Position Statement 2023-02
Enteral Calcium, Phosphate and Potassium Supplementation in Neonates and Children

Take Home Summary

- Neonates and children receive enteral calcium, phosphate or potassium supplements for a range of indications.
- There are no licensed oral liquid calcium or phosphate products available in the UK. There is a single licensed 1mmol/mL oral potassium solution, but there is no licensed alternative if this is not available.
- NPPG would welcome development of the following as licensed oral calcium and phosphate liquid products:
  - A solution providing 1mmol/mL of elemental calcium.
  - A solution providing 1mmol/mL of phosphate.
- Administration of a portion of a licensed effervescent calcium, phosphate or potassium tablet is common, and this off-label practice is challenging and prone to error.
- The visual appearance of effervescent tablets and their packaging can be similar, particularly in the case of Sando K® and Phosphate Sandoz®. This not infrequently leads to dispensing or administration errors, and extra vigilance is required, especially in patients using multiple effervescent tablet products.
- Where effervescent tablets are dissolved in water and an aliquot used to give the required dose:
  - Follow the recommendations in Tables 1, 2 and 3.
  - There will be some dosing inaccuracy and variability which cannot be eliminated or easily quantified. Close monitoring of patient response and appropriate dose adjustment is necessary.
  - Doses should be rounded to enable measurement. A suggested approach is provided in Table 4.
  - Any liquid remaining after giving a dose should be discarded; a new tablet should be used for each dose.
- When dispensing effervescent tablet products and only a portion is needed to administer the required dose, Hospital and Community Pharmacy staff should ensure that:
  - Clear instructions are provided on the dispensing label, supported wherever possible by direct education of patients/carers.
  - Appropriate equipment is provided. This can be flexible and tailored to patient/carer needs and local practice, but the following is suggested:
    1. A 20mL oral/enteral syringe to measure the initial volume of water required to disperse the tablet.
    2. A reusable, plastic medicine pot in which the tablet can be dispersed in water.
    3. A smaller oral/enteral syringe for measurement and administration of the required dose. For dose volumes of less than 1mL, a 1mL syringe is required.
- Effervescent tablets often contain significant amounts of sodium as an excipient. This should be considered when selecting the most appropriate product for an individual patient or cohort of patients.
- Unlicensed phosphate oral solutions are available in the United Kingdom and may allow for safer supplementation in some patient groups, particularly in the neonatal setting. The risks presented by using an unlicensed product in preference to off-label use of a licensed product should be considered when determining the right approach for an individual patient or a cohort of patients.

Additional Resources

Additional resources are available to support the implementation of recommendations above:

- Specialist Pharmacy Service – Medication safety - Managing the risks of using effervescent tablets in children.
- Medicines for Children. Information for parents and carers: How to give calcium, phosphate or potassium from effervescent tablets – Medicines For Children .

Table 1: Calcium Supplementation

Product	Manufacturer	Calcium Content per Tablet	Instructions for the Administration of "Part Tablet Doses"	Additional Information[1,2,3]
Calcium 500mg Effervescent Tablets	Accord-UK Ltd (SmPC)	12.5mmol	1. Dissolve each 12.5mmol tablet in 12mL water *(each tablet displaces approximately 0.5mL of water and so the final concentration obtained will be approximately 1mmol/ mL)*. 2. Once the tablet has fully dispersed and fizzing has stopped, which is usually after about 5 minutes, use the necessary volume of 1mmol/mL solution to administer the required dose. 3. Discard the remaining solution.	Equivalent product formerly marketed as Cacit® 500mg Effervescent Tablets. Each tablet also contains 0.87mmol of sodium, meaning that for each mmol of calcium administered the patient will also receive 0.07mmol of sodium. Also contains sunset yellow (E110) as an excipient.
Calvive® 1000 Effervescent Tablets	GlaxoSmithKline Consumer Healthcare (SmPC)	25mmol	1. Dissolve each 25mmol tablet in 20mL water *(each tablet displaces approximately 5mL of water and so the final concentration obtained will be approximately 1mmol/mL)*. 2. Once the tablet has fully dispersed and fizzing has stopped, which is usually after about 5 minutes, use the necessary volume of 1mmol/mL solution to administer the required dose. 3. Discard the remaining solution.	Equivalent product formerly marketed as Sandocal 1000® Tablets. Each tablet also contains 5.95mmol of sodium, meaning that for each mmol of calcium administered the patient will also receive 0.24mmol of sodium.
Effervescent Calcium Gluconate Tablets BP 1g	Accord-UK Ltd (SmPC)	2.23mmol	1. Dissolve each 2.23mmol tablet in 20mL water *(each tablet displaces approximately 0.5mL of water and so the final concentration obtained will be approximately 0.1mmol/mL)*. 2. Once the tablet has fully dispersed and fizzing has stopped, which is usually after about 5 minutes, use the necessary volume of 0.1mmol/ mL solution to administer the required dose. 3. Discard the remaining solution.	Each tablet also contains 4.5mmol of sodium, meaning that for each mmol of calcium administered the patient will also receive 2mmol of sodium. *Calculations based on rounded value of 2.2mmol calcium per tablet for ease of measurement)*.

