
RENAL CARE

# ELISIO™ HX

## A NOVEL SHARP CUT-OFF DIALYZER

NIPRO MEDICAL EUROPE


# A novel sharp cut-off, next-generation HD dialyzer

## Elisio™ HX

Chronic kidney disease (CKD) affects more than 10% of the world's population. For end stage renal disease patients, dialysis is one of the main life-sustaining treatments. However, **dialysis patients have several comorbidities and variable medical needs**.

**Inflammation** is at the core of the CKD leading to protein energy wasting, **anemia, malnutrition and cardiovascular (CV) diseases**.[1]

**Sarcopenia**, characterized by the loss of muscle mass and **frailty** also **increases CV risk and overall mortality**.[2]

With the continuous advancement in dialysis technology, a wider range of uremic toxins can be cleared in patients. High volume HDF has become the gold standard in several countries with superior survival rates.[3]

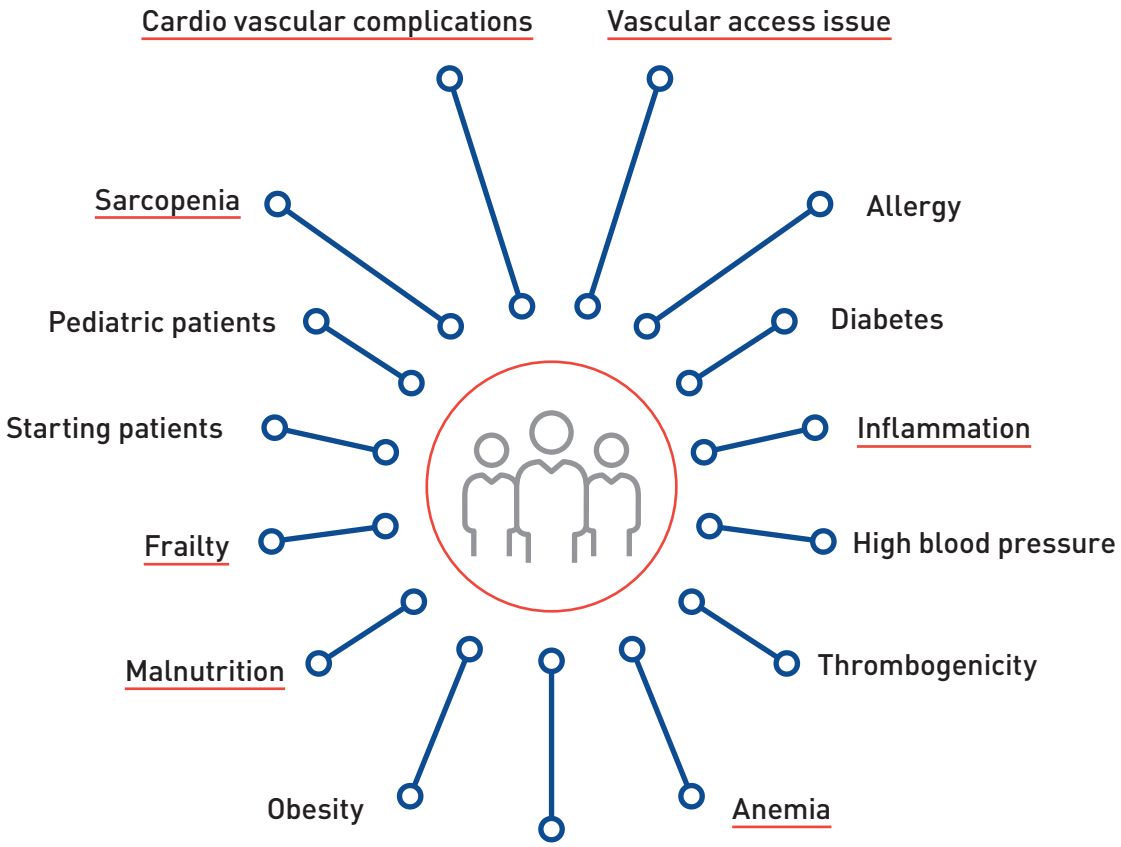
However, some patients are **not eligible for the HDF treatment** due to:

- **unsuitable vascular access**

single needle, malfunctioning central venous catheter, new fistula, low access flow not permitting the blood flow of at least 300 mL/min

- **inability to reach the efficient convective volumes (> 25 L post dilution)**[4]
- **clotting problems**
- **high hematocrit levels**

