



# International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher  
SciFormat Publishing Inc.  
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,  
Calgary, Alberta, T3E0A7,  
Canada  
+15878858911  
editorial-office@sciformat.ca

---

## ARTICLE TITLE

THE EFFICACY AND SAFETY OF GLECAPREVIR/PIBRENTASVIR THERAPY IN THE TREATMENT OF HCV INFECTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE – A REVIEW OF CURRENT LITERATURE

---

## DOI

[https://doi.org/10.31435/ijitss.2\(50\).2026.5234](https://doi.org/10.31435/ijitss.2(50).2026.5234)

---

## RECEIVED

23 February 2026

---

## ACCEPTED

13 May 2026

---

## PUBLISHED

18 May 2026

---

## LICENSE



The article is licensed under a **Creative Commons Attribution 4.0 International License**.

---

© The author(s) 2026.

This article is published as open access under the Creative Commons Attribution 4.0 International License (CC BY 4.0), allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

# THE EFFICACY AND SAFETY OF GLECAPREVIR/PIBRENTASVIR THERAPY IN THE TREATMENT OF HCV INFECTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE – A REVIEW OF CURRENT LITERATURE

**Patrycja Krawczyk** (Corresponding Author, Email: [krawczyk.patrycja@gmail.com](mailto:krawczyk.patrycja@gmail.com))  
Provincial Hospital in Kielce, Kielce, Poland  
ORCID ID: 0009-0001-0536-4570

**Beata Szreder**  
Medical University of Gdansk, Gdansk, Poland  
ORCID ID: 0009-0008-7876-2159

**Tamara Chodań**  
Collegium Medicum of the Nicolaus Copernicus University in Bydgoszcz, Bydgoszcz, Poland  
ORCID ID: 0009-0001-5891-7925

**Milena Lewicka**  
Medical University of Gdansk, Gdansk, Poland  
ORCID ID: 0009-0006-2919-9537

**Maja Łapaj**  
Hospital of the Ministry of Interior and Administration in Katowice, Katowice, Poland

**Piotr Pietrzyk**  
Mazovian Bródno Hospital in Warsaw, Warsaw, Poland

**Joanna Ślusarczyk**  
Provincial Hospital in Kielce, Kielce, Poland  
ORCID ID: 0009-0008-6405-5963

**Natalia Stanek**  
Hospital of the Ministry of Interior and Administration in Katowice, Katowice, Poland

**Zuzanna Noweta**  
Collegium Medicum of the Nicolaus Copernicus University in Bydgoszcz, Bydgoszcz, Poland  
ORCID ID: 0009-0009-8086-8101

**Aleksandra Jagiello**  
Mazovian Bródno Hospital in Warsaw, Warsaw, Poland  
ORCID ID: 0009-0005-6310-6755

**ABSTRACT**

**Background:** Chronic hepatitis C virus (HCV) infection remains a major global health concern and is associated with chronic kidney disease (CKD). HCV infection may represent both a contributing factor to the development of chronic kidney disease (as an extrahepatic manifestation) and a consequence of CKD-related exposures, particularly in patients undergoing dialysis. Historically, patients with advanced CKD and those undergoing dialysis had limited and poorly tolerated antiviral treatment options. The advent of direct-acting antivirals, including the fixed-dose combination of glecaprevir/pibrentasvir (G/P), has substantially changed therapeutic management in this high-risk population.

**Aim:** To summarize current evidence regarding the efficacy and safety of G/P therapy in adults with HCV infection and concomitant CKD, including patients receiving hemodialysis or peritoneal dialysis.

**Methods:** A narrative review of the literature was conducted using the PubMed/MEDLINE database. Studies published within the last six years reporting original clinical data on adults with CKD treated with G/P were included. Phase III trials and real-world cohort studies were analyzed, focusing on sustained virologic response at 12 weeks (SVR12) and safety outcomes.

**Results:** Across clinical trials and large real-world cohorts, G/P achieved SVR12 rates ranging from 97% to 100%, irrespective of CKD stage, dialysis status, or HCV genotype. The regimen was well tolerated, with predominantly mild adverse events and no clinically significant deterioration in renal function.

**Conclusion:** Glecaprevir/pibrentasvir demonstrates high antiviral efficacy and a favorable safety profile in patients with CKD, including those undergoing dialysis.

