

## Action Plan to Reach the Global Availability of Adrenaline Auto-Injectors

**Short running title: Anaphylaxis in ICD-11**

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## ABSTRACT

Adrenaline is the first-line treatment for anaphylaxis and, therefore, listed as an essential medication for the treatment of anaphylaxis by the World Health Organization (WHO). However, the availability of auto-injector (AAI) forms for use in the first-aid treatment is **limited to only 32% of all 195-world countries**, mostly high-income countries. The key issues leading to the lack of availability of AAIs include cost but also national regulations, lack of regional evidence about the value of epinephrine and the limited accurate data about the epidemiology of anaphylaxis. For these reasons, regional and international allergy academies support the initiatives to narrow these gaps. Our WHO Collaborating Centre is deeply involved in this process and the purpose of this document is serving as baseline to reach: (I) an adequate access to AAI in affordable cost for all patients/societies and (II) the development of disease/patient-specific approaches. Therefore, we propose a 5 steps action plan (gather accurate anaphylaxis epidemiological data and AAI consumption indicators, confirm partnerships, strengthen awareness and include AAI into the WHO Model List of Essential Medicine), which should be considered in combination. A prioritized research agenda should encapsulate all these steps in the frame a global initiative against anaphylaxis. More than calling for the global availability of AAIs for best management of anaphylaxis, we propose an action plan as baseline of a global initiative against anaphylaxis. We strongly believe the combined efforts are a strong public health and societal move, leading to optimal care of allergic patients and best practice of allergology.

**KEY WORDS:** anaphylaxis, adrenaline/epinephrine auto-injectors, classification, epidemiology, essential medicine, International Classification of Diseases, prevention, World Health Organization

## RESUMEN

La adrenalina es el tratamiento de primera línea de la anafilaxia y, por lo tanto, está catalogada como un medicamento esencial en su tratamiento por la Organización Mundial de la Salud (OMS). Sin embargo, la disponibilidad de los autoinyectores de adrenalina (AIA), indispensables en las fases iniciales del manejo de la anafilaxia, está limitada a solo el 32% de los 195 países del mundo, en su mayoría países con economías de primer orden. Los problemas clave que conducen a la falta de disponibilidad de los AIA incluyen el costo, pero también la regulación nacional, la falta de evidencia locales sobre el valor de la epinefrina y la escasez de datos precisos sobre la epidemiología de la anafilaxia. Por estas razones, las sociedades científicas de alergia, nacionales e internacionales dan apoyo a las iniciativas encaminadas a reducir estas brechas. Nuestro Centro Colaborador de la OMS está profundamente involucrado en este proceso y el propósito de este documento es servir de punto de partida para alcanzar: (I) un acceso adecuado a los AIA a un costo asequible para todos los pacientes / sociedades y (II) el desarrollo de un abordaje específico para el binomio paciente/enfermedad. Por todo ello, proponemos un plan de acción en 5 pasos: recopilar datos epidemiológicos de calidad sobre la anafilaxia e indicadores de consumo de AIA, establecer alianzas entre todos los agentes implicados, reforzar la importancia del uso adecuado de los AIA e incluirlos en el listado de medicamentos esenciales de la OMS), que deben darse de forma conjunta. Una agenda de investigación priorizada debe incluir todos estos pasos en el marco de una iniciativa global contra la anafilaxia. Más que exigir la disponibilidad global de los AIA para un mejor abordaje de la anafilaxia, proponemos un plan de acción como base de una iniciativa mundial contra la anafilaxia. Creemos firmemente que estos esfuerzos combinados a nivel societal y de salud pública conllevarán un cuidado óptimo de los pacientes alérgicos y la mejor práctica de la Alergología.

PALABRAS CLAVE: anafilaxia, autoinyectores de adrenalina/epinefrina, clasificación, epidemiología, medicina esencial, Clasificación Internacional de Enfermedades, prevención, Organización Mundial de la Salud.

Accepted Article

## ADRENALINE AUTO-INJECTOR AVAILABILITY: A MATTER OF LIFE OR DEATH

### *The usefulness of adrenaline*

Adrenaline (epinephrine) is the first-line treatment for anaphylaxis. Definitions of anaphylaxis for clinical use by healthcare professionals all state the concepts of a serious, generalized, allergic or hypersensitivity reaction that can be life-threatening and even fatal [1-4]. Anaphylaxis can be considered a condition with a constellation of features and signs, not pathognomonic of only one disease [5]. Since adrenaline is the only medication documented to prevent hospitalizations, hypoxic sequelae and fatalities in anaphylaxis, as a clear, critically important tertiary prevention measure, its availability in some countries is taken for granted and it is widely available in the community for first-aid treatment.