**For this wide array of patients** with variable medical needs, the best dialyzer should lose minimal albumin while maintaining high clearance of uremic toxins.[1]



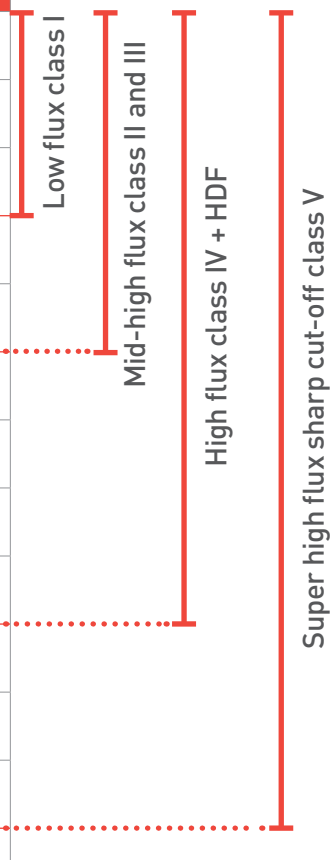

Patients with residual renal function

**Nipro's novel super high flux sharp cut-off dialyzer, Elisio HX, with the combination of a bigger pore size and a specific geometry, is designed to remove a wide range of middle molecule uremic toxins (12-60 kDa) which have serious clinical impact on patients.[2]**

## Japanese classification of dialyzers

In the absence of HDF, conventional HD with high flux dialyzers fall short in removing **larger middle molecule uremic toxins**. To overcome this limitation, the **super high flux dialyzers** with bigger pore sizes are introduced. In Japan, this class of dialyzers – also known as high-performance membranes – are used for the treatment of more than 90% of patients on hemodialysis and are associated with **higher survival rates**.[5]

| Uremic toxin | Molecular weight* |
|---|---|
| Urea | 60 Da |
| Phosphate | 96 Da |
| PTH | 9500 Da |
| Beta-2 microglobulin | 11.8 kDa |
| Myoglobin | 17 kDa |
| Complement factor D | 23.7 kDa |
| Interleukin-6 | 24.5 kDa |
| Kappa free light chain | 25 kDa |
| Alpha-1 microglobulin | 33 kDa |
| YKL-40 | 40 kDa |
| Pentraxin 3 | 41 kDa |
| Lambda free light chain | 45 kDa |
| Albumin | 67 kDa |




*approximate values

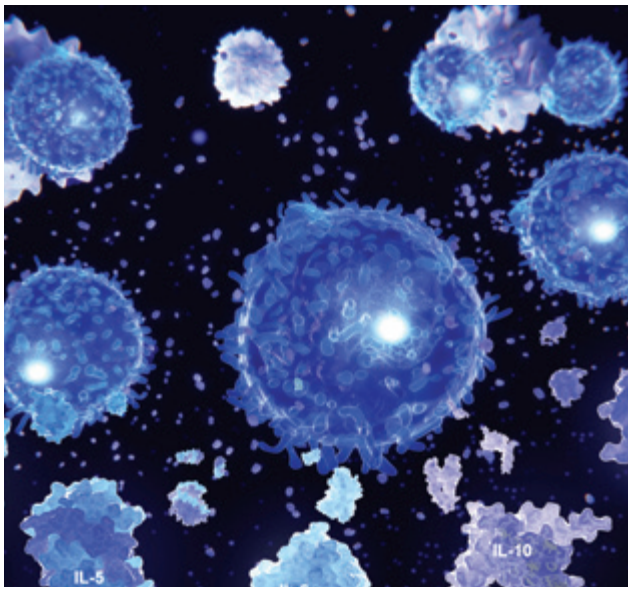
# Efficacy of class V dialyzers in removing clinically impactful middle molecules

## CLINICAL IMPACT OF MIDDLE MOLECULES

### Inflammation

Inflammation is at the **core of the CKD pathology** leading to several complications. A **21% increase of 1st year mortality rate** has been shown **for high levels of C-reactive protein**.[6]

The RISCAVID study has demonstrated a higher **CV and all-cause mortality** risk with higher levels of **IL-6 and IL-8**.[7] **IL-18** is also linked with a higher risk of **cardio vascular mortality** in dialysis patients.[8]




