Medicines & Healthcare products
Regulatory Agency

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Dear Professor Gøtzsche,

Re: False information in package inserts for antidepressants about a "chemical imbalance."

Thank you for your letter dated 20 January 2025 asking MHRA to check the package inserts for all antidepressants approved in the UK and to remove what you define as a misleading message about the cause of depression.

It is widely recognised that depression has a multifactorial aetiology. The wording 'chemical imbalance' is one of several terminologies used to explain to patients, in plain English, one of the several scientific paradigms which have been adopted in the psychiatry scientific literature to attempt to provide the basis, in part, for complex psychiatric conditions such as depression. We are aware of several recent publications proposing other aetiological mechanisms which may form the basis for depression and related conditions. The totality of evolving evidence remains under close review and forms part of the ongoing benefit and risk balance assessments for the selective serotonin reuptake inhibitor medicines.

All currently licensed antidepressants have an impact on serotonin and other monoamines and their transporters and shown efficacy in treating depression within clinical trials.

There are significant constraints within the patient information leaflets (PILs) to explain the basis for efficacy of medicinal products and it is not possible to describe all the possible mechanisms of effect for each individual antidepressant or the clinical trials data on which the positive benefit risk ratio was determined. The requirement for a PIL to undergo consultation with target patient groups (user testing) was enacted from 2005 with a three-year transition period. Therefore by 2008, all UK licensed medicines would be compliant with this requirement and so all leaflets have been tested by patients for clarity of message. The main purpose of the patient leaflet is to support a discussion between the healthcare

professional and patient about the risks and benefits of a medicine and the PIL is not intended to replace that discussion. Individual prescribers can describe the aetiology of an individual patient's depression in ways not described in product information. The patient leaflet must convey in lay language the contents of the Summary of Product Characteristics (SmPC) for healthcare professionals which in the case of several classes of antidepressant describes the impact of the medicine on serotonin and other monoamines.

Although there are currently no plans to remove the text referring to a chemical imbalance from the PILs for all antidepressants, we are currently reviewing how some of the risks are explained to patients and as part of that review improvements are likely to be made to the format and presentation of information within the PIL.

Yours sincerely,

Customer Experience Centre