New guidelines on the preparation of medicinal products in hospital pharmacy services

Publication of the Guide for the preparation of medicinal products in hospitals and of Royal Decree 477/2014 on advanced therapy medicinal products not industrially manufactured

Background

In June, the new guidelines on the preparation of medicinal products in hospitals have become available. Two documents on the activities of these institutions, long awaited due to their particular importance on the preparation of medicinal products in hospital pharmacy services, have been approved: Royal Decree 477/2014 on the authorization of advanced therapy medicinal products not industrially manufactured (Spanish Official Journal nº 144, 14 June 2014) and the Good Practice Guide. Both documents are available on the website of the Ministry of Health, Social Security and Equality and also on our website.

Rules on the preparation of advanced therapy medicinal products not manufactured industrially

Under Regulation 2004/726/EC, advanced therapy medicinal products include products for gene therapy and somatic cell therapy, tissue engineered products, and combined medicinal products for advanced therapy. European law contemplates that some of these products may be placed in the market without obtaining a prior marketing authorization. This applies to the products that are occasionally prepared in hospitals, following an individualized prescription for a specific patient and under the physician's responsibility.

These products will however need an authorization for use which shall be issued by the Spanish Agency for Medicinal Products and Medical Devices (AEMPS). Royal Decree 477/2014 establishes the requirements for obtaining said authorization, as well as for the preparation and use of the product.

The authorization must be requested by the hospital management, and the hospital itself shall be the holder. The process for obtaining cells must be described in detail in the application, even though the preparation of the product may be entrusted to another hospital or entity authorized for the preparation of medicinal products. The product must be correctly identified and accompanied by information appropriate for the patient, whose consent must be previously obtained.

The AEMPS will have 210 calendar days to authorize or not the preparation and use of the product, after verifying that its quality, traceability and pharmacovigilance comply with standards equivalent to industrially manufactured medicinal products. The authorization must be renewed periodically.

Additionally, a transitional period is included for products with consolidated use that have been used regularly. Hospitals may continue using them provided they inform the AEMPS, before 14 October 2014, of their intention to request an authorization for use for such products.

Guide on the preparation of medicinal products in hospital pharmacy services

On the other hand, the Ministry of Health has published the Good Practices Guide on the preparation of medicines in hospital pharmacy services, with guidelines and recommendations for the preparation of medicinal products both sterile and non-sterile.

These guidelines finally develop Royal Decree-Law 16/2012, which approved with urgent character the possibility that the Autonomous Regions authorize hospital pharmacy services to carry out operations of splitting, dose customizing, and other processing and transforming operations of medicinal products. For that purpose, compliance with the good practice guidelines elaborated by the General Directorate of Basic Services Portfolio of the National Health System and Pharmacy, with the collaboration of the AEMPS and experts of well-known prestige had to be guaranteed.

The guide comes out two years after the approval of Royal Decree-Law 16/2012, and after various vicissitudes that reveal how complex the process has been. The processing of commercial presentations has been an activity traditionally oriented to attend special needs of individual patients who could not be covered by such presentations. This is the only case where Law 29/2006 and Royal Decree 1015/2009 allow the use of a commercial presentation in conditions different to those included in its marketing authorization and SmPC. The Guide, logically, seems to be orientated to the same purpose and expresses that its guidelines are applied to "*any operation which permit adequate a medicinal product to the specific needs of a patient and/or adapt it for its administration or use*".

As regards its content, its objective is to guarantee that the preparation of medicinal products in hospitals answers to quality and safety standards comparable to the ones required for industrial manufacture. The service must perform its activities under the responsibility of a specialist pharmacist, and have qualified personnel and facilities and equipments suitable for the operations that will be carried out. Additionally, there must be a guide on the procedures, instructions, registries, sampling and control protocols for each of the preparations, after having analyzed the risk level associated to them. The guide, moreover, must include the quality and qualification requirements related to the facilities, equipments and personnel.

The preparations must be correctly identified and labeled, and guarantee their traceability. The activities must be carried out in the service's facilities, although low risk extemporaneous preparations (reconstitution of medicinal products, doses individualization, etc.) may be performed in other units such as nursing units. The preparation zone for steriles must be a clean room and separated from the rest. Preparations that could pose a danger (cytotoxic and biohazards products), must be performed in a confined zone which assures safe manipulation under biologic safety cabinets.

Raw materials and conditioning materials must comply with pharmacopeia and other applicable regulation. In the case of active ingredients which have been controlled and released in the European Union, it is sufficient to verify that the certificate of analysis complies with the specifications of the product defined by the pharmacopeia, and a visual inspection of the batch. Commercial presentations can only be used as starting materials if they have obtained a marketing authorization in Spain so therefore, they do not require a specific quality control analysis.

The pharmacy service is the ultimate responsible for the quality of the medicinal products prepared and for their release, but is important to highlight that the responsibility of carrying out the preparation must be assumed jointly by the prescribing doctor and the pharmacist responsible for the preparation.