### Vascular calcification

An association between **serum Beta-2 microglobulin (B2M) levels and vascular calcification** has been observed suggesting the role of B2M in CV events.[9] A study with a follow-up of 6 years demonstrated this molecule as an independent predictor of **all-cause mortality**.[10]

Classically, the elevated B2M can deposit in the form of protein fibrils in various places in patients known as the **dialysis-related amyloidosis**. The effect of accumulated modified B2M is the stimulation of inflammatory molecules in the surrounding tissue leading to **tendonitis, back and neck pain** in patients.[11]

### Maladaptive immunity

Plasma levels of free light chains (FLCs) increase as a result of their diminished removal in CKD patients or their excess production in diseases such as multiple myeloma.[12] The increased serum levels of FLC can interfere with the apoptosis of leukocytes leading to **increased inflammation**.[13] The **free kappa and lambda light chains** are associated with **vascular calcification**, and a higher level of the light chains may be a risk factor for **increased mortality** in CKD patients.[14-15]

## Oxidative stress

In CKD, chronic inflammation, oxidative stress, and accumulation of the uremic toxins lead to the accumulation of the **advanced glycation end products (AGEs)** which can in turn aggravate the **oxidative stress and inflammation**. This vicious circle can lead to decreased muscle mass and the advancement of sarcopenia.[2]

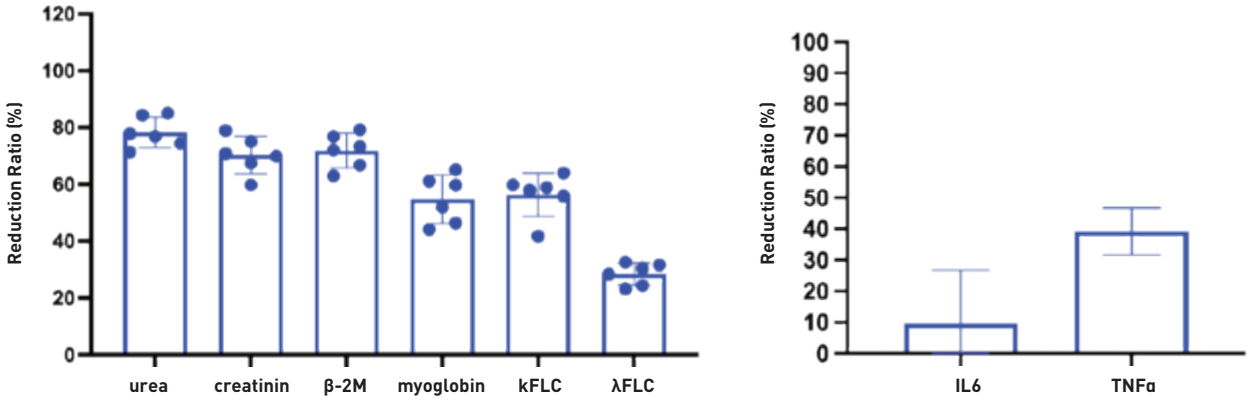
## Dialysis quality dose

The glycoprotein YKL-40, an inflammatory mediator, is a significant predictor of all-cause and CV mortality in dialysis patients.[16]

The **lower serum YKL-40 concentration is associated with the higher dose (Kt/V) in dialysis**.[17] The use of the high convective volumes in this study to increase the efficiency of dialysis highlights that the **removal of middle molecules requires a higher dialysis efficacy**.

# Optimal removal of middle molecule uremic toxins by Elisio HX

The objective of this prospective, single-center study was to determine the performance of the Elisio HX dialyzer in the removal of the following uremic toxins in 6 maintenance hemodialysis patients:[18]




Blood flow rate: 300 mL/min ; Dialysate flow rate: 500 mL/min; Treatment time: 240 min; N=6. Blood was collected pre- and post-dialysis to measure the reduction ratios.

