Collagenase for Dupuytren's contracture: Added benefit not proven

July 12 2012

Collagenase extracted from Clostridium histolyticum (trade name: Xiapex) was approved in the beginning of 2011 for the treatment of people with Dupuytren's contracture. In an early benefit assessment pursuant to the "Act on the Reform of the Market for Medicinal Products" (AMNOG), the German Institute for Quality and Efficiency in Health Care (IQWiG) examined whether collagenase offers an added benefit in comparison with conventional regimens. However, such an added benefit cannot be inferred from the dossier, as the drug manufacturer presented either no data or unsuitable data.

Collagenase is to break down thickened connective tissue fibres

Dupuytren's contracture is a disorder of the hand in which connective tissue fibres in the palmar side of the hand (fasciae) thicken and harden. As a result, one or several fingers become permanently bent and can no longer be straightened. Collagenase is injected into the lesions to break down the thickened connective tissue fibres. One day later, the rupture of these fibres through passive digital extension is attempted in order to restore the stretching ability of the affected finger.

G-BA specifies different comparator therapies depending on disease stage

When specifying the appropriate comparator therapy, the Federal Joint

Committee (G-BA) assumed that the choice of (conventional) treatment depends on how severely the function of the fingers and hand is impaired.

Hence, the G-BA stipulates four treatment alternatives and assigns them to different disease stages. The appropriate comparator therapies are specified as follows:

- no treatment" in stage N, where no contracture yet exists;
- percutaneous needle fasciotomy" (PNF), a minimally invasive technique, in stages N/I, I and II;
- partial fasciectomy" (PF), open surgery of the hand, in stages III and IV.

If PF is not suitable for advanced-stage patients, a PNF can be performed.

No assessment performed for three of four possible comparisons

However, the manufacturer deviated from the G-BA's specifications and chose PF as a comparator therapy for the whole indication. IQWiG regards this deviation to be insufficiently justified.

Regarding the G-BA's first, second and fourth research questions (patients with stage N, stages N/I, I and II, as well as patients with advanced stages for whom PF is not an option), the manufacturer neither performed any assessment nor indicated studies for such comparisons in the study list.

An added benefit for these three sub-indications is thus not proven.

Requirements for an indirect comparison not fulfilled

For the third research question (patients with stage III or IV without contraindications for PF), the manufacturer met the G-BA's specifications in the submitted dossier, choosing PF as the comparator therapy. However, there is no study available that directly compares PF and collagenase. As an alternative, the manufacturer presented data from an indirect comparison.

The legal ordinance on AMNOG explicitly allows for the option that added benefit may also be proven by means of such indirect comparisons. However, certain preconditions apply here, which the manufacturer did not fulfil. Due to a lack of suitable data, an added benefit is therefore not proven for this research question either.

G-BA decides on the extent of added benefit

The procedure for inferring the overall conclusion on the extent of added benefit is a proposal from IQWiG. The G-BA, which has opened a formal commenting procedure, decides on the extent of added benefit.

Provided by Institute for Quality and Efficiency in Health Care