---

**KEYWORDS**

Glecaprevir/Pibrentasvir, Chronic Kidney Disease, Hemodialysis, Peritoneal Dialysis, Hepatitis C Virus, Sustained Virologic Response

---

**CITATION**

Patrycja Krawczyk, Beata Szreder, Tamara Chodań, Milena Lewicka, Maja Łapaj, Piotr Pietrzyk, Joanna Ślusarczyk, Natalia Stanek, Zuzanna Noweta, Aleksandra Jagiełło. (2026) The Efficacy and Safety of Glecaprevir/Pibrentasvir Therapy in the Treatment of HCV Infection in Patients with Chronic Kidney Disease – A Review of Current Literature. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5234

---

**COPYRIGHT**

© **The author(s) 2026.** This article is published as open access under the **Creative Commons Attribution 4.0 International License (CC BY 4.0)**, allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

---

**Introduction**

Infection with Hepatitis C virus (HCV) affects approximately 50 million people worldwide, with an estimated 1 million new infections occurring annually (*Updated Recommendations on Treatment of Adolescents and Children with Chronic HCV Infection, and HCV Simplified Service Delivery and HCV Diagnostics*, 2022). It remains a major global health concern, contributing substantially to liver-related morbidity and mortality. In response, the World Health Organization (WHO) has set an ambitious target to eliminate HCV as a public health threat by 2030, defined as a 90% reduction in new chronic infections and a 65% reduction in HCV-related mortality compared with 2015 levels. (IDSA, n.d.) HCV infection may present as acute or chronic disease. Although acute infection is frequently asymptomatic, approximately 30% of individuals spontaneously clear the virus within six months without antiviral therapy. However, the remaining 70% progress to chronic infection, which may lead to serious complications such as liver fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). Beyond hepatic pathology, HCV infection is associated with a range of extrahepatic manifestations such as depression, diabetes mellitus, and chronic kidney disease (CKD) (*Updated Recommendations on Treatment of Adolescents and Children with Chronic HCV Infection, and HCV Simplified Service Delivery and HCV Diagnostics*, 2022). The relationship between HCV and kidney disease is complex and bidirectional. HCV may contribute to the development or acceleration of kidney damage through immune-mediated mechanisms, including cryoglobulinemia and glomerulonephritis, whereas patients with CKD—particularly those receiving maintenance dialysis—are at increased risk of acquiring HCV due to repeated healthcare exposure and invasive procedures. First identified in 1989, HCV has posed a serious therapeutic challenge, particularly in patients with CKD and end-stage renal disease (ESRD). (Wang et al.,

2025) Historically, interferon-based regimens, including peginterferon alfa-2a and ribavirin, required dose adjustments in these patients and were associated with limited efficacy and significant adverse effects, including deterioration of renal function (Jasso-Baltazar et al., 2022). The introduction of direct-acting antivirals (DAAs) revolutionized HCV therapy. The pan-genotypic fixed-dose combination of glecaprevir/pibrentasvir (G/P), has emerged as a particularly valuable option for patients with CKD and ESRD. This regimen provides high antiviral efficacy without the need for dose adjustment in patients with impaired renal function, including those undergoing hemodialysis, and presents minimal nephrotoxic risk (*Patients with Renal Impairment – HCV Guidance*, n.d.; Wang et al., 2025).

The aim of this review is to summarize the current evidence regarding the efficacy and safety of G/P therapy in patients with CKD, including those undergoing hemodialysis or peritoneal dialysis, based on literature published within the last six years.

### Methodology

This study was conducted as a narrative literature review. A structured search of the PubMed/MEDLINE electronic database was performed to identify relevant publications from the past six years. The search strategy combined controlled vocabulary terms (e.g., MeSH) and free-text keywords related to „hepatitis C virus infection”, „HCV”, „glecaprevir/pibrentasvir”, „chronic kidney disease”, „renal impairment” and „dialysis”, as well as the names of key clinical trials, including EXPEDITION-4 and EXPEDITION-5.

Eligible studies reported original clinical data on adult patients with CKD, including those receiving dialysis, who were infected with HCV and received treatment with G/P. Only studies providing data **on treatment efficacy** (e.g., sustained virologic response) and/or **safety outcomes** were included. Studies involving pediatric populations were excluded. Additionally, publications were excluded if they reported duplicate data identified through searches using different keywords, involved patients without CKD, without HCV infection, with co-infection with hepatitis B virus (HBV), or patients treated without antiviral regimens as G/P.

