# Vutrisiran: Use in Patients Undergoing Dialysis

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## SUMMARY


- Patients with severe renal impairment or ESRD were excluded from the phase 3 HELIOS-A and HELIOS-B studies.[1,2] However, patients developing an eGFR of <30 mL/min/1.73 $m^2$ after inclusion remained in the HELIOS-B study.[3]
- There is limited data available on the use of vutrisiran in patients on dialysis.
- An analysis was conducted to assess the effect of vutrisiran on renal outcomes and the impact of baseline renal function amongst patients in HELIOS-B. There were 2 patients in the vutrisiran arm and 2 patients in the placebo arm that started renal replacement therapy with dialysis during the double-blind period.[3]
- A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any safety concerns with the use of vutrisiran in patients with severe renal impairment or ESRD.[4,5]


## INDEX



## CLINICAL DATA

### Clinical Pharmacology Information

Across various clinical pharmacology studies including both healthy subjects and patients with hATTR-PN, the mean serum $t_{1/2}$ ranged from 4 to 7.5 hours following subcutaneous administration of vutrisiran. After reaching the $C_{max}$, vutrisiran concentration declined rapidly to the LLOQ by 24 to 48 hours. Clinical pharmacology data have shown that renal clearance is not a major route of elimination of vutrisiran.[6]

### HELIOS-B Study

HELIOS-B was a phase 3, global, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy and safety of vutrisiran in patients with ATTR-CM, including both hATTR and wtATTR. Patients were randomized (1:1) to receive either vutrisiran 25 mg (n=326) or

placebo (n=329) every 3 months by subcutaneous injection for up to 36 months. The primary endpoint was the composite endpoint of all-cause mortality and recurrent CV events (CV hospitalizations and urgent heart failure visits) at the end of the double-blind period in the overall population and in the monotherapy population (patients not receiving tafamidis at baseline). After the double-blind treatment period, all remaining eligible patients were allowed to receive vutrisiran in an OLE for up to 24 months.[7]

**HELIOS-B Post-hoc Analysis**

An analysis was conducted to assess the effect of vutrisiran on renal outcomes and the impact of baseline renal function among patients in HELIOS-B. Adverse events in patients who advanced to CKD stage ≥4 were assessed [vutrisiran (n=31) and placebo (n=32)]; four patients initiated renal replacement therapy with dialysis during the double-blind period (2 patients in the vutrisiran arm and 2 patients in the placebo arm). Reduction in TTR levels during vutrisiran treatment remained consistent after dialysis was initiated in these patients. One patient receiving dialysis in the vutrisiran arm died on day 939 and 1 patient survived and continued into the OLE. The 2 patients receiving dialysis in the placebo arm died during the DB period (day 89 and day 98).[3]

## GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any safety concerns with the use of vutrisiran in patients with severe renal impairment or ESRD.[4,5]

## AMVUTTRA PRESCRIBING INFORMATION – RELEVANT CONTENT

The **USE IN SPECIFIC POPULATIONS** section provides the following information[8]:

***Renal Impairment***

*No dose adjustment is recommended in patients with mild or moderate renal impairment (estimated glomerular filtration rate [eGFR] ≥30 to <90 mL/min/1.73 $m^2$). AMVUTTRA has not been studied in patients with severe renal impairment or end-stage renal disease.*

The **CLINICAL PHARMACOLOGY** section provides the following information[8]:

***Pharmacokinetics***

*The pharmacokinetic (PK) properties of AMVUTTRA were evaluated following a single dose in healthy subjects and multiple doses in patients with hATTR amyloidosis, as summarized in Table 2.*

