Capsulas

New regulatory framework for allergen products

Ministerial Order SND/778/2023, of 10 July, regulating certain aspects of the authorisation of allergen products

Background

We currently find allergen products for both human and veterinary use that do not have marketing authorisation (MA). On the other hand, for identical indications and allergens, we also find medicinal products that have an MA (and therefore proven quality, safety and efficacy).

Although the reasons for not having an MA can vary, they are generally related to the concept of Named Patient Programmes (NPPs) and its non-industrial manufacturing processes. These cases are exceptions to the general rule laid down in Spanish and European legislation that medicinal products must have a marketing authorisation before being placed on the market. However, many of these medicinal products that lack marketing authorisation do not align with the stated justifications: they are not individualised preparations and/or at least part of their manufacturing process is industrial. This is the case, for example, of some NPPs which, far from being individualised preparations made for a particular patient in accordance with a prescription, are manufactured using industrial methods, often starting before the prescription is issued.

This anomalous situation has been the subject of studies and work for several years with the aim of regularizing the situation. In July 2020, the CMDh published recommendations for Member States to harmonise the legal basis of allergen products. Among others, the recommendations aim to reinforce the exceptional nature of NPPs and emphasise that their regulation should not be used to circumvent the requirement to obtain an MA. Thus, the recommendations relegate NPPs to exceptional cases where no authorised alternative exists; also advise against accepting NPPs for certain highly relevant and highly prevalent allergens (listed in an annex); and require that the manufacturing of NPPs not commence prior to doctor's prescription.

In July 2023, marking the conclusion of a process initiated years ago, the Ministry of Health published Order SND/778/2023, which we are now discussing. This Ministerial Order outlines a procedure that enables the regularization of the current situation of allergen-based medicinal products.

What does the Ministerial Order cover?

(i) Allergen products for specific immunotherapy manufactured in isolation for the individual treatment of a patient (NPP).

NPPs must be manufactured on a case-by-case basis and cannot be used if other industrial or semi-industrial manufactured alternatives are available.

NPPs do not require an MA, but the Spanish Agency for Medicine and Medical Devices (AEMPS) must be informed of the start of the manufacturing process, which can only take place in authorised facilities and in accordance with good manufacturing practices.

(ii) Industrially manufactured allergen products for immunotherapy or in vivo diagnostics (Industrially Manufactured Medicinal Products).

These medicinal products require an MA, as would any other industrially manufactured medicinal product.

(iii) Allergen products for specific individualised immunotherapy, prepared from one or more industrially manufactured "bulk allergens", for a specific patient following the requirements of a specialist physician (Allergen Bulk-Based Medicinal Products).

This is a hybrid situation, halfway between NPPs and the Industrially Manufactured Medicinal Products. It covers "semi-industrial" products, i.e. products manufactured according to a doctor's prescription for a specific patient, but partly using an industrial process, where at least one of its active substances ("bulk allergens") has been industrially manufactured.

According to the Ministerial Order, "bulk allergens" are allergen preparations manufactured by an industrial process and intended to be part of mixtures with other bulks or dilutions of the bulk itself for a specific immunotherapy treatment, according to the specific requirements of a specialised physician, to meet an individual prescription.

"Bulk allergens" are treated as normal medicinal products and therefore require an MA (albeit a simplified one). Companies must submit the bulk data to the AEMPS, excluding the finished product sections and sections 4 (non-clinical reports) and 5 (clinical reports). Applicants must also provide a list of any mixtures in which the bulk may be included. These mixtures must be justified by stability and clinical utility data.

Regularisation process

As per above, there are currently Industrially Manufactured Medicinal Products and "bulk allergens" (which may subsequently be incorporated into Allergen Bulk-Based Medicinal Products) that do not have an MA.

The Ministerial Order recalls that these medicinal products require an MA and provides for a regularisation process.

The Ministerial Order grants a six-month period (i.e. until January 2024) during which companies manufacturing or marketing Industrially Manufactured Medicinal Products or "bulk allergens" without an MA must notify the AEMPS.

At the end of this six-month period, companies will have to submit the MA application. The deadline for submission will be set by the AEMPS (presumably after assessing the volume of notifications received for these products).

Products subject to the regularisation process may remain on the market until the AEMPS has taken a decision on the granting or refusal of the relevant MA. However, products that have not been notified in due time and form must cease to be marketed at the end of this six-month period, "with the exception of those being used in a specific treatment".

Our comments

The Ministerial Order brings clarity to a group of medicinal products that have been in regulatory limbo due to their uniqueness. It also lays the groundwork for beginning to regularise a completely anomalous situation, such as

the coexistence for certain indications and allergens of medicinal products with an MA with others that have not been subject to the same regulatory requirements.

Notwithstanding the above, and although the Ministerial Order is a step in the right direction, there is still a long way to go. The regularisation process is uncertain (the Ministerial Order does not set a maximum timeframe for all medicines to be regularised) and there is a risk that it will take longer than it should. In addition, there are aspects of the Ministerial Order and the general allergen regime (e.g. its public funding regime) that remain unclear and will require clarification. It will be crucial to follow this up over the coming months. The road to regularisation has begun, but there is still a long way to go.

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