

# Public Summary Document

**Product:** Collagenase clostridium histolyticum, lyophilised powder for injection, 900 micrograms powder for injection, Xiaflex<sup>®</sup>

**Sponsor:** Actelion Pharmaceuticals Australia Pty Ltd

**Date of PBAC Consideration:** July 2013

## 1. Purpose of Application

The submission requested an Authority required listing for the treatment of Dupuytren's contracture in patients who are unable to simultaneously place the affected finger and palm flat on a table due to a Dupuytren's contracture with a palpable cord.

The submission was considered under the TGA/PBAC parallel process. At the time of consideration by the PBAC in July 2013, the Clinical Evaluation Report, TGA delegates Overview and the Advisory Committee on Prescription Medicines (ACPM) recommendation were available.

## 2. Background

Collagenase Clostridium Histolyticum (CCH) has not previously been considered by the PBAC

## 3. Registration Status

CCH was TGA registered on 7 August 2013 for the treatment of Dupuytren's contracture in adult patients with a palpable cord.

## 4. Listing Requested and PBAC's View

An Authority required listing was sought for collagenase clostridium histolyticum (CCH) for use in the treatment of Dupuytren's contracture in patients who are unable to simultaneously place the affected finger and palm flat on a table due to Dupuytren's contracture with a palpable cord. The listing requested CCH be administered by a trained specialist. The PBAC foreshadowed that any PBS restriction should state that CCH be administered by an accredited specialist.

The basis of the requested listing is a cost minimisation analysis based on non-inferiority of CCH versus surgical fasciectomy in terms of comparative efficacy and safety.

## 5. Clinical Place for the Proposed Therapy

Dupuytren's contracture is a progressive fibro-proliferative disorder involving irreversible contraction of the palmar fascia of the hand and fingers, primarily affecting the metacarpal-phalangeal (MCP) and/or proximal inter-phalangeal (PIP) joints of the 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> fingers. Dupuytren's contracture is associated with progressive functional disability of affected hands, with an average time for progression from a mild to a severe contracture of 4.7 years (Rodrigo et al. 1976). Recurrence of disease following successful treatment is common.

Current treatment is surgical fasciectomy (excision of the Dupuytren's cord), open or percutaneous needle fasciotomy (division of the cord by needle or fine blade) or amputation in the most severe cases. Long term, aggressive and recurrent disease (i.e. severe contracture) responds less favourably to treatment due to remodelling of surrounding ligaments and joints.

CCH is an enzyme produced by the bacterium *Clostridium histolyticum*, composed of two microbial collagenases, (AUX-I and AUX-II) in a defined mass ratio. These two collagenases synergistically hydrolyse the collagen subtypes that predominate in the diseased Dupuytren's cord (mostly type I and III collagens), causing disruption of the cord (completed by manual manipulation of the affected digit) and improved elasticity and mobility of the affected joint.

The submission proposed that the place in therapy of CCH is as an alternative to surgical fasciectomy in patients who are unable to simultaneously place the affected finger and palm flat on a table due to a Dupuytren's contracture with a palpable cord (the Hueston table top test).

## **6. Comparator**

The submission nominated surgical fasciectomy as the comparator. The PBAC accepted the nominated comparator. The PBAC considered the CCH would also potentially replace fasciotomy in clinical practice. Therefore, fasciotomy should be regarded as a secondary comparator and should be included in the clinical management algorithm.

## **7. Clinical Trials**

The submission presented a meta-analysis of three randomised trials comparing CCH to placebo (DUPY 303, CORD I and CORD II), informally compared with outcomes of a systematic review of 68 observational studies reporting efficacy and safety outcomes for surgical correction of Dupuytren's contracture by fasciectomy. Data from the CCH long term extension study AUX CC 860 (patients continuing from the CORD I and CORD II trials) were also included in the comparison of safety and the economic evaluation. The DUPY 303 trial was terminated early for administrative reasons after recruiting 35 of the target 116 patient sample. The CORD I trial (N=308) was conducted in 16 US sites and the CORD II trial (N=66) was conducted in 5 Australian sites.

For the comparator of surgical fasciectomy, 68 observational surgical studies were grouped by outcomes or safety, which included 14 studies reporting data for the outcome of clinical success, 39 studies for the outcome of recurrence (inconsistently defined) and 41 studies for safety outcomes.

