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Direct Healthcare Professional Communication

22nd November 2017

Communication on potential product defect with BUCCOLAM (midazolam) prefilled plastic syringes

Dear Healthcare Professional,

Shire Services BVBA, in agreement with the European Medicines Agency and the UK Medicines and Healthcare products Regulatory Agency (MHRA), would like to inform you of the following:

Summary

- **There have been reports of a product quality defect related to BUCCOLAM pre-filled plastic syringes.**
- **In a very small number of cases, the translucent tip-cap has remained on the syringe tip when pulling the red cap off.**
- **If the translucent tip cap remains on the syringe tip it will prevent administration of BUCCOLAM.**
- **If this occurs, the translucent tip cap needs to be removed manually.**
- **We ask that you share this information with your patients' parents and caregivers, and with age-appropriate patients, to ensure they are aware of this issue when handling the product.**

Background on the safety concern

Shire has received reports that, when removing the red cap off the syringe prior to use, the translucent tip-cap has, in a very small number of cases, remained on the syringe tip (see **Figure 2** below) instead of being removed with the red cap as it should (see **Figure 1** below). The presence of the inner translucent tip-cap on the syringe will prevent administration of the medication and will therefore need to be removed manually to prevent the inner translucent tip-cap falling into the patient's mouth upon application of extreme pressure. This has never been reported to date, but cannot theoretically be excluded.

Figure 1. Translucent syringe tip-cap correctly removed, i.e. embedded in the red cap (normal removal - correct)

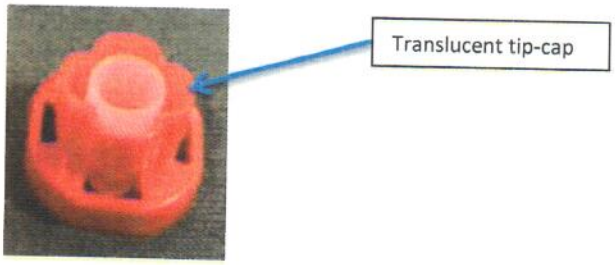

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Figure 2. Upon removing the red cap, the translucent tip-cap remains on the syringe (abnormal removal reported) *for illustrative purposes, not UK pack*

Shire is evaluating options to quickly resolve this issue. In the meanwhile, please help us counsel patients, caregivers, and other healthcare providers about this potential defect during medical consultations, dispensing of the product at the pharmacy, or any other setting in which you have interactions with patients or caregivers.

Further information

BUCCOLAM is approved in the European Union, Iceland, Norway and Liechtenstein for the following therapeutic indication:

- Treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from 3 months to < 18 years).

BUCCOLAM must only be used by parents/caregivers where the patient has been diagnosed to have epilepsy. For infants between 3-6 months of age treatment should be in a hospital setting where monitoring is possible and resuscitation equipment is available.

Detailed information on this product is available on the website of the European Medicines Agency: http://www.ema.europa.eu

Call for reporting

Please report any suspected adverse reactions to any medicine to the Medicines and Healthcare products Regulatory Agency (MHRA) through the Yellow Card Scheme. Please report:

- All suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.
- All suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

It is easiest and quickest to report ADRs online via the Yellow Cards website - www.yellowcard.mhra.gov.uk

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Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gov.uk
- at the back of the BNF, MIMS, ABPI Compendium or ordered by calling the Yellow Card Information Service freephone on 0800 731 6789
- or by downloading and printing a form the Yellow Card section of the MHRA website.

Any suspected adverse reactions observed during use of BUCCOLAM 2.5 mg , 5 mg , 7.5mg and 10 mg oromucosal solution may also be reported to Shire at +44 (0)1256 894000 or emailed to: drugsafety@shire.com

Company contact point

Should you have any questions or require additional information on the use of BUCCOLAM 2.5 mg , 5 mg, 7.5 mg and 10 mg oromucosal solution, please contact please contact Medical Information at Tel: 0800 055 6614 or by email at MedinfoEMEA@shire.com

Sincerely,

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Shire

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Shire