



Baxter

HDx THERAPY

Enabled by **MCO THERANOVA**

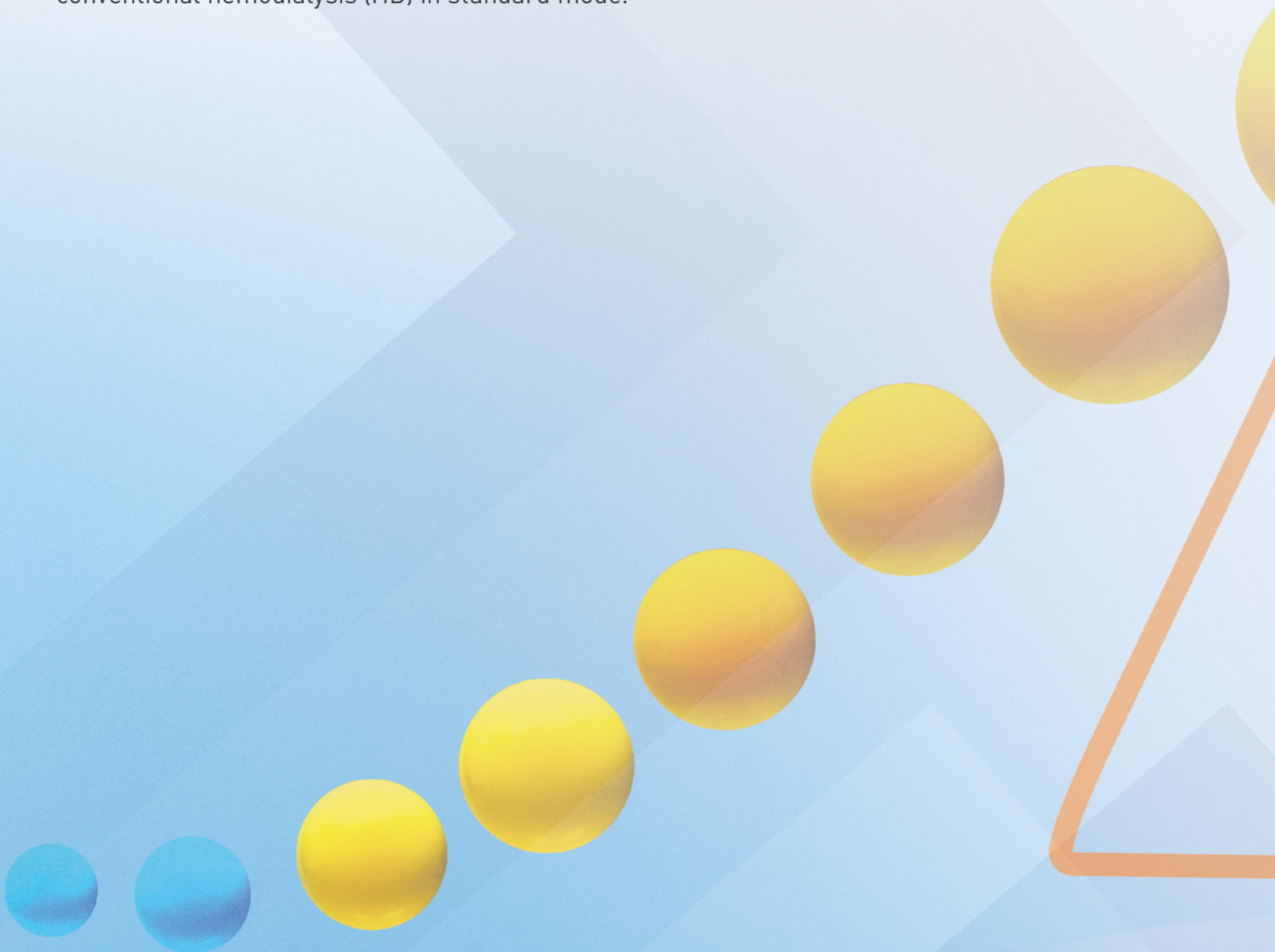
Discover how HDx Expanded Hemodialysis
may make **A WORLD OF DIFFERENCE** for
patients, clinicians & healthcare systems



