Medicines and Healthcare Products Regulatory Agency

151 Buckingham Palace Road
Victoria
London SW1W 9SZ
United Kingdom

Emma Brown
Area Coroner
Birmingham and Solihull
50 Newton Street
Birmingham B4 6NE

7 December 2016

Dear Ms Brown

RE: RAYMOND CHARLES WOODWARD, DECEASED, date of death 19/02/16 (Ref: 113062)

Thank you for your report dated 26th August 2016 regarding the investigation and inquest into the death of Raymond Charles Woodward (Regulation 28 Report to Prevent Future Deaths).

The MHRA as a regulatory agency has a responsibility to ensure that medicines are efficacious and acceptably safe and that guidance on the use of a medicine, including warnings and precautions for prescribers and patients, is appropriately described in the authorised product information, the Summary of Product Characteristics (SmPC) and Patient Information Leaflet.

A post-mortem of Mr Woodward showed that he died from cardiorespiratory arrest due to coronary artery disease and a reaction to intravenous Buscopan Ampoules, which had been administered as part of a barium enema investigation. Buscopan Ampoules, administered intramuscularly or intravenously, are licensed to reduce bowel spasm in diagnostic procedures, such as barium enema. Your report highlights a concern that the risk of life-threatening adverse reactions to Buscopan Ampoules in patients with coronary heart disease is not adequately addressed in the SmPC. Specifically, you refer to the following warning in section 4.4 of the SmPC for Buscopan Ampoules:

"Buscopan Ampoules should be used with caution in conditions characterised by tachycardia such as thyrotoxicosis, cardiac insufficiency or failure and in cardiac surgery where it may further accelerate the heart rate."

You note that the term "cardiac insufficiency" does not relate to a specific diagnosis and does not necessarily encompass patients with coronary heart disease. In your report you state that the Deceased's Consultant Physician, [redacted] has suggested that this point can be addressed by including the following statement in section 4.4 of the SmPC for Buscopan Ampoules:

"Additional caution should be exercised in administering IV Buscopan to patients with ischaemic heart disease."

To determine what regulatory action, if any, is required with respect to Buscopan Ampoules we have analysed all the reported deaths in the UK that were suspected as being caused by Buscopan Ampoules and reviewed the current product information.

From our safety database we have identified eight reported fatal cases in the UK (including the death of Mr Woodward) where a causal relationship between Buscopan Ampoules and a fatal outcome is likely. In two of these eight fatal cases, there were pre-existing cardiac conditions. In three of the remaining six fatal cases medical history was not reported and in the other three cases there was no mention of cardiac disease in the medical history, although the cases were not well described.

Section 4.8 of the SmPC of Buscopan Ampoules lists several side effects which could be more serious in patients with coronary heart disease. These include tachycardia, blood pressure reduced and serious allergic reactions (anaphylaxis), which can cause a severe drop in blood (shock) and in more serious cases can result in cardio-respiratory arrest. Several publications have noted that anaphylaxis is more likely to be fatal in patients with underlying coronary heart disease.[1,2]

Given that the risk of serious cardiac side effects due to Buscopan Ampoules is more likely in patients with cardiac conditions, such as coronary heart disease, we agree that the product information should be updated to more clearly communicate and minimise this risk in these patients. We have therefore written to the Company who hold the licence for Buscopan Ampoules and requested that they update the product information accordingly. The Company has agreed to revise the warning in section 4.4 of the SmPC which you highlighted as not adequately describing the risk in patients with coronary heart disease. The warning will recommend caution when using Buscopan Ampoules in patients with cardiac disease, including coronary heart disease, because of the risk of tachycardia, hypotension and anaphylaxis. In addition, the revised warning will recommend monitoring of these patients and that emergency equipment and personnel trained in its use must be readily available. The wording will be finalised once the Company submits an application to vary the product information, but is expected to be in line with the following:

"Buscopan Ampoules can cause tachycardia, hypotension and anaphylaxis, therefore use with caution in patients with cardiac conditions, such as cardiac failure, coronary heart disease, cardiac arrhythmia or hypertension, and in cardiac surgery. Monitoring of these patients is advised. Emergency equipment and personnel trained in its use must be readily available."

At the time that the product information is updated we also propose to communicate these new recommendations through an article in our MHRA newsletter, Drug Safety Update, which will be circulated to relevant healthcare professionals.

I will write to you again once the product information has been updated and the DSU article is published.

Thank you for drawing our attention to this important issue.

Yours sincerely

Dr Ian Hudson,
Chief Executive Officer
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1. Mueller UR. Cardiovascular disease and anaphylaxis. Curr Opin Allergy Clin Immunol 2007;7:337-41.
2. Triggiani M, Patella V, Staiano RI, et al. Allergy and the cardiovascular system. Clin Exp Immunol 2008;153:7-11.