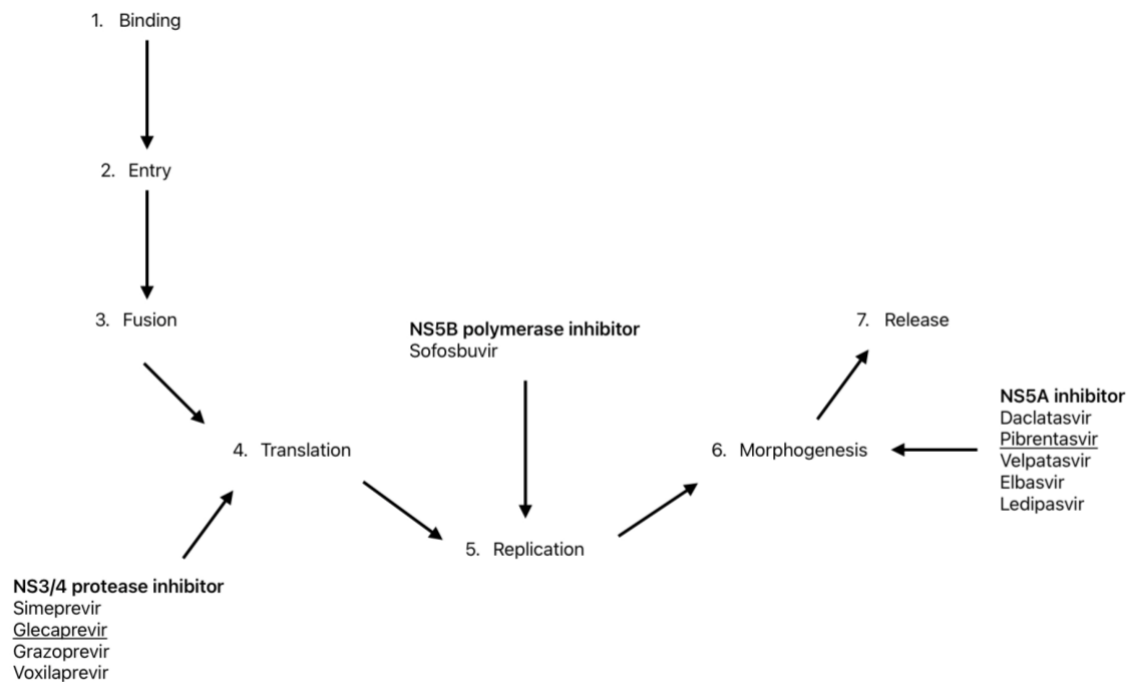
The primary focus of this review was on contemporary clinical evidence and real-world data reflecting routine clinical practice in patients with CKD, including those receiving dialysis. Although the principal search strategy was limited to studies published within the last six years, the pivotal EXPEDITION-4 trial was also included, despite being published outside this predefined time frame, as it represents a key reference study for the evaluation of glecaprevir/pibrentasvir in patients with advanced CKD.

### Pharmacology

G/P is a fixed-dose combination of two direct-acting antivirals targeting distinct nonstructural proteins critical for hepatitis C virus (HCV) replication. Direct-acting antivirals target specific steps in the viral life cycle and have revolutionized HCV therapy due to their high efficacy, short treatment duration, and favorable safety profile. (Bhattacharya et al., 2023) Glecaprevir is a inhibitor of the NS3/4A serine protease, which blocks cleavage of the viral polyprotein into functional components required for viral replication. Pibrentasvir inhibits the NS5A protein, a multifunctional phosphoprotein involved in viral RNA replication and virion assembly. The complementary inhibition of NS3/4 and NS5A provides pan-genotypic activity against HCV genotypes 1–6 and contributes to a high barrier to resistance (*Summary of Product Characteristics (SmPC) - (Emc) | 763*, n.d.; Xu et al., 2020) (**Figure 1**).

Following oral administration, both agents are rapidly absorbed, reaching peak plasma concentrations within several hours. Glecaprevir is primarily metabolized by cytochrome P450 3A (CYP3A), whereas pibrentasvir undergoes minimal metabolic transformation. Both compounds are substrates of drug transporters, including P-glycoprotein (P-gp) and organic anion transporting polypeptides (OATP1B1/3), which has implications for drug-drug interactions with strong inducers or inhibitors of these pathways (*Summary of Product Characteristics (SmPC) - (Emc) | 763*, n.d.).

Both compounds are predominantly eliminated via the hepatobiliary route, with minimal renal excretion (<1%). Pharmacokinetic studies demonstrate only modest increases in systemic exposure (AUC) in patients with severe CKD, which are not clinically significant. Dialysis does not meaningfully remove either compound. Consequently, no dose adjustment is required for patients with CKD stage 4–5 or for those receiving dialysis (Lawitz et al., 2020).



**Fig. 1.** Replication of HCV and DAAs targets.

Integrated pharmacokinetic analyses confirm comparable exposure profiles across all stages of renal function, supporting standard dosing regardless of CKD severity (Lawitz et al., 2020; Xu et al., 2020) (**Table 1**).

