

## **VI.2 Elements for a public summary**

### ***VI.2.1 Overview of disease epidemiology***

Adrenaline is a naturally occurring substance secreted by the body in response to exertion or stress. It is a potent stimulant and its effects on target organs are complex. It is used to provide rapid relief of hypersensitivity reactions to allergies or to forms of anaphylaxis (which include symptoms of generalised flushing of the skin, swelling of throat and mouth, difficulty in swallowing or speaking, alterations in heart rate).

Adrenaline has a strong action in constricting blood vessels. This activity counteracts the relaxation of blood vessels leading to a drop in blood pressure, which are the major features in anaphylactic shock. Adrenaline stimulates the airways in the lungs and helps relax the airways, thereby allowing air into the lungs which alleviates the feeling of an asthma attack which is another potential symptom of anaphylaxis. Adrenaline also alleviates pruritus (itching of the skin), urticaria (rash)

and angioedema (swollen hands, arms, feet or eyes) associated with anaphylaxis.

The overall effect of adrenaline depends on the dose used. In resuscitation procedures it is used to increase the efficacy of basic life support. It is a positive cardiac inotrope (stimulating the heart to contract more).

Adrenaline belongs to a group of medicines known as adrenergic and dopaminergic agents.

Adrenaline may be used to provide rapid relief of severe hypersensitivity reaction to drugs and other allergens, and in the emergency treatment of anaphylactic shock.

Some people with severe allergies may experience life-threatening reactions, known as anaphylaxis or anaphylactic shock. The anaphylactic reaction can originate from a variety of sources which include:

- Food allergies e.g. peanuts
- Allergies to materials e.g. latex
- Allergies to animals of animal bites/stings
- Hives (urticaria)
- Eczema
- Contact dermatitis
- Asthma

### **VI.2.2 Summary of treatment benefits**

Adrenaline has been tested in various Clinical Trials worldwide to be effective in each of the indications stated above. In a review article, *Dhami et al<sup>1</sup>*, looked at 56 studies investigating adrenaline use in anaphylaxis. There was evidence regarding the optimum route, site and dose of administration of adrenaline from trials studying people with a history of anaphylaxis.

This suggested that administration of intramuscular adrenaline into the middle of vastus lateralis muscle is the optimum treatment. Furthermore, fatality register studies have suggested that a failure or delay in administration of adrenaline may increase the risk of death.

The benefits of using Adrenaline in such situations was evident in all studies. Treatment responses were rapid, seen in all age groups, effective in reversing the anaphylaxis, and causing no long term problems.

### **VI.2.3 Unknowns relating to treatment benefits**

Based on the currently available data, no gaps in knowledge about efficacy in the target population were identified (except the elderly), that would warrant post-authorisation efficacy studies. Furthermore, there is no evidence to suggest that treatment results would be different in any subgroup of the target population, for any of the indications, taking into account factors such as age, sex, race or organ impairment.

However, there is minimal information on the dosage for the treatment of elderly patients.

#### **VI.2.4 Summary of safety concerns**

##### **Important identified risks**

<b>Risk</b>	<b>What is known</b>	<b>Preventability</b>
Necrosis (vascular constriction at the injection site)	Injection of adrenaline causes vasoconstriction which if permanent can lead to tissue necrosis	The PIL instructs patients to inform their doctor or pharmacist if they have had any adverse reaction following administration
ventricular arrhythmias including fibrillation (possibly fatal)	Adrenaline can cause potentially fatal ventricular arrhythmias including fibrillation, especially in patients with organic heart disease or those receiving other drugs that sensitise the heart to arrhythmias.	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences.
allergic-type reactions, including anaphylaxis due to sodium metabisulphite	Adrenaline Injection contains sodium metabisulphite that can cause allergic-type reactions, including anaphylaxis and life-threatening or less severe asthmatic episodes, in certain susceptible individuals.	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences.

Peripheral ischaemia	Adrenaline can have a powerful vasoconstriction effect on peripheral blood vessels leading to an ischaemia in small blood vessels.	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences.
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**Important potential risks**

Risk	What is known
None	N/A

**Missing information**

Risk	What is known
dosage regimes for adrenaline injection in elderly patients	The safety and efficacy of use in the elderly has not been studied.

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

All medicines have a Summary of Product Characteristics (SmPC) which provides 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 minimisation measures.

No additional risk minimisation activities are required.—Routine pharmacovigilance activities are considered sufficient to monitor the benefit-risk profile of the product and detect any safety concerns.

**VI.2.6 Planned post authorisation development plan (if applicable)**

There are no studies in the post authorisation development plan.

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

N/A