Hemlibra in Patients with Renal Impairment or Requiring Dialysis

This article responds to your request for information on Hemlibra® (emicizumab) in patients requiring dialysis. This response was developed according to the principles of evidence-based medicine and includes information from pharmacokinetic studies and case reports.

In brief

- Hemlibra is not contraindicated in patients with renal impairment or requiring dialysis, however no dedicated studies on the PK, safety, or efficacy of Hemlibra in these patients have been conducted.
    - Mild or moderate renal impairment does not appear to impact the PK of Hemlibra. No dose adjustments are recommended in patients with renal impairment.
- Hemlibra has a molecular mass of approximately 146 kDa and is expected to be retained by dialysis membranes.
- Two case reports have been published on the use of Hemlibra in patients with severe hemophilia A requiring haemodialysis. In both both patients, Hemlibra plasma levels remained stable throughout HD.

Abbreviations

CrCL=creatinine clearance

ESRD=end stage renal disease

FVIII=factor VIII

HD=haemodialysis

kDa=kilodaltons

PK=pharmacokinetics

rFVIII=factor VIII

Considerations for the use of Hemlibra in patients with renal impairment or requiring dialysis

The use of Hemlibra has not been formally assessed in patients with renal impairment.[1] There are limited data available on the use of Hemlibra in patients with mild to moderate renal impairment. No data are available on the use of Hemlibra in patients with severe renal impairment or requiring dialysis.

Administering Hemlibra to patients with renal impairment or requiring dialysis is not contraindicated, however it would be a decision to be made by the treating physician, and should be based upon an appropriate risk-benefit assessment.

Pharmacokinetics of Hemlibra in patients with renal impairment

No dedicated studies on the effect of renal impairment on the PK of Hemlibra have been conducted.[1] In a population PK analysis, most patients had normal renal function:

- Normal renal function (CrCL ≥90mL/min) — 332 patients
- Mild renal impairment (CrCL 60-89 mL/min) — 27 patients

- Moderate renal impairment (CrCL 30-59 mL/min) — 2 patients
- No patients had severe renal impairment.

Mild or moderate renal impairment did not appear to have an impact on the PK of Hemlibra.[1] No dose adjustments are recommended in patients with renal impairment.

Metabolism of Hemlibra

The metabolism of Hemlibra has not been studied, however as Hemlibra is a monoclonal antibody it is expected that it is cleared via catabolism rather than renal or hepatic metabolism.[1]

Permeability of dialysis membranes

Dialysis membranes are typically permeable to molecules up to 15 kDa.[2] Larger molecules are retained by dialysis membranes.

Hemlibra is a recombinant bispecific monoclonal antibody with a molecular mass of approximately 146 kDa.[3] Therefore it is not expected that Hemlibra would be filtered out and it should be retained in the serum during and following dialysis.

Case reports on the use of Hemlibra in patients requiring dialysis

Hemlibra initiation in a patient undergoing chronic intermittent HD

Weise et al. published a case report of a 64-year-old male patient with severe haemophilia A undergoing chronic intermittent HD who was newly started on Hemlibra.[4] Laboratory parameters, including FVIII, Hemlibra plasma levels and thrombin generation, were assessed before and up to 122 days after Hemlibra initiation.

Hemlibra was initiated on a HD-free day and a bolus of 200 IU rFVIII was administered after every HD session for 13 days after Hemlibra initiation to prevent bleeding during the loading period.[4] Haemodialysis was run without heparin and no arteriovenous shunt dysfunction occurred.

Hemlibra plasma levels remained stable throughout HD without washout or accumulation.[4] The patient remained free of bleeds.

Commencing HD in a patient being treated with Hemlibra

Funding and Rix reported on a patient with severe haemophilia A with inhibitors and progressive renal failure, being treated with Hemlibra.[5] The patient had substantial proteinuria due to AA-amyloidosis and developed ESRD, requiring chronic intermittent HD.

Hemlibra plasma levels were measured regularly in the two years leading up to HD, and before and after HD procedures on four occassions.[5] Bleeding episodes and treatment was recorded as a measure of Hemlibra efficacy.

The authors concluded that Hemlibra remains stable and effective as prophylaxis during progression of renal impairment and with HD.[5]

References

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4. Weise M, Siegemund A, Böhme L, et al. Emicizumab treatment in chronic intermittent haemodialysis. Haemophilia 2022;28:e20-e22. https://www.ncbi.nlm.nih.gov/pubmed/34687109

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