Adrenaline (epinephrine) is listed as an essential medication for the treatment of anaphylaxis by the World Health Organization (WHO) [6]. It is a life-saving non-selective adrenergic agonist. Its  $\alpha$ 1-adrenergic vasoconstrictor activity prevents and relieves laryngeal edema, hypotension, and shock. Its  $\beta$ 1-adrenergic activity produces inotropic and chronotropic effects [2], increasing the force and rate of cardiac contractions. Its  $\beta$ 2-activity includes bronchodilation and decreases release of mediators of inflammation. Its effects are time-dependent, mandating a recommendation for prompt administration. Despite its pivotal role, the auto-injectable form is *not* readily available in the majority of countries [7] in which best management of patients with anaphylaxis is therefore impossible.

### *Current status of the global availability of adrenaline auto-injectors*

Adrenaline auto-injectors (AAIs) are commercially available in many devices in doses suitable for most, but not all, adults and children. For instance, in France four commercial forms are available (Table 1), but it does not reflect the commercial availability from other countries. However, the availability of AAIs for use in the first-aid treatment of anaphylaxis is **limited to only 32% of all 195-world countries** [7], mostly high-income countries (Figure 1). In some countries in which AAIs are not

available through official distribution networks, they are available through distribution by special license arrangements, through distribution on a “named-patient” basis, or through the so-called “suitcase trade”. This latter, unofficial, source is unreliable because of the possibility of interruptions in the supply, and shipping and storing AAI under conditions outside the recommended temperature range, leading to increased possibility of degradation of the adrenaline (epinephrine) content. Although not ideal, in specific situations, where AAI are not available through official distribution networks, some patients and families can afford to order them online from an international pharmacy or travel to another country to purchase them [8-10]. Lack of availability of this first-aid medication for immediate injection in an anaphylactic reaction increases the risk of progression to a severe episode and death.

#### **ACTION PLAN TO REACH ADRENALINE AUTO-INJECTORS FOR THE PREVENTION OF ANAPHYLAXIS WORLDWIDE**

According to the WHO constitution, health is defined by *state of complete physical, mental and social well-being and not merely the absence of disease or infirmity, and the enjoyable of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, population belief, economic or social condition* [11]. With the aim of ensuring good health and care for all, there is a pressing need to step up international and national action on prevention of anaphylaxis and, to understand factors that put subjects at risk of developing anaphylaxis and death secondary to this condition.

A main concern of the allergy community is related to secondary/tertiary preventions focused on accurate diagnosis and management of allergic or hypersensitivity diseases in order to avoid new exacerbations or reactions. In the context of anaphylaxis, since dealing with a multi-system and potentially fatal disorder, all health care professionals should be prepared to recognize and manage it promptly and properly. Patients, too, should be prepared to recognize and self-treat

anaphylaxis promptly. Therefore, AAI as the first-line treatment should be globally available in both private and public (e.g., school) settings and health networks to be used for any individual who develops anaphylaxis [7].

Approaches may differ from country to country, depending on the national/regional policies, regulations and economical status. However, the final purpose of this document is serving as baseline to reach: (I) adequate access to AAI in affordable cost for all patients / societies and (II) disease/patient-specific approaches. For this, we here propose a 5 steps action plan (Table 2), which should be considered in combination:

- (I) To reach accurate anaphylaxis morbidity and mortality statistics
- (II) To confirm partnership: collaboration with national bodies and stakeholders in order to reach health and/or social security administrations
- (III) To strengthen awareness
- (IV) To include AAI into the WHO Model List of Essential Medicine
- (V) To provide worldwide data regarding the consumption of AAI

Countries with different economical conditions have specific priorities and requirements. The proposed action plan should support countries with different needs. For instance, steps I, II and IV would be crucial for middle and low-income countries in which AAI is still missing. On the other hand, steps II and V would allow reach the AAI in affordable prices and cover by the health national securities. Action III is a key step in every country to decrease the number of avoidable deaths.