**Table 1.** Pharmacokinetic profile of glecaprevir/pibrentasvir according to renal function

Parameter	Normal renal function	CKD Stage 4-5	Dialysis	Clinical implication
Primary elimination	Hepatobiliary	Hepatobiliary	Hepatobiliary	Unaffected by renal impairment
Renal excretion	<1%	<1%	<1%	Clinically negligible
Glecaprevir exposure (AUC)	Reference	Mild increase	Comparable to CKD 4-5	No dose adjustment
Pibrentasvir exposure (AUC)	Reference	Mild increase	Comparable to CKD 4-5	No dose adjustment
Removal by dialysis	Not applicable	Minimal	Not significantly removed	No timing modification required

### Efficacy

Effective treatment of hepatitis C virus (HCV) infection is particularly important in patients with CKD, as viral eradication may reduce the risk of progressive liver disease and potentially confer additional renal benefits. (Bhattacharya et al., 2023) Glecaprevir/pibrentasvir demonstrates high and consistent antiviral efficacy in patients with chronic HCV infection and renal impairment across controlled clinical trials and large real-world cohorts.

In the EXPEDITION-4 phase III study, 104 patients with CKD stage 4–5, including a majority on dialysis, achieved a sustained virologic response (SVR) at 12 weeks post-treatment of 98%, with a favorable safety profile. Patients with various HCV genotypes were enrolled in the study. Genotype 1 accounted for 52% of the study population, genotype 2 for 16%, genotype 3 for 11%, and 21% of patients were infected with genotypes 4, 5, or 6. Regardless of genotype, patients treated with the G/P regimen achieved a high rate of virologic response (Gane et al., 2017) (**Table 2**).

EXPEDITION-5 (phase III study) enrolled 101 patients with CKD stage 3b–5 (approximately 76% had stage 5 and were undergoing hemodialysis or peritoneal dialysis) and observed an SVR12 rate of 97%, with consistent responses across genotypes and renal subgroups. The study included patients infected with HCV

genotypes 1–4. Similarly to EXPEDITION-4, a high rate of virologic response was observed independent of HCV genotype (Lawitz et al., 2020) (**Table 2**).

Moreover, analysis of 19 phase III clinical trials including approximately 4,612 patients confirmed an overall SVR12 rate of about 97.5%, with high SVR12 rates (97,7%) observed across various subgroups, including 217 patients with renal impairment (Xu et al., 2020) (**Table 2**).

Importantly, large real-world evidence from a nationwide hepatitis C registry in Taiwan (n=1,054) reported an SVR12 of 99.6% among patients with CKD, demonstrating that the high antiviral efficacy of G/P translates into routine clinical practice. Furthermore, antiviral therapy was associated with improvement in renal function, suggesting potential nephroprotective benefits. Notably, a significant reduction in proteinuria was observed following viral eradication (Wang et al., 2025) (**Table 2**).

In a retrospective, multicenter real-world cohort from Taiwan including patients with CKD stage 4 or 5, all 108 individuals treated with G/P achieved undetectable HCV RNA at the end of therapy, with SVR12 rates of 99.1% in the evaluable population and 100% in the per-protocol population. By CKD stage, SVR12 was 100% in stage 4 and 98.7% in stage 5 patients, confirming the high effectiveness of the regimen in this advanced renal disease cohort (C. Liu et al., 2020) (**Table 2**).

Smaller real-life cohort study, including CKD 4–5 on hemodialysis and end-stage renal disease populations, similarly documented high SVR12 rates (100%), confirming robust effectiveness in diverse clinical settings (Jasso-Baltazar et al., 2022) (**Table 2**).

In a retrospective cohort of 837 patients with chronic hepatitis C, including 102 individuals with chronic kidney disease (CKD), the efficacy and safety of direct-acting antiviral regimens were assessed, with particular emphasis on G/P. Treatment with G/P demonstrated high antiviral effectiveness across different stages of renal impairment. Among patients undergoing peritoneal dialysis, eight individuals received G/P therapy, and all achieved sustained virologic response at 12 weeks post-treatment (SVR12), corresponding to a 100% cure rate. Comparable outcomes were observed in patients treated with elbasvir/grazoprevir (Hung et al., 2024) (**Table 2**).

Collectively, these data indicate that glecaprevir/pibrentasvir provides consistently high antiviral efficacy in patients with CKD across a range of genotypes and renal subgroups, with clinical trial outcomes closely mirrored in real-world practice, without the need for dose adjustment or treatment prolongation.