The clinical outcomes included in the informal comparison of CCH and fasciectomy were (i) the proportion of patients achieving less than or equal to 5° contracture 30 days post procedure in primary joints (most severely affected), and (ii) the rate of recurrence (defined as greater than or equal to 30° contracture at time of review compared to post-treatment baseline). Rate of recurrence was not an outcome in the clinical trials of CCH (DUPY 303, CORD I and CORD II), and therefore data from the long term extension study AUX CC 860 was compared to selected observational studies of surgical fasciectomy.

The PBAC considered that the risk of bias within the CORD I and CORD II trials was low and that the risk of bias was high in the surgical studies because most of these were single arm observational studies. The risk of bias across the informal comparison was therefore also high.

The PBAC accepted that the proportion of patients achieving less than or equal to 5° contracture is an appropriate and clinically relevant outcome. However, the PBAC considered the more stringent definition of recurrence defined as greater or equal to 20° contracture rather than greater than or equal to 30° contracture is appropriate.

The details of the published trials presented in the submission are shown in the following table:

<b>Trial ID/ First author</b>	<b>Protocol title/ Publication title</b>	<b>Publication citation</b>
CORD I Hurst L et al.	Injectable collagenase <i>Clostridium histolyticum</i> for Dupuytren's contracture.	<i>New England Journal of Medicine</i> 2009; 361(10):968-79.
CORD II Gilpin D et al.	Injectable collagenase <i>Clostridium histolyticum</i> : a new nonsurgical treatment for Dupuytren's disease.	<i>Journal of Hand Surgery (Am)</i> 2010; 35(12):2027-38.
DUPY 303 Badalamente MA et al.	Collagen as a clinical target: non operative treatment of Dupuytren's disease.	<i>Journal of Hand Surgery (Am)</i> 2007; 32A(6):767-74.
Abe Y. et al.	Surgery for Dupuytren's disease in Japanese patients and a new preoperative classification.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 2004; 29:B(3):235.
Adam R. et al.	Prognosis in Dupuytren's disease.	<i>The Journal of Hand Surgery</i> 1992; 17A:312.
Andrew J et al.	Segmental aponeurectomy for Dupuytren's disease: a prospective study.	<i>Journal of Hand Surgery (Brit)</i> 1991; 16 B(3):255.
Anwar M. et al.	Results of surgical treatment of Dupuytren's disease in women: a review of 109 consecutive patients.	<i>The Journal of Hand Surgery (USA)</i> 2007; 32(9):1423.
Anwar M. et al.	The lateral digital flap for Dupuytren's fasciectomy at the proximal interphalangeal joint - A study of 84 consecutive patients.	<i>The Journal of Hand Surgery (Eur)</i> 2009; 34(1):90.
Armstrong J. et al.	Dermofasciectomy in the management of Dupuytren's disease.	<i>The Journal of Bone and Joint Surgery (Brit)</i> 2000; 82(1):90.
Ashley F.	A two-stage operation for Dupuytren's contracture, with a report of 38 cases.	<i>Plastic and Reconstruction Surgery</i> 1953;12(1):79.
Balaguer T. et al.	Histological staging and Dupuytren's disease recurrence or extension after surgical treatment: A retrospective study of 124 patients.	<i>Journal of Hand Surgery (Eur)</i> 2009; 34(4):493.
Beyermann K. et al.	Severe contracture of the proximal interphalangeal joint in Dupuytren's disease: Does capsuloligamentous release improve outcome?	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 2004; 29 B(3):240.
Bismil Q. et al.	The development of one-stop wide-awake Dupuytren's fasciectomy	<i>Journal of The Royal Society of Medicine Short Reports</i> 2012;

