May 2017

Direct Healthcare Professional Communication

Discontinuation of Pharmalgen (Bee Venom and Wasp Venom) Initial kits and implementation of serial dilution protocol for up-dosing: risk of dosing errors

Dear healthcare professional,

ALK-Abelló Ltd (ALK), in agreement with the Medicines and Healthcare Products Regulatory Agency (MHRA), would like to inform you of the following:

Summary

- A changed dilution procedure for up-dosing of Pharmalgen Bee Venom and Wasp Venom will be introduced after discontinuation of the following strengths: 0.1 µg/ml, 1 µg/ml, and 10 µg/ml
- The remaining product presentation (100 µg/ml) can be diluted for the diagnostic and dosing instructions defined in the Summary of Product Characteristics (SPC)
- When initiating new patients, a serial dilution protocol will be needed locally to achieve the desired doses for the up-dosing schedule. The dilution procedure is described in the revised SmPC and patient information leaflet (PIL). We have also issued a dilution chart.
- Healthcare professionals should be aware that errors in the dilution process could lead to administration of a higher dose, which can put patients at a risk of developing a systemic allergic reaction (including anaphylactic shock)

Further information

ALK has discontinued production of Pharmalgen Bee and Wasp Venom Initial kits in the following concentrations: 0.1 µg/ml, 1 µg/ml and 10 µg/ml. Pharmalgen Bee and Wasp Venom in the highest concentration of 100 µg/ml will continue to be available.

All necessary doses lower than 100 µg/ml can be prepared through performing serial dilutions. By introducing several dilution steps, the risk of dilution errors increases. This could lead to the use of too-low or too-high concentrations during the up-dosing phase, particularly when the patient is undergoing up-dosing treatment.

In case of errors in the dilution process leading to administration of a higher dose than intended, a serious systemic allergic reaction (anaphylactic reaction or anaphylactic shock) could occur.

Serial dilutions have been used in other European countries using the 100 µg/ml vial for several years. No reports related to dilution errors of the reconstituted Pharmalgen product have been identified in ALK´s global safety database as of March 2017.

However, ALK acknowledges that there is a potential risk for dilution errors. To survey the situation, ALK, together with the MHRA, has initiated a post-authorisation safety study. This study will monitor the occurrence of medication errors and systemic allergic reactions related to the change in dilution procedure. We expect results of the study to be reported in about 2 years. You should report any dilution errors such as difficulty in understanding the dilution procedure, mistakes in doses, etc.

ALK has considered the consequences of discontinuing the lower-strength vials. To mitigate the concern of more dilution steps, and thereby the potential risk of causing additional medication errors, the following actions have been taken:

- The SmPCs and PILs for Pharmalgen have been updated to include information regarding the serial dilution procedure. The Pharmalgen Bee Venom and Pharmalgen Wasp Venom SmPCs can be found on the EMC website http://www.medicines.org.uk/emc/
- Educational material (Pharmalgen dilution chart) describing the dilution protocol will be provided to healthcare professionals who administer Pharmalgen
- All specialist allergy centres will be offered training by ALK´s Key Account Managers

Recommendations

- Read the revised SmPC, especially section 4.2 and 6.6, which are related to the up-dosing and the serial dilutions of Pharmalgen. Please share this information with all relevant healthcare professionals in your Trust
- Label all vials with allergen, concentration, date of dilution, and expiry date to avoid any confusion between the different diluted vials
- Be aware that the expiry date of the highest concentration (100 µg/ml) reconstituted product is 6 months (storage at +2°C to +8°C). For each subsequent dilution prepared (10 µg/ml, 1 µg/ml and 0.1µg/ml), the expiry date is a maximum of 24 hours after first dilution, and the solution should be discarded after use
- Use a brand new sterile syringe for each dilution stage

Call for reporting

Please continue to report suspected adverse reactions (ADRs) including dilution errors with Pharmalgen to the MHRA through the Yellow Card Scheme online at www.mhra.gov.uk/yellowcard

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

It is easiest and quickest to report ADRs online via the Yellow Cards website: www.mhra.gov.uk/yellowcard Alternatively, prepaid Yellow Card reporting is available:

- By writing to FREEPOST YELLOW CARD (no other address details are necessary)
- By emailing yellowcard@mhra.gsi.gov.uk
- At the back of the British National Formulary (BNF)
- By telephoning the Commission on Human Medicines (CHM) free phone line: 0800 731 6789
- Or by downloading and printing a form from the Yellow Card section of the MHRA website

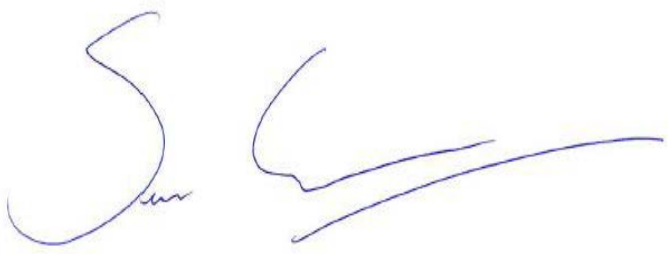
When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

Reports can also be made to the ALK´s Pharmacovigilance department at drugsafetyuk@alk.net or by calling 01189 037940.

Company contact point

If you have any questions about this letter or any enquiry, please contact ALK´s local Pharmacovigilance department at drugsafetyuk@alk.net or by calling 0118 903 7940. If you would like additional copies of the Pharmalgen dilution protocol chart, please contact ALK Customer Services on 0118 903 7940 or email info@uk.alk-abello.com

Yours faithfully,



Sean Connor
General Manager ALK-Abelló Ltd.