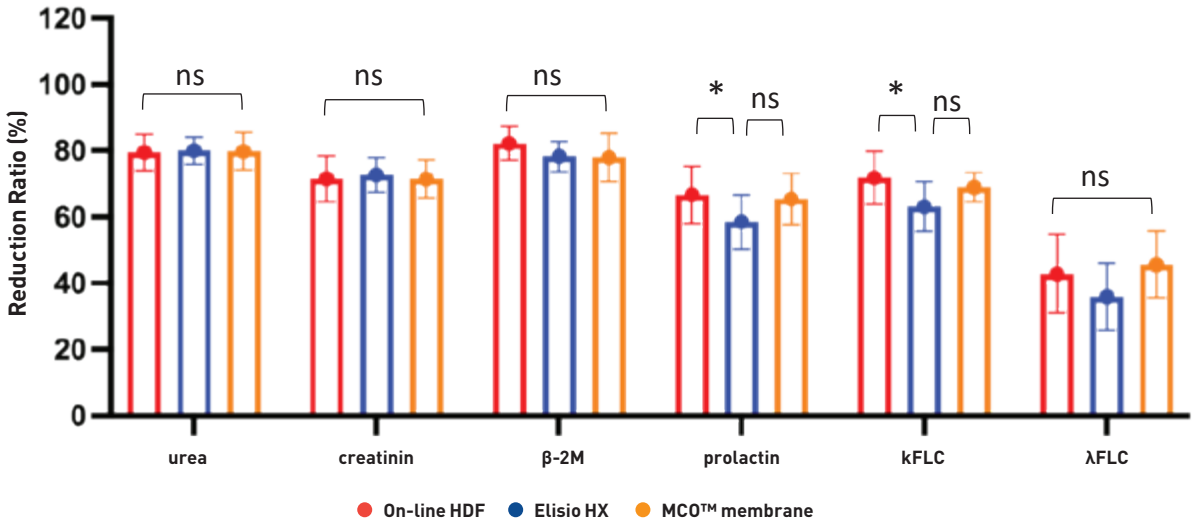
## Removal of high middle molecule uremic toxins:

- reduces inflammation and oxidative stress
- improves immune response
- improves cardiovascular co-morbidities
- improves quality of life

# Similar to hemodiafiltration and the medium cut-off membrane

This prospective, randomized, cross-over, single-center study was performed to determine the safety and efficacy of Elisio HX in comparison to a medium cut-off membrane and on-line HDF. 14 patients receiving HDF as baseline treatment were randomized to either Elisio HX or the medium cut-off membrane for 1 week. The results demonstrate that the removal of the middle molecules was mainly similar between Elisio HX and the medium cut-off as well as between Elisio HX and on-line HDF.[19]

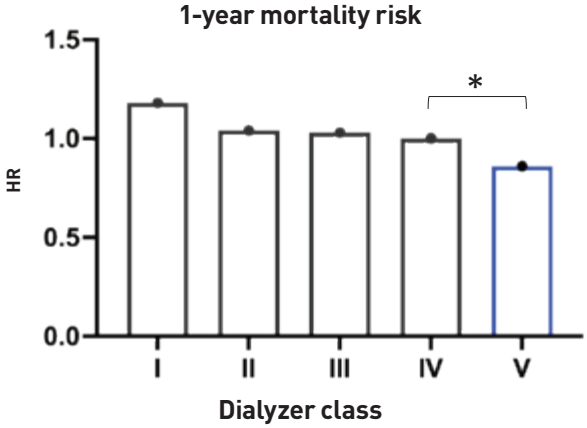
**This study indicates that the treatment with Elisio HX is a suitable alternative to on-line HDF and can be utilized for patients for whom HDF treatment is not possible.**




N=14; blood flow > 370 mL/min; replacement volume > 21 L; *p< 0.05; ns: not significant

# Higher dialyzer performance, higher survival

Japan has been using a distinct 5-grade classification of the dialyzers based on the clearance of B2M at the blood and dialysate flow of 200 and 500 mL/min respectively. Based on this classification, **class IV and V**, also known as **super high flux** dialyzers, are identified by B2M clearance of <70, ⩾ 70, and are used for the treatment of more than 90% of patients.



