ALLIANCE
Breathing life into medicines

27 April 2015

New restrictions for hydroxyzine-containing medicines to further minimize the known risk of QT prolongation

Dear Doctor,

This letter is sent in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) to inform you of strengthened warnings related to the safety of hydroxyzine by the two marketing authorisation holders for hydroxyzine, UCB Pharma Ltd and Alliance Pharmaceuticals.

Summary

Further restrictions are being introduced for hydroxyzine-containing medicines. These include:

- Hydroxyzine is contraindicated in patients with known acquired or congenital QT interval prolongation or with a known risk factor for QT prolongation
- In elderly patients hydroxyzine is not recommended
- In adults, the maximum daily dose should be 100 mg.
- In children up to 40 kg of body weight, the maximum daily dose should be 2mg/kg/day

Hydroxyzine should be used at the lowest effective dose, for the shortest possible treatment duration.

Further information on the safety concern and the recommendations

The risk of QT prolongation with hydroxyzine is already known and all the EU SmPCs contain a contraindication for patients with pre-existing prolonged QT interval and a warning for patients who have known risk factors. In most countries, the maximum daily dose in adults is currently 300 mg. In order to better characterise the known risk of QT prolongation with hydroxyzine and to define appropriate risk minimisation measures, UCB initiated further analysis of new *in vitro* study data and post-marketing experience with hydroxyzine. This led to subsequent review by the European Medicines Agency which included published studies and post-marketing data and consultation with experts in the treatment of children and the elderly. The previously known risk of QT prolongation and torsade de pointes was confirmed and risk factors were identified.

As a result of this analysis and review, new restrictions have been introduced with the aim of reducing exposure to the medicine, particularly in the most vulnerable groups.

ALLIANCE
Breathing life into medicines

In addition to the above mentioned restrictions the following information will be included in the product information:

- If hydroxyzine is prescribed to elderly patients, despite not being recommended in this age group, the maximum daily dose is 50 mg.
- Patients who are co-medicated with drugs inducing hypokalaemia and bradycardia should be treated with caution
- Examples of risk factors for QT interval prolongation are:
    - cardiovascular disease, family history of sudden cardiac death, significant electrolyte imbalance such as hypokalaemia or hypomagnesaemia, significant bradycardia, concomitant use with other drugs known to prolong QTc and/or induce Torsade de Pointes

Hydroxyzine is indicated in most European countries for a range of indications including pruritus and anxiety disorders.

Further information on the European procedure for hydroxyzine can be found on the European Medicines Agency's website at www.emea.europa.eu

Call for reporting

Reporting of suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed below.

https://yellowcard.mhra.gov.uk/

Company contact point

Dr Sarah Lawn
Local Safety Officer
UCB Pharma Ltd
208 Bath Road
Slough
Berkshire
SL1 3WE
01753 447853
sarah.lawn@ucb.com
ds.uk@ucb.com

Dr Lucy Cook
Medical Affairs Manager
Alliance Pharmaceuticals
Avonbridge House
Bath Road
Chippenham
SN15 2BB
01249 466966
medinfo@alliancepharma.co.uk
pharmacovigilance@alliancepharma.co.uk