

Assessing the Safety of Manufacturer Provided Measuring Devices for Oral Dosing in a Paediatric Setting.

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Background

At a recent conference, two paediatric emergency departments each discussed a 10-fold overdose involving Levetiracetam (Keppra™) oral liquid. Both of these overdoses occurred in the outpatient setting, following administration of the oral liquid by the parents to their child in the home. In both cases the oral liquid was supplied to the family by a community pharmacist. These two cases highlighted the poor suitability of the Keppra™ oral syringe in measuring doses less than 1mL and prompted a review of all oral syringes supplied by the Pharmacy Department at Princess Margaret Hospital (PMH).

Aim

To assess the safety of manufacturer supplied oral dosing devices in the outpatient setting.

Methods

Given the lack of legislative guidance provided by the TGA, or state-wide policy covering the manufacture and supply of oral measuring devices, investigators were led to consider the qualities of a safe and effective oral measuring device for use.

An online search found non-binding recommendations published by the FDA in 2011, which were later adapted in to a policy statement published by the American Journal of Paediatrics. Using some of these published recommendations, together with the experience of the investigators, a set of criteria were formulated to allow assessment and ranking of measuring devices according to their relative safety;

Assessment Criteria:

1. Do the graduations on the device appear in mL?
2. Do the graduations on the device appear in suitable increments of 0.1 or 0.2mL?
3. Do the increments on the device originate at zero volume?
4. Do the graduations originate at the tip end of the syringe or dropper and base of the cup or spoon?
5. Are the graduations easily readable?
6. Does the device allow for the medication to be clearly seen when measured?

7. Does the device hold the maximum dose?
8. Do the graduations appear in an appropriate direction for measurement to be taken? Bottles without bungs; graduations should read left to right. Bottles with bungs; graduations should read right to left. For the purposes of this assessment bungs supplied by the manufacturer are assumed to be used.
9. Does the device specify for oral/enteral use only?
10. Do the graduations include trailing zeros?
11. For 1mL devices, do graduations less than 1mL include a leading zero? A trailing zero is acceptable at the 1mL graduation only.
12. Is the device a syringe?

128 liquid oral medications on the PMH formulary were reviewed, and of these, 48 were supplied with a measuring device and included in the assessment. Measuring devices were graded against the criteria and were awarded 1 point if they satisfied the criterion. The enteral syringes used by the hospital were also included in the assessment, these being Nutrisafe 2™ syringes. The medicines assessed included unscheduled, S2, S3 and S4 medications. The measuring devices in this review include syringes, cups, spoons and droppers.



