

Donepezil - Reports of Rhabdomyolysis

Donepezil* is a specific and reversible inhibitor of acetylcholinesterase which has been authorised in Ireland since 1997 for use for the symptomatic treatment of mild to moderately severe Alzheimer's dementia.

Reports of rhabdomyolysis associated with donepezil were recently reviewed by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC). Rhabdomyolysis is a clinical and biochemical syndrome that results from the breakdown of skeletal muscle and the release of intracellular contents into the circulatory system. Rhabdomyolysis can cause serious and sometimes fatal abnormal heart rhythms, kidney damage and kidney failure, but is generally treatable if recognised promptly.

The PRAC considered cases of rhabdomyolysis from post-marketing spontaneous reports and clinical trials. Whilst the individual cases do not provide strong evidence of a causal association between donepezil and rhabdomyolysis, based on the cumulative information from 11 cases in particular, a causal or contributory role for donepezil in these cases of rhabdomyolysis and other less serious muscle disorders including weakness and pain cannot be excluded.

Rhabdomyolysis has been reported to occur independently of Neuroleptic Malignant syndrome (NMS) and in close temporal association with donepezil initiation or dose increase.

Rhabdomyolysis can also be a feature of NMS, a potentially life-threatening condition characterised by hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated serum creatine phosphokinase levels. NMS has been reported to occur very rarely in association with donepezil, particularly in patients also receiving concomitant antipsychotics. Additional signs may include myoglobinuria (rhabdomyolysis) and acute renal failure. If a patient develops signs and symptoms indicative of NMS, or

presents with unexplained high fever without additional clinical manifestations of NMS, treatment should be discontinued.

Advice for Healthcare Professionals

- Rhabdomyolysis has been reported very rarely in patients treated with donepezil and has occurred independently of NMS and in close temporal association with donepezil initiation or dose increase.
- Patients and carers should be made aware of and advised to immediately report any signs or symptoms of rhabdomyolysis experienced (e.g. muscle weakness, tenderness or pain particularly, if at the same time, they feel unwell, have a high temperature or have dark urine.)
- The product information for donepezil (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)) will be updated accordingly shortly.

Key message

Rhabdomyolysis has been reported very rarely in patients treated with donepezil and has occurred independently of NMS and in close temporal association with donepezil initiation or dose increase.

Patients and carers should be alerted to signs and symptoms of these conditions and told to inform their doctor immediately if any experienced.

*Brands include Aricept, Donesyn, Dozept, Donecept. See www.hpra.ie for further details.

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