

# Impact of displacement values of powders

for solution for injection or infusion on drug doses administered to children

## Background

Paediatric patients receive drug dosages based on their body weights. With drug powders for solution for infusion often only part of a vial is required. Failing to take into account significant displacement (dp) values can result in under-dosing. A literature search found no recent studies regarding the size of under-dosing resulting from ignored dp values.

## Purpose

To investigate whether dp values of powders for reconstitution are taken into account in the hospital's guide for preparation and administration of i.v. drugs on the paediatric ward.

To categorize and calculate the percentage of the resulting under-dosing in drugs where the dp values were omitted.

## Materials and methods

- The guide was studied to see whether dp values were stated.
- The size of the deviation between the estimated concentration (where the dp value was addressed) and the specified concentration was calculated.
- Dp values were obtained through a literature search and through the marketing authorization holders.

## Results

- No dp values were directly stated in the guide.
- Dp values were taken into account in only 1 in 7 drug powders in the guide.
- The omitted dp values were all in antibiotics, and resulted in potential under-dosing ranging from 4-12%, see the table.

## Investigated drug powders for reconstitution and under-dosing as a result of omitted displacement values

Drug powder name		Selexid 1 gram	Pentrexyl 500 mg	Cefuroxim Villerton 250 g	Ceftriaxon Villerton 1000 mg	Benzylpenicillin Panpharma 600 mg	Cefuroxim Fresenius Kabi 750 mg	Piperacillin/ Tazobactam Fresenius Kabi 2 gram
i.v. drug guide <sup>1</sup> accounts for displacement value?		Yes	No	No	No	No	No	No
Concentration after reconstitution (mg/ml)	stated <sup>2</sup>	100	100	100	100	100	100	200
	estimated <sup>3</sup>	100	96,2	96,2	94,3	93,8	93,8	176
Displacement value (ml/gram)		0,6	0,4	0,4	0,6	0,67	0,67	0,67
<b>Resultant underdosing in %</b>		n.a.	3,9	3,9	5,7	6,3	6,3	12

<sup>1</sup> The preparation and administration guide for i.v. drugs at the paediatric ward C2, Hospitalsenheden Vest, Central Denmark Region.

<sup>2</sup> Concentration after reconstitution stated in drug guide.

<sup>3</sup> Concentration after reconstitution calculated addressing the displacement values, nominal drug doses and added volume of solvent.

## Discussion

The omitted dp values could originate in their omission from SPCs and/or PILs. An article<sup>1</sup> states that only 20 in 56 datasheets on drug powders for reconstitution account for dp values. The PILs/SPCs of the investigated drugs were not studied for information on dp values.

The estimated concentrations in the table do not include any possible overfilling of powder. Therefore the calculated 12% under-dosing probably is an overestimation. Despite this, it's an example of the significant impact an omitted dp value can have on the accuracy of the dispensed dosage, especially when a high weight of drug powder that possesses a high dp value is reconstituted in a low volume of solvent.

A way to avoid inaccurate calculations of reconstituted drug concentrations is by knowing the volume of solvent that takes account of both any possible drug powder surplus and dp value.

## Conclusion

The dp values were generally not taken into account, in the hospital's guide for preparation and administration of i.v. drugs on the paediatric ward.

Ignored dp values have been estimated to result in under-dosing ranging from 4-12 %.

Care should be taken when dispensing includes withdrawal of a fraction from a reconstituted drug:

Assure that the solvent volume takes dp value and drug powder surplus into account.

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+ 10ml



= ?ml

1. Displacement values of powder injections. The Pharmaceutical Journal of Great Britain 1993;251:14