A WORLD OF DIFFERENCE

ONE CHANGE CAN TRANSFORM HD TREATMENT

Expanded Hemodialysis is a dialysis treatment where diffusion and convection are conveniently combined along a hollow fiber dialyzer equipped with a High Retention Onset (HRO) membrane¹ – defined as medium cut-off, with no special requirement of a particular hardware, preparation of replacement fluid, or additional nursing skill, compared to the necessary ones required to perform conventional hemodialysis (HD) in standard mode.²



WHAT A DIFFERENCE AN X MAKES

01

POSITIVE OUTCOMES

HDx therapy may reduce the burdens of hemodialysis therapy.^{3,4}

[Read more](#)

02

REMOVING LARGE-MIDDLE MOLECULES

The efficient removal of large-middle molecules may reduce the risk of inflammation, toxicity, and organ damage.²

[Read more](#)

03

UNIQUE MEMBRANE

A different membrane design allows for a filtration profile that is close to that of the natural kidney.¹

[Read more](#)

04

PROVEN RESULTS

HDx therapy's large and growing evidence-base.^{4,7}

[Read more](#)



HOW CAN HDx OPEN UP A WHOLE WORLD IN HD THERAPY?

ANSWERING CRITICAL PATIENT NEEDS

Patient-reported symptom burden has a significant impact on patient quality of life.⁷

PATIENT-REPORTED OUTCOMES



PRURITUS

UREMIC PRURITUS

HDx may significantly lower uremic pruritus, a predictor of poor sleep, in HD patients.⁸

[Read more](#)



RESTLESS
LEGS

RESTLESS LEGS SYNDROME

HDx may reduce the occurrence of restless legs syndrome (RLS), common in HD patients.^{5,9}

[Read more](#)



POOR RECOVERY
TIME

RECOVERY TIME

HDx may significantly reduce recovery time, positively associated with hospitalization and mortality, after dialysis treatments.^{10,11,12}

[Read more](#)



CREATING POSITIVE HEALTHCARE OUTCOMES

HDx can help free resources and relieve the strain on healthcare systems.^{3,14,31}

ECONOMIC OUTCOMES



HOSPITALIZATION
RATE

HOSPITALIZATION RATES

HDx may reduce hospitalization rates.^{3,31}

Read more



MEDICATION
USAGE

MEDICATION USAGE

HDx has been associated with decreases in medication usage.^{15,16,17}

Read more



COST OF CARE

COST OF CARE

HDx may reduce pressures on healthcare systems and total cost of care.^{3,13,14,16,31}

Read more



A BETTER NIGHT'S SLEEP CAN MAKE A WORLD OF DIFFERENCE

UREMIC PRURITUS

Daily bouts of itching that tend to worsen at night and may prevent sleep.⁸

IMPLICATIONS FOR PATIENTS¹⁸

>42%



of HD patient suffer from moderate to severe pruritus

Poor quality of life scores

Depression

Cardiovascular disease

Impaired sleep

Higher mortality risk

HDx MAY IMPROVE PATIENT-REPORTED PRURITUS

One randomized clinical study found **HDx** to deliver statistically significant improvements in key aspects of patient-reported uremic pruritus compared to conventional HD.⁸

MOLECULE ASSOCIATION

IL-6 is a pleiotropic cytokine that regulates the immune and inflammatory response and affects hematopoiesis, metabolism and organ development.¹⁹ IL-6 is commonly observed in Chronic Kidney Disease (CKD) patients and markedly increased in HD patients with uremic pruritus²⁰, which is caused by increased generation resulting from oxidative stress, chronic inflammation and fluid overload.¹⁹

INTERLEUKIN-6 (IL-6)

[25 kDa]

