



SELLING THE VALUE OF HDx THERAPY TO YOUR CUSTOMERS

How to use the **Theranova** Concept Brochure

HDx Therapy

Enabled by the **Theranova** Dialyser

For internal use only

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THE ANNOTATED THERANOVA CONCEPT BROCHURE (HDx THERAPY)

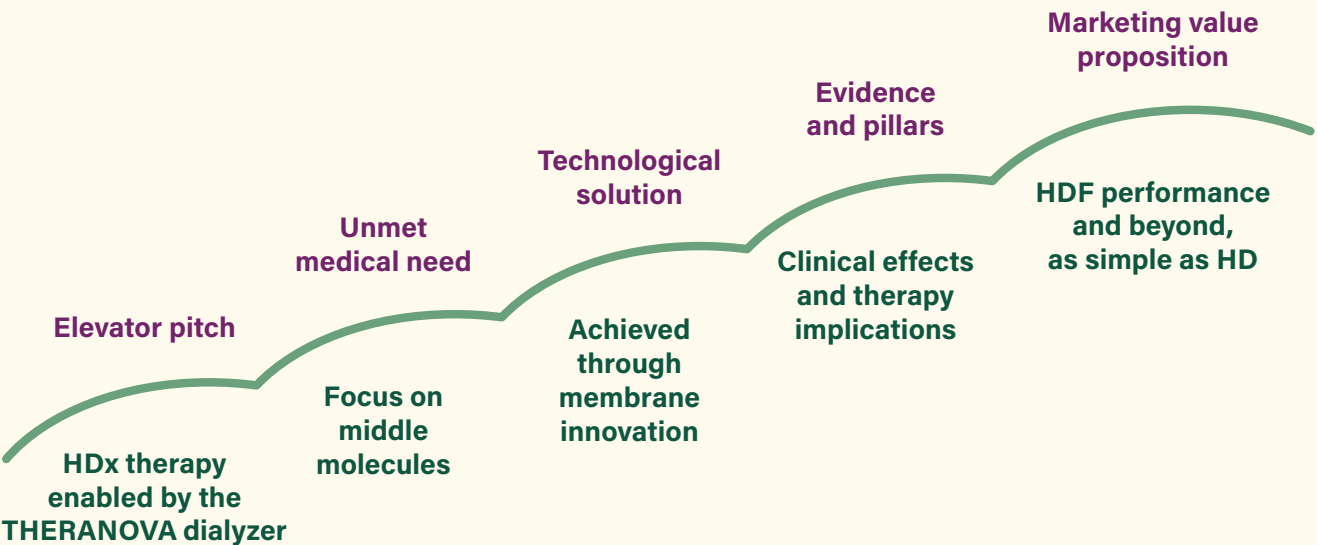
HOW TO USE THIS GUIDE

IN THIS GUIDE YOU WILL FIND:

- > Elevator pitch – a quick introduction to the HDx therapy value proposition
- > Conversation starters on each spread – simple questions to help your customers recognize the value and potential of the HDx therapy
- > Answers to conversations in the form of key benefits and supporting proof-points

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ELEVATOR PITCH

HDx THERAPY ENABLED BY THE THERANOVA DIALYZER



**DO NOT USE THERANOVA DIALYZERS FOR HDF OR HF DUE TO HIGHER PERMEABILITY
OF LARGER MOLECULAR WEIGHT PROTEINS SUCH AS ALBUMIN**

WHAT THE ELEVATOR PITCH GIVES YOU?

Is your opportunity to briefly tell the core story in the time it would take to ride an elevator.

It is the main value that new HDx therapy, enabled by the **Theranova** dialyzer, can bring to the customer by providing an alternative high-performance therapy to all chronic HD patients, focusing on the removal of large middle molecules.

HDF PERFORMANCE AND BEYOND AS SIMPLE AS HD:

The **Theranova** dialyzer, featuring an innovative membrane, effectively targets large middle molecules not efficiently removed by currently available dialysis treatments.

It provides the opportunity for an expanded hemodialysis therapy, HDx, providing HDF performance and beyond in the removal of middle and larger middle molecules, using regular HD infrastructure.

The premium performance and simplicity of the HDx therapy, enabled by the **Theranova** dialyzer, opens up another option for patients with chronic renal failure requiring hemodialysis.

MEDICAL UNMET NEED

HDx THERAPY: FOCUS ON LARGE MIDDLE MOLECULES

KEY MESSAGES TO CONVEY FROM THIS SPREAD

1. Removal of larger middle molecules is a new paradigm in dialysis.
2. Clearance is limited with high-flux filters used in HD or HDF and there is a need for more permeable and selective membranes.