#### ***Step I: To reach accurate anaphylaxis morbidity and mortality statistics***

From a public health perspective, morbidity and mortality data are key parameters of health status, which are the basis for population health care and prevention planning and interventions.

Currently, the principal and most reliable source for establishing and monitoring public health policies is information derived from Causes of Death statistics. While this type of source is well established and provides reliable and comparable public data collection for most of world countries, anaphylaxis has never

been a possible Cause of Death in death certificates. A recognized reason for under-notification of anaphylaxis deaths is the difficulty of coding anaphylaxis fatalities under the World Health Organization (WHO) International Classification of Diseases (ICD) system, as demonstrated by Brazilian mortality data [12]. Lack of accurate anaphylaxis mortality information prevents reaching comprehensive picture of public health and health interventions and investments, such as the availability of adrenaline auto-injectors.

A regular and systematic data collection and dissemination of statistics on diagnoses-based morbidity does not exist at a global level [13]. The reason behind this is that from a methodological and operational point of view, the collection of morbidity statistics is an extremely complex exercise, in particular with regards to comparability of data across countries. Population-based morbidity data mainly uses the ICD as the way of harmonizing data. However, a limited number of ICD-10 codes is able to capture anaphylaxis data. Only two terms in ICD-10 for anaphylaxis are hidden within section T78 of *Other and unspecified effects of external causes* under the unsatisfactory title *Adverse effects, not elsewhere classified*. So far these difficulties have hampered attempts to establish a morbidity data collection based on (mainly) administrative data similar to those already existing for causes of death or for health care data based on hospital discharges. Anaphylaxis regional epidemiological data differ considerably according to many variables and it is still unclear whether the increasing incidence published is real or the results reflect different methods used to define and characterize anaphylaxis [14].

Anaphylaxis mortality and morbidity statistics may gain new perspectives with the implementation of the ICD-11 in the forthcoming years. The ICD-11 revision provided the possibility of a better representation of anaphylaxis through the pioneer section "Allergic and hypersensitivity conditions" under the "Disorders of the Immune system" chapter [15, 16]. This achievement was a result of combined international academic and based-evidence trajectory acknowledged by the Joint Allergy Academies, composed by 6 regional international allergy academies (the American Academy of Allergy Asthma and Immunology, the European Academy of

Allergy and Clinical Immunology, the World Allergy Organization, the American College of Allergy Asthma and Immunology, the Asia Pacific Association of Allergy, Asthma and Clinical Immunology, and the Latin American Society of Allergy, Asthma and Immunology) and the ICD WHO representatives [12, 15, 17-29]. Meanwhile, we have been working to change the WHO mortality coding rules in order to consider anaphylaxis as underlying cause of death in death certificates [30]. The new ICD-11 will not solve all the problems related to population-based mortality and morbidity statistics, such as presence of over or under-diagnosis by coding by persons not experts in this disease (doctors or coders). For this reason, our WHO CC is preparing learning tools to prepare worldwide end-users for the implementation of the ICD-11.

Field-testing and validation procedures have been performed to support the implementation of the ICD-11. The utility of the new "Anaphylaxis" section has been evaluated from the morbidity and mortality perspectives [25-29]. One of the tasks of our WHO Collaborating Center (WHO CC) is to follow the "Allergic and hypersensitivity conditions" section and promote the required refinements.

***Step II: Confirm partnership: collaboration with national bodies and stakeholders in order to reach health and/or social security administrations***

A coordinated action plan is required, supported by the highest persons of governments and that inserts health concerns into all policy-making, from trade and finance to education and environmental planning. Action needs to go beyond government and should bring in civil society, academia, business, and other stakeholders to promote health. For instance, the French Ministry of Health, in coordination with the State Secretariat for Higher Education and Research, implements a proactive policy based on the mobilization of health / research professionals and patients' associations in order to improve quality diagnosis, management and prevention of the 3 million patients affected by rare diseases in France. They use the INSERM (French National Institute for Health and Medical Research) portal Orphanet containing all useful information on rare diseases and orphan drugs, for both physicians and patients. Created in 1997 in France it was

