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Review Article

SOFOSBUVIR: TREATMENT OF CHRONIC HEPATITIS C AND THE MAIN TRENDS IN PATENT PROTECTION

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ABSTRACT

The purpose of the study was to analyze and systematize the literature data on the benefit/risk ratio of sofosbuvir administration in the treatment of patients with chronic hepatitis C and the main trends in its patent protection. Studies were conducted using databases on the Internet: Ukrainian patent office, the European patent office, the US patent office, the Food and drug administration, European Medicines Agency (EMEA), State enterprise "The State Expert Center" of the Ministry of Health of Ukraine. It has used retrospective, logical, systematic and analytical methods. Data from clinical studies abroad and meta-analyses indicate that sofosbuvir is one of the most promising drugs for the treatment of chronic HCV infection. Its indisputable advantages are that this drug can be used with different genotypes of the virus, decompensated liver function, it is well tolerated. Sofosbuvir has an improved safety profile and a low probability of viral resistance. The high cost of sofosbuvir is due to the powerful patent protection. As mechanisms for working with patent barriers, it is recommended to use the flexible mechanisms of the TRIPS Agreement: the grant of compulsory licenses, the implementation of parallel imports, the tightening of the criteria for patentability (prohibition of patenting new forms that do not improve therapeutic efficacy).

Keywords: Sofosbuvir, Patent, Chronic hepatitis C, TRIPS

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INTRODUCTION

According to World Health Organization, morbidity and mortality associated with hepatitis C virus (HCV) infection continue to increase worldwide. Each year about 700,000 people die from HCV-related complications, including liver cirrhosis and hepatocellular carcinoma [1-6]. For Ukraine, the problem of HCV infection is really not only medically, but also socio-economically important. In Ukraine, infection with the hepatitis C virus of people over the age of 15 reaches 9% and up to 11,000 people die from its effects every year [7, 8]. According to the results of selective monitoring of risk groups, the level of HCV infection among some of them is much higher than the world average rates and reaches 40–60%. It should be noted that thanks to scientific breakthroughs towards the treatment of HCV infection, significant progress has been made in the treatment of this pathology and in fact, chronic hepatitis C has been transferred to the category of fully curable diseases.

Until recently, in Ukraine, the combination of pegylated interferon with ribavirin during 48-56 w was considered to be the recognized standard of therapy for this pathology. The effectiveness of this treatment was approximately 50%, that is, only half of the patients undergoing therapy had a chance of cure. But, in almost all cases this therapy was a peculiar kind of trial because of side effects, namely the "flu-like syndrome", which accompanied the patient during the entire course of therapy [7].

Taking into account international recommendations, as well as proven high efficacy and favorable safety profile of direct-acting antiviral agents (DAAs) in the treatment of chronic HCV, the Unified clinical protocol on primary, secondary, tertiary care "Viral hepatitis C in adults" was updated by Order of the Ministry of Health of Ukraine dated July 18, 2016 No. 729. The HCV treatment regimens of all genotypes were revised in the updated document.

There is no doubt that effective antiviral therapy leading to the eradication of HCV infection reduces the risk of progression of hepatic and extrahepatic HCV infection manifestations, especially if the treatment is carried out before the formation of liver cirrhosis [9-17].

At least 6 genotypes and dozens of subgenotypes of HCV, the distribution of which differs in different countries of the world, are currently described. In Russia, the United States, Europe and some other countries, the most common virus is genotype 1 (HCV-1), while HCV-3 is the second most common (22-30% of patients) [18-20].

As a result, interferon-free regimens with the use of DAAs were included in the treatment regimens of patients infected with HCV: sofosbuvir+ribavirin; sofosbuvir/ledipasvir; sofosbuvir+simeprevir; ombitasvir/paritaprevir/ritonavir and dasabuvir [21].

The purpose of the study was to analyze and systematize the literature data on the benefit/risk ratio of sofosbuvir administration in the treatment of patients with chronic hepatitis C and the main trends in its patent protection.

MATERIALS AND METHODS

Studies were conducted using databases on the Internet: Ukrainian patent office, the European patent office, the US patent office, the Food and drug administration, European Medicines Agency (EMEA), State enterprise "The State Expert Center" of the Ministry of Health of Ukraine. It has used retrospective, logical, systematic and analytical methods.

RESULTS AND DISCUSSION

The recommendations of the World Health Organization [22], the European Association for the Study of the Liver (EASL) [23] and the American Association for the Study of Liver Diseases (AASLD/The Infectious Diseases Society of America (IDSA), which consider current approaches to the treatment of chronic hepatitis C were published. All these recommendations proposed to use regimens that include sofosbuvir as one of the main regimens of antiviral therapy for chronic hepatitis [24].

Sofosbuvir is a nucleotide pan-genotypic inhibitor of the main replicative enzyme, the RNA-dependent RNA polymerase of the NS5B region of HCV. Sofosbuvir is a prodrug that, during intracellular metabolism, is transformed into a pharmacologically active analogue of uridine triphosphate. The standard dose of sofosbuvir is one 400 mg pill, which is taken as a single piece after a meal. After administration, sofosbuvir is rapidly absorbed. Sofosbuvir (mainly in the form of an inactive metabolite leaving hepatocytes after dephosphorylation) is characterized by an active