



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 October 2017
EMA/787779/2017
Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): collagenase clostridium histolyticum (treatment of Dupuytren's contracture and treatment of Peyronie's disease)

Procedure No. EMEA/H/C/PSUSA/00000871/201702

Period covered by the PSUR: 28 August 2016 to 27 February 2017

Medicinal product no longer authorised



Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR for collagenase clostridium histolyticum (treatment of Dupuytren's contracture and treatment of Peyronie's disease), the scientific conclusions of CHMP are as follows:

The MAH submitted with this PSUR a cumulative review of reported cases of cold intolerance covering this PSUR's period. Cumulatively 5 cases of temperature intolerance, 5 cases of peripheral coldness, 3 cases of peripheral vascular disorder and 5 cases of Raynaud's phenomenon were reported. Two of these cases had a positive dechallenge, 8 had a negative dechallenge/remain unresolved, and in 8 cases the outcome is unknown. From available information it can be seen that the fingers which were treated are affected, and that in response to cold weather become white and/or cold. The phenomenon developed in some cases after several months after injection. However, development of peripheral coldness can be considered a serious side effect with influence on the ability to work for some patients. Symptoms can include pain, altered sensation or colour changes and it can cause debilitating morbidity affecting patients' lives. It is also known for fasciectomy and might be present after surgical intervention or trauma on the upper limbs. In addition two cases were reported in the literature following collagenase clostridium histolyticum treatment of Dupuytren's contracture with new onset of cold intolerance. The pathophysiology of cold sensitivity as a complex of symptoms occurring after injuries is not well understood, and to date there are no known therapies which can prevent development of the syndrome or manage it. The symptoms tend either to disappear or exacerbate with time passing. Based on the available evidence the PRAC concluded that 'cold intolerance in the treated finger' should be added as a new adverse drug reaction with a frequency 'uncommon' in section 4.8 of the SmPC and section 4 of the Package Leaflet.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation

On the basis of the scientific conclusions for collagenase clostridium histolyticum (treatment of Dupuytren's contracture and treatment of Peyronie's disease) the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing collagenase clostridium histolyticum (treatment of Dupuytren's contracture and treatment of Peyronie's disease) is unchanged subject to the proposed changes to the product information.

The CHMP recommends that the terms of the marketing authorisation should be varied.