THERANOVA dialyzers are indicated for treatment of chronic and acute renal failure by Hemodialysis

Do not use in Hemodiafiltration or Hemofiltration mode or isolated Ultrafiltration



HDx CAN GIVE PATIENTS A LEG UP

RESTLESS LEGS SYNDROME (RLS)

A neurological condition characterized by an irresistible urge to move the limbs accompanied by uncomfortable sensations.²³

IMPLICATIONS FOR PATIENTS



HDx MAY PREVENT DISCOMFORT

A large observational study in prevalent HD patients found an approximate 55% reduction in the number of patients meeting RLS criteria after 12 months on **HDx** therapy.⁹

MOLECULE ASSOCIATION

A1M is a microglobulin, belonging to a protein family. It is described as a circulating “waste bin” which continuously removes free radicals and oxidizing agents, particularly heme, from the tissues. It is subsequently transported to the kidneys, where it is broken down. A1M’s urinary excretion is associated with faster Chronic Kidney Disease (CKD) progression and high mortality as well as restless syndrome.²⁵

a1-MICROGLOBULIN (A1M)

[33 kDa]

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HDx CAN HELP PATIENTS ENJOY MORE OF LIFE

RECOVERY TIME

The time in minutes that it takes a patient to recover after a hemodialysis session.²⁸

IMPLICATIONS FOR PATIENTS

68%



patients report >2 hours to recover¹²

Poor quality of life scores¹²

Activities of daily living¹²

Dialysis-related stress¹²

Associated with hospitalization¹²

Higher mortality risk^{12,28}

FASTER RECOVERY WITH HDx THERAPY

HDx therapy may significantly reduce dialysis recovery time and improve perceived fatigue level.¹¹

MOLECULE ASSOCIATION

IL-6 is a pleiotropic cytokine that regulates the immune and inflammatory response and affects hematopoiesis, metabolism and organ development.¹⁰ In people on chronic HD, fatigue appears associated with the serum level of interleukin, supporting that inflammation plays a role.³⁰

INTERLEUKIN-6 (IL-6)

[25 kDa]

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HELP PATIENTS SPEND **LESS** **TIME** IN YOUR WORLD

HOSPITALIZATION RATES

Research reveals that **HDx** is likely to significantly lower hospitalization rates.^{3,31}

REDUCTION IN HOSPITALIZATION EVENTS

A randomized controlled trial of 171 prevalent HD patients showed a **45%** lower all-cause hospitalization rate over 12 months with **HDx** therapy compared to the control high-flux HD arm.³¹

Health resource utilization	THERANOVA (n = 86)	high-flux HD (n = 85) ^a	p-value
Hospitalization events	18	31	-
Total hospital days	74	139	-
Total patient-years	32.4	30.5	-
Hospitalization rate per PY [SE]	0.56 (0.13)	1.02 (0.12)	0.042
Hospital length of stay [mean days [SE]]	4.11 (0.57)	4.63 (0.58)	0.406

a One high-flux HD randomized participant did not complete baseline.



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WHERE LESS CAN BE MORE

FEWER MEDICATIONS

HDx has the potential to reduce the need for medication for conditions related to uremic toxins such as anemia and inflammation.¹⁶

LOWER DOSES

Research has shown that patients under **HDx** therapy may have a decreased Erythropoietin Resistance Index (ERI). Also, these patients may need a lower ESA dose over time without a concomitant reduction in hemoglobin level, when compared with patients under High-Flux HD and HDF therapies.^{14,15,16,17}

MEDICATION UTILIZATION PER PATIENT YEAR

ESA – INTERNATIONAL UNITS^a

HD HF mean (95% CI) N = 81	HDx mean (95% CI) N = 81	Percent change HDx vs HD HF
181318	168124^a	-7%

IRON – MILIGRAMS

HD HF mean (95% CI) N = 81	HDx mean (95% CI) N = 81	Percent change HDx vs HD HF
959	759^a	-21%

INSULIN – INTERNATIONAL UNITS

HD HF mean (95% CI) N = 81	HDx mean (95% CI) N = 81	Percent change HDx vs HD HF
5383	3434^a	-36%

HYPERTENSION MEDICATIONS – TABLETS

HD HF mean (95% CI) N = 81	HDx mean (95% CI) N = 81	Percent change HDx vs HD HF
1183	731^a	-38%

^a Statistically significant difference found in corresponding univariate GLM analysis of outcome on **HDx**. All had a P-value <0.01.