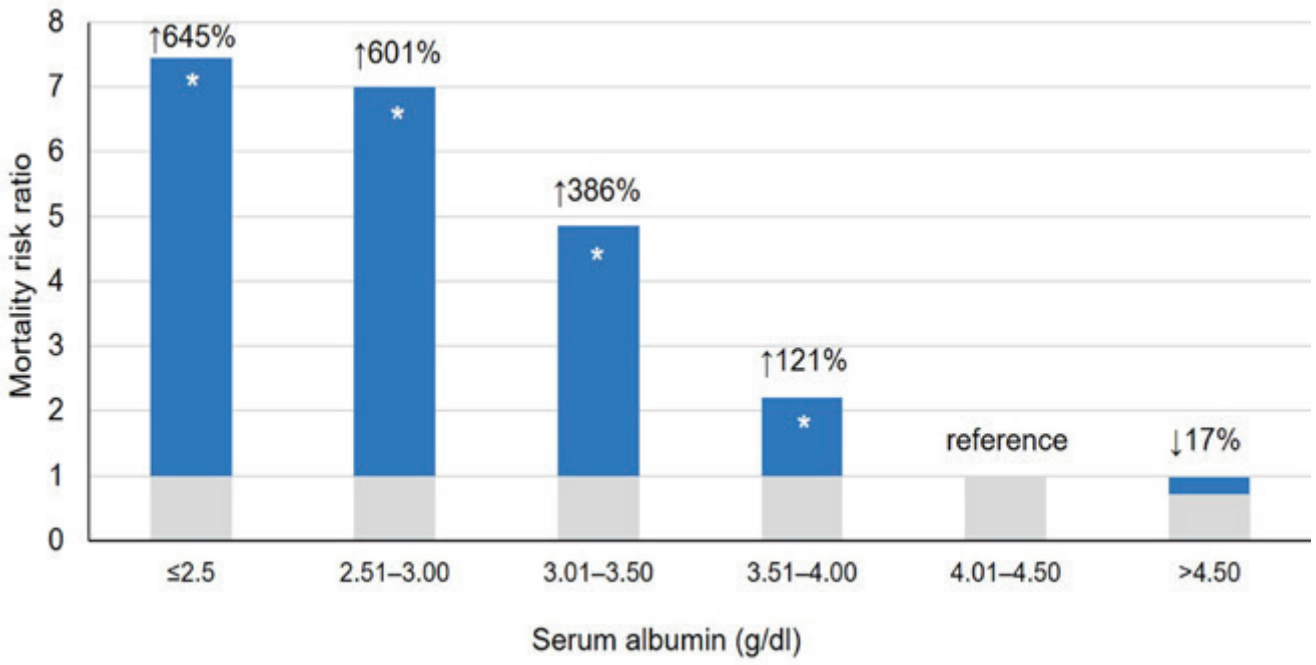

Using the nation-wide data of the Japanese society for dialysis therapy renal data registry in a large cohort of more than 200,000 patients, **this study has revealed a significantly lower risk of all-cause mortality for class V super high flux dialyzers including the sharp cut-off Elisio HX**.[5]

Graph from Abe et al.[5] 1-year all-cause mortality risk compared to class IV as reference. Cox proportional hazard regression. * p<0.05. Dialyzer classification based on B2M clearance (mL/min): I <10, II <30, III <50, IV <70, V ⩾ 70.

# Minimal albumin loss in Elisio HX

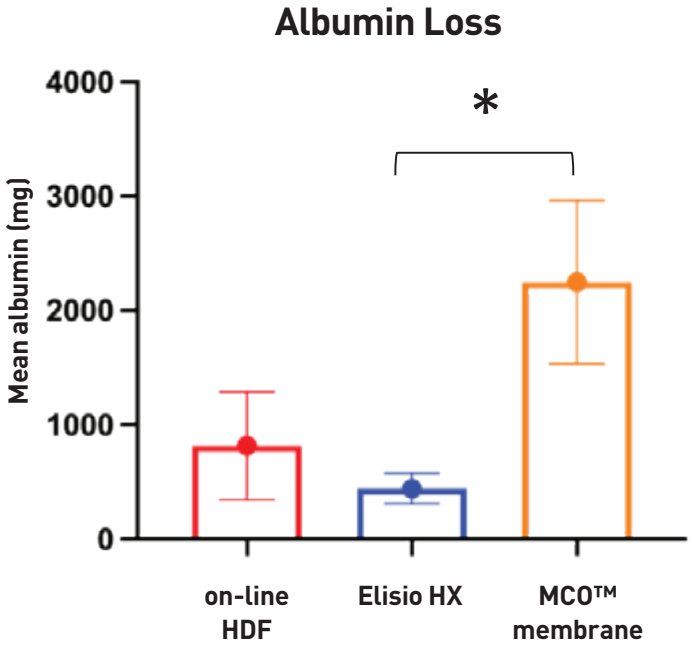
**Hypoalbuminemia** is common amongst the CKD patients and is a **strong predictor of mortality**.[20,21] Dialysis can increase this condition by the extra loss of albumin through the dialyzer's pores.[1]

The type of therapy and the type of membrane can impact the patients' albumin levels.[22, 23]




Graph from.[1] Relative risk of death by albumin level among 19,746 patients receiving incenter hemodialysis.[20]

The minimal albumin loss in Elisio HX, distinguishes it as a sharp cut-off membrane in the larger class of medium cut-off membranes.[19]




N=14; blood flow > 370 mL/min; replacement volume > 21 L; *p< 0.05; ns: not significant

The sharp cut-off feature of Elisio HX distinguishes this membrane for patients vulnerable to loss of albumin such as patients with malnutrition, frailty, sarcopenia or anemia.

