Dialyse hemodialyse: sofosbuvir 7243

GFR = glomerulaire filtratie snelheid, ESRD = eindstadium nierfalen, SVR = sustained virological response

Onderbouwend	Bewijs	Effect	Opmerkingen
SPC Sovaldi 6-11-2019 (rev 19)	0	Hemodialyse kan op doeltreffende wijze de belangrijkste circulerende metaboliet GS-331007 verwijderen (extractieverhouding 53%). Een hemodialysesessie van 4 uur verwijderde ongeveer 18% van de toegediende dosis. Toename blootsteling bij HCV-geïnfecteerde patiënten met Clcr < 30 ml/min resp. ESRD met dialyse: - sofosbuvir: ↑ met factor 2 resp. 1.9 - GS-331007 ↑ met factor 7 resp. 21	De veiligheid en de juiste dosis zijn niet vastgesteld bij patiënten met eGFR < 30 ml/min/1,73 m2 of een terminale nieraandoening die hemodialyse vereist. ► Werkgroep: het is niet bekend of door cumulatie van de inactieve metaboliet (GS-331007) onverwachte bijwerkingen kunnen optreden

Overig	Opmerkingen
EPAR Sovaldi	Safe use of SOF in patients with severe renal impairment or ESRD has not been established and no dosing recommendation is available. Normalising the exposure of GS-331007 in patients with severe renal impairment would require 5- to 10-fold lower dose of SOF. This may lead to suboptimal treatment. Therefore, to facilitate the use of SOF in these patients, further clinical safety and efficacy data in this population is needed and will be obtained from a study performed by the applicant as an additional pharmacovigilance activity (study GS-US-334-0154). Safety margins calculated from results of toxicology studies are 5.4 to 11.6 for SOF and 1.6 to 3.5 for GS-331007 in subjects with mild and moderate renal impairment. The haemodialysis extraction ratio for GS-331007 was approximately 50%. Treatment of patients with severe renal impairment/end-stage renal disease (ESRD) is not recommended.
HCV Richtsnoer (versie oktober 2019) geraadpleegd 10-2-2020. https://hcvrichtsnoer.nl/nierinsufficientie/	Expert opinion: Sofosbuvir is niet geregistreerd voor patiënten met een creatinine klaring < 30 ml/min. Gezien de beschikbaarheid in Nederland van andere wel voor deze groep patiënten, geregistreerde middelen adviseert de richtsnoercommissie geen sofosbuvir bevattende regimes te gebruiken bij patienten met CrCL <30 ml/min en/of hemodialyse.
Bhamidimarri KR ea. Urgent treatment with sofosbuvir based regimen for hepatitis C genotype 1 patients with severe renal insufficiency (GFR < 30ml/min). Hepatology 2014;**60 (Suppl):** 688a-9a. Poster	4 HCV geïnfecteerde patiënten met Clcr < 30 ml/min (3 op dialyse) werden behandeld met sofosbuvir 400 mg om de dag icm simeprevir 150 mg/dag of ribavirine 200 mg/dag. 3 van de 4 patiënten bereikten een SVR12.
Saxena K ea. Safety and efficacy of Sofobuvir-containing regimens in Hepatitis C infected patients with reduced renal function: real-world experience from HCV-TARGET. J Hepatol 2015.62: S263. Poster	HCV-TARGET studie waarin 18 patiënten met eGFR <30 ml/min (waarvan 5 op dialyse) behandeld werden met SOF 400 mg/dag. Auteurs: Frequencies of SVR with SOF-containing regimens are high and not influenced by renal impairment. However, patients with reduced baseline renal function have a higher frequency of anemia, worsening renal dysfunction and serious adverse events regardless of use of RBV. Close monitoring during treatment is warranted.

