Evidence for Self-Medication
International Review Journal

Safety of fexofenadine as over-the-counter treatment for allergic rhinitis in Italy

Marina Volonté, DVM, Mohamed Amessou, PhD, MBA, and Maria Chiara Uboldi, PhD

Switches of oral antihistamines (OAHs) from prescription drug to over-the-counter (OTC) status may raise safety concerns due to misuse or abuse, as seen with first-generation antihistamines. A real-world study by Carnovale et al. [1] showed no difference in number of adverse events after switching second generation OAHs to OTC, indicating a similar safety profile and supporting the use of larger pack sizes.

Over-the-counter (OTC) medicines provide accessible self-care solutions, as they are sold without a physician's prescription. Switching of drugs from prescription to OTC may raise concerns among healthcare professionals (HCPs) over the safety (misuse or abuse) of these drugs [2]. To reach an OTC status, medication must have a well-established safety profile and efficacy suitable for self-medication [3]. The number of people favouring OTC medicines for allergy treatment has increased from 66% in 2009 to 75% in 2015 [4].

Allergic rhinitis (AR) is an inflammation caused by allergens with symptoms of runny, itchy and stuffed nose; sneezing; and red and watery eyes. Fexofenadine is a second-generation oral antihistamine (OAH) available OTC for symptomatic treatment of AR in most European countries, and since 2016 in Italy. Cetirizine and loratadine, also second-generation OTC OAHs, require a prior pharmacist's consultation in Italy. Unlike some European countries where a pack size of 7–100 OAH tablets is marketed as OTC, only packs of

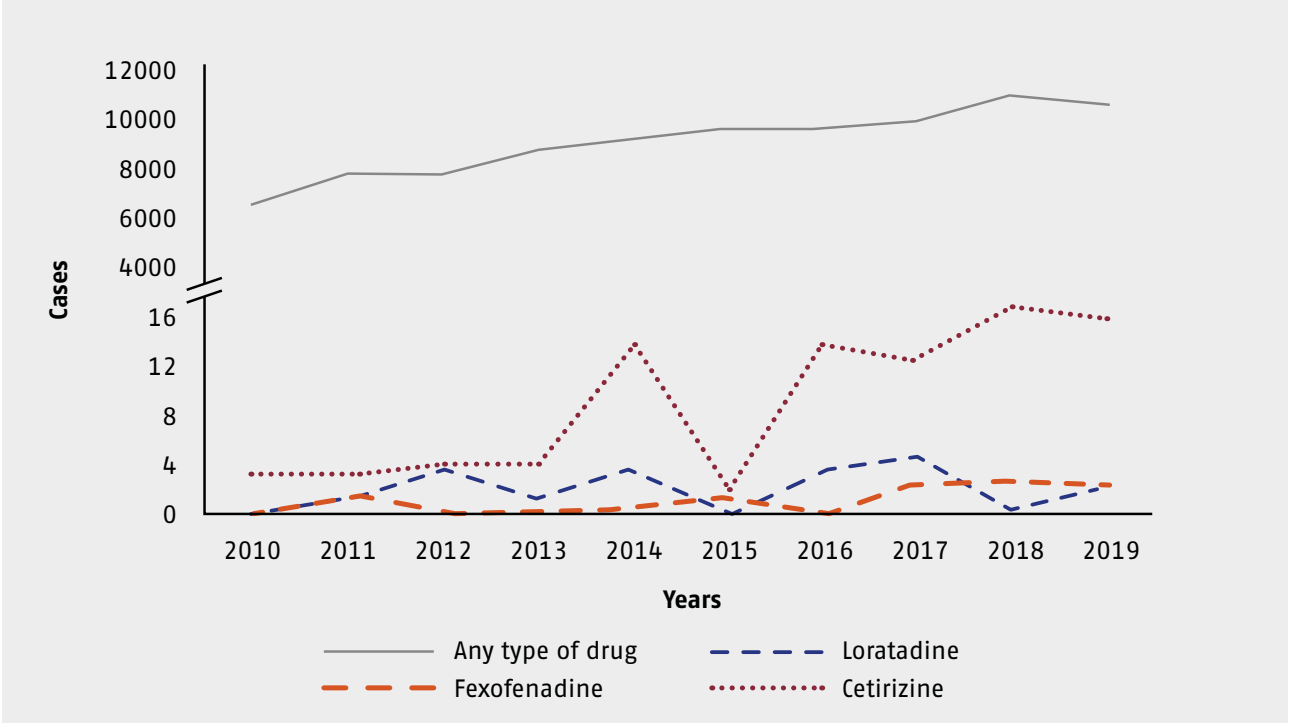

Fig. 1. Number of annual serious adverse events (SAEs) related to fexofenadine compared to loratadine and cetirizine, reported between January 2010 and June 2019 in Italy (Adapted from Carnovale C, et al. 2022)

Evid Self Med 2023;3:230023 | https://doi.org/10.52778/efsm.23.0023
Affiliation/Correspondence: Marina Volonté, DVM, Sanofi Consumer Health Care, Viale Bodio 37/B, 20158 Milan, Italy (marina.volonte@sanofi.com); Mohamed Amessou, PhD, MBA, Sanofi, Gentilly, France; Maria Chiara Uboldi, PhD, Sanofi, Milan, Italy

