Thalidomide, the story goes on

Talidomida, la historia continúa

Dear Editor,

It has been almost 10 years since we published an editorial in *Anales de Pediatría* under the title ''Thalidomide: an unfinished history''.[1] After this time interval, recently there have been news about the reauthorisation for the marketing of thalidomide in Spain, and, as regards those affected by it, the story remains unfinished 10 years later.

Sixty years after the discovery of the severe teratogenic effects of thalidomide, the drug is once again being marketed in Spain since February 2, 2023 (Spanish Agency of Medicines and Medical Devices, AEMPS).[2] To date it had only been available as a drug subject to special medical control since 1985, a foreign drug and later on an orphan drug for treatment of multiple myeloma authorised by the European Medicines Agency (EMA) since 2001. Its exceptional and controlled use has also been authorised for other diseases, such as erythema nodosum or actinic prurigo, when there are no other treatment options. In multiple myeloma in particular, one of its derivatives, lenalidomide, which is authorised for use in Spain, has been replacing thalidomide in many cases.

Contrary to its initial marketing authorisation, the prescription and dispensation of thalidomide are now restricted to a single authorised indication (first-line treatment, in combination with melphalan and prednisone, in patients with untreated multiple myeloma, aged $\geq$65 years or ineligible for high-dose chemotherapy) and subject to a strict pregnancy prevention programme (PPE) and controlled access system (AEMPS)[3]: the same surveillance and control system established for thalidomide analogues with more recent marketing authorisations, such as lenalidomide and pomalidomide.

In fact, the system calls for strict safety requirements, and it is similar to the one established by the Food and Drug Administration (FDA) to prevent teratogenicity, the System for Thalidomide Education and Prescribing Safety (STEPS), which was implemented in 1998 with the initial approval in the United States of thalidomide as an orphan drug for treatment of erythema nodosum, which was then extended to multiple myeloma.[4] It is worth mentioning that, paradoxically, in the 1960s the United States had rejected the initial application submitted by Chemie Grünenthal for the marketing of thalidomide for symptomatic treatment of nausea and vomiting during pregnancy due to a lack of safety data.

We ought to remember that the teratogenic effects that affected more than 10,000 newborns worldwide marked a turning point in the process of authorization and marketing of drugs for human use, setting the foundations of the current system for monitoring the safety of drugs pre and post marketing (drug surveillance) and specifically recommendations concerning use during pregnancy and/breastfeeding (international classification of pregnancy categories for drugs based on foetal risk). These are indispensable principles today for conducting preclinical and clinical research on new drugs.

Still, what has happened in the past 10 years to the individuals affected by thalidomide in Spain?

At present, in our country, contrary to Germany, the Netherlands or Portugal, where all thalidomide victims have been awarded compensation, the Association of Victims of Thalidomide of Spain (AVITE) is still fighting to gain recognition for affected survivors (more than 300) and compensation for individuals born with malformations known to result from thalidomide exposure between the 1950s and 1985 (Royal Decree of 2018).[5] Financial support payments should have been effected in 2019, but the benefits were never paid due to noncompliance with Law 6/2018 on the General State Budget. In response to this, AVITE filed a suit against the government and the state, but since the cassation appeal was dismissed by the Supreme Court of Spain, it has announced future demonstrations once the political campaigns for the upcoming elections start to claim the payment of due compensations.[5]

The story goes on...

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