***Table 2: Pharmacokinetic Parameters of Vutrisiran***

| | ***Vutrisiran*** |
|---|---|
| ***General Information*** | |
| ***Dose Proportionality*** | *Vutrisiran $C_{max}$ showed dose proportional increase while $AUC_{last}$ and $AUC_{inf}$ were slightly more than dose proportional following single subcutaneous doses ranging from 5 to 300 mg (i.e., 0.2 to 12 times the recommended dose)* |
| ***Accumulation*** | *No accumulation of vutrisiran was observed in plasma after repeated every 3 months dosage[a]* |
| ***Absorption*** | |

| | |
|---|---|
| ***$T_{max}$ [Median (Range)]*** | *4 (0.17, 12.0) hours[b]* |
| ***Distribution*** | |
| ***Estimated Vd/F (%RSE)*** | *10.1 (5.8) L[c]* |
| ***Protein Binding*** | *80%[d]* |
| ***Organ Distribution*** | *Vutrisiran distributes primarily to the liver after subcutaneous dosing* |
| ***Elimination*** | |
| ***Half-Life [Median (Range)]*** | *5.2 (2.2, 6.4) hours[b]* |
| ***Apparent Clearance [Median (Range)]*** | *21.4 (19.8, 30) L/hour[b]* |
| ***Metabolism*** | |
| ***Primary Pathway*** | *Vutrisiran is metabolized by endo- and exonucleases to short nucleotide fragments of varying sizes within the liver* |
| ***Excretion*** | |
| ***Primary Pathway*** | *The mean fraction of unchanged vutrisiran eliminated in urine was approximately 19.4% at the recommended dose of 25 mg. The mean renal clearance of vutrisiran ranged from 4.5 to 5.7 L/hour[e]* |

*$AUC_{inf}$ = area under the concentration-time curve from the time of dosing extrapolated to infinity; $AUC_{last}$ = area under the concentration-time curve from the time of dosing to the last measurable concentration; $C_{max}$ = maximum plasma concentration; CV = coefficient of variation; RSE = relative standard error; $T_{max}$ = time to maximum concentration; Vd/F = apparent volume of distribution*

*[a]After 25 mg every 3 months dosage in hATTR amyloidosis patients*

*[b]After 25 mg single dose in healthy subjects*

*[c]Based on population PK model estimation*

*[d]Vutrisiran plasma protein binding was concentration-dependent and decreased with increasing vutrisiran concentrations (from 78% at 0.5 mcg/mL to 19% at 50 mcg/mL)*

*[e]After single subcutaneous vutrisiran dose from 5 to 300 mg (i.e., 0.2 to 12 times the recommended dose) in healthy subjects*

## ABBREVIATIONS

$AUC_{0-24}$ = area under the concentration time curve from 0 to 24 hours; $AUC_{inf}$ = area under the concentration-time curve from the time of dosing extrapolated to infinity; $AUC_{last}$ = area under the concentration-time curve from the time of dosing to the last measurable concentration; $C_{max}$ = maximum plasma concentration; CV = coefficient of variation; DB = double-blind; ESRD = end-stage renal disease; hATTR-PN = hereditary transthyretin amyloidosis with polyneuropathy; LLOQ = lower limit of quantification; OLE = open-label extension; PD = pharmacodynamics; PK = pharmacokinetics; RSE = relative standard error; $t_{1/2}$ = half-life; $T_{max}$ = time to maximum concentration; TTR = transthyretin; Vd/F = apparent volume of distribution.

*Updated 13 May 2026*

## REFERENCES


1. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2300015.
2. Protocol for: Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. 2025;392(1):33-44. doi:10.1056/NEJMoa2409134
3. Sheikh FH, Dang J, Fontana M, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy and renal Impairment: Analyses from HELIOS-B. *J Card Fail*. 2026;32(5):853-863. doi:10.1016/j.cardfail.2026.02.049
4. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2400036.
5. Alnylam Pharmaceuticals. Data on file. MED-ALL-VUTRI-2600002.
6. European Medicines Agency. Amvuttra : EPAR - Public Assessment Report. Published July 21, 2022. Accessed May 13, 2026. https://www.ema.europa.eu/en/documents/assessment-report/amvuttra-epar-public-assessment-report_en.pdf.
7. Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. 2025;392(1):33-44. doi:10.1056/NEJMoa2409134
8. AMVUTTRA (vutrisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.