	service: a retrospective review.	3(7):48.
Bulstrode N. et al.	The complications of Dupuytren's contracture surgery.	<i>The Journal of Hand Surgery (USA)</i> 2005; 30(5):1021.
Citron N. et al.	Recurrence after surgery for Dupuytren's disease: A randomised trial of two skin incisions.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 2005; 30(6):563.
Clibbon J. et al.	Palmar segmental aponeurectomy for Dupuytren's disease with metacarpophalangeal flexion contracture.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 2001; 26 B(4):360.
Coert J. et al.	Results of partial fasciectomy for Dupuytren disease in 261 consecutive patients.	<i>Annals of Plastic Surgery</i> 2006; 57(1):13.
De Maglio A. et al.	Dupuytren's disease: recurrence and extension treated by selective aponeurectomy.	<i>Chirurgia degli Organi di Movimento</i> 1996; 81(1):43.
Denkler K.	Dupuytren's fasciectomies in 60 consecutive digits using lidocaine with epinephrine and no tourniquet.	<i>Plastic and Reconstruction Surgery</i> 2005; 115(3):802.
Dias J. et al.	Dupuytren's contracture: an audit of the outcomes of surgery.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 2006; 31(5):514.
Dickie W. et al.	Dupuytren's contracture, a review of the late results of radical fasciectomy.	<i>British Journal of Plastic Surgery</i> 1967; 20(3):311.
Donaldson O. et al.	The association between intraoperative correction of Dupuytren's disease and residual postoperative contracture.	<i>Journal of Hand Surgery (Eur)</i> 2010; 35(3):220.
Ebskov L. et al.	Day care surgery for advanced Dupuytren's contracture.	<i>The Journal of Hand Surgery</i> 1997; 22 B(2): 191.
Edmunds I. et al.	A new surgical approach to Dupuytren's disease.	<i>Journal of Hand Surgery (Eur)</i> 2011; 36(6):485.
Engstrand C. et al.	Evaluation of activity limitation and digital extension in dupuytren's contracture three months after fasciectomy and hand therapy interventions,	<i>Journal of Hand Therapy</i> 2009; 22(1): 21.
Evans R. et al.	A clinical report of the effect of mechanical stress on functional results after fasciectomy for Dupuytren's contracture.	<i>Journal of Hand Therapy</i> 2003; 15(4): 331.
Foucher G. et al.	A modified open palm technique for Dupuytren's disease. Short and long term results in 54 patients.	<i>International Orthopaedics</i> 1995; 19(5):285.
Foucher G. et al.	Open palm technique for Dupuytren's disease. A five-year follow-up.	<i>Annals of Hand and Upper Limb Surgery</i> 1992; 11(5):362.
Gelberman R. et al.	Wound complications in the surgical management of Dupuytren's contracture: A comparison of operative incisions.	<i>The Hand</i> 1982; 14(3): 248.
Hakstian R.	Long-term results of extensive fasciectomy.	<i>British Journal of Plastic Surgery</i> 1966; 19(2):140.
Hall P. et al.	Skin replacement in Dupuytren's disease.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 1997; 22(2):193.
Hogemann A. et al.	Results of total aponeurectomy for Dupuytren's contracture in 61 patients: A retrospective clinical study.	<i>Archives of Orthopaedic and Trauma Surgery</i> 2009; 129(2):195.
Honner R. et al.	Dupuytren's contracture. Long term results after fasciectomy.	<i>The Journal of Bone and Joint Surgery</i> 1971; 53(2):240.
Horner R. et al.	Dupuytren's contracture. Analysis of 100 consecutive surgical cases.	<i>Rocky Mt Medical Journal</i> 1971; 68(10): 49.
Hueston J.	Recurrent Dupuytren's contracture.	<i>Plastic and Reconstruction Surgery</i> 1963; 31(1): 66.

