<27 November 2014>

Submission of comments on 'Reflection Paper on the use of patient reported outcome (PRO) measures in oncology studies-Draft' (EMA/CHMP/292464/2014)

Comments from:

Name of organisation or individual
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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).

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	IQWiG appreciates the opportunity to comment on the reflection paper on the use of patient reported outcome (PRO) measures in oncology studies.	

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
Lines 27-30 PRO definition		Comment: According to the executive summary, the reflection paper acknowledges the importance of the patients' point of view on their health status and addresses the possible use of this information in regulatory decision making about the treatment effects of drugs. This objective should be considered when defining PRO for the context of the reflection paper. From IQWiG's point of view, treatment adherence should not be included in the definition of a PRO in the context of the reflection paper. Measures of treatment adherence can be reported by patients; however, treatment adherence does not describe a health status or any other (patient-relevant) health outcome of an intervention. An increased treatment adherence does not per se constitute a benefit for the patient; it only represents an advantage if it results in an improved health outcome. Treatment adherence is a process measure rather than a health outcome. As such it should not be included in a PRO definition, which aims to evaluate intervention effects on health outcomes. It is possible that improved process measures such as	

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		treatment adherence can result in improved health outcomes. However, it is also possible that changes in treatment adherence achieved by an intervention do not result in relevant changes in health outcomes. Health outcomes should therefore be measured directly, rather than relying on process measures to assess the effect of an intervention. From IQWiG's point of view, the inclusion of satisfaction with treatment in the PRO definition in the context of the assessment of intervention effects on health outcomes also seems questionable. So far, a clear concept describing relevant components of patient satisfaction based on health outcomes is missing. Proposed change (if any): A PRO includes any outcome evaluated directly by the patient him- or herself and based on the patient's perception of a disease and its treatment(s). Patient reported outcome is an umbrella term covering both single dimension and multi-dimension measures of symptoms, health-related quality of life (HRQL), health status, etc.	
Lines 147-155		Comment: It is somewhat unclear what is meant in this paragraph. While (double) blinding in a trial may not always be successful, it is nevertheless an essential instrument to avoid bias. Even more, there is no common understanding of how to assess unblinding and how to interpret tests of unblinding	

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		(Hróbjartsson & Boutron. Clin Pharmacol Ther. 2011 Nov;90(5):732-6). There is no reason to dispense with (double) blinding, except in rare situations where the effort would be unacceptable. We believe that tumour-related symptoms have more value when assessing the patient-relevant benefit of treatments than so-called objective measures of tumour response or delay in progression. This is the case in both placebo-controlled and active-controlled trials. Proposed change (if any): Delete this paragraph.	
Lines 156 - 158		Comment: Please see comment above. The given example where (double) blinding is allegedly not possible does not seem to be convincing. Proposed change (if any): If there are doubts that (double) blinding can be successfully achieved in the trial, extensive planning in advance is required to increase the credibility of study data. …	
Lines 288 -292		Comment: The text in this paragraph seems to limit the possible use of PRO measures to certain situations (i.e. late line palliative setting, maintenance therapy, and in studies comparing agents with similar efficacy but different safety profiles).	

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		This limitation seems to be inconsistent with the statement in lines 69 to 71, where the general value of PROs is described ("In summary, PRO measures may provide important patient perspective on the disease and the treatment received; an evaluation that provides clinically important information that is not captured by conventional anti-tumour efficacy data and adverse event reporting"). From IQWiG's point of view, PRO results (reflecting patient-relevant health outcomes) could generally be relevant, because they provide the patients' perspective of a treatment's effects, which might not be covered by other measures. Proposed change (if any):	

Please add more rows if needed.