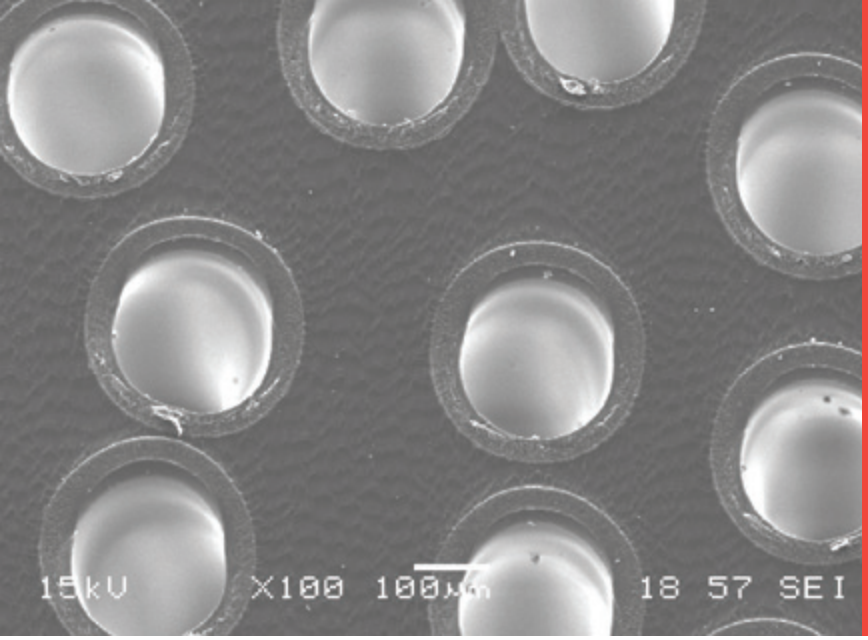



Image obtained in R&D center Japan.

## ELISIO-HX

**a Polynephron™ membrane made with polyethersulfone (PES) that is beneficial for the patients and the environment:**

- Clearances of middle molecular weight (MW) molecules[18,19]
- Retention of albumin[19]
- Not made with BPA
- Less $CO_2$ emission [27]

# Conclusion

**Following the shift of the paradigm from one-size-fits-all to a patient-centric approach, meeting the specific needs of dialysis patients is becoming increasingly important.**

HDF, as the gold standard of dialysis removes a wide array of uremic toxins associated with cardiovascular and all-cause mortality.[24] However for patients not medically eligible for HDF, the best qualitative dialysis treatment is necessary.

**For patients with no access to HDF, a quality dialysis treatment should:**

- remove the larger middle molecules (related to inflammation and CV diseases)[25]
- improve **amyloidosis, restless leg syndrome and pruritis**[26]
- improve the quality of life

The high performance dialyzers known as class IV and V in the Japanese classification, have shown superior survival rates and unharmful albumin losses.[5] In patients with lower capacity for albumin synthesis, or with poor nutrition, retaining sufficient **albumin is vital**.[1]

Elisio HX, with the combination of **bigger pore size and a specific geometry** is able to remove a wide range of middle molecule uremic toxins with **minimal albumin loss.** This provides a **quality dialysis treatment** for both standard and vulnerable patients.