1. LARGE MIDDLE MOLECULES: A NEW PARADIGM IN DIALYSIS

- > Classification of uremic solutes: there is a world beyond β_2 -microglobulin
- > Removal with current high-flux dialysis therapies (HD or HDF) remains limited by membrane permeability



CONVERSATION STARTER:

Introduce your customers to the classification of uremic solutes and to the limited reach in larger middle molecules with current high-flux therapies (HD, HDF).

Typical questions:

- > How important is the removal of larger middle molecules, beyond β_2 -microglobulin?
- > Did you know that the removal of the larger middle molecules may remain very limited with high-flux membranes, even when convection (HDF) is applied?

2. THE NEED FOR MORE PERMEABLE MEMBRANES

There is a growing evidence about the relevance and toxicity of large middle molecules. Removal of these molecules requires membrane with higher permeability than standard current high flux dialyzers.

TECHNOLOGICAL SOLUTION

HDx THERAPY: ACHIEVED THROUGH MEMBRANE INNOVATION

KEY MESSAGES TO CONVEY FROM THIS SPREAD

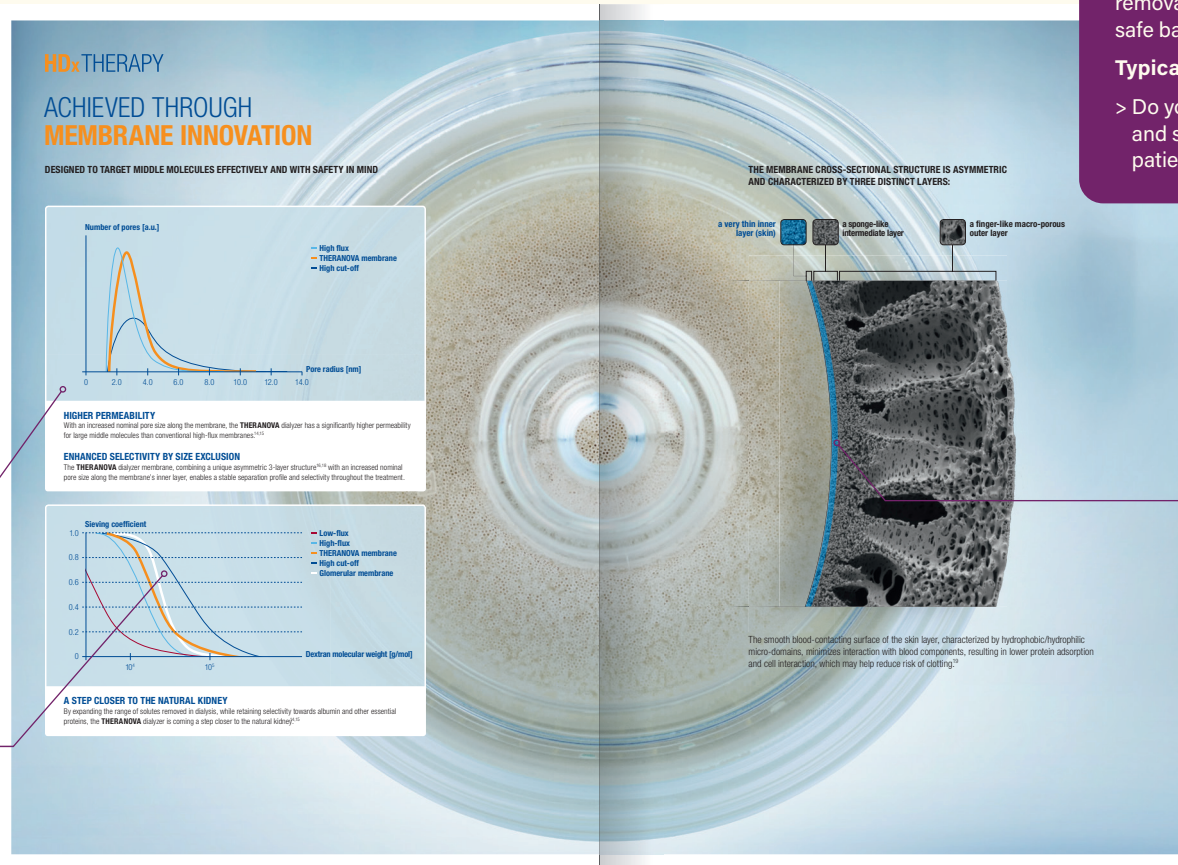
1. **Theranova** is the next logical membrane innovation, combining higher permeability with enhanced selectivity.
2. Stable selectivity throughout the treatment is ensured by pore size control and the proprietary membrane 3-layer-structure.
3. The **Theranova** artificial kidney membrane is a step closer to the glomerular (natural) kidney.