extended to all Europe in 2000 thanks to grants of the European Commission (<https://www.orpha.net/consor/cgi-bin/index.php?lng=EN>). Although severe anaphylaxis is still not into the list of rare diseases, this move would allow, in first instance, the allocation of resources to better understand the national and global epidemiology of anaphylaxis as a disease; monitor the patterns of this disorder to follow hospitalizations, mortality, avoidable deaths and costs. Having more precise epidemiological data may support the global availability of adrenaline auto-injectors worldwide at affordable price addressed to the patients' care through argumentation with national bodies and stakeholders. The above health intervention / policy model can be taken as an example in different countries in order to implement essential actions according to individual national needs, such as the availability of adrenaline auto-injectors in low income countries [14]. Whether this strategy will achieve more financial resources than previous strategies considering anaphylaxis as a disease more frequent than previously though, with a probable increase in its prevalence in the latter decades, mainly due to the increase of atopy and food allergies and therefore with the need for more resources to promote their prevention and treatment is unknown but worth trying, mainly because it is indeed an epidemiological fact that such an approach would eventually prove and the program will be carried on (or disprove and the program will be moved out).

Anaphylaxis epidemiological publications are hampered by the inclusion of all severity degrees of anaphylaxis. Mild reactions in which manifestations are generally limited to one organ or system, such as the skin, usually do not incur any risk of death. The inclusion of these cases in the epidemiological studies provides mistaken perception of high and increasing incidence of severe anaphylaxis. Our focus would be addressing severe reactions in which the risk of mortality is strong and requires additional prevention measures and a coordinated management such as the one provided by the rare disease network in our country. To date, there is no available data regarding severe cases of anaphylaxis in Europe. French data suggests that **less than 30,000 people are affected by severe anaphylaxis** and, 9.2 per 100,000 person-years based on the University Hospital of Montpellier data [28]. Australian data

demonstrated the increasing number of patients at risk of anaphylaxis, from 0.98% in 2009 reaching 1.38% in 2014 in school aged children. In contrast, the number of adrenaline auto-injectors activated (severe cases) per year per 1000 students at risk of anaphylaxis was 6 and 8 in 2010 and 2014 respectively [31]. If taken as isolated data of patients at risk, it can drive readers to think that anaphylaxis is increasing in this country. However, the administration of the treatment as objective data indicates that severe anaphylaxis can be considered as rare disease.

As the only WHO CC for classifications of allergic and hypersensitivity conditions, we intend to establish close collaboration with national bodies in order to implement actions for better patients' care, monitor and prevention, developments in research and launch measures in order to reduce avoidable deaths. Also, we intend to extend these actions internationally with the support of the WHO-Family of International Classifications, academic and scientific networks, the Joint Allergy Academies, stakeholders and patients' organizations. Our WHO Collaborating Center will provide the means through which governmental and nongovernmental collaborating parties can combine their strengths to achieve focused objectives, avoiding wasting energy and resources. The position of a WHO CC would allow us a more bilateral dialog with these bodies and faster easier communication with health organizations. Our aim is starting the actions plan applied to anaphylaxis as a model, but we may extend to other allergic and hypersensitivity conditions in the coming period. Human and financial resources will be required and may be achieved through the support from the mentioned bodies involved, robust research projects and structured collaborations. We intend to take all the support to move on the proposed action plan. For that, structured collaborations are under construction.

In the field of anaphylaxis, it is mandatory to sensitize the different levels of the health system in order to trigger more involvement and proactiveness. The first key goal of the work is to ensure the availability of essential medications for patients, therefore the AAI in low and middle-income countries and to promote better management and education in high-income countries.

**Step III: To strengthen awareness**

The main goal of prevention interventions includes reducing the negative impact or progression of an already-established condition and reducing complications and the risk of new reactions. In higher income countries, great achievements have been reported at individual and population levels (Figure 2) in the past by improving awareness and diagnostic work-up methods. However, we still observe discrepancies in lower- and lower-middle income countries, where some supplementary diagnostic tools, such as the tryptase measurements, and high priority medications are not available [7].

Increased awareness in the field of anaphylaxis is a key step forward in order to optimize the patients' time frame in health care pathways up to the full allergological work-up. Consistent and bilateral collaboration with general practitioners, pediatricians, different specialties and other health professionals is required.

Personalized health plan including personal educational guidance based on specific structured educational diagnosis and prevention measures would be key steps to decrease the number of avoidable hospitalizations and deaths. This should include for instance education programs to avoid inadvertent causes of exposures such as food or how to recognize episodes of anaphylaxis by patients or relatives since reasons for delayed application of adrenaline during the acute phase of anaphylaxis and increased risk of death are due to: (i) difficulties in recognizing the manifestations, (ii) absence of the first-line treatment drug at the time of the reaction, (iii) lack of familiarity on managing the adrenaline auto-injector devices.

