

## IN USE PRODUCT SAFETY ASSESSMENT REPORT FOR Dexamethasone injection

### SUMMARY OF ASSESSMENT AND ITS FINDINGS

#### BACKGROUND

There are two main issues with dexamethasone sodium phosphate injection:

1. Concerns continue to be raised about how the content and dose of dexamethasone are expressed in packaging and labelling as well as in standard resources such as the BNF. Incidents are still reported where confusion leads to dosage errors. Manufacturers use different approaches to describe dexamethasone content and dose.
2. Aspen has acquired the product licence for the Organon preparation and re-formulated the injection to harmonise the formulations of dexamethasone solution for injection available from the company within the EU Market. This has resulted in changes to concentration (from 4mg/mL to 3.8mg/mL), storage conditions and presentation (see table). With two other dexamethasone injections of lower concentration on the market and prescribers accustomed to prescribing 4mg (and multiples of) doses of dexamethasone, there may be a potential risk for administration of incorrect doses.

#### DETAILS OF PRODUCT (S) ASSESSED

	Organon	Aspen	Hameln	Hospira
Dexamethasone base (on packaging)	4.0mg/mL	3.8mg/mL	3.3mg/mL	3.3mg/mL
Volume equivalence of 4mg base	1ml	1.05ml (only 1ml will be available in each glass vial)	1.2ml (only 1ml will be available in each glass ampoule)	1.2ml (only 1ml will be available in each glass ampoule)
Dexamethasone sodium phosphate	5.25mg/mL	5.0mg/mL	4.3 mg/mL	4.3mg/mL
Dexamethasone phosphate	Not stated	Not stated	4.0mg/mL	4.0mg/mL
Propylene glycol content	None	None	20mg/mL	None
Storage	Store below 25°C	Store in a refrigerator (2-8°C)	Store below 25°C	Store below 25°C
Presentation	Glass ampoule	Glass vial	Glass ampoule	Glass ampoule

Table reproduced with thanks as per [CMU memo](#)

When dexamethasone is prescribed, doses are generally expressed in terms of dexamethasone base, therefore:

4mg dexamethasone base  $\equiv$  1.2mL of Hospira/Hameln preparations and 1.05mL of Aspen preparations

8mg dexamethasone base  $\equiv$  2.4mL of Hospira/Hameln preparations and 2.10mL of Aspen preparations

## CONCLUSION FOLLOWING APPLICATION OF VALIDATED ASSESSMENT TOOL

There are 4 key issues highlighted in this report:

**1. Dosage inconsistency** - the expression of dexamethasone doses varies, with different doses for similar or identical indications published in SPCs, in guidelines and in formularies. The dose of dexamethasone prescribed relates to dexamethasone base and familiarity with using the 4mg/mL strength in practice may risk the inadvertent administration of only 1mL (instead of 1.2mL) of the Hameln/Hospira brand, with the potential to under-dose patients by about 20%; for the Aspen product, administration of 1mL will result in a dose of 3.8mg, a 5% under-dose. This lack of clarity means that some patients may receive an incorrect dose, how critical this is depends on area of use since for many doses adjustment is made based on clinical response. However, protocols and guidance should be consistent in how the dose is reflected.

**2. Storage** - the Aspen product requires storage at 2-8 deg C whereas the other products (Hameln/ Hospira) are stored at standard room temperature. There is a potential for confusion and risk of products being stored at the wrong temperature at pharmacy and ward/clinic level.

**3. Labelling** - the labelling on the amps/vials is not consistent with the terminology used on packaging and in the product literature.

**4. Propylene glycol** - This is used as a solubiliser and is potentially toxic in some patients who are not able to adequately metabolise and eliminate this excipient. These patients are mainly infants and children below the age of 4 years, pregnant women, patients with hepatic or renal failure, and patients treated with disulfiram or metronidazole. According to a recent assessment by the CHMP, no recommendation on a safe dose for propylene glycol can be made based on the current available data; and correlations between exposure, patient characteristics and reported adverse events are not established. The amount of propylene glycol that a neonate is exposed to from the small dose of dexamethasone is probably not clinically significant. Specialists will need to assess this risk in these patients groups.

The inconsistencies in presentation are not new. The addition of another dexamethasone product with a different strength to the available choices further increases the potential for errors in prescribing/administration and storage to occur.

Many hospitals have already produced internal guidance for prescribers about the differing strengths of dexamethasone to minimise confusion. They will have to update this guidance now that a product with a different strength and storage conditions has entered the market.

## POTENTIAL NEXT STEPS AND MITIGATION ACTIONS

- 1. Local action** - Hospitals and CCGs need to ensure that all prescribers are aware of the differences between each product in terms of dose and storage and how this may affect their clinical practice. They need to have a process in place to ensure that all protocols and guidelines recommending use of 4mg dose are reviewed as well as correct storage in all settings.
- 2. National action** - national bodies such as NHS England, the MHRA and NICE/BNF could work towards ensuring standardisation in the way that dose and content of dexamethasone products are expressed by manufacturers and in guidelines.
- 3. UKMI** - to update Injectable Medicine Guide for dexamethasone injections.

Note: This is similar to the issue addressed by MHRA in 2013 where they advised that all caffeine products be named and prescribed consistently as caffeine citrate to avoid errors of dosing when prescribed as caffeine

(<http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON300399>)

This report was produced in September 2014 using photographic images (not physical products) of licensed dexamethasone sodium phosphate available at the time of assessment. Images were obtained primarily from pharmaceutical companies, but also from the Commercial Medicines' Unit PharmaQC database (<http://cmu.dh.gov.uk/medicines/pharmaqc-database/>) and from various sources within the NHS.

This report summarises individual product assessments undertaken by: South West Medicines Information and Training and East Anglia Medicines Information Service. Thanks to Northwick Park Medicines Information Centre and London and South East Medicines Information Centre for additional comments.

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