PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
REF: 13/63 FINAL
APC BOARD DATE: 8 MAY 2013

COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (Xiapex®▼)
for Dupuytren’s contracture

The Pan Mersey Area Prescribing Committee recommends COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (Xiapex®▼) as a treatment option for Dupuytren’s Contracture in adult patients with a palpable cord.

The Pan Mersey Area Prescribing Committee recommends collagenase Clostridium histolyticum (Xiapex®▼) as a treatment option for Dupuytren’s contracture in adult patients with a palpable cord. Treatment **must** be undertaken in the outpatient setting.

In light of the high cost of Xiapex®▼, the Pan Mersey Area Prescribing Committee recommends the use of Xiapex®▼ in the following specified groups:

> in patients with two or fewer palpable cords per hand and;
> for whom needle fasciotomy is not appropriate†.

Xiapex®▼ has been added to the NICE workplan. This statement will be reviewed when NICE guidance becomes available.

The only identified national guidance on the management of Dupuytren’s contracture was published by the British Society for Surgery of the Hand (BSSH) which recommended Xiapex®▼ as a possible treatment option for moderate Dupuytren’s contracture.† This guidance was published before Xiapex®▼ was licensed in the UK.

Xiapex®▼ is not appropriate for a shared care scheme with primary care physicians.

†**Needle fasciotomy is the subject of NICE Interventional Procedure Guideline 43 and remains a treatment option for Dupuytren’s contracture. Some specialists in this region do not routinely offer this treatment due to concerns over safety and recurrence rates.**

**Note:** Patients who are not eligible for treatment under this policy 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. If appropriate an exceptional funding request will be required following the usual locally defined process.

Version: 1.3
Review date: November 2017
(or earlier if there is significant new evidence relating to this recommendation)
COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (Xiapex®▼) for Dupuytren’s contracture

**EFFECTIVENESS**
Evidence for the efficacy of Xiapex®▼ comes from two pivotal, double-blind, placebo-controlled RCTs of identical design (CORD-1 and CORD-2)2,3. The primary end point was the proportion of all primary joints with a contraction angle of ≤5° 30 days after the last injection. CORD-1 included 306 patients and demonstrated efficacy of 64% compared to 7% with placebo (p < 0.001).2 CORD-2 included 66 patients and demonstrated efficacy of 44% compared to 5% with placebo (p < 0.001).3

Long-term follow-up from pooled data of all phase-III studies showed that the nominal recurrence rate for the 623 joints previously treated successfully was 34.8%. Recurrence defined as >20° change or medical intervention required.4

As yet, Xiapex®▼ has not been directly compared to standard surgical interventions in a randomised, controlled trial.

**SAFETY**
Nearly all patients receiving Xiapex®▼ in clinical trials reported at least one adverse effect.2,3 The majority of these were mild or moderate in severity. The most common adverse effects included peripheral oedema, contusion, injection site pain, tenderness, swelling at the injection site, localised itching, injection site haemorrhage and lymphadenopathy.2,5 Serious adverse reactions include tendon rupture.2

Antibodies to the two collagenases (AUX-1 and AUX-2) contained in Xiapex®▼ have been reported to occur in ≥85% of patients after 1 injection and 100% after ≥2 injections.2,3 However, no clinically significant consequences appear to be associated with the emergence of these antibodies.

Xiapex®▼ is a black triangle drug. All suspected adverse drug reactions, including minor reactions, should be reported via the Yellowcard scheme.

**COST**
Xiapex®▼ is available as a single use vial containing powder for reconstitution. Cost per vial is £650 (exc. VAT).5

See detailed cost impact summary overleaf.

**PATIENT FACTORS**
Xiapex®▼ is contraindicated in patients with hypersensitivity to the active ingredient or any of the excipients. Its use is not recommended in patients who have received anticoagulants in the previous 7 days or tetracyclines in the previous 14 days.6 No dosage adjustments are necessary in the elderly or in patients with renal or hepatic impairment.6 In clinical trials, Xiapex®▼ produced better results when used in patients with less severe baseline contractions and when used in metacarpophalangeal (MCP) rather proximal interphalangeal (PIP) joints.2,3

Refer to the SPC for the most current prescribing information [www.medicines.org.uk/emc](http://www.medicines.org.uk/emc)

**PRESCRIBING INFORMATION**6
Xiapex®▼intralesional injection should only be repeated at intervals of 4 weeks and only one cord should be treated at a time.

The recommended dose of Xiapex®▼ is 580 micrograms per injection into a palpable Dupuytren’s cord. For an MP joint, each dose is administered in an injection volume of 0.25ml (requiring 0.39ml solvent for reconstitution). For a PIP joint, each dose is administered in an injection volume of 0.2ml (requiring 0.31ml solvent for reconstitution). Xiapex®▼ must be administered by a surgeon appropriately trained in the correct administration of the product and experienced in the diagnosis and management of Dupuytren’s disease.