**Table 2.** Comparative SVR12 of Glecaprevir/Pibrentasvir Across Clinical Trials and Real-World Studies in Patients (pts) with Renal Impairment

Study/Reference	Population	CKD stage/Dialysis	Treatment Duration	SVR12 (%)
EXPEDITION-4	104 pts	CKD 4-5 (82% on dialysis)	12 weeks	98,0
EXPEDITION-5	101 pts	CKD 3b-5 (76% on dialysis)	8-16 weeks	97,0
Phase III analysis	217 pts	Severe renal impairment	8-12 weeks	97,7
Taiwan Registry real - world	1054 pts	Early CKD & pre-ESRD	8 weeks	99,6
Taiwan multicenter CKD 4-5 cohort	108 pts	CKD 4-5	8-12 weeks	~100
Real-life cohort study	25 pts	CKD on hemodialysis	8 weeks	100
Retrospective cohort study	8 pts	CKD on peritoneal dialysis	8-12 weeks	100

### Safety

The fixed-dose G/P is generally well tolerated in patients with CKD, including those undergoing dialysis. Integrated analyses of phase II and III clinical trials, including EXPEDITION-4 and EXPEDITION-5, indicate that the most commonly reported adverse events (AEs) are fatigue, pruritus, nausea, and headache (Gane et al., 2017). Serious AEs considered related to G/P therapy are rare and occur at rates comparable to placebo (Xu et al., 2020).

Renal safety is particularly important in advanced CKD and dialysis populations (Yang et al., 2024). G/P is eliminated predominantly via the hepatobiliary route, with minimal renal excretion (<1%). Pharmacokinetic studies demonstrated only modest and clinically insignificant increases in systemic exposure in patients with severe renal impairment (X. Liu & Hu, 2021). Real-world evidence indicates that estimated

glomerular filtration rate (eGFR) remains stable, or may even improve slightly, during and after therapy in patients with CKD, suggesting minimal nephrotoxicity and potential renal benefits (Wang et al., 2025). These findings are consistent across CKD stages 3-5, including patients receiving hemodialysis or peritoneal dialysis, confirming that standard dosing is safe and does not require adjustment (Hung et al., 2024; Ryu et al., 2022).

G/P also exhibits a generally favorable drug–drug interaction (DDI) profile, which is an important consideration in clinical practice, especially among patients with CKD who often require multiple concomitant medications. According to the Summary of Product Characteristics (SmPC), glecaprevir and pibrentasvir are inhibitors of P-glycoprotein (P-gp), organic anion transporting polypeptides (OATP1B1/3) and breast cancer resistance protein (BCRP). Administration of G/P may increase plasma concentrations of certain drugs such as statins and digoxin. Conversely, the use of strong cytochrome P-450 (CYP) 3A and P-gp inducers, including rifampin, carbamazepine, St. John's wort (*Hypericum perforatum*), and phenobarbital, is contraindicated, as these agents may significantly reduce plasma levels of G/P, potentially leading to subtherapeutic antiviral exposure, insufficient treatment response, and decrease the chance of HCV eradication. G/P components are substrates of efflux transporters P-gp and BCRP, and glecaprevir is additionally a substrate of the transporters OATP1B1/3. Concomitant administration of OATP1B1/3 inhibitors, such as elvitegravir, ciclosporin, darunavir, and lopinavir, may increase systemic exposure to glecaprevir. In patients receiving tacrolimus, therapeutic drug monitoring is recommended, as co-administration with G/P may elevate tacrolimus plasma concentrations and necessitate dose adjustment (*Summary of Product Characteristics (SmPC) - (Emc) | 763*, n.d.; X. Liu & Hu, 2021).

Overall, real-world and pharmacokinetic data indicate that G/P is generally safe and associated with a low risk of clinically significant drug–drug interactions. Nevertheless, particular attention is required in patients receiving multiple concomitant medications (Curry et al., 2021). This is especially relevant in individuals with CKD/ESRD, who frequently require complex pharmacotherapy and therefore warrant careful review of concomitant therapies and appropriate monitoring (Sommer et al., 2020).

## Discussion

Patients with CKD and ESRD, including those requiring dialysis, represent a particularly challenging population in the management of coexisting chronic diseases. For many years, the treatment of HCV infection in this population was associated with substantial clinical limitations. Renal impairment may occur as an extrahepatic manifestation of HCV infection, but CKD itself—especially in patients undergoing long-term hemodialysis—also increases the risk of HCV acquisition due to repeated vascular access and healthcare exposure (Gane et al., 2017). Effective antiviral therapy is therefore of critical importance both for individual patient outcomes and for infection control within dialysis units (*Updated Recommendations on Treatment of Adolescents and Children with Chronic HCV Infection, and HCV Simplified Service Delivery and HCV Diagnostics*, 2022).

For many years, treatment strategies for HCV infection yielded unsatisfactory outcomes in this patient population. Prior to the introduction of DAAs, the historical regimen based on pegylated interferon combined with ribavirin was used reluctantly in clinical practice due to its limited efficacy and suboptimal safety profile, particularly among patients with ESRD and those undergoing dialysis. In addition, these therapies were associated with a high incidence of adverse events. Ribavirin required dose modification in advanced renal impairment and was frequently associated with hematologic toxicity, complicating management in this population (Fabrizi et al., 2021).