Jurisc D. et al.	Dupuytren's disease characteristics in Primorsko-goranska County.	<i>Collegium Antropologicum</i> 2008; 32(4):1209.
Kartik I.	Data on the recurrence and the progression of Dupuytren's contracture.	<i>Acta Chirurgiae Plasticae</i> 1963; 5(4): 253.
Kjeldal I. et al.	Out-patient surgery for Dupuytren's disease under intravenous regional anaesthesia.	<i>The Journal of Hand Surgery</i> 1988; 13 B(3):257.
Kobus K. et al.	Evaluation of treatment results of patients with Dupuytren's contracture - Our clinical experience.	<i>Ortopedia Traumatologia Rehabilitacja</i> 2007; 9(2):134.
Loos B. et al.	50 years' experience with Dupuytren's contracture in the Erlangen University Hospital--a retrospective analysis of 2919 operated hands from 1956 to 2006.	<i>BMC Musculoskeletal Disorders</i> 2007; 8:60.
Macnicol M.	The open palm technique for Dupuytren's contracture.	<i>International Orthopaedics</i> 1984; 8(1):55.
Maekela E. et al.	Dupuytren's contracture: the long-term results after day surgery.	<i>Journal of Hand Surgery (Brit)</i> 1991; 16 B(3):272.
Matton G. et al.	Our experience with 186 operated Dupuytren hands. Comparison of two techniques.	<i>Acta Orthopaedica Belgica</i> 1982; 48(5): 775.
Mavrogenis A. et al.	Partial fasciectomy for Dupuytren's contractures.	<i>Journal of Surgical Orthopaedic Advances</i> 2009; 18(2):106.
McFarlane R et al.	Dupuytren's contracture. The management of one hundred patients.	<i>The Journal of Bone and Joint Surgery</i> 1966; 48(6):1095.
Meathrel K. et al.	Abductor digiti minimi involvement in Dupuytren's contracture of the small finger.	<i>Journal of Hand Surgery (USA)</i> 2004; 29(3):510.
Misra A. et al.	Predicting the Outcome of Surgery for the Proximal Interphalangeal Joint in Dupuytren's Disease.	<i>The Journal of Hand Surgery</i> 2007; 32(2): 240.
Moermans J.	Long-term results after segmental aponeurectomy for Dupuytren's disease.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 1996; 21 B (6):797.
Moermans J.	Segmental aponeurectomy in Dupuytren's disease.	<i>Journal of Hand Surgery (Brit)</i> 1991; 16 B(3):243.
Nieminen S. et al.	Resection of the palmaris longus tendon in surgery for Dupuytren's contracture.	<i>Annales Chirurgiae et Gynaecologiae</i> 1986; 75(3):164.
Olmeda A. et al.	The treatment of Dupuytren's contracture by radical aponeurectomy.	<i>Italian Journal of Orthopaedics and Traumatology</i> 1986; 12(3):305.
Orlando J. et al.	Dupuytren's contracture: a review of 100 patients.	<i>British Journal of Plastic Surgery</i> 1974; 27(3):211.
Rank B. et al.	Surgery for Dupuytren's contracture: A long-term review.	<i>Australia New Zealand Journal of Surgery</i> 1978; 48(4):398.
Razemon J.	Lateral digital rotation flaps in the treatment of forms of Dupuytren's contracture.	<i>Annales de Chirurgie de la Main</i> 1982; 1(3):199.
Rebelo J. et al.	Dupuytren's disease: Analysis of 110 patients on a long-term follow-up.	<i>European Journal of Plastic Surgery</i> 1995; 18(1):32.
Robins R. et al.	Day care surgery for Dupuytren's Contracture.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 1993; 18B:494.
Rodrigo J. et al.	Treatment of Dupuytren's contracture. Long term results after fasciotomy and fascial excision.	<i>The Journal of Bone and Joint Surgery</i> 1976; 58-A(3):380.
Rombouts J. et al.	Prediction of recurrence in the treatment of Dupuytren's disease: evaluation of a histologic classification.	<i>The Journal of Hand Surgery</i> 1989; 14A: 644.

