

## Scientific summary

### **CHALLENGES IN THE IMPLEMENTATION OF EAACI GUIDELINES ON ALLERGEN IMMUNOTHERAPY: A GLOBAL PERSPECTIVE ON THE REGULATION OF ALLERGEN PRODUCTS**

Patients suffering from an allergic disease can be treated by allergen immunotherapy. This treatment is intended to reduce the symptoms of the allergy, for example sneezing and itchy nose or eyes or, in the best case, cure the disease.

However for allergen immunotherapies to be effective, patients need medicines for allergen immunotherapy that actually work (good efficacy), are safe for use (acceptable safety) and are of sufficient quality (e.g. the correct type and amount of ingredients and the purity). To make sure that only high quality medicines are used by physicians and patients, regulatory agencies are involved. These agencies decide on whether or not a medicine may be released to the market, which means prescribed to and used by patients. For this, they intensely check all properties of a specific medicine and also evaluate on whether or not the safety and efficacy has been proven for a specific medicine in clinical studies, meaning that they have been tested on humans and proven to work and are safe to use.

Most allergen immunotherapy products are allowed on the market by the countries own regulatory agency. This means that each country looks at these products from their own perspective and their own regulations. This is why in different countries, different allergy immunotherapies products are available to patients and doctors.

When we look at the way these different regulatory agencies around the world deal with allergy immunotherapy products, we do see some things that are the same. For example, allergen immunotherapy products are considered to be medicines in all regions, meaning that they are regulated as such. Also they are most commonly made available by one of two ways. Either by a full marketing authorisation, where all aspects (quality, safety, and efficacy) are independently checked by the regulatory agency and only products are made available to the patients where these aspects have been proven to be favorable. Alternatively, they are specifically manufactured by companies on the basis of a prescription for an individual patient. In this case, the allergen immunotherapy products are in most cases not independently checked for their quality, safety or efficacy by the regulatory agencies but only by the manufacturer itself. This also means that some aspects, such as efficacy, may be uncertain for these products. In some countries, certain allergen immunotherapy medicines may also be imported from other countries. The different ways countries regulate and examine immunotherapies means that the products available for the patients differ widely in different regions of the world.

### **Challenges in the implementation of EAACI AIT Guidelines: Allergen manufacturing and quality aspects for allergen immunotherapy in Europe and the United States**

It is important for patients to use medicines that are of high quality. To make sure that this is the case, different aspects need to be looked at to make sure that the specific medicine is of good quality. For example, it must be clear that what is in the medicine are the ingredients it is supposed to have (correct identity). Also, each ingredient should be in there at the right amount as written on the label (correct quantity). In addition, it is important that all the ingredients are pure, not mixed with other ingredients you do not want in there (purity).

Medicines for allergen immunotherapy are intended to reduce the symptoms of the allergy, for example sneezing and itchy nose or eyes or, in the best case, cure the disease. The manufacturing of allergen immunotherapy medicines can be a difficult and complicated process. Most of the time, these medicines are made from ingredients that come from natural sources. For example, birch pollen would be collected in nature and then processed in the factory to become the most important ingredient in the allergen immunotherapy medicine to treat birch pollen allergy. This can be a challenge. The birch pollen immunotherapy medicine has to be of the same quality all the time even if the natural birch pollen may change over time.

For those products that have a marketing authorization, regulatory agencies decide on whether or not a specific medicine may be made available to patients by independently evaluating these medicines, including the quality. Looking at allergen immunotherapy in two major regions of the world, it becomes clear that many aspects concerning the quality requirements in the European Union and the United States are similar.

Nevertheless, there are also essential differences in the regulation of these medicines, resulting in differences in the type of medicinal products available in the two regions.

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