**Step IV: To include AAI into the World Health Organization Model List of Essential Medicines**

The WHO Model List of Essential Medicine (EML), published by the WHO, contains the medications considered to be most effective and safe to meet most

important needs in the health system. The list is frequently used by countries to support the development of their own local lists of essential medicine [6, 32].

The first list was published in 1977 and included 212 medications. The 20<sup>th</sup> edition was published in 2017 and comprises 433 drugs [32]. Although adrenaline (epinephrine) is listed as the treatment of anaphylaxis, the auto-injector form is still missing in the EML. If present in EML, it could be published in national lists of countries in which these drugs are not available. For this reason, the discussions with the WHO EML representatives are ongoing and the proposal will be formally submitted for the forthcoming edition. This move can support argumentations to advocate for the adequate treatment of anaphylaxis worldwide.

***Step V: To provide the worldwide data regarding the consumption of AAI***

Feasibility, effectiveness and affordability of prevention and management strategies are critical to reduce preventable deaths. Knowledge on prescription and consumption of AAI are key data to forecast the auto-injectors market. According to the Global auto-injectors market analysis & forecast, anaphylaxis segment dominated the global auto-injectors market by indication in terms of revenue in 2015 and the trend is projected to sustain throughout the forecast period [33, 34]. Anaphylaxis segment has been pointed as the most attractive segment in the field with an attractiveness index of 3.55 over the forecast period. Revenue from the anaphylaxis segment is anticipated to register a compound annual growth rate of 15% over 2016-2026, to reach more than US\$ 6,000 Mn by 2026 [33].

Understanding the trends of the market of essential medications, such as the AAI, can support the allergy community to substantiate: (I) accurate data about the burden of global anaphylaxis; (II) national interventions to ensure availability in countries in which these medications are absent; (III) national health policies in order to have them available in both private and public settings; (IV) the dialog with national bodies, regulators and stakeholders to reach medications in affordable price to all or full reimbursement from national security.

Criticism related the availability of AAls as public health measure can be considered as it only benefits individuals who can also access a correct diagnosis, afford and maintain a safe unexpired supply of the devices. Nevertheless, according to the United States Internal Revenue Service, from the prevention perspective, medications are preventive care when taken by a person who has developed risk factors for a disease that has not yet manifested itself or not yet become clinically apparent, or to prevent the recurrence of a disease from which a person has recovered [35].

As an example, in 2013, President Obama signed the School Access to Emergency Epinephrine Act into law. This federal legislation provides a financial incentive for states to enact their own laws requiring schools to keep student non-specific epinephrine auto-injectors in case of an emergency [36]. Nearly every state has passed legislation regarding stocking undesignated epinephrine auto-injectors in K-12 schools. As another example, the state of Florida passed a law to allow public facilities such as amusement parks, sports leagues, camps, city parks, restaurants and other businesses to maintain a large number of epinephrine auto-injectors for emergency treatment of anaphylaxis [37]. AAI manufacturers recently introduced generic versions in the market in order to reduce the overall cost of the device. The initial pack of two devices was sold at US\$ 600 till December 2016, which was reduced to US\$ 300 to the generic form from January 2017. This has increased the affordability of insured as well as non-insured patients to obtain the medication [33].

Governmental and nongovernmental bodies, international and national allergy organizations, manufacturers, and humanitarian agencies should work together to encourage companies with established distribution networks to include adrenaline auto-injectors in their distribution networks. National allergy organizations play a key position to “lobbying” the discussions and actions with national regulators and governmental bodies.

The key issues leading to the lack of availability of AAls include cost but also national regulations, lack of regional evidence about the value of epinephrine and

the limited accurate data about the epidemiology of anaphylaxis morbidity and mortality data. Over the last several years, an increasing number of clinical databases have been developed to capture reliable anaphylaxis epidemiological data at both national and regional levels [38-45]. However, a substantial proportion of the current data on the epidemiology of anaphylaxis has come from registries with limited scope and population source. Different methods have been applied in an attempt to reach reliable epidemiological data, but most of the studies have focused on specific triggers or at-risk populations. Lack of harmonized strategies to record anaphylaxis cases hampers collection of comparable epidemiological data. In general, registries are representative sources to reach epidemiological data, and are applied only if the reporting of the conditions is mandatory and the data are validated. For these reasons, regional and international allergy academies support the initiatives to narrow these gaps.