Table 2: Phosphate Supplementation

Product	Manufacturer	Phosphate Content per Tablet	Instructions for the Administration of "Part Tablet Doses"	Additional Information[4]
Phosphate Sandoz® ***Note: risk of confusion with Sando K®***	Alturix Limited (SmPC)	16.1mmol	1. Dissolve each 16mmol tablet in 15mL water *(each tablet displaces approximately 1mL of water and so the final concentration obtained will be approximately 1mmol in 1mL)*. 2. Once the tablet has fully dispersed and fizzing has stopped, which is usually after about 5 minutes, use the necessary volume of 1mmol/mL solution to administer the required dose. 3. Discard the remaining solution.	Each tablet also contains 20.4mmol of sodium and 3mmol of potassium, meaning that for each mmol of phosphate administered the patient will also receive 1.27mmol of sodium and 0.19mmol of potassium. *(Calculation based on rounded value of 16mmol phosphate per tablet for ease of measurement)*.

Table 3: Potassium Supplementation

Product	Manufacturer	Potassium Content per Tablet	Instructions for the Administration of "Part Tablet Doses"	Additional Information[5]
Sando K® ***Note: risk of confusion with Phosphate Sandoz®***	Alturix Limited (SmPC)	12mmol	1. Dissolve each 12mmol tablet in 11mL water *(each tablet displaces approximately 1mL of water and so the final concentration obtained will be approximately 1mmol in 1mL).* 2. Once the tablet has fully dispersed and fizzing has stopped, which is usually after about 5 minutes, use the necessary volume of 1mmol/mL solution to administer the required dose. 3. Discard the remaining solution.	

Supporting Information

Enteral supplementation of calcium, phosphate and potassium is common in paediatric and neonatal practice. In some cases, supplementation is short-term to treat acute deficiency, whereas in other scenarios such as Osteopenia of Prematurity or Fanconi syndrome treatment may be long term.

There are no licensed oral liquid calcium or phosphate products available in the UK, which is not ideal, especially when treating neonates and infants requiring small doses. Instead, caregivers must administer the required dose using a portion of an effervescent tablet. This practice is off-label and error prone, but is unavoidable given the lack of licensed products. In the case of calcium, the risks are further exacerbated by the fact that the available effervescent tablet preparations all contain differing amounts of calcium, variably expressed in terms of mass units (e.g. g, mg) or mmol, and/or in terms of calcium salt or elemental calcium. There is a licensed 1mmol/mL potassium chloride oral solution, Kay-cee-L, available and this should be used in preference to using a portion of an effervescent potassium tablet when available and clinically suitable.

Dosing Accuracy when Administering a Dose by Taking a Portion of a Dissolved Effervescent Tablet

Effervescent tablets can displace significant volumes of water on dissolution, creating complexity when only part of the final solution is used to administer a dose. Displacement values are not published in the relevant Summaries of Product Characteristics (SmPCs)[1-5], and direct communication with the respective manufacturers revealed that they do not hold this information on file[6-10]. Water is displaced both by tablet components directly and by gas generated during the effervescence process, and so the extent of displacement is likely to be dynamic as much of the dissolved gas will eventually come out of solution and disperse into the surrounding air.

Failure to consider displacement will lead to dosing inaccuracy. However, uncertainty around the extent of displacement means that making definitive recommendations is difficult. The instructions provided in Tables 1-3 take displacement into account based on pragmatic experience in paediatric centres in the UK. Whilst there will be some variation in final volumes obtained when following these recommendations, any resultant dose inaccuracy is unlikely to be clinically significant; using a consistent method of preparation will minimise variation. Nonetheless, close monitoring of patient response and appropriate dose adjustment is required.

