Montelukast – Safety update

- On March 4, 2020, the FDA announced that they are adding a *Boxed Warning* to the drug label for all brand and generic Singulair® (montelukast) products regarding serious behavior and mood-related changes.

- Montelukast should only be reserved to treat allergic rhinitis in patients who are not treated effectively with or cannot tolerate other allergy medicines.

- Montelukast prescribing information already includes warnings about mental health side effects, including suicidal thoughts or actions; however, many health care professionals and patients/caregivers are not aware of the risk.

- Montelukast is FDA-approved for asthma and allergies. It is a prescription medicine approved to prevent asthma attacks and for long-term treatment of asthma in adults and children ≥ 1 year of age. It is also approved to prevent exercise-induced asthma in patients ≥ 6 years of age. In addition, it is approved to help control the nasal symptoms of seasonal outdoor allergies in patients ≥ 2 years of age and year-round indoor allergies in those ≥ 6 months of age.

- Patients and parents/caregivers should stop montelukast and discuss with a healthcare professional right away if they experience behavior or mood-related changes while taking the medicine. These changes may include:

    — agitation, including aggressive behavior or hostility; attention problems; bad or vivid dreams; depression; disorientation/confusion; feeling anxious; hallucinations; irritability; memory problems; obsessive-compulsive symptoms; restlessness; sleepwalking; stuttering; suicidal thoughts and actions; tremor/shakiness; trouble sleeping; and uncontrolled muscle movements

- Patients should take montelukast for allergic rhinitis or hay fever only if other medicines cannot be tolerated or they do not work. Many other safe and effective allergy medicines are widely available, including over-the-counter medicines. Patients should discuss alternatives with a healthcare professional.

    — These include antihistamines such as loratadine (Alavert®, Claritin®), fexofenadine (Allegra®), cetirizine (Zyrtec®), levocetirizine (Xyzal®), and diphenhydramine (Benadryl®), as well as steroid nasal sprays such as fluticasone (Flonase®), triamcinolone (Nasacort®), and budesonide (Rhinocort®).
    — Alternatively, allergy immunotherapy has been shown to decrease symptoms of allergic rhinitis.

- Patients should discuss any history of mental illness with their healthcare provider before starting montelukast treatment.

- To lessen allergy symptoms, patients may take measures such as avoiding exposure to allergy triggers, keeping indoor air clean and taking allergy medicines.

- Healthcare professionals should consider the risks and benefits of montelukast when deciding to prescribe or continue patients on the medicine. Patients receiving montelukast should be counseled about mental health side effects, and advise them to stop the medicine and contact a healthcare professional immediately if they develop any symptoms as described above.

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  - In many cases, symptoms resolved after stopping montelukast; however, in some cases symptoms persisted after discontinuation from therapy or were reported after discontinuation of therapy.
  - Events have occurred in patients with and without pre-existing psychiatric disease.

- The safety update is based on case reports, an observational study using the FDA's Sentinel System, and reviewed observational and animal studies in the published literature. The FDA also reevaluated the benefits and risks of use of montelukast.

- The FDA continues to receive reports of mental health side effects reported with montelukast use. Consistent with the FDA's prior evaluations, a wide variety of mental health side effects have been reported, including completed suicides.

  - Some reports occurred during montelukast treatment and resolved after stopping the medicine. Other reports indicated that mental health side effects developed or continued after stopping montelukast.
  - The Sentinel study, which studied asthma patients ≥ 6 years of age, and other observational studies did not find an increased risk of mental health side effects with montelukast compared to inhaled corticosteroids. However, these studies had some limitations which may affect interpretation of results.
  - Animal studies showed that montelukast given orally reaches the brain in rats.

- Although this data is limited, the FDA decided to require a *Boxed Warning*. Due to the wide availability of alternative safe and effective allergy medicines with long histories of safety, the FDA has reevaluated the risks and benefits of montelukast and has determined it should not be the first choice treatment particularly when allergic rhinitis symptoms are mild.