EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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European Medicines Agency

Dear Mr. Destrebecq,

I thank you for your letter dated 8 November calling on the European Medicines Agency to adopt guidelines on the off-label use of medicines to support healthcare practitioners and to protect public health.

We fully agree that off-label use of medicines is an important concern for public health. As referred to in your letter, the European Medicines Agency is currently awaiting the results of a study initiated by the European Commission on the off-label use of medicines in the European Union. Based on these results, the European Commission and EMA will determine what specific actions may need to be taken regarding off-label use.

Off-label use *per se* is not regulated within the current EU legislation and is inherently linked to clinical practice and national policies. However, a number of important regulatory initiatives in the European Union have led to changes that reduced the need for off-label use of medicines in certain areas:

In the field of paediatrics, off-label use has been a concern for many years as many medicines authorised in Europe for adults were neither authorised nor adequately studied for use in children. The Paediatric Regulation which came into force in 2007 has prompted research of medicines in children in order to reduce off-label use in this population.

In the field of orphan diseases, the orphan drug legislation has successfully increased the development and authorisation of medicines in these areas of high medical need.

In addition, compassionate use programmes and the granting of 'conditional marketing authorisation' further allow faster access to medicines which can contribute to reducing the need for the off-label use of medicines.

Unfortunately, we cannot comment on the use of medicines off-label for purely economic reasons. However, we hope that the study by the European Commission will shed further light on this.

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Please also note that the European regulatory framework provides strong safeguards for off-label use. Since the implementation of the European pharmacovigilance legislation in 2012, the definition of adverse drug reactions has been broadened to include adverse reactions arising from off-label use. In practice this means that the European Medicines Agency now collects adverse reactions from medicines used off-label, and can evaluate these data and make recommendations to protect public health as necessary. In this respect, EMA fully supports the recommendation of the Declaration on Good Off-Label Use Practice that physicians and patients should report adverse events and outcomes linked to the use of the off-label product through established routes.

One of the key elements of the pharmacovigilance legislation has been the establishment of a dedicated committee responsible for assessing and monitoring the safety of medicines which is called the Pharmacovigilance Risk Assessment Committee (PRAC). Through the review of Periodic Safety Update Reports and other pharmacovigilance data, the PRAC routinely considers off-label use when monitoring the safety of a given medicine and takes specific measures when it identifies a safety concern. This could be, for example, in the form of a letter to healthcare professionals highlighting risks associated with a given off-label use or the reflection of a particular safety concern in the product information. As part of this process, adverse reactions due to off-label use are now captured and collected through the Agency's EudraVigilance database, which is used to continuously monitor and analyse the benefit-risk balance of medicines.

We would like to thank you again for your letter, interest and willingness to work with the agency in this important issue. We will involve relevant stakeholders in due time and once the Commission releases the results of their study.

I hope this letter reassures you of our commitment to continue to promote the safe and rational use of medicines in Europe.

Yours sincerely,

Guido Rasi
Executive Director