# Performance Data

| Clearance: Qf = 0 mL/min* | Qb/Qd (ml/min) | 11HX | 13HX | 15HX | 17HX | 19HX | 21HX |
|---|---|---|---|---|---|---|---|
| Urea | 200/500 | 191 | 195 | 197 | 198 | 199 | 200 |
| | 300/500 | 255 | 266 | 275 | 281 | 287 | 290 |
| | 400/500 | 296 | 313 | 327 | 338 | 348 | 355 |
| Creatinine | 200/500 | 179 | 185 | 190 | 194 | 197 | 198 |
| | 300/500 | 230 | 244 | 255 | 266 | 275 | 280 |
| | 400/500 | 260 | 280 | 297 | 310 | 321 | 331 |
| Phosphate | 200/500 | 173 | 180 | 186 | 190 | 194 | 196 |
| | 300/500 | 212 | 227 | 241 | 252 | 261 | 268 |
| | 400/500 | 235 | 253 | 272 | 286 | 299 | 310 |
| Vitamin $B_{12}$ | 200/500 | 126 | 139 | 150 | 159 | 167 | 174 |
| | 300/500 | 146 | 163 | 179 | 192 | 203 | 214 |
| | 400/500 | 158 | 178 | 196 | 210 | 223 | 235 |
| Myoglobin | 200/500 | 69 | 80 | 92 | 102 | 112 | 121 |
| | 300/500 | 76 | 88 | 100 | 110 | 122 | 132 |
| | 400/500 | 81 | 96 | 108 | 119 | 130 | 142 |

| Clearance Qf = 10 mL/min* | Qb/Qd (ml/min) | 11HX | 13HX | 15HX | 17HX | 19HX | 21HX |
|---|---|---|---|---|---|---|---|
| Urea | 200/500 | 193 | 197 | 199 | 199 | 200 | 200 |
| | 300/500 | 257 | 268 | 276 | 282 | 288 | 292 |
| | 400/500 | 298 | 316 | 329 | 341 | 351 | 358 |
| Creatinine | 200/500 | 181 | 188 | 193 | 196 | 198 | 199 |
| | 300/500 | 233 | 247 | 258 | 270 | 277 | 283 |
| | 400/500 | 263 | 284 | 300 | 314 | 325 | 334 |
| Phosphate | 200/500 | 175 | 182 | 187 | 191 | 194 | 197 |
| | 300/500 | 216 | 232 | 245 | 255 | 264 | 271 |
| | 400/500 | 239 | 256 | 274 | 290 | 302 | 314 |
| Vitamin $B_{12}$ | 200/500 | 129 | 142 | 153 | 162 | 170 | 177 |
| | 300/500 | 150 | 168 | 183 | 195 | 206 | 217 |
| | 400/500 | 162 | 182 | 200 | 214 | 226 | 240 |
| Myoglobin | 200/500 | 74 | 88 | 97 | 108 | 118 | 128 |
| | 300/500 | 81 | 94 | 105 | 116 | 127 | 139 |
| | 400/500 | 86 | 100 | 113 | 124 | 137 | 148 |

## Ultrafiltration Coefficient**

| | | | | | | |
|---|---|---|---|---|---|---|
| KUF (mL/hr/mmHg) | 47 | 53 | 60 | 67 | 75 | 82 |

## Sieving Coefficient**

| | | | | | |
|---|---|---|---|---|---|
| Vitamin $B_{12}$ | 1.00 | $\beta_2$-microglobulin | 1.00 | Albumin | 0.0024 |
| Inulin | 0.97 | Myoglobin | 0.86 | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Effective Surface Area ($m^2$) | 1.1 | 1.3 | 1.5 | 1.7 | 1.9 | 2.1 |
| Priming Volume (ml) | 68 | 80 | 90 | 102 | 114 | 125 |
| Effective Length (mm) | 228 | 245 | 259 | 271 | 281 | 290 |
| Inner Diameter (µm) | 200 | 200 | 200 | 200 | 200 | 200 |
| Membrane Thickness (µm) | 40 | 40 | 40 | 40 | 40 | 40 |
| Maximum TMP (mmHg) | 500 | 500 | 500 | 500 | 500 | 500 |

| | | | |
|---|---|---|---|
| Material | Membrane: Polynephron™ | Housing and Header: Polypropylene | Potting Compound: Polyurethane |
| Sterilization Method | Dry Gamma | | |
| Package | 24 pcs/box | | |

* *In vitro* test condition (EN1283/ ISO8637-1:2017): Qd 500 mL/min, Qf 0 mL/min & Qf 10 mL/min.

Clearance data obtained in Japan. Clearance data can vary slightly depending on the test setup, lot nr. and production site.