Roy N. et al.	Fasciectomy and conservative full thickness skin grafting in Dupuytren's contracture.	<i>Acta Orthopaedica Belgica</i> 2006; 72(6): 678.
Sennwald G.	Fasciectomy for treatment of Dupuytren's disease and early complications.	<i>The Journal of Hand Surgery</i> 1990; 15(5): 755.
Shaw D. et al.	Dupuytren's disease treated by palmar fasciectomy and an open palm technique.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 1996; 21 B(4):484.
Sinha R. et al.	Functional benefit of Dupuytren's surgery.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 2002; 27B(4):378.
Tonkin M. et al.	Dupuytren's contracture: a comparative study of fasciectomy and dermofasciectomy in one hundred patients.	<i>The Journal of Hand Surgery</i> 1984; 9(2): 156.
Tonkin M. et al.	The proximal interphalangeal joint in Dupuytren's disease.	<i>The Journal of Hand Surgery</i> 1985; 10(3): 358.
Tripoli M. et al.	The "Jacobsen Flap" for the treatment of stages III-IV dupuytren's disease: A review of 98 cases.	<i>Journal of Hand Surgery (Eur)</i> 2008; 33(6):779.
Ullah A. et al.	Does a 'firebreak' full-thickness skin graft prevent recurrence after surgery for Dupuytren's contracture? A prospective, randomised trial.	<i>The Journal of Bone and Joint Surgery</i> 2009; 91-B(3):374.
van Giffen N. et al.	Dupuytren's disease: Outcome of the proximal interphalangeal joint in isolated fifth ray involvement.	<i>Acta Orthopaedica Belgica</i> 2006; 72(6): 671.
van Rijssen A. et al.	A Comparison of the Direct Outcomes of Percutaneous Needle Fasciotomy and Limited Fasciectomy for Dupuytren's Disease: A 6-Week Follow-Up Study.	<i>Journal of Hand Surgery (Brit &amp; Eur)</i> 2006; 31(5):717.
van Rijssen A. et al.	Five-year results of a randomised clinical trial on treatment in Dupuytren's disease: percutaneous needle fasciotomy versus limited fasciectomy.	<i>Plastic and Reconstruction Surgery</i> 2012; 129(2): 469.
Vigroux J. et al.	A natural history of Dupuytren's contracture treated by surgical fasciectomy: The influence of diathesis (76 hands reviewed at more than 10 years).	<i>Annals of Hand and Upper Limb Surgery</i> 1992; 11(5):367.
Weckesser E.	Results of wide excision of the palmar fascia for dupuytren's contracture: special reference to factors which adversely affect prognosis.	<i>Annals of Surgery</i> 1964; 160:1007.

## 8. Results of Trials

### Comparison of CCH versus fasciectomy

The meta-analysis of three randomised trials comparing CCH to placebo (DUPY 303, CORD I and CORD II) showed that the weighted, placebo-corrected clinical success rate of CCH was 63.1%. Once the DUPY 303 was removed from the analysis due to the trial's early termination and small sample size, the weighted, placebo-corrected clinical success rate was 50%.

The analysis of 14 surgical studies showed the weighted clinical success rate was 69%. A re-analysis excluding studies conducted between 30 and 50 years ago and those reporting less stringent or non-comparable outcome measures of clinical success showed a weighted mean clinical success rate of 82%.

During the evaluation, the PBAC concluded that the most relevant figures for assessing comparative benefit were 69.0% for surgery success and 50.0% for CCH success.

The PBAC noted that in the pre-PBAC response and the hearing during the PBAC meeting the sponsor demonstrated a clinical success rate of CCH to be 60.5% by simply lumping numbers from CORD I and CORD II trials. The PBAC considered this is not appropriate. The PBAC accepted that the appropriate comparison of efficacy of CCH vs surgery is 50% vs 69%.

The submission presented the recurrence rate of contracture following CCH vs surgical fasciectomy as 13% vs 25% at year 2 and 28% vs 21% at year 4 for a less stringent measure of recurrence ( $\geq 30^\circ$  contracture). For a more stringent measure ( $\geq 20^\circ$  contracture), the recurrence rate of contracture following CCH vs surgical fasciectomy was 19% vs 26% at year 2 and 42% vs 24% at year 4.

The PBAC noted the lower rates of long-term clinical success with CCH, and was concerned that there is potential for CCH to delay, rather than replace, surgical fasciectomy.

#### CCH meta-analysis versus placebo

Larger proportions of patients were able to achieve  $\leq 5^\circ$  of contracture (clinical success) at Day 30 after injection with CCH compared to placebo.

Similarly, results for the proportion of patients achieving  $\geq 50\%$  improvement in contracture (RD 0.78; 95% CI [0.60, 0.95]), mean relative decrease in contracture from baseline (WMD 65.14; 95% CI [51.87, 78.41]) and mean change in range of finger motion from baseline (WMD 36.66; 95% CI [24.65, 48.68]) 30 days after the last injection with CCH, all statistically significantly favour CCH over placebo.

