European Medicines Agency

London, 26 April 2007
Doc. Ref. EMEA/CHMP/EWP/156308/2007

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

CONCEPT PAPER ON THE CLINICAL DEVELOPMENT OF MEDICINAL PRODUCTS FOR THE TREATMENT OF HEPATITIS C INFECTION

AGREED BY THE EFFICACY WORKING PARTY	April 2007
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	26 April 2007
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 July 2007

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KEYWORDS	*Hepatitis C, guidance, HCV*

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1. INTRODUCTION

Hepatitis C virus (HCV) is a leading cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma, as well as the most common indication for liver transplantation in many European countries. Worldwide, the number of chronically infected persons is estimated at 170 million, or 3% of the global population. About 20-30% of chronically infected persons will advance to cirrhosis within 20 years.

In Europe around 1/3 of HIV-infected patients are co-infected with hepatitis C, with a prevalence of 50% in some regions in southern Europe. Compared to HCV mono-infected patients, these patients have faster progression of liver fibrosis; the risk for manifest cirrhosis is doubled for a middle-aged man carrying both infections.

2. PROBLEM STATEMENT

The current treatment mainstay of CHC is (pegylated) interferon alpha in combination with ribavirin. A large number of direct-acting anti-virals, however, is now under development including protease inhibitors and nucleoside analogues and one compound was recently submitted for marketing authorisation through the centralised procedure.

Available data indicate that HCV resistance development may be seen very rapidly in patients on mono-therapy with direct-acting anti-virals and from this perspective it is of importance to take into account what has been learnt over the years in relation to treatment of HIV. Similarly, the potential for pharmacokinetic (PK) interactions appear high for the compounds now under development, especially for patients co-infected with HIV

Issues to be discussed in a future guideline include:

- Appropriate endpoints
- Assays for quantification of viral load and appropriate cut-off values
- Resistance testing
- Testing of activity against HIV
- Design of exploratory and confirmatory mono- and combination studies
- Predictive factors for response
- Design of the PK interaction package
- Design of studies in HIV co-infected patients
- Design of studies in immune suppressed patients in general, patients with (advanced) cirrhosis, liver transplant patients
- Paediatric programme

3. DISCUSSION (ON THE PROBLEM STATEMENT)

There is a need for new and improved therapies in the treatment of CHC, especially of patients infected with HCV genotype 1 and with high viral load and in patients co-infected with HIV. These groups of patients, however, constitute a major risk with respect to resistance development. This appears to form the major challenge in the development of direct-acting anti-virals for the treatment of CHC.

4. RECOMMENDATION

The Efficacy Working Party recommends that a guideline is written on the development of medicinal products for the treatment of patients infected with hepatitis C virus.

5. PROPOSED TIMETABLE

It is anticipated that the first draft guideline may be available 3 months after adoption of the concept paper.

6. RESOURCE REQUIREMENTS FOR PREPARATION

Preparation of this Guideline will involve the EWP, the ad hoc HIV drafting group, the PK drafting group and the anti-viral SAG.

7. IMPACT ASSESSMENT (ANTICIPATED)

It is anticipated that a guideline will facilitate the interaction between regulatory agencies within Europe and Sponsors developing products for the treatment of CHC.

Until such time as this guideline comes into operation, EMEA/CHMP scientific advice is recommended.

8. INTERESTED PARTIES

- European Association for the study of the Liver
- European Society of Clinical Microbiology and Infectious Diseases
- EATG