Adapted after Ariza: An initial evaluation of **HDx** on hospitalizations, drug utilization, costs, and patient utility in Colombia.¹⁶

LOWER USE

Patients receiving **HDx** therapy may have a decreased use of supportive medications such as iron, insulin and antihypertensive medications vs those treated with conventional high-flux HD.¹⁶

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BETTER CARE CAN LOWER EXPENSES

FREEING UP RESOURCES

Recently published research has shown promising signs that **HDx** has the potential to positively impact the burden on healthcare systems.^{14,16,31}

REDUCING THE COST OF CARE

HDx therapy may offer health care systems the opportunity to reduce the total cost of care, primarily driven by potential reduction of cardiovascular events, infections, medication usage, all-cause hospitalizations, hospitalization rate and length of stay.^{3,13,14,16,17,31}

ECONOMIC OUTCOMES

HOSPITALIZATION EVENTS³¹

Probabilistic analysis determined that **THERANOVA** was associated with lower costs in **96%** of the 10,000 simulations.

Item	Unit cost [USD]	Per-patient cost		
		THERANOVA	high-flux HD	Difference
All-cause Hospitalization ^a	\$2518 per day	\$5756	\$11,853	-\$6097
Dialyzer cost ^b	\$15.00 ea/ \$6.50 ea	\$2340	\$1014	\$1326
Cumulative		\$8096	\$12,867	-\$4771

a All-cause hospitalization was defined as any serious adverse event that resulted in hospitalization

b **THERANOVA** dialyzer was priced at \$15 in the United States and high-flux dialyzer was assumed to cost \$6.50

Adapted after Blackowicz: Economic evaluation of expanded hemodialysis with the **THERANOVA 400** dialyzer: A post hoc evaluation of a randomized clinical trial in the United States.³¹

MEDICATION UTILIZATION¹⁶

Percentage change in average annual cost analysis HDx vs HD-HF			
ESA*	IRON	INSULIN	ANTIHYPERTENSIVES
-7.27%	-20.83%	-32.64%	-30.16%

*Erythropoietin stimulating agents

Adapted after Ariza: An initial evaluation of **HDx** on hospitalizations, drug utilization, costs, and patient utility in Colombia.¹⁶

CARDIOVASCULAR EVENTS

A retrospective, observational study found that **HDx** compared to HD-HF is likely to significantly lower nonfatal cardiovascular events by **35%**.³



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IS IT POSSIBLE TO GET CLOSER TO THE NATURAL KIDNEY?

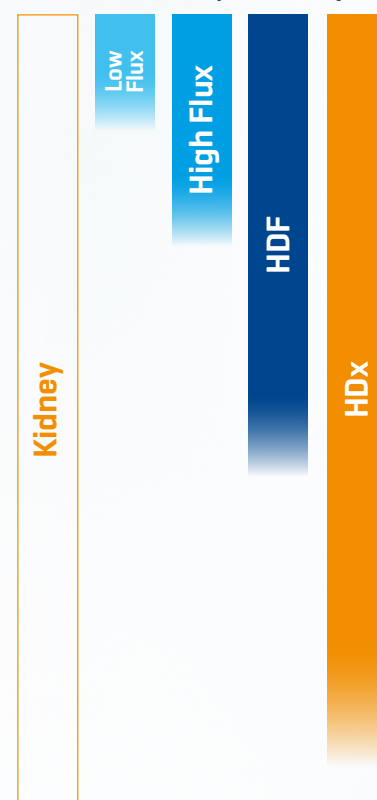
USING A MEMBRANE WITH EXPANDED PERMEABILITY AND SELECTIVITY¹

Until now, current dialytic therapies have had limited capability in removing large-middle molecule uremic toxins.^{32,48} Large-middle molecules can contribute to inflammation, cardiovascular events and other dialysis-related co-morbidities.⁴⁸

