

HDx Therapy | Patient Information Sheet

BUILDUP OF TOXINS CAN CONTRIBUTE TO SYMPTOM BURDEN IN PATIENTS WITH KIDNEY FAILURE

When kidneys are damaged, they don't effectively remove toxins through urine, and these toxins build up in the bloodstream. That's why the dialyzer is perhaps the most important part of hemodialysis treatment. The dialyzer acts like an artificial kidney to remove fluid and toxins from the body.

However, traditional (high-flux) dialyzers have limited ability to remove certain toxins - called large-middle molecules¹⁻³ - that are known to cause some of the symptoms that dialysis patients suffer, like itching,^{4,5} fatigue,^{5,6} difficulty sleeping^{5,6} and restless legs.⁷⁻⁹

Uremic toxins by class and linkage with clinical symptoms and outcomes¹

Uremic toxin class	Relevant clinical effects and symptoms	Removed by
Small Molecules	<ul style="list-style-type: none"> General Uremic Toxicity^{10,11} Vascular Calcification,⁸ Chronic Kidney Disease-Mineral and Bone Disorder¹² 	Traditional (high flux) HD
Small-middle Molecules	<ul style="list-style-type: none"> Chronic Kidney Disease-Mineral and Bone Disorder¹² Amyloidosis/Carpal Tunnel Syndrome^{10,11} 	HDx therapy
Medium-middle Molecules	<ul style="list-style-type: none"> Oxidative Stress and Mitochondrial Dysfunction¹⁴ Multiple Toxicity^{21,23} Contributor to Proinflammatory Status of Uremia¹⁴ Pruritus,⁴ Recovery Time,¹⁵ Chronic Inflammation,¹⁶ Cardiovascular Disease,¹⁸ Protein-Energy Wasting in CKD¹⁸ 	HDx therapy
Large-middle Molecules	<ul style="list-style-type: none"> Sepsis,¹¹ Chronic Inflammation,¹⁶ Cardiovascular Disease,¹⁶ Protein-Energy Wasting in CKD¹⁶ Secondary Immunodeficiency, Cardiovascular Disease² Restless Leg Syndrome (RLS)²⁴ Inflammation¹⁶ Chronic Inflammation, Secondary Immunodeficiency¹¹ 	HDx therapy
Large Molecules	<ul style="list-style-type: none"> Toxin Binding¹¹ 	Kidney

HDx THERAPY DELIVERS EXPANDED HEMODIALYSIS AND IS ONE STEP CLOSER TO THE NATURAL KIDNEY^{3,17}



Unlike traditional hemodialysis, HDx therapy is made possible by a specialized membrane within the **Theranova** dialyzer, designed to remove the unwanted large-middle molecules (the “bad” stuff) while retaining the essential large molecules, like albumin (the “good” stuff).¹⁷⁻¹⁹

The ability to perform HDx therapy is very straightforward. Doctors can simply prescribe the **Theranova** dialyzer instead of the current, traditional dialyzer. There is no need for different machinery or any other change from the normal treatment.²⁰ The **Theranova** dialyzer is the only available dialyzer that delivers HDx therapy.

AFTER SWITCHING TO HDx THERAPY ENABLED BY THERANOVA DIALYZERS, PATIENTS HAVE REPORTED



Reduction in itchiness,²¹ restless leg syndrome²² and dialysis recovery time²³



Improved sleep quality, energy level and general well-being⁶

*Symptoms and responses to any treatment may vary so it's important to talk to a healthcare provider and to follow a doctor's recommendations.

SHARE THIS INFORMATION WITH CARE TEAMS

Talk with nurses and nephrologists about HDx therapy enabled by the **Theranova dialyzer**.*

Some conversation starters with care teams...



Know about HDx therapy? Or about large-middle molecules?

HDx therapy is one step closer to the natural kidney,³ targeting the removal of large-middle molecules linked to chronic inflammation, cardiovascular disease (CVD), immunodeficiency and symptom burden.^{2,3,19}

Show the uremic toxins chart (above) showing the linkage of uremic toxins to clinical outcomes and symptoms.



Why might patients be experiencing itchiness, fatigue, difficulty sleeping and/or restless legs?

Traditional (high flux) dialyzers have limited ability to remove these toxins that cause these symptoms.¹⁻³

Show the uremic toxins chart (above) showing medium- and large-middle molecule linkage to these dialysis-related symptoms.



How is the **Theranova dialyzer different than traditional dialyzers?**

The **Theranova** dialyzer's membrane has a larger and more uniform pore size than traditional (high-flux) dialyzers, allowing better clearance of large-middle molecules while retaining essential large molecules, like albumin.^{18,25}



For which patients is the **Theranova** dialyzer an option?

The **Theranova** dialyzer can be used for chronic kidney disease (CKD) patients prescribed intermittent hemodialysis in any setting – home, clinic or hospital.²⁴ Ask a doctor about **HDx** therapy enabled by the **Theranova** dialyzer.

