



Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life practice

To the Editor:

On behalf of Merck & Co., Inc., Kenilworth, NJ, USA (“MSD”), this letter is in response to the article by BENARD *et al.* [1].

We noticed that the abstract section of the referenced manuscript contains the following statement:

“Although montelukast is generally well tolerated, postmarketing studies have reported serious neuropsychiatric adverse drug reactions (ADRs) leading to a United States Food and Drug Administration black box warning.”

MSD, which manufactures Singulair® (montelukast sodium), would like the Editor to take note that this statement is incorrect. The US Product Information for Singulair does not contain a Black Box warning and, thus, it is inaccurate to state that the US Food and Drug Administration (FDA) required the inclusion of a Black Box warning related to serious neuropsychiatric drug adverse reactions. A link to the US Product Information for Singulair is provided for reference [2].

Please note that MSD updated the US Product Information for Singulair to contain safety information related to neuropsychiatric events in the Warnings and Precautions section (5.4 Neuropsychiatric Events) and Adverse Reactions section (6.2 Post-Marketing Experience).

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Conflict of interest: Disclosures can be found alongside this article at erj.ersjournals.com

References

- 1 Benard B, Bastien V, Vinet B, *et al.* Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life practice. *Eur Respir J* 2017; 50: 1700148.
- 2 Singulair® (montelukast sodium) Tablets, Chewable Tablets, and Oral Granules. www.merck.com/product/usa/pi_circulars/s/singulair/singulair_pi.pdf

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From the authors:

We thank Eduardo Urdaneta, from Merck & Co., Inc., for his correspondence regarding our paper [1] and appreciate the opportunity to reply to his concern.

In 2008, the US Food and Drug Administration (FDA) was investigating a possible association between the use of Singulair and behaviour/mood changes, suicidality (suicidal thinking and behaviour) and suicide. It issued a warning about an increased risk of psychiatric events associated with montelukast. This



warning was not a black box warning, however; and we respectfully request that these words be removed from the abstract [2].

In 2012, the label warning was maintained and worded as follows:

“Neuropsychiatric events have been reported with SINGULAIR. Instruct patients to be alert for neuropsychiatric events. Evaluate the risks and benefits of continuing treatment with SINGULAIR if such events occur.”

In 2014, the FDA analysed post-marketing cases in the paediatric population and maintained the warnings and precautions in the labelled safety issues for prescribers.

“Patients and prescribers should be alert for neuropsychiatric events. Patients should be instructed to notify their prescriber if these changes occur. Prescribers should carefully evaluate the risks and benefits of continuing treatment with montelukast sodium if such events occur.”

The latest 2016 label maintains this warning [3]:

“Neuropsychiatric events have been reported with SINGULAIR. Instruct patients to be alert for neuropsychiatric events. Evaluate the risks and benefits of continuing treatment with SINGULAIR if such events occur.”

Given the high rate of neuropsychiatric events we observed in our paediatric cohort study, we strongly encourage all physicians to pay attention to the current FDA warning for prescribers and patients to be alert for the possibility of neuropsychiatric events. In addition, it is our opinion that, before contemplating montelukast, physicians should consider, and discuss with patients and parents, the risk of neuropsychiatric events with montelukast.

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- 1 Benard B, Bastien V, Vinet B, *et al*. Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life practice. *Eur Respir J* 2017; 50: 1700148.
- 2 US Food and Drug Administration. Early Communication About an Ongoing Safety Review of Montelukast (Singulair). <https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/ucm070618.htm> Date last updated: April 18, 2013.
- 3 Singulair® (montelukast sodium) Tablets, Chewable Tablets, and Oral Granules. www.merck.com/product/usa/pi_circulars/s/singulair/singulair_pi.pdf

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