A prioritized research agenda should encapsulate all the previous steps in the frame a global initiative against anaphylaxis. More than calling for the global availability of AAls for best management of anaphylaxis to prevent undue morbidity and mortality, we here propose an action plan as baseline of a global initiative against anaphylaxis. We strongly believe the combined efforts are a strong public health and societal move, leading to optimal care of allergic patients and best practice of allergology.

**ABBREVIATIONS:**

AAls: Adrenaline auto-injectors (AAls)

EML: WHO Model List of Essential Medicine

ICD: International Classification of Diseases

WHO: World Health Organization

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The authors declare that they do not have conflict of interests related to the contents of this article.

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All authors contributed to the construction of the document (designed the study, analyzed and interpreted the data, and wrote the manuscript).

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Accepted Article

## LIST OF TABLES

Table 1: Adrenaline auto-injectors commercially available in France (2018)

**ADRENALINE AUTO-INJECTORS COMERCIAALLY AVAILABLE IN FRANCE (2018)**

<b>Product</b>	<b>ANAPEN®</b> 	<b>EMERADE®</b> 	<b>EPIPEN® / Jr</b> 	<b>JEXT®</b> 
<b>Doses (mg)</b>	0.15 0.3	0.15 0.3 0.5	0.15 0.3	0.15 0.3
<b>Number of actions to activation</b>	3	1	2	2
<b>Length of the needle (mm)</b>	10 (+/- 1.5)	16 23 23	16 23	23
<b>Maintaining time (seconds)</b>	10	5	10 (3)	10
<b>Cost* (€/2 auto-injector) (Nov. 2017) * reimbursement: 65%</b>	66.91	64.63 64.63 66.91	74.07	66.91

**Table 2: General timeline of the action plan to reach worldwide availability of adrenaline auto-injectors**

ACTION PLAN TO REACH WORLDWIDE AVAILABILITY OF ADRENALINE AUTO-INJECTORS FOR THE PREVENTION OF ANAPHYLAXIS	CURRENT STATUS	LONG-TERM PROCESS
<p><b>Reach accurate anaphylaxis epidemiological data</b></p>	<ul style="list-style-type: none"> <li>- Strengthen standard international definitions, notification, classification and coding (<i>e.g.</i>, International Classification of Diseases) to support monitoring morbidity and mortality</li> <li>- Alignment with the WHO for the implementation of the ICD-11</li> <li>- Changes in the WHO mortality coding rules</li> <li>- Alignment with the Joint Allergy Academies, institutions and experts in the field</li> </ul>	<ul style="list-style-type: none"> <li>- Implementation of the ICD-11 and application of the WHO mortality coding rules</li> <li>- Surveillance and monitoring</li> </ul>
<p><b>Confirm partnerships</b></p>	<ul style="list-style-type: none"> <li>- Acknowledgement from the Joint Allergy Academies, experts in the field and collaboration with the WHO</li> <li>- Establishment of the WHO Collaborating Centre for Classification Scientific Support</li> </ul>	<ul style="list-style-type: none"> <li>- To establish close collaboration with national bodies in order to implement actions for better patients' care, monitor and prevention, developments in research and launch measures in order to reduce avoidable deaths</li> <li>- To extend these actions internationally with the support of the WHO-Family of International Classifications, academic and scientific networks, the Joint Allergy Academies, stakeholders and patients' organizations</li> <li>- To provide the means through which governmental and nongovernmental collaborating parties can combine their strengths to achieve focused objectives</li> </ul>
<p><b>Strengthen awareness</b></p>	<ul style="list-style-type: none"> <li>- The Allergy academies have been promoting education activities, anaphylaxis guidelines and public campaigns regarding the possible manifestations of anaphylaxis</li> </ul>	<ul style="list-style-type: none"> <li>- Increase health professionals' awareness through education and continuing education programs (<i>e.g.</i>, breastfeeding, latex avoidance, early food diversification for infants).</li> <li>- Support dissemination of accurate information to the public (<i>e.g.</i>, EAACI Anaphylaxis</li> </ul>

