



Salt or base? Clear labeling of the reference value to prevent dosing errors: A case study



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Background

The availability of medicinal products containing identical active substances but expressed in different reference values (active base versus salt form) entails a substantial risk of errors in dose calculation and in the compounding of individualised preparations.¹ For example, confusion between caffeine and caffeine citrate results in a twofold dosing error.² Awareness of this issue varies among those involved in the medication process, and dosing information in the literature is frequently unclear.

Aim and Objectives

To prevent dosing errors associated with medicinal products expressed in different reference values, relevant monographs in Kinderformularium.DE, a German web-based database for evidence-based dosing information during childhood, were identified and supplemented with explicit information regarding the respective reference value.

Materials and Methods

An interprofessional expert panel of pharmacists and paediatricians from university children's hospitals, as well as members of the Paediatrics Committee of the Federal Association of German Hospital Pharmacists (ADKA e.V.) discussed the issue of differing reference values in round-table meetings. The panel developed a standardized process to ensure the unambiguous designation of reference values in Kinderformularium.DE and revised monographs of active substances present in salt form as described in Figure 1.

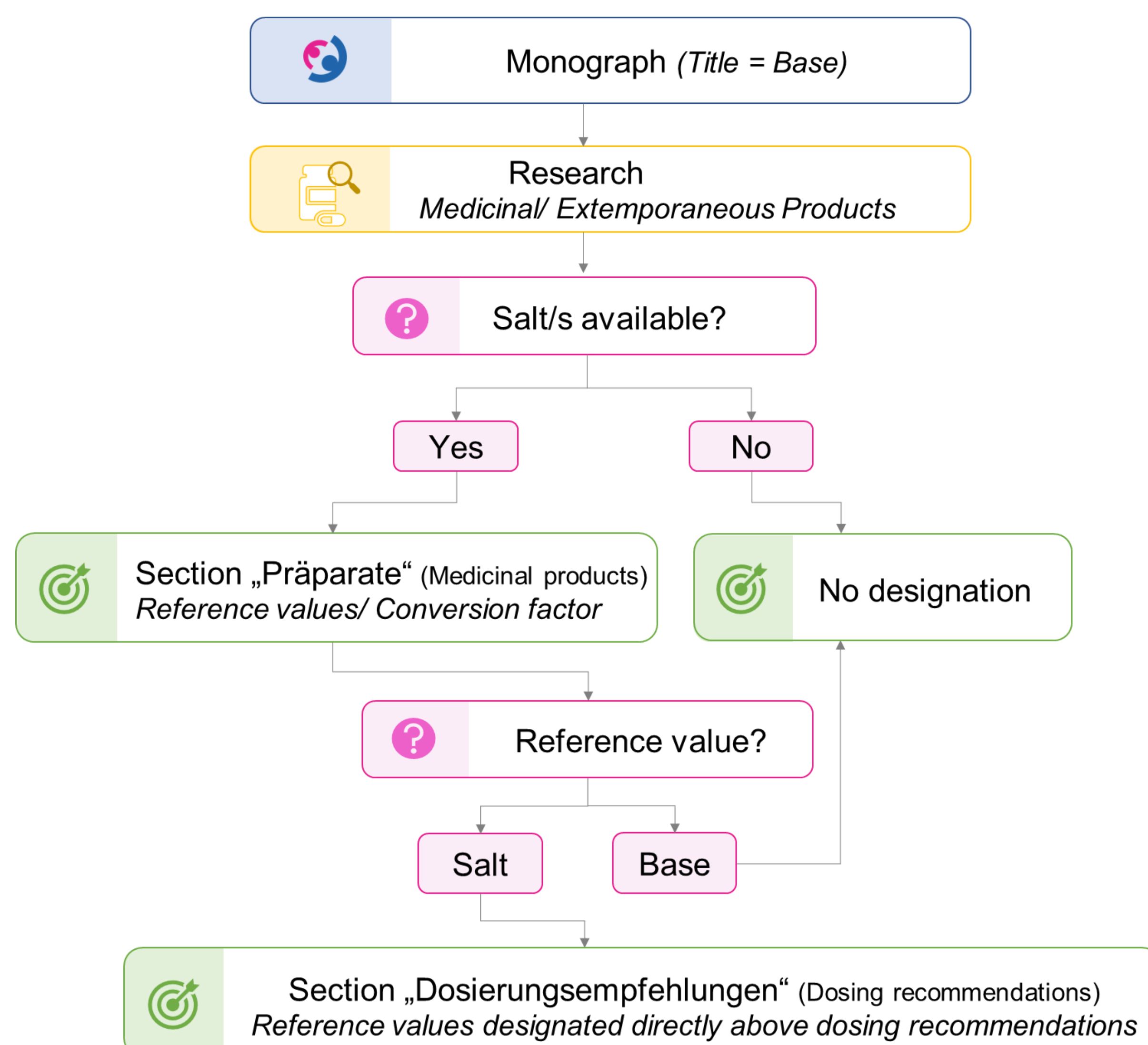


Figure 1: Process of designating reference value in Kinderformularium.DE

Using scientific evidence and clinical experience, the panel defined criteria for selecting relevant monographs in Kinderformularium.DE for which a specific designation by means of a note box is appropriate. These criteria include, among others, the availability of different salt forms of an active substance and a narrow therapeutic range, both of which increase the risk of (potentially serious) dosing errors.

References

- Daniel L, Prohotsky D. A survey of top 200 drugs—inconsistent practice of drug strength expression for drugs containing salt forms. *J Pharm Sci.* 2012;101(1):1-6.
- Chiesi GmbH. SmPC Peyona 20 mg/mL Infusionslösung und Lösung zum Einnehmen (EU/1/09/528/002). Oktober 2020.
