EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

30 July 2010

Submission of comments on 'the concept paper on the need for revision of the guideline on the clinical development of medicinal products for the treatment of hepatitis C' (EMA/CHMP/EWP/825749/2009)

Comments from:

Name of organisation or individual
The European Liver Patients Association (ELPA) www.elpa-info.org ELPA emerged from a desire amongst European liver patient groups to share their experiences of the often very different approaches adopted in different countries. ELPA was formally launched in Paris on April 14th 2005 during the annual conference of the European Association for the Study of the Liver (EASL) and now has 20 members from 17 countries. ELPA's aim is to promote the interests of people with liver disease by furthering awareness and prevention among healthcare professionals, policymakers and the public at large; by addressing the low profile of liver disease compared to other disease areas; by sharing experience of successful case examples as regards the management of the disease; by working with professional bodies such as EASL to ensure that treatment and care are aligned across Europe to the highest standards.

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 *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	ELPA greatly welcomes the European Medicine's Agency intention to adopt a new guideline for the assessment of medicinal products for the treatment of hepatitis C. In this context, ELPA refers to the new resolution by the WHO assembly WHA63.18 which defines viral hepatitis as a serious global public health problem where action needs to be taken with regard to health promotion, diagnosis and treatment. The resolution hence represents an undisputable recognition of the urgent need to support and accelerate scientific research, with a view to preventing the notorious and dreadful complications which are typical of the disease. The WHO further points out that hepatitis C is still not preventable by vaccination and that 80% of hepatitis C virus infections become a chronic infection. It finally points to the need for a promotion of access to treatment technologies, recognising the need to make new drugs available to the broadest community of patients. This is currently not the case: With hepatitis C being a largely asymptomatic condition and without sufficient efforts to promote early diagnosis, there are ten thousands of "difficult to treat" (i.e. those at highest risk of dieing and hence most in need of treatment) hepatitis C patients. Their sole chance of survival in the short-run lies in the immediate access to new drugs, i.e. usually access to clinical trials with expanded access programmes or on a compassionate use basis. In the	

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	face of death, the concept of "risk minimisation" naturally does not apply to these "difficult to treat" patients in the same way as it does to "ordinary" patients. "Difficult-to-treat" patients include • Patients with cirrhosis related to HCV • Patients awaiting liver transplantation related to HCV • Patients with decompensated cirrhosis • Transplanted patients with recurrent HCV; • Patients with HIV co-infection "Ordinary" hepatitis C patients are usually considered as those who have slight or medium fibrosis and are not at risk of suffering from complications in the short term (mainly naïve, relapsers and non-responder patients). However, for "difficult to treat" hepatitis C patients, access on a compassionate use basis/ access to expanded access programmes and to confirmatory studies proves difficult in practice, since pharmaceutical companies still fear potential negative consequences for the development of their drugs targeted "ordinary patients" The situation of these patients is very similar to that of HIV patients in the early 1990s. Once, the urgency for intervention had been acknowledged, the pharmaceutical industry and regulators agreed to a flexible approach and pathways for early access to clinical trials were created (fast-track procedure and expanded access programmes) and lives could be saved. ELPA sees urgent need for a similar action for the benefit	

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	of hepatitis C patients who are difficult to treat. Whilst we understand that this issue is still largely regulated at national level, we consider an EU-wide approach as necessary. We hence call on the EMA to actively support the provision of incentives for the establishment of expanded access/ compassionate use programmes for "difficult-to-treat" hepatitis C patients. There is urgent need for the access to clinical trials of phase IIa, IIb and phase III for these "difficult-to-treat" patients. Furthermore, the EMA should look further in the promotion of separate regulatory pathways for such trials. It is important to ensure that pharmaceutical companies who provide early access for these "difficult to treat patients" will not be penalised for negative outcomes during their clinical trials, but that instead their CSR efforts should be recognised. Otherwise, the development of new hepatitis C drugs for naïve or non-responder patients is at risk by being delayed or adversely influenced. This way, the EMA would make an active contribution to the implementation of the new WHO assembly resolution WHA62.18 on viral hepatitis.	

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)*
		ELPA largely agrees with the issues raised by EMA for new or updated guidance, and has the following remarks: 1) The implementation of genetic predictors of SOC activity should be considered in different type of studies: a) in exploratory and confirmation studies using one or more DAA in combination with SOC. This would stratify enrolled patients so as to understand the impact of DAA addition to SOC in patients with different genomic profile, and in patients with different kinetics of response to eventual SOC lead in phases; b) in exploratory studies using only combinations of DAA where patients with higher probability of response to SOC could be selected in order to minimize the risk of not having future options in case of occurrence of resistance. 2) The implementation of exploratory studies on the re-treatment of patients with resistance to one or more DAA. 3) The definition of stopping rules for studies using	

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		combinations of DAA in order to minimize the risk of resistance. 4) Different classes of DAA have shown different levels of resistance risk. Thus guidelines on the design of exploratory studies on combinations of DAA should be calibrated on the number and type of drug classes combined together to treat HCV (ie nn polymerase inhibitors + PI or Nucleoside polymerase inhibitors + PI etc.) 5) The need for urgent confirmatory studies with combinations of DAA in categories of patients where usage of these drugs could be life saving (patients with decompensated cirrhosis with or without HIV coinfection, patients with severe HCV disease or post transplant severe relapses of HCV non responders to SOC). 6) The possibility to extend exploratory/feasibility studies to patients undergoing liver transplant with high risk of HCV recidivism, with or without interaction studies. ELPA is grateful for the scientific advice of Ph.D Massimo Puoti, Associate Professor, Department of Infectious Diseases, University of Brescia, P.zzle Spedali Civili 1, I-25123 Brescia	

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		Proposed change (if any):	
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