HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Quinine – Reminder of Safety Profile and Potential Drug-Drug Interactions Particularly Where Used for Nocturnal Leg Cramps

The European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) recently concluded a routine periodic review of medicinal products containing the active substance quinine.

In Ireland, medicinal products containing quinine are licensed as a sulphate salt for the treatment and prevention of nocturnal leg cramps in adults and the elderly (when cramps cause regular disruption of sleep). At higher doses, medicinal products containing quinine are also indicated for the treatment of malignant tertian malaria including chloroquine-resistant malaria.

Having examined the available evidence, the PRAC considered that while the risk-benefit balance of medicinal products containing quinine in both licensed indications remains unchanged, the product information for these medicines should be updated to advise caution in patients predisposed to QT-prolongation, and in patients with atrioventricular block.

Additionally, the EU review recommended that prescribers be reminded of appropriate use of quinine for the treatment and prevention of nocturnal leg cramps. As already described in the product information, patients should have an initial trial of 4 weeks. During this period, patients should be closely monitored for hypersensitivity reactions known to be associated with quinine (for example, thrombocytopenia). Quinine should be discontinued after 4 weeks if there is no benefit. Treatment should be interrupted every 3 months to re-assess continuing need.

Background to the Review

Quinine is an isomer of quinidine, a class 1a antiarrythmic which reduces the velocity of cardiac conduction. The product information already advises that quinine should be used with caution in patients with atrial fibrillation or other serious heart disease, and that in excessive doses the QT interval may be prolonged. However, two recent publications (Gjesing et al., 2015, Sheehan et al., 2016) suggest that patients with multiple risk factors for QT prolongation or atrioventricular block may also be at risk of cardiotoxicity even at therapeutic doses.

Also arising from this routine assessment of the active substance and based on pharmacokinetic data, a warning will be added to product information regarding the potential for quinine to increase levels of phenobarbital and of carbamazepine.

Advice to Healthcare Professionals

- Quinine should be used with caution in patients with conditions which predispose to QT-prolongation and in patients with atrioventricular block.
- Caution is advised when administering quinine with drugs which could prolong the QT-interval.
- As described in the product information, when used for the treatment and prevention of nocturnal leg cramps, quinine should be discontinued after the first 4 weeks if there is no benefit. Quinine should be interrupted every 3 months to re-assess continuing need.

Key Message

- Quinine should be used with caution in patients with conditions which predispose to QT-prolongation, in patients with atrioventricular block, or when quinine is co-administered with drugs which could prolong the QT interval.
- When used for nocturnal leg cramps, the need for continuing treatment should be re-assessed regularly.

Further details on quinine-containing medicinal products are available on www.hpra.ie.

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