Ganaxolone: Adis Evaluation

Clinical Considerations

- A selective, high-affinity positive allosteric modulator of synaptic and extrasynaptic $GABA_A$ receptors
- Administered orally three times daily with food
- More effective than placebo (as an adjunct to existing antiseizure treatment) in reducing the frequency of major motor seizures; efficacy appears to be maintained during longer term treatment
- Generally well tolerated; somnolence is the most frequent adverse reaction

Plain Language Summary

Background and rationale

- Cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) is a rare, X-linked genetic disorder characterised by clinical features that include developmental delay and severe treatment-resistant epilepsy that begins soon after birth
- Treatment of CDD is symptom based; antiseizure medications suitable for the seizure types seen in CDD are widely used, but no one agent has been associated with seizure control and treatment becomes less effective over time
- Ganaxolone (ZTALMY®), an analog of the naturally occurring neuroactive steroid allopregnanolone (a potent anticonvulsant), has recently been developed and is the first approved treatment for seizures associated with CDD

Clinical findings

- In the phase 3 placebo-controlled Marigold trial in patients aged 2–19 years, ganaxolone was more effective than placebo (as an addition to existing antiseizure treatment) in reducing the frequency of seizures in patients with CDD
- The effectiveness of ganaxolone seems to be maintained during longer term treatment
- Ganaxolone was generally well tolerated in patients with CDD; the most common adverse reaction was somnolence

Conclusion

Oral ganaxolone is an effective and well-tolerated adjunct to existing treatment options for patients with CDD-associated seizures.