Patients may receive treatment with the **Theranova** Dialyzer if they have chronic kidney disease and are prescribed intermittent hemodialysis only. This dialyzer removes larger size middle molecules (toxins) that can play a pathologic role in the uremic clinical syndrome (fluid, electrolyte, hormonal, and metabolic abnormalities). Patients should know there are no known contraindications for the use of **Theranova** dialyzers. In rare cases, patients could experience a hypersensitivity reaction during dialysis, particularly at the onset of treatment. If this occurs, report abnormal symptoms immediately to the health care provider. If severe, the dialysis must be discontinued, and appropriate medical intervention administered. Isolated/sequential ultrafiltration (Fluid Removal Only) should NOT be applied when using **Theranova** dialyzers. For single use only.

Rx only. For the safe and proper use of this device, refer to the Instructions for Use.

1. Rosner MH, et al. Classification of Uremic Toxins and Their Role in Kidney Failure. Clin J Am Soc Nephrol. 2021;16(12):1918-1928.
2. Wolley M, et al. Exploring the Clinical Relevance of Providing Increased Removal of Large Middle Molecules. Clin J Am Soc Nephrol. 2018;13 (5):805-814.
3. Zweigart C, et al. Medium cut-off membranes - closer to the natural kidney removal function Int J Artif Organs. 2017;40(7):328-334.
4. Kimmel M, et al. The role of micro-inflammation in the pathogenesis of uraemic pruritus in haemodialysis patients. Nephrol Dial Transplant. 2006;21(3):749-755.
5. Pisoni RL, et al. Pruritus in haemodialysis patients: International results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant. 2006;21(12):3495-3505. Nephrol Dial Transplant. 2006;21:3495-3505.
6. Penny JD, et al. Impact of Expanded Hemodialysis Using Medium Cut-off Dialyzer on Quality of Life: Application of Dynamic Patient-Reported Outcome Measurement Tool. Hemodial Int. 2021;25(1):E10-E14.
7. Ronco C. Editor. Expanded Hemodialysis: Innovative Clinical Approach in Dialysis. Karger Medical and Scientific Publishers. 2017.
8. Sakurai K. Biomarkers for Evaluation of Clinical Outcomes of Hemodiafiltration. Blood Purif. 2013;35(Suppl 1):64-68.
9. Giannaki CD, et al. Epidemiology, impact and treatment options of restless legs syndrome in end-stage renal disease patients; an evidence based review. Kidney Int. 2014;85(6):1275-1282.
10. Ronco C, La Manna G. Expanded Hemodialysis: A New Therapy for a New Class of Membranes. Contrib Nephrol. 2017;190:124-133.
11. Ronco C, et al. Expanded Haemodialysis: from operational mechanism to clinical results. Nephrol Dial Transplant. 2018;33(suppl_3):iii41-iii47.
12. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease - Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl. (2011). 2017;7(1):1-59.
13. Desjardins L, et al. Association between Free Light Chain Levels, and Disease Progression and Mortality in Chronic Kidney Disease. Toxins (Basel). 2013;5(11):2058-2073.
14. Vanholder R, et al. Biochemical and Clinical Impact of Organic Uremic Retention Solutes: A Comprehensive Update. Toxins (Basel). 2018;10(1):33.
15. Bossola M, et al. Recovery Time after Hemodialysis Is Inversely Associated with the Ultrafiltration Rate. Blood Purif. 2019;47:45-51.
16. Lorenz G, et al. Mortality prediction in stable hemodialysis patients is refined by YKL-40, a 40-kDa glycoprotein associated with inflammation. Kidney Int. 2018;93(1):221-230.
17. Boschetti-de-Fierro A, et al. MCO Membranes: Enhanced Selectivity in High-Flux Class. Sci Rep. 2015;5(1):18448.
18. Kirsch AH, et al. Performance of hemodialysis with novel medium cut-off dialyzers. Nephrol Dial Transplant. 2017;32(1):165-172.
19. Hutchison CA, et al. The Rationale for Expanded Hemodialysis Therapy (**HDx**). Contrib Nephrol. 2017;191:142-452.
20. Ronco C. The Rise of Expanded Hemodialysis. Blood Purif. 2017;44:I-VIII.
21. Lim JH, Park Y, Yook JM, et al. Randomized controlled trial of medium cut-off versus high-flux dialyzers on quality of life outcomes in maintenance hemodialysis patients. Sci Rep. 2020;10(1):1-11.
22. Alarcon et al. Impact of medium cut-off dialyzers on patient-reported outcomes (PROs): COREXH Registry. Blood Purif. <https://doi.org/10.1159/000508803>.
23. Bolton S, Gair R, Nilsson LG, Matthews M, Stewart L, McCullagh N. Clinical Assessment of Dialysis Recovery Time and Symptom Burden: Impact of Switching Hemodialysis Therapy Mode. Patient Relat Outcome Meas. 2021 Nov 4;12:315-321. doi: 10.2147/PROM.S325016. PMID: 34764715; PMCID: PMC8575372.
24. Theranova Instructions for Use. 2021