**IMPLEMENTATION NOTES**
Xiapex®▼ is an option for the treatment of patients with Dupuytren’s contracture and two or fewer palpable cords per hand, for whom needle fasciotomy is not an appropriate treatment option. Xiapex®▼ should only be initiated by a hospital specialist experienced in the diagnosis and management of Dupuytren’s contracture and is not appropriate for a shared care scheme with primary care physicians. Xiapex®▼ should only be used in the outpatient setting.
COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (Xiapex®▼) for Dupuytren’s contracture

COST IMPACT SUMMARY

Xiapex represents the first pharmacological intervention for the management of Dupuytren’s contracture. Previously, only surgical intervention or hand therapy was available for this condition. Moderate disease can usually be managed using needle fasciotomy. Xiapex®▼ does not represent a cost-effective alternative to needle fasciotomy as displayed below. However, some specialists in the region do not offer needle fasciotomy due to concerns over safety and recurrence rates. Fasciectomy (either digital or palmar) represent more invasive and costly procedures for this condition. Xiapex®▼ represents an alternative option to fasciectomy. Dr Foster data shows that there were 98 episodes for digital fasciectomy and 166 episodes for palmar fasciectomy in this region in 2010/11.

<table>
<thead>
<tr>
<th></th>
<th>Needle fasciotomy</th>
<th>Digital or palmar fasciectomy</th>
<th>Collagenase injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPD appointment</td>
<td>New patient = £121</td>
<td>OPD appointment</td>
<td>New patient = £121</td>
</tr>
<tr>
<td>Pre-op assessment</td>
<td>not included in tariff</td>
<td>Pre-op assessment</td>
<td>not included in tariff</td>
</tr>
<tr>
<td>Day case procedure</td>
<td></td>
<td>Day case/inpatient procedure</td>
<td>OPD appointment</td>
</tr>
<tr>
<td>Needle fasciotomy</td>
<td></td>
<td>Digital fasciectomy</td>
<td>Follow up OPD = £71</td>
</tr>
<tr>
<td>HB55C = £837</td>
<td></td>
<td>Palmar fasciectomy</td>
<td>Collagenase = £650 (exc. VAT)</td>
</tr>
<tr>
<td>HB55B = £911</td>
<td></td>
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<tr>
<td>OPD appointment</td>
<td>Follow up OPD = £71</td>
<td>OPD appointment</td>
<td>Follow up OPD = £71</td>
</tr>
<tr>
<td>Hand therapy/physiotherapy appointments</td>
<td>Dependent on individual</td>
<td>OPD appointment (if 2nd injection)</td>
<td>Follow up OPD = £71</td>
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<td>Patient discharged</td>
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<td></td>
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<tr>
<td>Total predicted cost</td>
<td>£1,029 - £1,103</td>
<td>Total predicted cost</td>
<td>£1,114 - £2,036 (inc. VAT)</td>
</tr>
</tbody>
</table>

Table 1: Comparative costs of treatment options for a patient with one palpable cord.

Appointment costs assume patient seen in trauma & orthopaedic clinic (single professional clinic; codes WF01B and WF01A). Costs for plastics: new £126, F/U £64; rheumatology: new £217, F/U £100.

Ref: Department of Health PbR tariff 2013/14

In clinical trials, an average of 1.7 injections was required per cord to achieve the primary endpoint. Therefore, assuming that a patient requires two injections, treatment with Xiapex®▼ would cost £2,036, which represents a crude estimated saving of £706 per patient when compared to palmar fasciectomy coded as HB53Z. This should be interpreted as a minimum cost saving when treating patients with a single cord for several reasons:

1. the tariff price for digital fasciectomy, or procedures coded as HB51Z, is significantly higher;
2. costs associated with hand therapy/physiotherapy appointments are not included;
3. a small number of surgical cases require subsequent revision;
4. data emerging from clinical practice in the USA and UK suggests that, on average, 1.1 injections are required to treat each cord.

This final point should be interpreted with caution at the moment as data is only available from an abstract. The likely reason for this finding is that local anaesthetic use was prohibited in clinical trials but is commonly used in clinical practice.

Xiapex®▼ is not less costly than surgery in all patients. Patients with multiple cords in the same hand can have all cords operated on at the same time. Only one injection of Xiapex®▼ into a single cord is allowed at any one time. Repeated injections, either into the same cord (maximum of 3 injections per cord) or into
another affected cord, can be administered at 30 day intervals. The cost of 3 or 4 injections is, respectively, £2,958 and £3,880, which is more costly than surgical intervention (assuming palmar fasciectomy). Pooled data from the CORD-1 and CORD-2 studies suggest that approximately 20% of patients with only one or two affected joints received ≥3 injections.

Recurrence data for patients treated with Xiapex®▼ has been shown to be similar to that experienced with other standard treatments. Only 7% of the 623 joints achieving success during the pivotal phase III trials required surgery or other medical intervention during the 3-year follow-up period of the CORDLESS trial.

Pfizer’s (the manufacturer of Xiapex®▼) cost comparison model suggests that an annual cost saving of £166,940 could be made regionally by using Xiapex®▼ in patients with 2 or fewer palpable cords for whom needle fasciotomy is not appropriate. This cost saving is based on the previously stated Dr Foster data and assumes:

- Xiapex®▼ would take market share from palmar and digital fasciectomy based on the ratio between the two procedures in the current situation;
- no patients undergoing surgical intervention receive hand therapy or physiotherapy appointments post-operatively;
- 1.7 injections are required to treat each cord.

REFERENCES
5. BNF 65 (March-September 2013)
7. Department of Health Payment by Result Tariff 2013/2014