		<p>campaign, WAO Allergy week).</p> <ul style="list-style-type: none"> <li>- Specific interventions with early introduction of specific foods in the infant diets (<i>e.g.</i>, peanut).</li> <li>- Remove strong sensitizers from public places and workplace environments (<i>e.g.</i>, remove powdered latex gloves to prevent occupational latex allergy/ anaphylaxis, remove OTC use of pholcodine to prevent neuromuscular blocking agent anaphylaxis).</li> <li>- Individualize patient's education and provide specific information: environmental or behavior modifications to reduce patient's exposure to allergens, provide a written anaphylaxis emergency action plan.</li> </ul>
<p><b>Include AAI into the WHO Model List of Essential Medicine (EML)</b></p>	<p>- Proposal under preparation together with the WHO EML leadership</p>	<p>- After formal inclusion into the EML, this WHO statement will be offered for possible implementation in different countries</p>
<p><b>Provide worldwide data regarding the consumption of AAI</b></p>	<p>- Indicators mention anaphylaxis segment dominated the global auto-injectors market by indication in terms of revenue in 2015 and the trend is projected to sustain throughout the forecast period</p>	<p>- Understand trends and gather consistent data regarding prescription and consumption of AAI are key data to forecast the auto-injectors market. It will allow: (I) accurate data about the burden of global anaphylaxis; (II) national interventions to ensure availability in countries in which these medications are absent; (III) national health policies in order to have them available in both private and public settings; (IV) the dialog with national bodies, regulators and stakeholders to reach medications in affordable price to all or full reimbursement from national security.</p>

LIST OF FIGURES

Figure 1: Adrenaline auto-injectors are missing in more than 65% world countries

## GLOBAL AVAILABILITY OF ADRENALINE AUTO-INJECTORS:

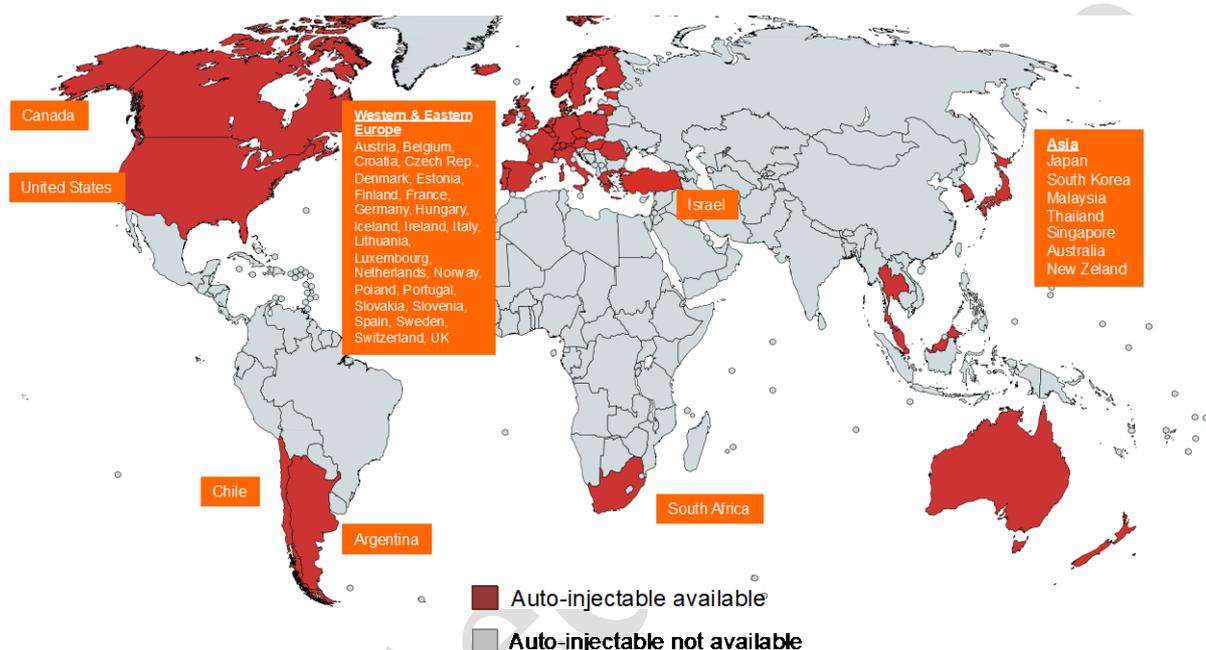


Figure 2: Strengthening awareness to prevent anaphylaxis

