Australian Paediatric Surveillance Unit

STUDY INFORMATION SHEET
Montelukast and Neuropsychiatric Events

COMMENCED
MAY 2020

BACKGROUND

Montelukast sodium has been available on the Australian Register of Therapeutic Goods since 1998 and listed on the Pharmaceutical Benefits Scheme since 2003. It is a selective leukotriene receptor antagonist and acts to prevent airway smooth muscle contraction and inflammation. Current indications in children include prophylaxis and treatment of chronic asthma in children >2 years of age, symptomatic treatment of allergic rhinitis and on streamlined authority for first line asthma preventer for children 2-14 years (as alternative to sodium cromoglycate or nedocromil sodium) and prevention of exercise induced asthma in children 6-14 years (also using optimal inhaled corticosteroid).

Neuropsychiatric events in adults and children treated with montelukast have been reported since 2000 and include depressed mood, suicidal ideation and attempts, aggressive behaviour and sleep and dream disturbance. The Therapeutic Goods Administration (TGA) Australia has received 313 reports for neuropsychiatric events since introduction of montelukast to end of August 2019, of which 204 were in children and adolescents 18 years or under. The most frequently reported events included aggression, anxiety, suicidal ideation, depression and nightmares. In 2017 an 18 year old died in Australia while taking montelukast, leading to increased community awareness and concern about its use. A systematic review of observational and pharmacovigilance studies found no statistically significant association in the four observational studies included but the pharmacovigilance studies did suggest a possible association. Further evidence from high quality epidemiological studies is required to determine risk. (Law et al)

In Australia product information for montelukast (PI) was updated by the TGA in response to international and local reports and currently contains detailed information about adverse events and precautions for prescribing. In addition, the TGA is undertaking ongoing review of montelukast and neuropsychiatric events in response to the recent reports and public concern and has requested the APSU conduct this 1 year study to inform this review.

STUDY OBJECTIVES

1. To estimate the frequency of neuropsychiatric events associated with montelukast in children managed by paediatricians
2. To describe the clinical presentation of these neuropsychiatric events
3. To describe the management and short term outcome of neuropsychiatric events

CASE DEFINITION

New onset of neuropsychiatric symptoms following prescription montelukast at any dose.

Symptoms may include:

- agitation
- anxiousness
- dream abnormalities/ nightmares
- tremor
- restlessness
- aggressive behaviour
- sleep disturbance
- irritability
- somnambulism
- suicidal ideation or behaviour
- depression
- disorientation

PRINCIPAL INVESTIGATOR

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FURTHER INFORMATION

For further information related to this study or assistance completing the Case Report Form, please contact the APSU by either:

- email: SCHN-APSU@health.nsw.gov.au or
- phone: (02) 9845 3005

SELECTED REFERENCES

- Product information for Montelukast: https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/PICMI?OpenForm&t=&q=montelukast
- Database of Adverse Event Notifications https://www.tga.gov.au/database-adverse-event-notifications-daen
- Law SWY, Wong AYS, Anand S, Wong ICK, Chan EW. Neuropsychiatric events associated with Leukotriene- Modifying Agents: as Systematic review. Drug Safety 2018;41(3):253-65.

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This study has been approved by a Human Research Ethics Committee properly constituted under NHMRC guidelines.