** KUF: Bovine blood (Hct 32 ±2%, Protein 60 g/L, 37°C), Qb 300 mL/min

*** SC (EN1283/ ISO8637-1:2017): Qb 300 mL/min, Qf 60 mL/min.

# References


1. Kalantar-Zadeh K, et al. Slipping through the pores: hypoalbuminemia and albumin loss during hemodialysis. Int J Nephrol Renovasc Dis. 2021
2. Dozio E, et al. Sarcopenia in chronic kidney disease: focus on advanced glycation end products as mediators and markers of oxidative stress. Biomedicines. 2021
3. Maduell F, et al. High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients. J Am Soc Nephrol. 2013
4. Maduell F, et al. ESHOL study reanalysis: All-cause mortality considered by competing risks and time-dependent covariates for renal transplantation. Nefrologia. 2016
5. Abe M, et al. High-performance dialyzers and mortality in maintenance hemodialysis patients. Sci Rep. 2021
6. Mc Causland FR, et al. C-reactive protein and risk of esrd: results from the trial to reduce cardiovascular events with aranesp therapy (treat). Am J Kidney Dis. 2016
7. Panichi V, et al. The RISCAVID study. NDT. 2008
8. Chang CH, et al. Elevation of interleukin-18 correlates with cardiovascular, cerebrovascular, and peripheral vascular events: a cohort study of hemodialysis patients. Medicine. 2015
9. Liabeuf S, et al. Plasma beta-2 microglobulin is associated with cardiovascular disease in uremic patients. KI. 2012
10. Foster MC, et al. CRIC Study. AJKD. 2016
11. Scarpioni R, et al. Dialysis-related amyloidosis: challenges and solutions. Int J Nephrol Renovasc Dis. 2016
12. Cohen G. Immune dysfunction in uremia 2020. Toxins. 2020
13. Cohen G, et al. Immunoglobulin light chains modulate polymorphonuclear leucocyte apoptosis. EJCI. 2003
14. Fraser SDS, et al. The association of serum free light chains with mortality and progression to end-stage renal disease in chronic kidney disease: systematic review and individual patient data meta-analysis. Mayo Clinic proceedings. 2017
15. Desjardins L, et al. Association between free light chain levels, and disease progression and mortality in chronic kidney disease. Toxins. 2013
16. Lorenz G, et al. Mortality prediction in stable hemodialysis patients is refined by YKL-40, a 40-kDa glycoprotein associated with inflammation. KI. 2018
17. Vega A, et al. The new marker YKL-40, a molecule related to inflammation, is associated with cardiovascular events in stable haemodialysis patients. Clin. Kidney J. 2020
18. Kreiter, et al. Internal study. 2021. Data on file
19. Puyol, et al. abstract submitted to EDTA 2022
20. Owen WF, et al. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl J Med. 1993
21. <https://www.dopps.org/DPM/Files/meanalbumingdl_c_overallTAB.htm. . 2020>
22. Maduell F, et al. Medium cut-off dialyzer versus eight hemodiafiltration dialyzers: comparison using a global removal score. Blood purif. 2019
23. van Gelder MK, et al. Albumin handling in different hemodialysis modalities. Nephrol Dial Transplant. 2018
24. Peters SA, et al. Haemodiafiltration and mortality in end-stage kidney disease patients: a pooled individual participant data analysis from four randomized controlled trials. NDT. 2016
25. Wolley M, et al. Exploring the clinical relevance of providing increased removal of large middle molecules. CJASN. 2018
26. Florens N, et al. Expanded haemodialysis: news from the field. NDT. 2018
27. Keoleian, et al. Life cycle material data update for GREET Model. University of Michigan. 2012.

Nipro Renal Care is part of Nipro Corporation Japan, a leading global healthcare company established in 1954. With over 35.000 employees worldwide, Nipro serves the Medical Device, Pharmaceutical, and Pharmaceutical Packaging industries.

Nipro Renal Care is a global market leader with over 6 decades providing renal solutions for dialysis and dialysis-related treatment. We specialize in developing dialysis machines, water treatment systems, and a comprehensive portfolio of disposable medical equipment.

In order to address the needs of patients, healthcare professionals, and procurement managers alike, Nipro Renal Care is driven by innovation and patient safety to offer the highest quality products that optimize time, effort, and costs.

## BECAUSE EVERY LIFE DESERVES AFFORDABLE CARE

www.nipro-group.com/en-en/our-company/our-locations

Please contact your local representative for more information.

MM-2213 - Bro-Elisio HX - EN - 18 Mar 2022

NIPRO MEDICAL EUROPE

**Nipro Medical Europe :** European Headquarters, Blokhuisstraat 42, 2800 Mechelen, Belgium
T: +32 (0)15 263 500 | F: +32 (0)15 263 510 | medical@nipro-group.com | www.nipro-group.com