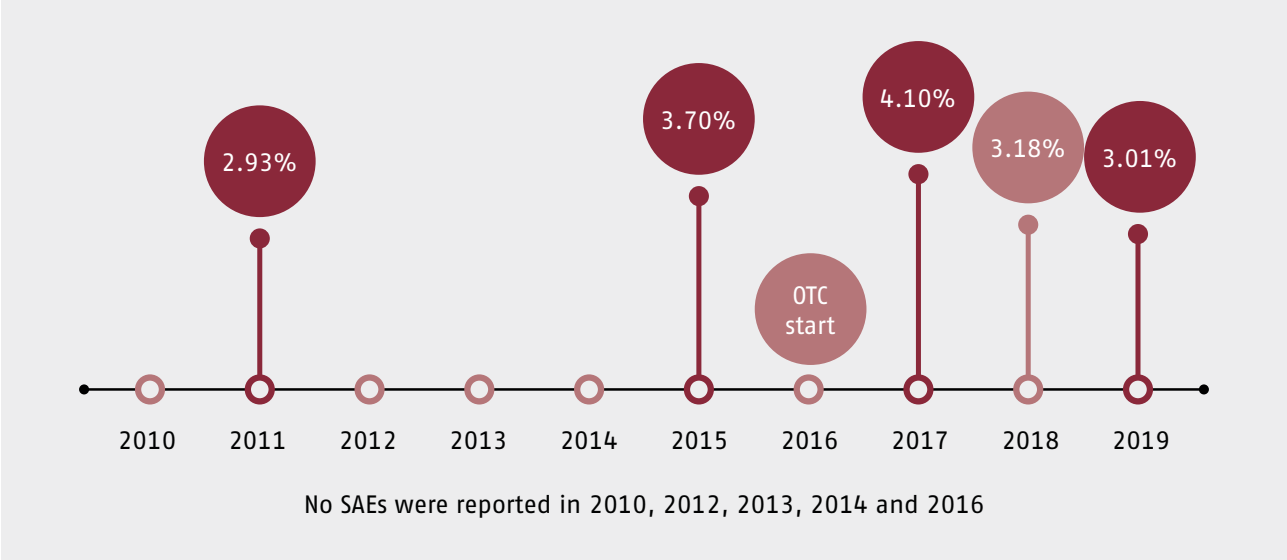

Fig. 2. Annual SAE reporting rate of fexofenadine in Italy (2010–2019) (Adapted from Carnovale C, et al. 2022)
OTC: over the counter; SAE: serious adverse event

7–10 OAH tablets are available for self-medication in Italy [1]. This real-world study compared the safety profile of fexofenadine before and after its OTC availability in Italy with that of other European countries where larger packs are available. Furthermore, a systematic literature review was conducted to evaluate the safety profile of fexofenadine and other second-generation OAHs in Europe. This case-by-case analysis of adverse events related to fexofenadine, loratadine and cetirizine in Italy (from January 2010 to June 2020) was based on using real-world data extracts of safety reports from a reliable database, i.e. the United States' Food and Drug Administration Adverse Event Reporting System (FAERS) [1].

Impact of OTC switch on fexofenadine safety profile

Among the 3760 reports of suspected fexofenadine-related serious adverse events (SAEs), 13 (8 after duplicate removal) were from Italy and categorised as possible for causality based on the application of Naranjo's algorithm but oscillating between 1 and 3 suggestive of a weak correlation. A slight increase in fexofenadine-related SAEs from 2010 to 2019 (range: 0–2 per year) was reported in Italy, which was in line with the general reporting trend of any type of drug, including loratadine and cetirizine, possibly reflective of a general intensification of pharmacovigilance activities (**Fig. 1**).

Fexofenadine had a low incidence of SAEs even in Europe where it is available as an OTC medication in larger packs (20–100 tablets), with only two to five reports per country.

The annual reporting rate of fexofenadine-related SAEs (i.e. the rate at which SAEs related to a drug occurred based on its annual utilisation) increased only faintly in Italy after it had gained the OTC status (in 2016), despite a large increase in OTC fexofenadine sales. The reporting rate plateaued at 3.01% in 2019, which was similar to the pre-OTC level of 3.70% seen in 2015 (**Fig. 2**).

A systematic review of 22 studies conducted in Europe [1] showed a wide use of second-generation OAHs in clinical practice and highlighted a favourable opinion on their use in self-medication by HCPs, including pharmacists.

Summary

The favourable safety profile of fexofenadine in self-medication shown also for larger pack sizes available in Europe supports their use in Italy as well. Finally, spontaneous reporting systems, such as FAERS, allow real-world safety data analysis and characterisation of OTC drugs in daily clinical use.

Literature

1. Carnovale C, Battini V, et al. Safety of fexofenadine and other second-generation oral antihistamines before and after the removal of the prescription requirement in Italy and other European countries: A real-world evidence study and systematic review. World Allergy Organ J. 2022;15(7):100658. doi: 10.1016/j.waojou.2022.100658.
2. Schifano F, Chiappini S, et al. Focus on over-the counter drugs' misuse: A systematic review on antihistamines, cough medicines, and decongestants. Front Psychiatr. 2021;12:657397. doi: 10.3389/fpsyt.2021.657397.
3. Stippler A, Eckstein N, et al. To switch or not to switch—first Germany-wide study from the perspective of pharmacists in the European environment. J Public Health. 2021;29(1):9–17. doi: 10.1007/s10389-019-01101-4.
4. Association CHP. Rx-to-OTC Switch, 2022. https://www.chpa.org/our-issues/otc-medicines/rx-otc-switch (accessed 27 February 2023).

Acknowledgements: The authors thank Paula Fontanilla, PhD, an employee of Sanofi, for critically reviewing the scientific content of this manuscript and Avinash Bardia and Ashwitha A, employees of Sanofi, for providing writing and editorial support.

Conflict of interest: M. Volonté, M. Amessou and M.C. Uboldi are employees of Sanofi.

Disclosure: Sanofi funded medical writing and publication of this manuscript.

Information regarding manuscript

Submitted on: 12.05.2023
Accepted on: 06.07.2023
Published on: 10.09.2023