



## Editorial

### Recall for Medications: The Fragile Balance Risk/Benefit



A recent paper published, as a scientific letter in JAMA Network Open, has evaluated the impact of the recall for varenicline from the North American market that occurred at July 2021, due to contamination with nitrosamines.<sup>1</sup> The study analyzes the impact in terms of prescription of effective and safe medications to help quit smoking. Data are given on how the prescription of the Canadian generic varenicline (apo-varenicline, which is not affected by nitrosamine contamination problems) and the prescription of bupropion and nicotine replacement therapy (NRT) have evolved. The figures speak up: the prevalence of smokers receiving varenicline treatment for smoking cessation decreased from 536 prescriptions per million subjects in June 2021 to 136 prescriptions per million in September 2021. This represented an absolute reduction of 74.7% in prescriptions for this effective and safe medication to quit smoking. Even the figures for June 2022 continued to remain at those same levels. But the most serious thing is that this reduction in the number of varenicline prescriptions was not followed by an increase in the number of prescriptions for other effective and safe medications to quit smoking such as bupropion and NRT: the percentages of prescriptions of these drugs remained constant from June 2021 to June 2022.<sup>1</sup>

Of course, this is a study that has some limitations, such as that it does not compute the NRT that has been prescribed Over The Counter (OTC), however, all that has been sold under medical prescription is computed and this is already an excellent marker of how it has evolved the behaviour of health professionals throughout the period analyzed.

Given the striking results of this study, it would be important to make some considerations.

The first consideration refers to the powerful impact that this recall for varenicline will have on the health of a large number of smokers who could have stopped smoking if they had used this medication and who, since they did not use this or any other of the effective and safety drugs, their chances of succeeding in that attempt were very significantly reduced and they would probably continue to be smokers, and more likely to become frustrated smokers, that is, desperate at the impossibility of quitting. Then the measure, which was supposedly carried out to protect the health of smokers, has not only not protected it but has put it at risk.

The second consideration refers to the fact that these types of measures taken against medications that are safe and effective in helping to quit smoking open a false door through which other types of therapies that are neither as effective nor as safe. We are referring to electronic cigarettes and heated tobacco products. Recently, North American CDC made a lukewarm statement about electronic cigarettes that drew the attention of a good number of

medical associations and societies about the use of these devices to quit smoking.<sup>2</sup> Statements like that and decision-making like the one made with varenicline are what make it easier for some smokers to stop using safe and effective medications to quit and are turning to the use of new forms of tobacco consumption. This situation is becoming evident in all the surveys.<sup>3</sup>

To finish we would like to make two attention calls. One addressed to the regulatory authorities so that they take into account that any decision they make in relation to medications to stop smoking can have important benefits for people's health, but also relevant risks and that before making them it is convenient that they make a detailed analysis of the risk/benefit binomial of their decisions. At the time, the decision to recall varenicline from the market due to contamination with nitrosamines was already highly discussed, since the figures reached were considerably smaller than those present in normal cigarettes and even smaller than those detected in electronic cigarettes (it is curious that these were not taken into account when that lukewarm statement about them that we talked about before was made).<sup>4</sup> Furthermore, that contamination was not detected in the Canadian generic varenicline, apo-varenicline, which could continue to be used. This data, although known, did not become more widespread until a few months later, already too late to recover its use and make up for the reduction in prescriptions.

We want to direct the other attention call to health professionals interested in smoking cessation treatments. Data that this study shows about how the frequency of NRT and bupropion prescriptions has not changed, despite the reduction in varenicline prescriptions, is very disappointing.<sup>1</sup> It seems that for many health professionals the only treatment to stop smoking was varenicline, as if there were not too many data on the efficacy and safety of NRT or bupropion as drugs for the treatment of tobacco addiction. Even the limited knowledge of these professionals about the availability of apo-varenicline in the US market speaks of the low interest in the treatment of smoking among those health professionals. With this we want to show that it is essential that all health professionals receive training, have knowledge and develop skills for the use of all pharmacological treatments to quit smoking. In this sense, Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) has just published a Clinical Practice Guide for pharmacological treatments of smoking cessation, which addresses this discipline and specifies which medications are safe and effective, and how they should be used; and with which protocols they should be used in daily clinical practice; all of this supported by the most rigorous scientific evidence and explained with clear algorithms.<sup>5</sup>

In summary, the decision to recall varenicline has had a significant impact on the rational use of smoking cessation medications, leading to a large number of smokers not having benefited from this drug and without being prescribed other drugs equally effective and safe. On the contrary, they will have directed their steps to the use of other ineffective and dangerous therapies such as electronic cigarettes or heated tobacco products. This reality should alert regulatory authorities to be prudent in making decisions about smoking cessation medications, and should also raise awareness among all health professionals so that they are well trained in the knowledge and use of all smoking cessation drugs.

### Ethical Approval

Nothing to declare.

### Conflict of Interest

Dr. Carlos A. Jiménez-Ruiz. CAJ-R has received honoraria for presentations, participation in clinical studies and consultancy from: Aflofarm, Bial, GSK, Menarini and Pfizer.

Dr. Carlos Rabade-Castedo. CR-C has received honoraria for speaking engagements, sponsored courses, and participation in clinical studies from Aflofarm, GSK, Menarini, Mundipharma, Novartis, Pfizer, and Teva.

Dra. Eva de Higes-Martinez. EH-M has received fees for presentations, conferences and courses sponsored by: Astra-Zéneca, Bial, Boehringer, Chiesi, Esteve, Faes Farma, Ferrer, GSK, Mundipharma, Menarini, Novartis, Pfizer and Rovi.

Dr. Jose Ignacio de Granda-Orive. JIG-O has received honoraria for speaking, scientific consulting, clinical study participation, or

publication writing for the following: Astra-Zéneca, Chiesi, Esteve, Faes, Gebro, Menarini, and Pfizer.

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