The introduction of pangenotypic DAAs in 2013 fundamentally transformed HCV management in patients with CKD. These agents achieve high SVR rates and demonstrate favorable safety profiles. Owing to minimal renal elimination in most currently available regimens, dose adjustment is generally unnecessary in patients with CKD or ESRD, including those undergoing dialysis (Jasso-Baltazar et al., 2022). Notably, some studies have demonstrated that treatment with the G/P regimen, followed by successful HCV eradication, was associated with a reduction in proteinuria and improvement in renal function in the studied patient population (Wang et al., 2025).

According to the 2022 clinical practice guideline from *Kidney Disease: Improving Global Outcomes*, pangenotypic DAA regimens are recommended as first-line therapy for patients with CKD stages G1–G5, including, those with kidney failure requiring dialysis and kidney transplant recipients. In circumstances where pangenotypic agents are unavailable, genotype-specific regimens (e.g., grazoprevir/elbasvir or daclatasvir/asunaprevir) may be considered; however, their antiviral activity is restricted to specific HCV genotypes and subtypes. Importantly, grazoprevir/elbasvir-based therapy can be safely administered in patients

with CKD stages G4–G5 and in those with kidney failure requiring maintenance dialysis, owing to hepatic metabolism via CYP3A and predominant biliary/fecal excretion. Nevertheless, its clinical applicability remains limited by activity confined to HCV genotypes 1 and 4 (Jadoul et al., 2022).

In 2019, the **U.S. Food and Drug Administration (FDA)** expanded approval for sofosbuvir-containing regimens to include patients with severe renal impairment (eGFR <30 mL/min/1.73 m<sup>2</sup>) and those undergoing hemodialysis. Previously, sofosbuvir use had been limited only to patients with preserved or moderately impaired kidney function (CKD stages G1–G3b and eGFR ≥30 mL/min/1.73 m<sup>2</sup>) (Fabrizi et al., 2021). Accumulating real-world evidence has demonstrated high SVR rates in this population, ranging from 94% to 100% depending on CKD stage, thereby confirming the effectiveness of sofosbuvir-based therapy even in advanced CKD (Fabrizi et al., 2021; Mohammad & Khan, 2024).

However, the pharmacokinetic profile of sofosbuvir warrants careful consideration in patients with kidney failure, as approximately 80% of the drug and its predominant inactive metabolite are eliminated via renal excretion. This characteristic may necessitate dose adjustment and careful clinical monitoring in individuals with severely reduced kidney function (Fabrizi et al., 2021).

In this context, G/P therapy appears to represent a more favorable option, as it undergoes predominantly hepatic metabolism with negligible renal elimination and therefore does not adversely affect kidney function. Moreover, large real-world cohorts, including a nationwide registry from Taiwan (n = 1,054), demonstrated not only excellent virologic efficacy in HCV infection but also reductions in proteinuria and stabilization or improvement of renal function parameters following treatment. These findings suggest that beyond viral eradication, G/P therapy may confer additional renal benefits, potentially through reduction of HCV-mediated glomerular injury and systemic inflammation (Wang et al., 2025).

Our results indicate that SVR12 rates with G/P therapy were consistently high (97–100%) across CKD stages, independent of dialysis status or HCV genotype.

This consistency underscores the robustness of G/P therapy in a population historically considered difficult to treat. Safety outcomes reported in these studies have likewise been favorable, with no unexpected adverse events and stable renal function during treatment (Yen et al., 2020). Collectively, the available evidence supports the preferential use of pangenotypic DAAs—particularly G/P—in patients with advanced CKD or ESRD, especially when compared with genotype-restricted regimens or therapies characterized by substantial renal elimination. These findings are aligned with current KDIGO recommendations advocating pangenotypic regimens as first-line therapy in this population (Jadoul et al., 2022).

### Limitations

Despite the evidence supporting the efficacy and safety of glecaprevir/pibrentasvir in patients with CKD, several limitations should be acknowledged. Sample sizes in some subgroups, particularly patients with stage 4–5 CKD or those on dialysis, remain relatively small, potentially limiting the generalizability of the findings. Additionally, the follow-up period in many studies is short, which restricts the assessment of long-term renal outcomes, durability of SVR, and potential late-emerging adverse events. Finally, while improvements in renal parameters have been observed, the underlying mechanisms remain speculative, and causality cannot be definitively established from current data.

