and serious treatment related adverse effects included corporeal rupture (n=3) and penile haematoma (n=3). In the IMPRESS 1 and 2 studies, positive Xiapex™ antibodies were measured in 98-99% of men by 52 weeks although no systemic immunological events were reported.(5) In the open label and the PIIb studies, the safety profile of Xiapex™ was similar to that seen in the IMPRESS studies. There were 3 serious treatment related adverse effects; two penile haematomas and a corporal rupture, which were resolved with treatment. As with the IMPRESS studies, all men developed antibodies to Xiapex™ by the end of the studies.(12;13) Longer term safety data would be valuable in order to assess the durability of Xiapex™ treatment using the licensed dosing regimen.(14)

4.2.2. Risk assessment.

The EMA granted conditional approval of Xiapex™ for PD which required an educational programme be in place prior to launch. The programme focusses on safe use of Xiapex™ in PD and contains information about:(6,7)

- Injection technique, appropriate volumes for reconstitution and injection and dosing interval. There is potential risk of misplaced administration and care must be taken when marking the plaque. A surgical marker should be used to mark the plaque when the penis is erect. The dose of Xiapex™ should then be administered into that lesion when the penis is flaccid. Xiapex™ is contraindicated in men whose penile plaques involve the urethra due to potential damage to the urethra. Physicians should therefore examine the location of the plaque before considering Xiapex™.
- Recognition and treatment of severe immune-mediated reactions, including anaphylaxis and information on the potential risk of matrix metalloproteinases (MMP) cross-reactivity, including the development of musculoskeletal syndrome and exacerbation/initiation of autoimmune disorders. The SPC advises that the patient be observed for 30 minutes after injection. Physicians are reminded to inform the patient about the signs and symptoms associated with the treatment and when to seek attention from the health care provider.
- Information on bleeding risk in men with coagulation disorders including those on concurrent anticoagulants because the efficacy and safety of Xiapex™ in men with PD receiving anticoagulants is unknown. In the three pivotal studies, 73 % of Xiapex™ treated men reported bruising and 38 % reported bleeding at the injection site.

3.3.Potential advantages and disadvantages over existing technologies

3.3.1. Convenience and healthcare resource utilisation

Xiapex™ is an effective treatment for PD that is less invasive, possibly less risky and less resource intensive compared to surgery. Whereas Xiapex™ is intended to manage moderate penile curvature; surgery is indicated for more severe curvature. For men eligible for either treatment modality, using Xiapex™ can help to free up theatre space for other needs. Xiapex™ is only effective if administered in conjunction with penile modelling procedures. This requires the physician to be trained to administer Xiapex™ and to train the

patient to self-perform penile modelling too. The man must be willing and able to self-perform modelling. After the injection, the men must be monitored for at least 30 minutes in case of allergic reaction and some healthcare resource may be required for this. (7) Some men may find the administration of Xiapex™ and the associated modelling therapy to be embarrassing or painful. However, this issue is unlikely to have been captured by pivotal studies because these men probably declined to participate in these studies. Penile traction devices are another effective option. Xiapex™ is less time intensive but more invasive than these devices. Xiapex™ requires fridge storage and needs to be reconstituted and brought to room temperature before use which requires time and refrigeration facilities. Administration of regional or topical anaesthesia can be used prior to injection and a dressing can be applied after the injection, both of which will impact resources.(6)

3.3.2. Suitability for shared care

It is unlikely that Xiapex™ would be suitable for use outside of a specialist setting since it requires a trained specialist to administer it.

3.3.3. Drug cost and likely budgetary impact

As well as the cost of Xiapex™, single use syringes, needles, swabs, dressing and local anaesthetic may need to be added. Staff resource needs to be considered as a trained physician has to administer Xiapex™, perform the penile modelling, monitor for hypersensitivity afterwards and to train men to self-perform penile modelling. If successful, however, use of Xiapex™ may reduce the need for antidepressants and assisted conception in some men with PD who are trying to have a family.

4. Health Economics

No health economic data were identified. A 0.9mg vial of Xiapex™ powder and solvent for solution for injection costs £650.00, each cycle of two injections costs £1,300 and the maximum cost of a course of 8 injections amounts to £5,200.(7)

Budget Impact (6;7)

Population	**No per 100,000 population**
Male population >18 years	38,300
PD prevalence in adult men	3.2%
PD population	1,226
PD men with 30-60° curvature	34.5%
Men eligible for Xiapex™	423
Costing	
Cost per cycle per patient	£1,300
Cost for 8 cycles per patient	£5,200
Range of cost for Xiapex™ per 100,000 of the population	£549,900 to £2,199,600

5. Likely commissioning and funding pathway

Specified high cost drug.(7)

6. Suggested place in therapy

For men with PD who have moderate penile curvature, there are no treatments which are proven to be effective for PD except surgery or penile traction. Surgery is invasive and associated with risk of complications and morbidity. It is only suitable for men with severe penile curvature and requires recovery time and penile traction is time intensive to use. Xiapex™ is licensed in men with PD with a palpable plaque and curvature deformity of at least 30°.(6) Studies found Xiapex™ to be a modestly effective and minimally invasive pharmacological treatment option for men with PD who have a palpable non calcified penile plaque causing moderate (30-60°) penile curvature and no contraindications (such as having plaque that involves the urethra or being on oral anticoagulants). Xiapex™ is less invasive than surgery and less time intensive than penile traction, making it an alternative option. Ultimately, however, surgery may still be required for some men (particularly those with bulky plaques).(14-16)

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Search strategy

Medline: (Peyronie.ti.ab OR Peyronies.ti.ab.) AND (MICROBIAL COLLAGENASE/ OR [collagenase AND clostridium AND histolyticum] OR “collagenase clostridium histolyticum” OR Xiapex)
Embase: PEYRONIE DISEASE/dm,dr,dt,th AND (CLOSTRIDIOPEPTIDASE OR [collagenase AND clostridium AND histolyticum] OR “collagenase clostridium histolyticum” OR Xiapex)

Written by Sheena Vithlani, London Medicines Information Service, Northwick Park Hospital, Harrow, HA1 3UJ. [sheena.vithlani@nhs.net]. Pharmaceutical Company [Swedish Orphan Biovitrium] took the opportunity to carry out a factual check on this review. LMEN would like to thank Sarah Cavanagh and [Urologist] from [Ipswich Hospital] for comments on this review.