focus will make a change of direction possible in the basis of the healthcare relationship, given that we will go from examining solely the aim of doing good and doing no harm, even without patient consent, to a perspective whose main focus is autonomy and dignity. In this way, the patients' autonomy is increased without leaving them alone in the face of the decision. But this has to be a task performed jointly between the professionals and the patients.

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Tianeptine: Why has it not been classified as a narcotic in Spain?☆

Tianeptina: ¿por qué en España no ha sido catalogada como estupefaciente?

Sirs,

Tianeptine is a tricyclic antidepressant marketed in France since 1988 that has recently entered the Spanish market as a generic medicine.[1] It is a drug that is chemically similar to another amphetamine-type stimulant and antidepressant–amineptine, which was withdrawn from commercialisation in Spain (1999) and in other countries due to its addictive properties and adverse hepatic and cutaneous effects. The structural similarity of tianeptine to amineptine and the cases of abuse and addiction reported for it have given rise to many doubts about its safety profile.[2,3]

In 2012, France's National Agency for Medicines and Health Products Safety (*ANSM* is the acronym in French), at the request of the Narcotic Drugs and Psychotropic Substances Committee, decided to re-evaluate the benefit–risk ratio of Stablon® (the brand name of tianeptine in France). When that committee analysed the cases detected, the results permitted them to conclude that, in effect, there was a risk of abuse and addiction associated with its use.[4] The overall assessment of efficacy and safety led the French agency to decide that the benefit–risk ratio of tianeptine was favourable, but limited. With respect to its benefits for health, the agency's conclusions were: ''Given the available information, bearing in mind the therapeutic alternatives existing and the drug dependence problems identified, Stablon® does not present any benefit for the public health system''.[4]

As a consequence, tianeptine has been classified as a narcotic drug in France. Since 3 September 2012,[5] this antidepressant has been subject to the same prescription and supply restrictions as any other narcotic substance in List I, with a maximum length of prescription of 28 days. Before that, it had been withdrawn from marketing in Georgia and included in the list of psychotropic substances in Russia, Ukraine and Armenia. Tianeptine is not authorised in several Anglo-Saxon countries.

At present, the safety of tianeptine is still a concern. The well-known journal *Prescrire* has repeatedly denounced that its benefit–risk ratio is unfavourable.[6] Previously, the conclusion reached by the re-evaluation the ANSM performed had been noted and the reason that the French authorities had allowed this drug to continue to be funded had been questioned.[7] Tianeptine is included in the list of drugs to avoid that this journal publishes every year.[8] Up till now, the European Pharmacovigilance Risk Assessment Committee has not carried out an assessment of tianeptine, but the data recorded in EudraVigilance (a European database of reports on presumed adverse reactions) confirm that there is a risk of abuse and addiction associated with its use. Up to October 2015, of the 563 cases reported, 125 included abuse and 27, addiction.[9]

In spite of these antecedents, to date no restrictions in the prescription or supply of tianeptine (Zinosal®) have been established in Spain. Given that it is a generic medicinal product, the applicable regulation for obtaining its authorisation is much simpler and only requires bioequivalence studies against the reference compound. It

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is not known whether the Spanish Agency of Medicines and Medical Devices has assessed the safety of this drug and whether it has taken the measures adopted in other countries into consideration.

In similar situations, when the evidence of efficacy and safety of a new drug is questionable, its promoters have used information of little scientific reliability to back up their sales strategies. Among these are: (1) citing action mechanisms–described for laboratory animals–that distinguish the substance promoted from its competitors, but that are perhaps irrelevant for the indication sought and that sometimes do not distinguish it from the placebo; (2) using ambiguous terms that seem neuroscientific–such as ''neuroplasticity'' and ''regulation of glutamatergic transmission''–to justify its sales without specifying either how or on which of the hundred of elements that comprise such processes the substance being promoted acts, nor what relevance such an action (if it exists) has on the disorder in human beings; and (3) directly extrapolating the effects observed on experimental animals submitted to stress to therapeutic effects in complex human syndromes.

It is the reader who must decide if these strategies are applicable to the molecule in question based on the information provided and, consequently, the one who must decide upon the credibility of the information. Of course, this is a logical process that should precede any modification of clinical practice.

In short, tianeptine is a drug new to Spain, but it is one that has raised numerous issues elsewhere for years. Compared to other antidepressants, it does not present any advantages with respect to either efficacy or convenience (administration 3 times a day). In addition, its cost exceeds that of selective serotonin reuptake inhibitors considered to be first line treatments for depression. The justifiable uncertainties about its safety reinforce the idea that aspects as crucial as its funding or its classification as a narcotic substance have to be put to consideration again.

The authors declare that this article has been written in agreement with the accepted standards on transparency with regard to the publication of scientific articles.[10]

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