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Research and Development the Prescription of Sofosbuvir Tablets

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Abstract: The prescription of sofosbuvir tablets was screened to select the best prescription proportions. Methods: According to the prescription technology of foreign listed tablets "sovaldi®", experiments of diluents, disintegrating agents, binders, lubricants and coating process were investigated, including the stability study of self-made samples and reference tablets under the conditions of high temperature, high humidity and illumination. We aimed to screen a reasonable prescription process. Results: Prescription process was ultimately determined including: sofosbuvir 400 mg, mannitol 360 mg, microcrystalline cellulose 360 mg, cross-linked sodium carboxymethyl cellulose 60 mg, magnesium stearate 14 mg, gum arabic 6 mg, opadry film coating powder 36 mg, and chose purified water as a binder. Conclusion: The determined prescription process was stable, and the production process was not harsh, it was suitable for scale-up production. The results of stability study and the dissolution behavior in vitro were similar to those of commercial products, so the prescription is design reasonably.

Keywords: sofosbuvir tablets, stability study, prescription technology, reference tablet "sovaldi ®".

1. Introduction

The molecular formula of sofosbuvir is $C_{22}H_{29}FN_3O_9P$, with a relative molecular mass of 529.453[1-2]. Sofosbuvir is a direct acting antiviral drug, which inhibits the hepatitis C virus RNA depend on RNA polymerase, NS5B gene. Sofosbuvir is effective in the treatment of 1, 2,

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3 genotypes or genotype 4 HCV subjects, including the hepatocellular carcinoma subjects who are waiting for liver transplantation and meet with the Milan standard, and the HCV/ HIV-1 co-infected patients.

The traditional standard treatment for HCV infection is interferon α or peg interferon α combined with ribavirin; the treatment program is expensive with large adverse drug reactions. When it was used for the treatment of genotype 2 and 3 HCV infections, the sustained virological response (SVR) is 80%, while the SVR for HCV infected individuals of genotype 1 is only about 50%[3]. In order to replace the currently used interferon injection therapy, global market for the treatment of chronic hepatitis C have appeared telaprevir, boceprevir, sofosbuvir one after one, the first two are HCV nonstructural protein 3/4A serine protease inhibitors, which are suitable for HCV infection of gene type 1, but need to be combined with peg interferon α and ribavirin [4].

Sofosbuvir, approved by FDA on December 6, 2013, is a new type of anti HCV drugs, which is suitable for various genotypes of hepatitis C treatment [5]. Clinical trials confirmed that the SVR of sofosbuvir combined with peg interferon α and ribavirin was up to 90% for genotype 1 and 4 HCV infections, for genotype 2 HCV infections, the SVR of sofosbuvir combined with ribavirin was 89%~95%, for genotype 3 HCV infections, the SVR of sofosbuvir combined with ribavirin for 24 weeks was 84%.

In order to increase the range of clinical medication selection and reduce the cost of medication for patients, the prescription process was screened and optimized by referring to GILEAD's sovaldi® in this study. The prescription of sofosbuvir tablets was determined, the main technical parameters were verified, and the quality standard of the product was established and realized the expected industrialized production.

Table 1. The Prescription of Sofosbuvir

Ingredients	Function
Sofosbuvir	active ingredient
cross-linked sodium carboxymethyl cellulose	disintegrant
purified water	binder
microcrystalline cellulose	diluent
mannitol	diluent
gum arabic	lubricant
magnesium stearate	lubricant
opadry	coating material