Drug	Brand	1	2	3	4	5	6	7	8	9	10	11	12	Total Criteria	Total Criteria Met	Percentage
Nutrisafe2 Syringes		1	1	1	1	1	1	1	0	1	1	1	1	12	11	92%
Ciclosporin	Neoral	1	1	1	1	1	1	1	1	0	1	1	1	12	11	92%
Oseltamivir	Tamiflu	1	1	1	1	1	1	1	0	1	1	1	1	11	10	91%
Efavirenz	Stocrin	1	1	1	1	1	1	0	1	1	1	1	1	11	10	91%
Fluconazole	Diflucan	1	1	1	1	1	1	0	1	1	1	1	1	11	10	91%
Abacavir	Ziagen	1	1	1	1	1	1	0	1	1	1	0	1	11	9	82%
Lamivudine	3TC	1	1	1	1	1	1	0	1	1	1	0	1	11	9	82%
Lopinavir/Ritonavir	Kaletra	1	1	1	1	1	1	0	1	0	1	1	1	11	9	82%
Mycophenolate	Cellcept	1	1	1	1	1	1	0	1	0	1	1	1	11	9	82%
Oxcarbazepine	Trileptal	1	0	1	1	1	1	0	1	1	1	1	1	11	9	82%
Zidovudine	Retrovir	1	1	1	1	1	1	0	1	1	1	0	1	11	9	82%
Sirolimus	Rapamune	1	1	1	1	1	0	0	1	0	1	1	1	12	9	75%
Azithromycin	Zithromax	1	0	1	1	1	0	1	1	0	1	1	1	11	8	73%
Nystatin	Omegapharm	1	1	1	0	1	0	1	1	0	1	1	1	11	8	73%
Multivitamin	Pentavit	1	1	1	0	1	0	1	1	0	1	1	1	11	8	73%
Poloxamer	Coloxyl	1	1	1	0	1	0	1	1	0	1	1	1	11	8	73%
Simethicone	Infacol	1	1	1	0	1	0	1	1	0	1	1	1	11	8	73%
Rufinamide	Inovelon	1	0	1	1	1	1	0	1	0	1	1	1	11	8	73%
Valganciclovir	Valcyte	0	0	1	1	1	1	0	1	1	1	1	1	11	8	73%
Digoxin	Lanoxin	1	1	1	0	1	0	0	1	0	1	1	1	12	8	67%
Risperidone	Risperdal	1	1	1	0	1	0	0	1	0	1	1	1	12	8	67%
Clarithromycin	Klacid	1	0	1	1	1	0	0	1	0	1	1	1	11	7	64%
Fusidic acid	Fucidin	1	0	0	1	0	1	1	1	1	1	1	1	11	7	64%
Melatonin	Neomel	0	1	0	1	1	1	0	1	0	1	1	1	11	7	64%
Colecalciferol	Biological	0	1	0	1	1	0	1	1	0	1	1	0	12	7	58%
Tocofersolan	Vedrop	1	0	0	0	1	1	0	1	0	1	1	1	12	7	58%
Ibuprofen	ApoHealth	1	1	0	1	1	1	0	0	0	0	1	1	12	7	58%
Cetirizine	Little Allergies	1	0	1	0	1	0	0	1	0	1	1	1	11	6	55%
Nitazoxanide	Nizonide	1	0	0	1	0	1	1	1	0	1	1	1	11	6	55%
Paracetamol/Codeine	Painstop	1	0	0	1	0	1	1	1	0	1	1	1	11	6	55%
Posaconazole	Noxafil	1	0	0	1	0	1	1	1	0	1	1	1	11	6	55%
Voriconazole	Vfend	0	0	1	1	1	1	0	1	0	0	1	1	11	6	55%
Cefuroxime	Zinnat	1	0	0	1	0	1	0	1	0	1	1	1	11	5	45%
Cetirizine	Zyrtec	1	0	0	1	0	1	0	1	0	1	1	1	11	5	45%
Diazoxide	Proglycem	0	1	0	1	1	0	0	1	0	1	1	1	11	5	45%
Linezolid	Zyvox	1	0	0	1	0	1	0	1	0	1	1	1	11	5	45%
Mebendazole	Vermox	1	0	0	1	0	0	1	1	0	1	1	1	11	5	45%
Sulfamethoxazole/Trimethoprim	Bactrim	0	0	0	1	0	1	1	1	0	1	1	1	11	5	45%
D-Alpha tocopherol	Micel E	0	0	0	1	1	0	0	1	0	1	1	0	12	5	42%
D-Alpha tocopherol and Retinyl Palmitate	Biological	0	0	0	1	1	0	0	1	0	1	1	0	12	5	42%
Captopril	Capoten	1	0	0	1	1	0	0	1	0	1	0	0	12	5	42%
Amoxicillin	Sandoz	1	0	0	1	0	0	0	1	0	1	1	1	11	4	36%
Amoxicillin/Clavulanate	Curam	1	0	0	1	0	0	0	1	0	1	1	1	11	4	36%
Cefalexin	Sandoz	1	0	0	1	0	0	0	1	0	1	1	1	11	4	36%
Ranitidine	Zantac	1	0	0	1	0	0	0	1	0	1	1	1	11	4	36%
Ursodeoxycholic acid	Ursotalk	1	0	0	1	0	0	0	1	0	1	1	1	11	4	36%
Aripiprazole	Abilify	0	0	0	1	1	0	0	1	0	0	1	0	12	4	33%
Itraconazole	Sporanox	1	0	0	1	0	0	0	1	0	0	1	0	11	3	27%
Levetiracetam	AFT	0	0	0	0	1	0	0	1	0	0	1	1	11	3	27%

Results

- Of the 49 measuring devices assessed 5 devices scored 90% or above.
- The highest ranking devices came from Nutrisafe 2 syringes, Ciclosporin, Oseltamivir, Efavirenz and Fluconazole.
- The lowest ranking devices belong to the following medications, Cefalexin, Ranitidine, Ursodeoxycholic acid, Itraconazole, Levetiracetam. Scoring below 36% overall.
- The lowest ranking devices included measuring spoons, cups and syringes
- 20 of the 49 devices assessed scored below 50%

Attributes of a safe measuring device:

- Graduations are displayed only in mL and in the correct format,
- The graduations on the device are displayed in suitable increments for intended use.
- The increments on all devices begin at zero volume and originate at the tip end of the syringe.
- The graduations are easily readable; the device is transparent allowing the medication to be easily seen including possible air bubbles.
- None of the graduations contain trailing zeros and the devices used for the purpose of measuring doses under 1mL have graduations containing leading zeros.
- All the devices in the top 5 are syringes, the preferred measuring device for oral dosing.



Discussion and Conclusion

There are several factors which could have prevented the 10-fold overdoses described above:

- Improved education and awareness of the pharmacist and family regarding the appropriateness of the syringe supplied with the Keppra™ Oral Liquid.
- The suitability of the syringe supplied by the manufacturer in measuring doses less than 1mL.

While the legislative policy for manufacturers concerning the safety and suitability of oral measuring devices remains unclear, pharmacists have an important role in ensuring that patients and families are properly counselled on how to measure prescribed doses from commercially prepared oral liquid formulations.

Following this review, the outpatient pharmacy at PMH substitutes the measuring devices supplied by the manufacturer with an appropriately sized Nutrisafe2™. The outpatient pharmacy does not substitute the syringes provided with Ciclosporin, Sirolimus and Azithromycin since these are considered safe and fit for use.

References

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