Uremic Toxin Classes by molecular weight [Daltons]^{32,50}

Urea	[60 Da]	●	Small Molecules [<0.5 kDa]
Phosphate	[96 Da]	●	
PTH	[9.5 kDa]	●	Small-middle Molecules [0.5-15 kDa]
Beta ₂ microglobulin	[12 kDa]	●	
Myoglobin	[17 kDa]	●	Medium-middle Molecules [>15-25 kDa]
Kappa free-light-chains	[23 kDa]	●	
Complement factor D	[24 kDa]	●	
Interleukin-6	[25 kDa]	●	
TNF-alpha	[26 kDa]	●	Large-middle Molecules [>25-58 kDa]
FGF-23	[32 kDa]	●	
Alpha 1 microglobulin	[33 kDa]	●	
YKL-40	[40 kDa]	●	
Lambda free-light-chains	[45 kDa]	●	Large Molecules [>58 kDa]
Albumin	[67 kDa]	●	

Evolution of dialysis therapies



Adapted after Rosner M, et al. Classification of Uremic Toxins and Their Role in Kidney Failure.

Clin J Am Soc Nephrol. 2021;16(12):1918-1928³²






EUTOX Uremic Solutes Database. June 2022. Uremic-toxins.org⁵⁰



GOING BEYOND UREA AND BETA₂ MICROGLOBULIN

The clinical symptoms and conditions associated with uremic toxins differ according to their molecular weight, with the large-middle molecules being linked to several clinical effects.³²

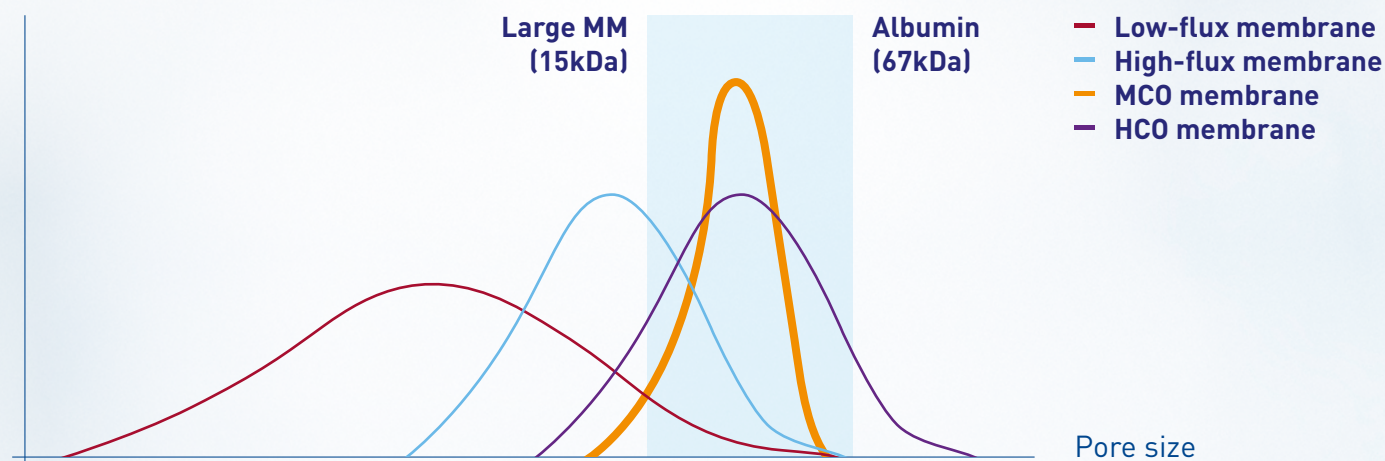
Large-middle molecule linkage with clinical symptoms and outcomes

