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### A PRACTICAL FRAMEWORK FOR THE ASSESSMENT OF RISKS AND BENEFITS OF OFF-LABEL PRESCRIBING IN PAEDIATRICS (ARBOP-P)

<sup>1,2,3</sup>TM Van der Zanden\*, <sup>4</sup>NJ Vet, <sup>3,4,5</sup>SN de Wilt. <sup>1</sup>Department of Paediatrics, Erasmus MC – Sophia Childrens Hospital, Rotterdam; <sup>2</sup>Department of Pharmacology and Toxicology, Radboud University Medical Center, Radboud Institute for Health Sciences, Nijmegen; <sup>3</sup>Dutch Knowledge Center Pharmacotherapy for Children, Den Haag; <sup>4</sup>Department of Paediatric Surgery, Erasmus MC – Sophia Childrens Hospital, Rotterdam; <sup>5</sup>Department of Pharmacology and Toxicology, Radboud Institute for Molecular Life Sciences, Nijmegen, The Netherlands

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**Background** Guidelines for off-label prescribing are emerging.<sup>1–6</sup> However, these guidelines do not provide practical guidance to assess the risk benefit balance and select the right paediatric dose. We, therefore, aimed to develop a practical framework to guide paediatric healthcare professionals to assess the risks and benefits of off-label use.

**Methods** We have reviewed available literature on the suggested criteria for appropriate off-label use and evaluated these criteria for relevance in paediatrics. For guidance on dose-selection we searched for regulatory guidance on paediatric drug development. Next, the literature was searched for strategies that can be applied to assess the risks and benefits of off-label use. Based on literature findings a framework was proposed to provide practical guidance to physicians for off-label prescribing. Finally, the framework was applied to a case.

**Results** The following conditions for appropriate off-label use were identified based on available literature: 1. *Medical need for off-label use*. 2. *Off-label use is based on ‘high quality evidence’*. As ‘high quality evidence’ in paediatrics is often lacking, we propose to replace the need for high quality evidence by a positive risk-benefit assessment based on available evidence. 3. *Parents and patients are informed*. This is not feasible for every single drug prescribed off-label, we propose a graded approach 4. *The outcomes of off-label use are followed up*.

The PROACT-URL framework<sup>7</sup> for decision-making as well as the FDA paediatric decision tree<sup>8</sup> seem helpful tools to guide decisions in real-life practice.

**Conclusion** We identified important aspects and tools to develop a framework (ARBOP-P) to guide healthcare professionals on how to systematically assess and balance the benefits and risks for off-label use, including dose selection, to ultimately optimize efficacy and safety of paediatric off-label prescribing.

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### EXTENDING THE DUTCH PAEDIATRIC FORMULARY ACROSS EUROPE: SUCCESSFUL DEVELOPMENT OF COUNTRY SPECIFIC, PARALLEL, PAEDIATRIC DRUG FORMULARIES

<sup>1,2,3</sup>T Van der Zanden\*, <sup>4</sup>A Neubert, <sup>4</sup>J Zahn, <sup>4</sup>S Wimmer, <sup>5</sup>M de Hoop, <sup>6,7</sup>T Rosness, <sup>8</sup>C Kjeldby-Høie, <sup>9,10</sup>A Teigen, <sup>11</sup>C Male, <sup>11</sup>E Rauch, <sup>12</sup>F Lagler, <sup>4</sup>W Rascher, <sup>2,3,13</sup>S de Wildt. <sup>1</sup>Department of Paediatrics, Erasmus MC – Sophia Childrens Hospital, Rotterdam; <sup>2</sup>Department of Pharmacology and Toxicology, Radboud University Medical Center, Radboud Institute for Health Sciences, Nijmegen; <sup>3</sup>Dutch Knowledge Center Pharmacotherapy for Children, Den Haag, The Netherlands; <sup>4</sup>Department of Paediatrics and Adolescents Medicine, Universitätsklinikum Erlangen, Erlangen, Germany; <sup>5</sup>KNMP, Den Haag, The Netherlands; <sup>6</sup>The Norwegian Medicines Manual for Health Personnel; <sup>7</sup>The Faculty of Mathematics and Natural Sciences, School of Pharmacy; <sup>8</sup>Sykehusapoteket, Rikshospitalet, Oslo; <sup>9</sup>Sykehusapoteka Vest HF, Stavanger; <sup>10</sup>Medicines for Children Network, Bergen, Norway; <sup>11</sup>Department of Paediatrics, Medical University Vienna, Vienna; <sup>12</sup>Institute for Inborn Errors of Metabolism, Paracelsus Medical University, Salzburg, Austria; <sup>13</sup>Department of Paediatric Surgery, Erasmus MC – Sophia Childrens Hospital, Rotterdam, The Netherlands

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**Backgrounds** As many drugs in paediatrics are used of off-label, prescribers across Europe face a lack of evidence-based dosing guidelines. The Dutch Paediatric Formulary (DPF) was developed to provide dosing guidelines based on best available evidence from registration data, investigator-initiated research, clinical experience and consensus (1). The DPF has recently joined forces with Germany, Norway and Austria aiming to develop multi-language, parallel, paediatric drug formularies based on the DPF.

### Methods

The DPF database and ICT framework were extended to a duplicate database for Germany. The dosing guidelines were translated to German and reviewed for fit with German practice. Relevant drugs and dosing recommendations were selected and country-specific information was added to address country-specific needs. Work-sharing on content development was studied in a small pilot.

**Results** The German Pediatric Formulary ([www.kinderformularium.de](http://www.kinderformularium.de)) was launched on 1 October 2018 within a German paediatric medication safety project (KiDSafe). At that time 119 of 769 drugs were reviewed and published in the German formulary. The dosing recommendations of the DPF show a good fit with German practice; i.e. adaptations were needed in less than 10% of the cases caused by differences in licensing status, national guidelines or availability of formulations. There were no differences in interpretation of evidence. Nine drugs - highly relevant for German practice, but not listed in the DPF, were added to the German formulary based on SmPC. The content