He YL ea. Safety and efficacy of sofosbuvir-based treatment of acute hepatitis C in end-stage renal disease patients undergoing haemodialysis. Aliment Pharmacol Ther 2018;47:526-32. doi: 10.1111/apt.14429.	We conducted a prospective and observational study of end-stage renal disease patients who were undergoing haemodialysis and were acutely infected with HCV. Patients received a half dose of sofosbuvir (200 mg) and a full dose of daclatasvir (60 mg) daily. The primary endpoint was the proportion of patients with sustained virological responses (SVRs); the other primary outcomes were safety and tolerability. Thirty-three patients were enrolled in the study. The median HCV RNA viral load at baseline was 6.8 log10 IU/mL. Twenty-four patients were infected with HCV genotype 2a, seven patients with 1b, and two patients with 2a+1b. All patients achieved a SVR at 12 weeks after the end of treatment. The treatment was well tolerated, and there were no drug-related serious adverse events. A half dose of sofosbuvir (200 mg once daily) plus a full dose of daclatasvir (60 mg once daily) were suitable for the treatment of acute HCV-infected patients who were undergoing end-stage renal disease and were on haemodialysis.
Surendra M ea. Ledipasvir and Sofosbuvir for untreated HCV genotype 1 infection in end stage renal disease patients: A prospective observational study. Hemodial Int 2018;22:217-21. doi: 10.1111/hdi.12604.	This is a single center prospective open label observational study to assess the safety and efficacy of Ledipasvir and Sofosbuvir in hemodialysis (HD) patients who were diagnosed with HCV genotype 1 infection. Eligibility criteria were treatment naive HD patients with normal liver histology. We administered Ledipasvir and Sofosbuvir combination tablet on alternate days for a period of 12 weeks. Primary efficacy end point was the assessment of sustained virological response (SVR12), and the safety end point was the discontinuation of therapy secondary to adverse drug effects. A total of 21 patients were treated with this regimen. Two patients expired during the study period and are not related to the therapy. SVR12 was achieved in all the 19 patients. None of the patients in our study discontinued the therapy or had severe adverse drug effects. One patient had headache and another patient had giddiness which were managed symptomatically. Ledipasvir and Sofosbuvir combination therapy on alternate days, is effective even in ESRD patients, with excellent SVR12 rates, and it is as safe as in other population groups, without any major adverse reactions.
Choudhary NS ea. Efficacy and safety of sofosbuvir-based regimens in chronic hepatitis C patients on dialysis. Indian J Gastroenterol 2017;36:113-6. doi: 10.1007/s12664-017-0735-7.	Sixteen consecutive patients of ESRD (on dialysis) and chronic hepatitis C were treated with sofosbuvir-based regimens as they were prospective kidney transplantation recipients, at a tertiary care center in north India. Sofosbuvir was given 400 mg on alternate days. Sixteen patients (12 males) aged 45±12 years received sofosbuvir-based treatment. These patients were on hemodialysis from 10 (2-48) months. Eleven of these patients had genotype 1, four had genotype 3, and one had genotype 4 infection; baseline RNA was 7 (5-8) log. The following treatment regimens were used: sofosbuvir, ribavirin, and low dose peginterferon (n = 8; 6 genotype 1 and one each had genotype 3 and 4); sofosbuvir and daclatasvir (n = 7); sofosbuvir, ribavirin, and daclatasvir (n = 1). Ten patients achieved end of treatment response and 8 (80%) of these achieved sustained virological response at 12 weeks (SVR12); six are on treatment. Two patients with genotype one (including one with cirrhosis) had relapse. Seven patients needed blood transfusion; interferon was stopped in one due to thrombocytopenia. Fatigue was present in 4 patients. Sofosbuvir-based regimens can be used in ESRD patients on dialysis with good efficacy.

Risicogroep	

Opmerkingen:

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	Wijziging kinetiek	**Effect dialyse**	**Actie**	**Datum**
Beslissing werkgroep	Ja	Ja: inactieve metaboliet GS-331007 Nee: sofosbuvir	Ja	16 november 2020