Direct Healthcare Professional Communication

July XX, 2021

CHAMPIX (varenicline) - lots to be recalled due to presence of impurity N-nitroso-varenicline above the Pfizer acceptable daily intake limit

Dear Healthcare Professional,

Pfizer, in agreement with the European Medicines Agency and <National Competent Authority> would like to inform you of the following:

Summary

- **Lots of CHAMPIX batches (varenicline) that were found to contain levels of N-nitroso-varenicline above Pfizer's acceptable level of daily intake are being recalled. As a precaution, Pfizer is pausing distribution of the medicine pending further testing.**
- **Based on the available data, there is no immediate risk to patients taking this medication.**
- **While EU authorities continue to assess the data, healthcare professionals should, as a precaution, not start new patients on CHAMPIX.**
- **The recall and pause in distribution will result in shortages of CHAMPIX.**
- **For patients who are already on CHAMPIX, it may not be possible to complete treatment and healthcare professionals may consider switching treatment to an alternative.**
- **Alternatives will vary from market to market but may include nicotine replacement therapy (NRT) and bupropion.**
- **Healthcare professionals should also take into account the need to consider dose tapering, as the summary of product characteristics (SmPC) states that "At the end of treatment, discontinuation of CHAMPIX was associated with an increase in irritability, urge to smoke, depression, and/or insomnia in up to 3% of patients."**
- **Healthcare providers should advise patients undergoing treatment not to discontinue CHAMPIX without consulting them, and to discuss any questions or concerns with their healthcare provider if needed.**

Background on the safety concern

CHAMPIX (varenicline) is indicated for smoking cessation in adults.

Pfizer tested CHAMPIX product lots for the presence of the CHAMPIX-derived nitrosamine, N-nitroso-varenicline. Test results indicated levels of N-nitroso-varenicline in certain lots exceeded the Pfizer product-specific acceptable daily intake (ADI) level.

N-nitroso-varenicline is a nitrosamine. Nitrosamines are classified as probable human carcinogens (substances that could cause cancer). Nitrosamines can be found at very low levels in water and foods, including cured and grilled meats, dairy products and vegetables. Nitrosamine impurities may increase the risk of cancer if people are exposed to them above acceptable levels over long periods of time. As a precaution, Pfizer is recalling product lots above the Pfizer derived ADI and pausing distribution of CHAMPIX, pending further testing. This nitrosamine finding is not associated with any change in CHAMPIX manufacturing.

Pfizer and the EMA are working together to assess information on this issue and are monitoring the situation closely, including any disruptions to the European market.

The expected benefits of CHAMPIX, intended to help patients quit smoking and with a limited use of 12 to 24 weeks, outweigh the low potential risks posed by temporary N-nitroso-varenicline exposure from CHAMPIX. CHAMPIX has a safety profile that has been established through the clinical development program and confirmed by data from over 15 years of marketing.

Call for reporting

Healthcare professionals are reminded to continue to report suspected adverse reactions associated with CHAMPIX in accordance with the National spontaneous reporting system. Healthcare professionals are asked to report any suspected adverse reactions.

Company contact point

[Insert local contact information e.g. Pfizer Medical Information/Communications

Department at XXX-XXX-XXXX]

Communication Plan for Direct Healthcare Professional Communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Champix (varenicline)
Marketing authorisation holder(s)	Pfizer Europe MA EEIG Boulevard de la Plaine 17 1050 Bruxelles Belgium
Safety concern and purpose of the communication	Lots of CHAMPIX (varenicline) that were found to contain levels of N-nitroso-varenicline above Pfizer's acceptable level of daily intake are being recalled. Out of an abundance of caution, Pfizer is pausing distribution of product pending further testing.
DHPC recipients	General practitioners, secondary care providers (i.e. cardiologists, pulmonologists, psychiatrists), smoking cessation clinics, Quit Lines, community pharmacists, hospital pharmacists, nurses, advanced practice nurses, professional societies, national associations, patient advocacy groups.
Member States where the DHPC will be distributed	All EU member states except Bulgaria where the product is permanently discontinued, as notified to EMA on 28 April 2021

Timetable *Delete steps which are not applicable*	**Date**
DHPC and communication plan (in English) agreed by CHMP	6 July 2021
Submission of translated DHPCs to the national competent authorities for review	8 July 2021
Agreement of translations by national competent authorities	13 July 2021
Dissemination of DHPC	15 July 2021