With regard to comparative harms, the adverse events related to the treatment of Dupuytren's contracture with CCH, while different in type, are similar to those associated with surgical fasciectomy (excepting adverse events associated with anaesthesia), in terms of severity and association with the physical disruption of the Dupuytren's cord. The PBAC agreed that CCH is less invasive and so is unsurprisingly associated with a lower potential for adverse events, and that these events are more likely to be localised and short-term.

## **9. Clinical Claim**

The submission described CCH as non-inferior in terms of comparative effectiveness and safety over surgical fasciectomy. The PBAC considered that this claim was not adequately supported in terms of efficacy, but was supported in terms of safety. The PBAC noted that the inclusion criteria of clinical trials (CORD I and CORD II) excluded patients with severe disease who would be eligible for treatment with CCH under the requested listing

## **10. Economic Analysis**

The submission presented a cost minimisation analysis based on its claim of non-inferiority of CCH versus surgical fasciectomy. The validity of the cost-minimisation analysis was challenged by the presented clinical evidence, which inadequately supports the claim of non-inferior efficacy.

The PBAC considered the cost of surgical fasciectomy was overestimated by including occupational therapy in the fasciectomy arm, which the sponsor agreed to remove in its Pre-PBAC response, and the cost of CCH treatment was underestimated due to a lower estimation of injections per joint (1.08 rather than 1.67 injections per joint) applied in the CCH cost calculation.

The PBAC noted that a reduced price was proposed in the pre-PBAC response. The PBAC considered that a further reduction of the revised price would be required for a listing restricted to 2 or less rays on a cost minimisation basis based on the sensitivity analyses.

## **11. Estimated PBS Usage and Financial Implications**

An estimated net cost per year to the PBS is less than \$10 million in Year 5. The PBAC considered that utilisation was a likely underestimate.

The PBAC noted that a risk share arrangement was proposed based on the number of CCH injections per patient. The PBAC considered that the proposal would be difficult to implement and is not likely to be workable.

## **12. Recommendation and Reasons**

The PBAC rejected the submission on the basis of the clinical evidence, which inadequately supports the claim of noninferior efficacy against surgical fasciectomy and an unacceptably high price of CCH.

The PBAC considered there is a higher long term recurrence rate after CCH therapy and the evidence inadequately supports a claim of non-inferiority for clinical efficacy compared to surgical fasciectomy. The PBAC accepted that CCH has a non-inferior or possibly superior safety profile compared to surgical fasciectomy. The PBAC noted that there is a moderate clinical need for CCH for the treatment of Dupuytren's contracture.

The PBAC considered that a further price reduction is essential to address the questionable cost-effectiveness of CCH as the PBAC considered that the efficacy of CCH is most likely to be less effective compared to fasciectomy and the proposed CCH price is unacceptably high. The PBAC also considered the future listing should be restricted to patients with 2 or less rays affected, and fasciotomy should be included in both the clinical management algorithm and the economic analysis.

The PBAC noted that hand surgeons currently claim MBS item 46366 (subcutaneous fasciotomy) for administration of CCH. The PBAC requested advice from MSAC and the Department to clarify whether this current claiming practice is appropriate, or whether it would be necessary to create a specific MBS item to administer CCH for the treatment of Dupuytren's contracture. The PBAC also requested advice on how CCH would be used in clinical practice compared with surgical fasciectomy, such as whether there would be

differences in the rates of regional block versus theatre to provide sufficient anaesthesia or whether there would be differences in the rates of imaging such as x-rays. Specifically advice was requested on the extent to which any other MBS items would be associated with the administration of CCH in comparison with the extent to which any other MBS items are associated with surgical fasciectomy and the costs to the MBS and to the health care system of any revealed differences.

The PBAC considered that CCH and surgical fasciectomy are not completely interchangeable: any PBS subsidy of CCH should be restricted to patients with Dupuytren's contracture with 2 or less rays affected who would otherwise undergo surgical fasciectomy.

The PBAC considered that any future resubmission of CCH should take the form of a major submission.

### **Outcome**

Rejected

### **13. Context for Decision**

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

### **14. Sponsor's Comment**

Actelion Pharmaceuticals Australia are disappointed with the PBAC outcome, but are working with the PBAC to understand the issues raised to make this important less-invasive therapeutic option available to Australian patients with Dupuytren's contracture.