An alternative approach of dispersing the tablet in a small amount of water and then further diluting to a final volume after effervescence is complete may result in a higher degree of accuracy. However, this two-step process is likely to be more error prone overall and/or prove impractical for busy caregivers.

It is recognised that the suggested dilution information in Tables 1-3 may result in dose volumes which may be excessive for some patients, especially if larger doses are being given. If it is necessary to deviate from the standard dilutions, the displacement values provided should still be used to enable accurate dosing.

Prescribers can round calculated doses of calcium, phosphate and potassium supplements, to aid accurate and easy administration. A suggested approach when using a 1mmol in 1mL solution is given in Table 4.

Table 4: Suggested Dose Rounding

Calculated Dose	Round to the Nearest
0.2-0.49mmol	0.02mmol
0.5-1.9mmol	0.1mmol
2 - 4.9mmol	0.2mmol
5 - 9.9mmol	0.5mmol
More than 10mmol	1mmol

In some cases, giving the same daily dose in fewer instalments may be appropriate if this aids accurate dose measurement.

Excipient Challenges with Effervescent Tablets

The sodium content of some calcium and phosphate effervescent tablets is significant and should be taken into account when selecting the most appropriate product for an individual patient or cohort of patients.

There are anecdotal reports of alkalosis when effervescent calcium tablets have been used in neonates. This is likely to be due to incomplete consumption of carbonate if the effervescence process has not been allowed to run its full course. Use of an alternative formulation may be justified if the problem persists.

Equipment Required to Administer Doses which are a Portion of an Effervescent Tablet

A combination of equipment is required to accurately measure and administer doses which are a portion of an effervescent tablet; this should be issued at the point of dispensing. The equipment provided can be flexible according to patient/carer needs, but the following is suggested:

- A 20mL syringe oral/enteral syringe to measure the initial volume of water required to dissolve the tablet. The volumes of water for tablet dissolution specified in Tables 1 and 2 have been rounded to allow use of a 20mL syringe.
- An open container such as a reusable plastic medicine pot for dissolution of the tablet.
- A second, oral/enteral syringe to draw up and administer the required dose. This syringe should be of appropriate size and have appropriate graduations to measure the required dose:
  - Where the dose volume is less than 1mL, a 1mL syringe should be used to minimise dosing inaccuracy. Use of larger syringes to measure these small volumes results in a greater degree of inaccuracy and variability, even if the required volume corresponds with the available graduations[11].
  - For dose volumes of 1mL or greater, it is not possible to make specific recommendations as the graduations on oral/enteral syringes are not standardised. The most appropriate device should be selected by the dispensing pharmacist.

Oral Liquid Alternatives

NPPG would welcome the development of licensed oral calcium and phosphate solutions. The ideal products would provide 1mmol/mL of elemental calcium or phosphate, as this would allow accurate dosing for both neonates and children. It is recognised that that these concentrations may be challenging to formulate.

References:

1. Summary of Product Characteristics – Calcium 500mg Effervescent Tablets. Accord-UK Ltd. Accessed on 17/07/24 [date of revision of text 09/06/2023].
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3. Product Characteristics – Calvive 1000 Effervescent Tablets (formerly Sandocal Tablets). GlaxoSmithKline Consumer Healthcare. Accessed via on 17/07/2024 [date of revision of text 08/12/2023].
4. Summary of Product Characteristics – Phosphate Sandoz. Alturix Limited. Accessed on 17/07/2024 [date of revision of text 09/11/2023].
5. Summary of Product Characteristics – Sando K. Alturix Limited. Accessed on 17/07/2024 [date of revision of text 22/05/2024].
6. Personal communication from Medical Information. Accord-UK Ltd. 02/08/2022.
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8. Personal communication from Medical Information. GlaxoSmithKline Consumer Healthcare. 09/08/2022.
9. Personal communication from Medical Information. Alturix Limited. 05/08/2022.
10. Personal communication from Medical Information. Alturix Limited. 24/07/2024.
11. Arenas-López S, Gurung K et al. Accuracy of enteral syringes with commonly prescribed paediatric liquid medicines. Arch Dis Child. 2017;102:655–659.

Disclaimer

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Key changes from Version 1 (published March 2023): • Addition of Sando K®.	
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