- Universitätsklinikum Erlangen, Kinder- und Jugendklinik. *Kinderformularium.DE: Coffein*. Last access: 16. April 2025. Access via: <https://kinderformularium.de/>
- Donnelly M, Zhang X, Jean-François M, et al. Narrow therapeutic index drugs: FDA experience, views, and operations. *Clin Pharmacol Ther.* 2025;117(1):116-129.

Results

As of April 2025, 183 of the 672 monographs (27.2%) in Kinderformularium.DE were identified for which specification of the reference value is relevant, and the „Präparate“ (Medicinal products) section was revised accordingly. In 86 monographs (12.8%), an additional specification of the reference value at the dosage level was implemented (e.g., propranolol, sildenafil, caffeine (Figure 2)).

Figure 2: Monograph Caffeine in Kinderformularium.DE.³ Extract from Section „Dosierungsempfehlungen“ (Dosing recommendations) with explanations regarding designation of salt/base

For monographs associated with an increased risk of error, a note box was included directly above the dosing recommendations (Table 1). The standardised revision of all monographs is being carried out on an ongoing basis.

Table 1: Monographs with note box concerning salt/ base designation (selection)

Monograph	Reason for use of note box
Caffeine	Extent of conversion factor (f=2), substance for extemporaneous products
Morphine	Medicinal products with different salts (-hydrochloride, -sulfate)
Erythromycin	Medicinal products with different salts (-estolate, -ethylsuccinate, -stearate), Dose regimen dependant on salt
Lithium	Narrow therapeutic range ⁴ , Extent of conversion factor (f=5,3)

Conclusion and Relevance

This projects aims to increase awareness of the risk of dosing errors associated with differing reference values. The clear and explicit designation implemented in Kinderformularium.DE enhances safety in prescribing and compounding and supports interprofessional communication. In the long term, harmonising the respective reference values in official documents – such as summaries of product characteristics and clinical study reports – should be pursued in order to further improve medication safety.

References

- Daniel L, Prohotsky D. A survey of top 200 drugs—inconsistent practice of drug strength expression for drugs containing salt forms. *J Pharm Sci.* 2012;101(1):1-6.
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