Large-middle molecules			Relevant clinical effects
TNF-alpha	[26 kDa]		<ul style="list-style-type: none">· Sepsis³³· Chronic Inflammation³³· Cardiovascular Disease³⁴· Protein-energy wasting in CKD³⁴
FGF-23 ⁵⁰	[32 kDa]		<ul style="list-style-type: none">· Secondary Immunodeficiency· Cardiovascular Disease³⁴
Alpha 1 microglobulin	[33 kDa]		<ul style="list-style-type: none">· Restless Legs Syndrome [RLS]^{35,36}
YKL-40	[40 kDa]		<ul style="list-style-type: none">· Inflammation³⁷
Lambda free-light-chains	[45 kDa]		<ul style="list-style-type: none">· Chronic Inflammation· Secondary Immunodeficiency³⁴

EXPERTISE IN MEMBRANE MANUFACTURING: MCO TO PERFORM HDx

Membrane formation technologies have enabled precise control of pore size distribution which results in a narrow pore size distribution with a significant number of pores that are large enough for middle molecules to penetrate, but small enough for albumin to not pass through.^{38,39}

Number of pores



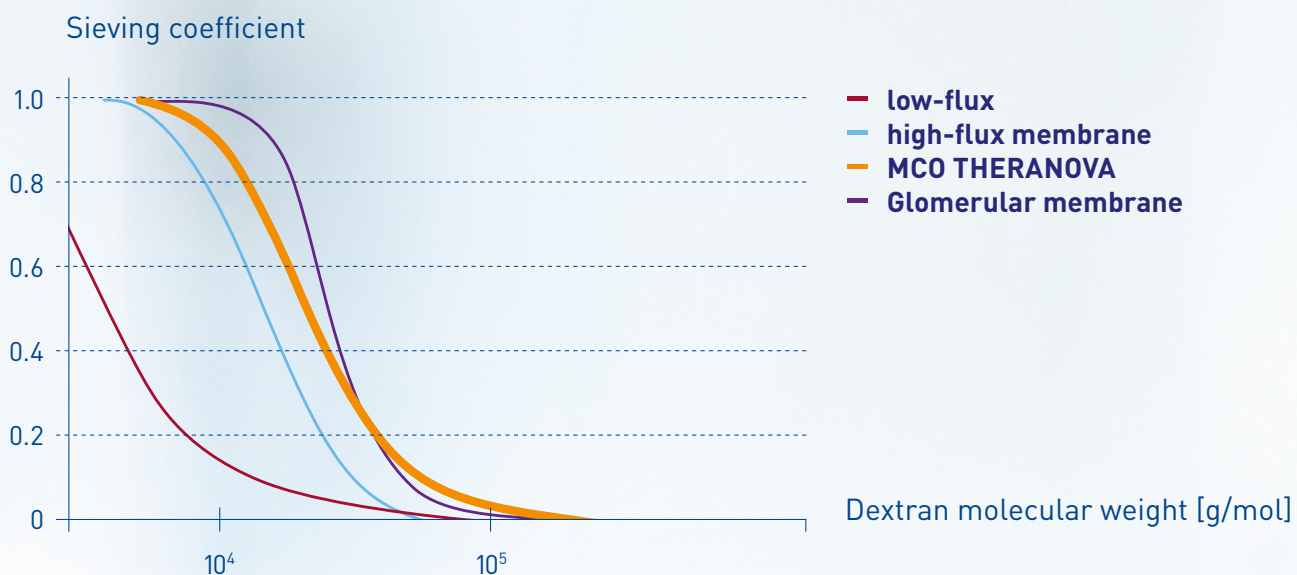
Adapted after Wolley: Exploring the Clinical Relevance of Providing Increased Removal of Large Middle Molecules.⁴⁹



