VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Jext is an auto-injector (a device) containing the active substance adrenaline tartrate. Jext is used for the emergency treatment of serious, potentially life-threatening allergic reactions (anaphylaxis) to insect stings or bites, foods, drugs and other allergens (substances causing an allergic reaction). Jext is also used to treat serious, potentially life-threatening allergic reactions caused by exercise or unknown reasons.

Anaphylaxis can affect the whole body (presenting with e.g. skin, respiratory, cardiovascular and gastrointestinal symptoms) and has a rapid onset. Anaphylaxis can rapidly become life-threatening. The typical signs and symptoms of anaphylaxis include nettle rash (hives) anywhere on the body, swelling of face, lips and/or throat, difficulty breathing, dizziness, nausea, vomiting, cramping abdominal pain, drop in blood pressure (weakness) and collapse/unconsciousness.

In 2006, The American College of Allergy, Asthma and Immunology estimated that in the US, approximately 50 to 2000 persons out of 100,000 persons are at risk of developing anaphylaxis. In Europe, the average incidence has been estimated to be 3%. These numbers are rising, especially for anaphylaxis caused by food.

The active substance of Jext, adrenaline tartrate, is a neurotransmitter and hormone naturally occurring in the body. Jext is designed so that patients or their caregivers can administer adrenaline as emergency treatment of severe allergic reactions. Adrenaline prevents worsening of allergic airway constriction, increases blood pressure and can be life-saving. If patients find it necessary to use Jext as immediate treatment for an acute episode of anaphylaxis, they will be instructed to contact emergency personnel after use in order to complete treatment under the care of a physician and to undergo an adequate observation period.

VI.2.2 Summary of treatment benefits

The effect of adrenaline in the treatment of severe allergic reactions is well-known from extensive use by physicians and emergency units. Adrenaline has a life-saving effect in the treatment of severe, potentially life-threatening allergic reactions (anaphylaxis). It is a recommended first-line treatment during anaphylaxis and a delay in administration can be fatal.

The use of adrenaline auto-injectors (e.g. Jext) is strongly recommended for patients experiencing serious allergic reactions with an unknown cause or causes that are difficult to avoid. Adrenaline auto-injectors have also been recommended for patients with a history of reactions to small amounts of an allergen or with limited access to nearby care. There are also some types of food (peanuts, tree nuts, fish and shellfish) which are related to the occurrence of severe allergic reactions. A prescription of an adrenaline auto-injector is recommended for patients with these types of food allergies.

VI.2.3 Unknowns relating to treatment benefits

The use of adrenaline to treat severe allergic reactions is well established as the recommended first-line emergency treatment, and no differences in benefit are expected with regards to age or ethnicity. Some reports indicate that adrenaline may not be delivered into the muscle by adrenaline auto-injectors in patients with large skin-to-muscle depths.

VI.2.4 Summary of safety concerns

The important identified risks are summarised in Table 37. Potential risks and missing information were not identified for Jext.

Table 37 Important identified risks

Risk	What is known	Preventability
Jext not working in an critical situation	Patients or caregivers may attempt to operate the device incorrectly, or apply insufficient force to activate the Jext. Failure to activate Jext during a severe allergic reaction may be fatal.	In order to avoid device failure in a critical situation, clear instructions with pictograms describing how to use Jext are provided in the PL, SmPC, patient information card and device label. In addition, an instructional video is available. Instructions can be found in the PL, SmPC, prescriber's checklist, patient information card and on the device clearly differentiating the parts of the pen (removable yellow cap, black injector tip). Ongoing signal detection and management. This allows analysis of data to identify potential risk factors and address these in a focused manner if required. In order for patients to get familiar with how to use Jext, trainer pens (Jext Trainer) are

Risk	What is known	Preventability
		available to physicians, patients and caregivers to practice correct activation. The label of Jext Trainer provides a clear instruction on how to use Jext Trainer. Educational material with instructions for use has been prepared in both printed, easy-to-carry form (patient information card) and in digital form (instructional video). The importance of training is emphasised in the SmPC and PL. Guidance text in the SmPC for Jext states the importance of device usage training. A prescriber's checklist is available for physicians to facilitate correct and sufficient instruction of patients with regards to the care and usage of Jext.
Accidental injection into hands or fingers/Accidental needle stick	Accidental injection into hands or fingers may occur for patients and/or caregivers trying to use Jext. This may be due to inadequate training in how to use Jext. Accidental injection into hands or fingers may result in pain and loss of blood flow to the affected area. The damage is usually reversible.	In order to avoid accidental injection/accidental needle stick, clear instructions with pictograms describing how to use Jext are provided in the PL, SmPC, patient information card and device label. In addition, an instructional video is available. Instructions can be found in the PL, SmPC, prescriber's checklist, patient information card and on the device clearly differentiating the parts of the pen (removable yellow cap, black injector tip). Ongoing signal detection and management. This allows analysis of data to identify potential risk factors and address these in a focused manner if required. In order for patients to get familiar with how to use Jext, trainer pens (Jext Trainer) are

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		available to physicians, patients and caregivers to practice correct activation. The label of Jext Trainer provides a clear instruction on how to use Jext Trainer. Educational material with instructions for use has been prepared in both printed, easy-to-carry form (patient information card) and in digital form (instructional video). The importance of training is emphasised in the SmPC and PL. Guidance text in the SmPC for Jext states the importance of device usage training. A prescriber's checklist is available for physicians to facilitate correct and sufficient instruction of patients with regards to the care and usage of Jext.
Lack of drug effect	A single dose of Jext may be inadequate for some patients to relieve the symptoms of severe allergic reaction (anaphylaxis). This may be due to the increased severity of the allergic reaction or delayed use of Jext. Lack of drug effect during a severe anaphylactic reaction is may be fatal if additional dose of adrenaline is not given.	It is stated in the SmPC and in the PL that a second Jext injection may be administered after 5-15 minutes if the symptoms are still present after the first injection. It is stated in the SmPC that it is recommended that patients are prescribed two Jext pens which they should carry at all times. It is stated in section 4.4 and 6.6 of the SmPC that the patient should seek emergency medical assistance immediately after administering the first dose of adrenaline for further treatment as required.