### Conclusions

The available clinical trial and real-world evidence demonstrates that G/P provides consistently high sustained virologic response rates and a favorable safety profile in patients with chronic kidney disease, including those with advanced renal impairment and dialysis dependence. In addition to effective viral eradication, emerging data suggest potential stabilization or improvement of renal parameters following treatment. Overall, G/P represents a particularly suitable therapeutic option in patients with CKD, given its high antiviral efficacy, favorable safety profile, and minimal renal elimination. Future research should aim to address these gaps by conducting prospective, multicenter studies with larger sample sizes and longer follow-up periods. Specifically, investigations into the long-term nephroprotective effects of HCV eradication with G/P, including its impact on proteinuria, eGFR decline, and progression to ESRD, are warranted.

## REFERENCES

1. Bhattacharya, D., Aronsohn, A., Price, J., Lo Re, V., Heald, J., Demisashi, G., Durzy, E., Davis-Owino, A., Tynes, S., & American Association for the Study of Liver Diseases–Infectious Diseases Society of America HCV Guidance Panel. (2023). Hepatitis C guidance 2023 update: American Association for the Study of Liver Diseases–Infectious Diseases Society of America recommendations for testing, managing, and treating hepatitis C virus infection. *Clinical Infectious Diseases*, *ciad319*. <https://doi.org/10.1093/cid/ciad319>
2. Curry, M. P., Flamm, S. L., Milligan, S., Tsai, N., Wick, N., Younossi, Z., & Afdhal, N. H. (2021). Prevalence of drug-drug interactions with pangenotypic direct-acting antivirals for hepatitis C and real-world care management in the United States: A retrospective observational study. *Journal of Managed Care & Specialty Pharmacy*, *27*(9), 1239–1248. <https://doi.org/10.18553/jmcp.2021.20550>
3. Fabrizi, F., Cerutti, R., & Messa, P. (2021). An updated view on the antiviral therapy of hepatitis C in chronic kidney disease. *Pathogens*, *10*(11), Article 1381. <https://doi.org/10.3390/pathogens10111381>
4. Gane, E., Lawitz, E., Pugatch, D., Papatheodoridis, G., Bräu, N., Brown, A., Pol, S., Leroy, V., Persico, M., Moreno, C., Colombo, M., Yoshida, E. M., Nelson, D. R., Collins, C., Lei, Y., Kosloski, M., & Mensa, F. J. (2017). Glecaprevir and pibrentasvir in patients with HCV and severe renal impairment. *New England Journal of Medicine*, *377*(15), 1448–1455. <https://doi.org/10.1056/NEJMoa1704053>
5. Glecaprevir/pibrentasvir 100 mg/40 mg film-coated tablets—Summary of product characteristics (SmPC)—(emc) | 763. (n.d.). Retrieved March 1, 2026, from <https://www.medicines.org.uk/emc/product/763/smpc>
6. Hung, H.-Y., Hung, W.-L., Gu, Y., & Chen, C.-Y. (2024). Direct-acting antivirals in hepatitis C treatment for renal impairment: Liver safety concerns and effectiveness in peritoneal dialysis. *Biomedicines*, *13*(1). <https://doi.org/10.3390/biomedicines13010055>
7. IDSA. (n.d.). *HCV guidance*. Retrieved March 1, 2026, from <https://www.idsociety.org/practice-guideline/hcv-guidance/>
8. Jadoul, M., Awan, A. A., Berenguer, M. C., Bruchfeld, A., Fabrizi, F., Goldberg, D. S., Jia, J., Kamar, N., Mohamed, R., Pessôa, M. G., Pol, S., Sise, M. E., & Martin, P. (2022). KDIGO 2022 clinical practice guideline for the prevention, diagnosis, evaluation, and treatment of hepatitis C in chronic kidney disease. *Kidney International*, *102*(6), S129–S205. <https://doi.org/10.1016/j.kint.2022.07.013>
9. Jasso-Baltazar, E. A., Solís-Galindo, F. A., Muñoz-Hernández, M. A., & Quintal-Medina, I. A. (2022). Sustained virologic response in patients with hepatitis C and chronic kidney disease. *Revista Medica Del Instituto Mexicano Del Seguro Social*, *60*(3), 283–288.
10. Lawitz, E., Flisiak, R., Abunimeh, M., Sise, M. E., Park, J. Y., Kaskas, M., Bruchfeld, A., Wörns, M.-A., Aglitti, A., Zamor, P. J., Xue, Z., Schnell, G., Jalundhwala, Y. J., Porcalla, A., Mensa, F. J., & Persico, M. (2020). Efficacy and safety of glecaprevir/pibrentasvir in renally impaired patients with chronic HCV infection. *Liver International*, *40*(5), 1032–1041. <https://doi.org/10.1111/liv.14320>
11. Liu, C., Yang, S., Peng, C., Lin, W., Liu, C., Su, T., Tseng, T., Chen, P., Chen, D., & Kao, J. (2020). Glecaprevir/pibrentasvir for patients with chronic hepatitis C virus infection and severe renal impairment. *Journal of Viral Hepatitis*, *27*(6), 568–575. <https://doi.org/10.1111/jvh.13265>
12. Liu, X., & Hu, P. (2021). Efficacy and safety of glecaprevir/pibrentasvir in patients with chronic HCV infection. *Journal of Clinical and Translational Hepatology*, *9*(1), 125–132. <https://doi.org/10.14218/JCTH.2020.00078>
13. Mohammad, N., & Khan, D. (2024). Efficacy of sofosbuvir and velpatasvir combination in the treatment of hepatitis C virus (HCV) in chronic kidney disease (CKD) patients. *Cureus*, *16*(5), Article e60861. <https://doi.org/10.7759/cureus.60861>
14. Patients with renal impairment – HCV guidance. (n.d.). *HCVGuidelines.org*. Retrieved March 1, 2026, from <https://www.hcvguidelines.org/guidance/patients-with-renal-impairment/>
15. Ryu, J. E., Song, M. J., Kim, S.-H., Kwon, J. H., Yoo, S. H., Nam, S. W., Nam, H. C., Kim, H. Y., Kim, C. W., Yang, H., Bae, S. H., Song, D. S., Chang, U. I., Yang, J. M., Lee, S. W., Lee, H. L., Lee, S. K., Sung, P. S., Jang, J. W., . . . Yoon, S. K. (2022). Safety and effectiveness of direct-acting antivirals in patients with chronic hepatitis C and chronic kidney disease. *The Korean Journal of Internal Medicine*, *37*(5), 958–968. <https://doi.org/10.3904/kjim.2021.486>
16. Sommer, J., Seeling, A., & Rupprecht, H. (2020). Adverse drug events in patients with chronic kidney disease associated with multiple drug interactions and polypharmacy. *Drugs & Aging*, *37*(5), 359–372. <https://doi.org/10.1007/s40266-020-00747-0>
17. World Health Organization. (2022). *Updated recommendations on treatment of adolescents and children with chronic HCV infection, and HCV simplified service delivery and HCV diagnostics* (1st ed.).
18. Wang, S.-J., Huang, C.-F., Chang, T.-S., Lo, C.-C., Hung, C.-H., Huang, C.-W., Chong, L.-W., Cheng, P.-N., Yeh, M.-L., Peng, C.-Y., Cheng, C.-Y., Huang, J.-F., Bair, M.-J., Lin, C.-L., Yang, C.-C., Kuo, H.-T., Hsieh, T.-Y., Lee, T.-H., Lee, P.-L., . . . Yu, M.-L. (2025). Real-world efficacy and safety of universal 8-week glecaprevir/pibrentasvir in patients with chronic hepatitis C with early chronic kidney disease or pre-end-stage renal disease: Insights from a nationwide hepatitis C virus registry in Taiwan. *The Kaohsiung Journal of Medical Sciences*, *41*(2), Article e12929. <https://doi.org/10.1002/kjm2.12929>