HDx: DIFFUSION AND CONVECTION COMBINED INSIDE A DIALYZER

A HEMODIALYZER WITH AN EXPANDED SOLUTE REMOVAL PROFILE

HDx is a dialysis treatment where diffusion and convection are conveniently combined inside a hollow fiber dialyzer.¹ **MCO THERANOVA's** membrane provides the patented Molecular Weight Retention Onset (MWRO) and Molecular Weight Cut-Off (MWCO) range to target the efficient removal of large-middle molecules.^{5,6,38} This results in a sieving curve closer to the natural kidney.^{1,38}



Adapted after Boschetti-de-Fierro: MCO Membranes: Enhanced Selectivity in High-Flux Class.³⁸

A NEW CLASS OF DIALYZERS

THERANOVA is the only device falling in the classification of Hemodialyzers with an expanded solute removal profile, as defined by the US Food and Drug Administration (FDA).⁴⁰ **THERANOVA** also falls into the new class of medium cut-off dialyzers, based on the in vitro and clinical use methodology published by the Chinese Nephrology & Blood Purification Innovation Alliance.⁴⁵



FOUR THERAPEUTIC PRINCIPLES THAT MAKE HDx POSSIBLE

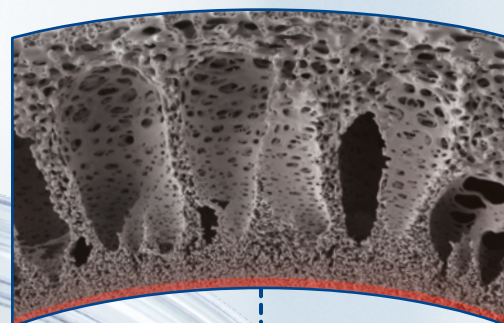
The clearance profile provided by **HDx** therapy enabled by **MCO THERANOVA** is made possible using regular HD workflow and infrastructure⁶ thanks to the combination of 4 principles in a single dialyzer device design.

The membrane structure is asymmetric and can be seen in cross section as **three distinct layers**⁴³

A finger-like macro-porous outer layer

A sponge-like intermediate layer

A very thin inner layer (skin)



1 HIGH PERMEABILITY TO LARGE-MIDDLE MOLECULES

Membrane with increased nominal pore size that provides significantly higher permeability for large-middle molecules when compared to high-flux membranes used for conventional HD and HDF.^{1,2,38}

2 EFFECTIVE SELECTIVITY BY SIZE EXCLUSION

A unique asymmetric 3-layer structure controls the distribution of pore sizes for a stable separation profile.³⁸

3 AUGMENTED INTERNAL FILTRATION

A reduced inner diameter increases the convective transport along the membrane, within the same hollow fiber dialyzer performing diffusion.^{1,2,38}

4 RETENTION OF ENDOTOXINS

The adsorptive properties of the **MCO** membrane make it a safe and effective barrier against potential dialysis fluid contaminants despite the higher permeability.^{2,38,42}

Internal filtration IF at 500mL/min Qd

Blood flow [QB], mL/min

IF mL/min

THERANOVA 400

300

400

29.7

41.6

THERANOVA 500

300

400

31.6

53.1

Adapted after Lorenzin: Classification of hemodialyzer clinical performance.⁴⁴



HOW HDx IS CHANGING DIALYSIS ONE STUDY AT A TIME

HDx therapy evidence on patient-reported, clinical and economic outcomes continues to grow.⁴⁶

If you want to visit the
Compendium of Studies
[click here](#)



A WORLD OF DIFFERENCE



Visit the HDx
therapy website
[click here](#)



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Medical devices of class IIb – Notified body: BSI, NL (CE 2797) – Legal manufacturer: Gambro Dialysatoren GmbH – Hechingen, Germany.¹

For single use only. For safe and proper use of these devices refer to the Instructions for Use.

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