Table 38 Important potential risks

Risk	What is known
Serious allergic reaction to sodium metabisulphite content	Jext contains sodium metabisulphite which may rarely cause severe hypersensitivity reactions including anaphylactic symptoms and bronchospasm in susceptible people, especially those with a history of asthma. The prevalence of metabisulphite among asthmatic individuals have been estimated to be xx. Patients with these conditions must be carefully instructed in regard to the circumstances under which Jext should be used.
Serious cardiovascular adverse reactions in predisposed patients	Side effects associated with adrenaline's alpha and beta receptor activity may include cardiovascular effects, and may exacerbate cardiovascular disease. Due to an increased risk of adverse reactions following administration of adrenaline, special caution should be taken in patients with cardiovascular diseases including angina pectoris, obstructive cardiomyopathy, cardiac arrhythmia, cor pulmonale, atherosclerosis and hypertension.

Table 39 Missing information

Risk	What is known
None	

VI.2.5 Summary of additional risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides the physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the Package Leaflet (PL). The measures in these documents are known as routine risk minimisations measures.

The Summary of Product Characteristics and the PL for Jext can be found in the Jext EPAR page.

This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures). Full details on these conditions and the key elements of any educational material can be found in Annex II of the product information which is published in Jext's EPAR page; how they are implemented in each country however will depend upon agreement between the manufacturer and the national authorities.

Additional risk minimisation measures are for the following risks:

Table 40 Risk minimisation measures for "Device not working in a critical situation" and "accidental injection/Accidental needle stick

Objective and rationale
Summary description of main additional risk minimisation measures • Jext Trainer (simulation device for training in the use of Jext) • Patient Information Card (printed, easy-to-carry material describing correct use of Jext and the symptoms of anaphylaxis) • Instructional video (audio-visual material available digitally demonstrating correct use of Jext) • Prescriber's checklist (tool to aid prescribers with instructing patients in the correct use and care of Jext) The overall objective of the additional risk minimisation measures available for Jext is to facilitate sufficient training of healthcare professionals, patients and caregivers in the use of Jext to ensure successful administration of adrenaline with the device in the event of anaphylaxis.

VI.2.6 Planned post-authorisation development plan

Table 41 List of studies in post-authorisation development plan

Trial/study/activity	Objectives	Safety concerns /efficacy issue addressed	Status	Planned date for submission of (interim and) final results
PK/PD study.	The objective of the planned study is to understand the influence of different factors on distribution, exposure and activity of adrenaline when administered via Jext.	The study addresses the potential safety concern relating to the adequacy of adrenaline auto-injector needle lengths to ensure intramuscular drug delivery in all patients regardless of skin-to-muscle-depth.	Planned	Protocol to be submitted 14 February 2016. Final trial report to be submitted 14 April 2017.

The above study is a condition of the marketing authorisation.

VI.2.7 Summary of changes to the risk management plan over time

Table 42 Major changes to the risk management plan over time

Version	Date	Safety Concerns	Comment
01	23 September 2009	• Device not working in a critical situation • Accidental injection/accidental needle stick • Lack of drug effect	New Risk Management Plan
02	09 April 2010	• Device not working in a critical situation • Accidental injection/accidental needle stick • Lack of drug effect	Description of risk minimisation measures was added to each identified safety concern
03	01 October 2010	• Device not working in a critical situation • Accidental injection/accidental needle stick • Lack of drug effect	Risk minimisation activities were added
04	14 May 2014	• Device not working in a critical situation • Accidental injection/accidental needle stick • Lack of drug effect	Update in accordance with the GVP Module V. Submitted in connection to the marketing authorisation renewal.
05	19 January 2016	Identified risks: • Device not working in a critical situation • Accidental injection/accidental needle stick • Lack of drug effect Potential risks: • Serious allergic reaction to sodium metabisulphite content • Serious cardiovascular adverse reactions in predisposed patients	Risk minimisation measures (educational materials) were added. Submitted as a condition to the MA as specified in the opion adopted by the EC on 14 August 2015 following the Article 31 procedure EMEA/H/A-31/1398.
06	05 February 2016	Identified risks: • Device not working in a critical situation • Accidental injection/accidental needle stick	Protocol was added to Appendix 8.

Version	Date	Safety Concerns	Comment
		• Lack of drug effect Potential risks: • Serious allergic reaction to sodium metabisulphite content Serious cardiovascular adverse reactions in predisposed patients	
07	13 October 2016	Identified risks: • Device not working in a critical situation • Accidental injection/accidental needle stick • Lack of drug effect Potential risks: • Serious allergic reaction to sodium metabisulphite content Serious cardiovascular adverse reactions in predisposed patients	Consolidated version combining version 05 and 06.