



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

<31/01/2018>

Submission of comments on 'Concept paper on the need for a paediatric addendum of the guideline on clinical investigation of medicinal products for the treatment and prophylaxis of venous thromboembolic disease)

EMA/230866/2017

Comments from:

Name of organisation or individual

TEDDY - European Network of Excellence for Paediatric Clinical Research

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).



1. General comments

Stakeholder number <i>(To be completed by the Agency)</i>	General comment (if any)	Outcome (if applicable) <i>(To be completed by the Agency)</i>
	This guideline addresses a highly relevant topic, since several clinical trials on new oral anticoagulants, acting on specific coagulation factors, are now ongoing.	

2. Specific comments on text

Line number(s) of the relevant text <i>(e.g. Lines 20-23)</i>	Stakeholder number <i>(To be completed by the Agency)</i>	Comment and rationale; proposed changes <i>(If changes to the wording are suggested, they should be highlighted using 'track changes')</i>	Outcome <i>(To be completed by the Agency)</i>
Line 25-27		<p>Comment and proposed addition: We suggest to change: "While the overall incidence rate for a VTE event in adults is approximately 100-200 per 100,000/year, the incidence of symptomatic thrombosis is approximately 1 case per 100,000 paediatric patients [4,5]. <u>The incidence increases to 18.8-58.0 VTE events per 10000 hospital admissions.</u> (Chan AK, Monagle P. Updates in thrombosis in pediatrics: where are we after 20 years? Hematology Am Soc Hematol Educ Program. 2012:439-43)</p>	
Lines 30-33		<p>Comment and proposed addition: We suggest inserting the Italian registry that includes some data that can be useful for the prevalence of thrombosis, risk factors and objective tests used for the diagnosis.</p> <p>(latest published update: Giordano P, Grassi M, Saracco P, Molinari AC, Gentilomo C, Suppiej A, Indolfi G, Lasagni D, Luciani M, Piersigilli F, Putti MC, Rota LL, Sartori S, Simioni; Paediatric Thrombosis Working Group of the RITI. Paediatric venous thromboembolism: a report from the Italian Registry of Thrombosis in Children (RITI). Blood Transfus. 2017 Jun 30:1-8)</p>	
Lines 40-43		<p>Comment: further details on the acceptability of including adolescents in VTE studies might be added in the guidance.</p>	
Lines 44-46		<p>Comment: We suggest to add supporting data from existing registries/epidemiological data to justify that in neonates and young children VTE occurs more often (60%) in the upper</p>	

Line number(s) of the relevant text <i>(e.g. Lines 20-23)</i>	Stakeholder number <i>(To be completed by the Agency)</i>	Comment and rationale; proposed changes <i>(If changes to the wording are suggested, they should be highlighted using 'track changes')</i>	Outcome <i>(To be completed by the Agency)</i>
		venous system (vs. only 2% in adults)	
Lines 44-51		Comment: Please consider that only 1/10 VTE is symptomatic (Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008;133(6 Suppl):381S-453S)	
Lines 58-61		<p>Comment: Some data on the practical approach to therapy can also be mentioned, considering the factual problems experienced by paediatricians in administering low-molecular weight heparin in childhood and infancy (Molinari AC, Banov L, Bertamino M, Barabino P, Lassandro G, Giordano P. A practical approach to the use of low molecular weight heparins in VTE treatment and prophylaxis in children and newborns. <i>Pediatr Hematol Oncol.</i> 2015 Feb;32(1):1-10.)</p> <p>We suggest to mention new available treatments (Law C and Raffini L, A Guide to the Use of Anticoagulant Drugs in Children. <i>Pediatr Drugs</i> (2015) 17:105–114; von Vajna E, Ruhaniyah A and Tsz-Yin S. Current Clinical Trials on the Use of Direct Oral Anticoagulants in the Pediatric Population. <i>Cardiol Ther</i> 2016 Jun;5(1):19-41; da Luz LT, Marchand M, Nascimento B, Tien H, Nathens A, Shah P. Efficacy and safety of the drugs used to reverse direct oral anticoagulants: a systematic review and meta-analysis. <i>Transfusion.</i> 2017 Jul;57(7):1834-1846).</p>	
Line 58-60		Comment: The length of treatment of VTE in children depends on the age.	

Line number(s) of the relevant text <i>(e.g. Lines 20-23)</i>	Stakeholder number <i>(To be completed by the Agency)</i>	Comment and rationale; proposed changes <i>(If changes to the wording are suggested, they should be highlighted using 'track changes')</i>	Outcome <i>(To be completed by the Agency)</i>
		The LMWH or oral anticoagulation with a vitamin K antagonist (VKA) are administrated for at least 3 months in younger children or for 5-7 days. There are not other oral anticoagulants approved in childhood that avoid the need to puncture the medication. In addition, there is no evidence on the adequate duration of anticoagulant treatment in childhood.	
Lines 97-102		Comment: Interested parties should also include reference paediatric scientific societies and relevant patients' associations (e.g Associazione Italiana di Ematologia e Oncologia Pediatrica - AIEOP, Associazione Italiana di Ematologia e Oncologia Pediatrica - ALT)	

Please add more rows if needed.