Kent and Medway Policy Recommendation and Guidance Committee
Policy Recommendation

Collagenase clostridium histolyticum (Xiapex®) for Dupuytren's contracture
PR 2012-04

Recommendation

The Kent, Surrey & Sussex (KSS) Policy Recommendation Committee has considered the available evidence of clinical effectiveness and safety of treatments; information on activity, resources, costs and provision of current treatments across the CCGs in Kent, Surrey and Sussex; views and opinions of local stakeholders; and the likely impact of implementation of a new policy across the area. Taking these into account, the Policy Recommendation Committee recommends that:

1. Collagenase clostridium histolyticum (Xiapex®) is not routinely funded within the local NHS as a treatment for Dupuytren's contracture.

2. Collagenase may only be considered an option for treating Dupuytren's contracture where special arrangements for clinical governance, consent and audit or research are in place, and where all the following criteria are met:
   - Use is restricted to patients with moderate disease (BSSH classification) as an alternative to fasciotomy or fasciectomy, at the same point in the treatment pathway that fasciotomy and fasciectomy would be considered.
   - Treatment is for primary disease with a clearly defined palpable cord.
   - Collagenase use is restricted to up to 2 affected joints, assuming 1 injection per joint.
   - Injection and finger extension is performed by specialist hand surgeons experienced in the management of Dupuytren's contracture.
   - Capacity permits finger extension within 24 hours of injection (as per Xiapex® protocol).
   - All stages of treatment (injection, finger extension and follow-up) are performed in, and/or costed as, outpatient appointments.

This policy recommendation will be reviewed in light of new evidence, especially long-term recurrence rates.

CCGs in Kent, Surrey, and Sussex will always consider appropriate individual funding requests (IFRs) through their IFR process.

Supporting Documents

Kent, Surrey & Sussex Health Policy Support Unit (2012). *Collagenase clostridium histolyticum (Xiapex®) for Dupuytren's contracture: Final report.*

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Key points and rationale

What is Dupuytren's contracture?

Dupuytren's contracture (DC) is a benign, slowly progressive condition, characterised by a thickening of the connective tissue in the palm of the hand – due to abnormal collagen deposition – into isolated nodules and eventually pathogenic cords. As the cords form, they contract the connective tissue, making it difficult for patients to extend their fingers fully. Affected fingers may eventually become permanently fixed in a contracted position that cannot be straightened without invasive medical intervention. Severe Dupuytren's contracture is therefore a disfiguring and sometimes painful deformity that can limit a patient's ability to work and undertake daily activities.

What is collagenase?

Collagenase clostridium histolyticum was launched in the UK in March 2011 as the first non-surgical treatment licensed for the treatment of DC. Collagenase isolated from *Clostridium histolyticum* is injected directly into the affected cord. The next day the treated joint is manipulated under medical supervision to disrupt the contracted cord, with the aim of regaining full flexion of the digit.

Why do we need a KSS-wide policy on access to collagenase?

Collagenase for Dupuytren's contracture is not currently planned for appraisal by NICE, however there exists a clinical desire to use this treatment in several CCGs throughout KSS. Collagenase has a relatively high purchase cost and widespread use may present a financial risk to CCG budgets. However used appropriately, this treatment option offers potential savings over standard treatment. A policy recommendation is required to aid commissioners in determining under what circumstances collagenase should be available for the treatment of DC in the context of current priorities and the available resources.

How is Dupuytren's contracture currently treated?

There is no cure for DC. Most patients do not require treatment because their condition is mild. Surgery is the current standard of care for moderate to severe cases of DC that require intervention. Common surgical procedures range from the minimally invasive fasciotomy to the more invasive fasciectomy. In fasciotomy, a needle is used to divide the diseased cord, in fasciectomy the hand is opened and the diseased tissue removed. Fasciotomy is performed in an outpatient setting, fasciectomy as a surgical day case. For fasciotomy, typically a single follow-up is required. For fasciectomy two follow-up appointments are expected and up to 7 hand therapy sessions may be required. The rate of recurrence is higher with fasciotomy compared to fasciectomy, but the complication rates and recovery times are less. Patient and clinician preference is the main determinant of the treatment undertaken and it is therefore not possible to identify specific indications for each procedure. In 2010-11, 1,198 procedures for the treatment of DC were undertaken in KSS. Of these, 969 were single procedure episodes (57 were fasciotomies and 786 fasciectomies).

What is the evidence base for collagenase?

Three high quality RCTs were identified comparing collagenase to placebo. In these studies, collagenase significantly reduced the degree of contracture and increased the range of movement compared to placebo. Clinical success (reduction in contracture to with 0–5°of full extension) was achieved with 1.4–1.5 injections per joint. Real-world data suggest that 1.1 injections can achieve satisfactory results. There are no studies comparing the efficacy and safety of collagenase to current standards of care (fasciectomy or fasciectomy), and there are no long-term data on safety or recurrence rates for collagenase. In addition, impact of treatment

with collagenase on subsequent surgery, if needed, and the effectiveness of re-treatment with collagenase in previously successfully treated patients with recurrent disease is unknown. In the absence of head-to-head RCTs and long term follow-up data, the clinical benefit of collagenase compared to standard treatment cannot be determined with certainty. The ability to compare results across studies assessing collagenase and surgery separately is complicated by the use of different outcome definitions – often inadequately described. Comparison of adverse events is especially difficult.
The policy recommendation reflects the inability to determine the long-term efficacy and safety of collagenase compared to standard treatment

How cost-effective is collagenase?
The cost effectiveness of this treatment is contingent on the number of injections administered, the setting of care and the 'per-hand' recurrence rate (which is currently unknown). If any treatment (or follow-up appointment) cannot be performed and/or costed as an outpatient appointment the cost effectiveness of this treatment is attenuated**.** Provided 'per-hand' recurrence does not exceed 60% for a hand treated with a single injection or 46% where treatment involves two injections over 5 years, this treatment option will be cost-saving to cost-neutral compared to standard treatment. If these recurrence rates are exceeded the cost of this treatment will exceed standard treatment. Since treatment with collagenase does not remove the diseased tissue, it is unlikely that the 5 year recurrence rate would be less than fasciectomy (21%) and more likely to be closer to that for fasciotomy (85%). The policy recommendation reflects the uncertainty around the recurrence rate of DC following treatment with collagenase and the conditions, necessary to be met, in order for this treatment to be considered cost-effective compared to standard treatment.

What are the risks of collagenase treatment?
Within the clinical trials, almost all of participants reported adverse events (AEs), however the majority were mild, transient in nature and did not require intervention. Serious adverse events were reported in 2% of cases and included tendon rupture. Trial based estimates of AEs for fasciectomy and fasciotomy are 5% and 0% respectively, however there is insufficient information on the nature, relative severity and management of events to enable accurate comparison.

Who should administered collagenase?
Collagenase's activity can affect any collagen-containing structure. Consequently, it can cause serious damage to tendons, ligamentous structures and articular cartilage if used incorrectly. Due to the potency of this agent and nature of complications, treatment should be restricted to secondary care by specialist hand surgeons experienced in the management of Dupuytren's contracture who have undergone appropriate training for the administration of this treatment.

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