19. Xu, H.-Q., Wang, C.-G., Xiao, P., & Gao, Y.-H. (2020). Efficacy and safety of glecaprevir/pibrentasvir for chronic hepatitis C patients: A systematic review and meta-analysis. *Journal of Clinical and Translational Hepatology*, 8(3), 267–276. <https://doi.org/10.14218/JCTH.2020.00047>
20. Yang, C.-C., Huang, C.-F., Chang, T.-S., Lo, C.-C., Hung, C.-H., Huang, C.-W., Chong, L.-W., Cheng, P.-N., Yeh, M.-L., Peng, C.-Y., Cheng, C.-Y., Huang, J.-F., Bair, M.-J., Lin, C.-L., Yang, C.-C., Wang, S.-J., Hsieh, T.-Y., Lee, T.-H., Lee, P.-L., . . . Yu, M.-L. (2024). Real-world efficacy and safety of universal 8-week glecaprevir/pibrentasvir for treatment-naïve patients from a nationwide HCV registry in Taiwan. *Infectious Diseases and Therapy*, 13(6), 1199–1213. <https://doi.org/10.1007/s40121-024-00968-5>
21. Yen, H.-H., Su, P.-Y., Zeng, Y.-H., Liu, I.-L., Huang, S.-P., Hsu, Y.-C., Chen, Y.-Y., Yang, C.-W., Wu, S.-S., & Chou, K.-C. (2020). Glecaprevir–pibrentasvir for chronic hepatitis C: Comparing treatment effect in patients with and without end-stage renal disease in a real-world setting. *PLOS ONE*, 15(8), Article e0237582. <https://doi.org/10.1371/journal.pone.0237582>