1. HIGHER PERMEABILITY

A higher nominal pore size and greater number of pores results in higher permeability.

3. A STEP CLOSER TO THE NATURAL KIDNEY

This is a result of membrane design and process engineering (spinning) innovation providing higher permeability and enhanced selectivity.



CONVERSATION STARTER:

Introduce **Theranova** as the logical next-step in dialysis innovation. This comes as a result of optimizing the balance between membrane permeability and selectivity. The higher permeability allows a delivery of HDF performance (and beyond for the large middle molecules) in HD mode, while the enhanced selectivity allows a controlled removal of essential solutes and acts as a safe barrier to endotoxins.

Typical question

> Do you use different membranes and surface areas to try optimizing patient care?

2. ENHANCED SELECTIVITY

Results from strict pore size control (narrow distribution) at the inner skin layer, and the proprietary 3-layer-structure of the membrane.

EVIDENCE AND PILLARS

HDx THERAPY: CLINICAL EFFECTS AND THERAPY IMPLICATIONS

KEY MESSAGES TO CONVEY FROM THIS SPREAD

The **Theranova** dialyzer effectively targets large middle molecules not efficiently removed by currently available dialysis treatments. It provides the opportunity for an expander hemodialysis therapy, HDx (1), providing HDF performance and beyond in the removal of middle and larger middle molecules (2), using regular HD infrastructure and protocol (3).

1. EXPANDING HD

Markedly greater clearances and intradialytic reduction ratios than regular HD – at ordinary blood flow rates (300 mL/min).

3. REGULAR HD INFRASTRUCTURE AND PROTOCOL

The four HDx therapy pillars:

- > Outstanding performance
- > For all patients, primarily for those requiring higher clearances of larger uremic toxins, without access to HDF
- > With standard fluid quality
- > On any HD monitor

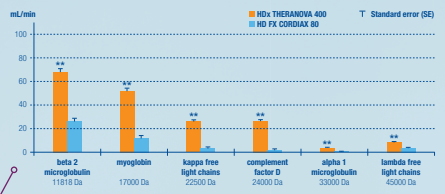
HDx THERAPY

TREATMENT EFFECTS AND THERAPY IMPLICATIONS

OVERALL CLEARANCE HDx vs. HD²³

HDx with THERANOVA 400 dialyzer HD with latest generation high-flux dialyzer
Q_b = 300 mL/min – Treatment Time = 4 h (Mean) – n = 19

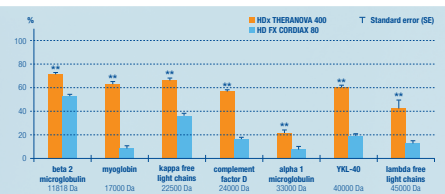
**p < 0.001 vs. high-flux HD



REDUCTION RATIO HDx vs. HD²³

HDx with THERANOVA 400 dialyzer HD with latest generation high-flux dialyzer
Q_b = 300 mL/min – Treatment Time = 4 h (Mean) – n = 19

**p < 0.001 vs. high-flux HD



Do not use THERANOVA dialyzers for HDF or HF due to higher permeability of larger molecular weight proteins such as albumin.



PERFORMANCE

Enhanced blood purification of a wide range of large middle molecules in two clinical studies, comparing to a best-generation high-flux dialyzer, the use of THERANOVA dialyzers in HD resulted in:

- Markedly greater clearances and intradialytic reduction ratios than regular HD – at ordinary blood flow rates²³
- Similar to greater removal in comparison to high-volume HDF²⁴
- Albumin removal limited to between 1 and 4 grams²³



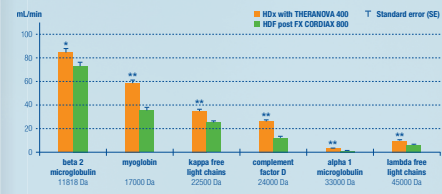
PATIENT

Patients requiring higher clearances of larger uremic toxins, without access to HDF

OVERALL CLEARANCE HDx vs. HDF²⁵

HDx with THERANOVA 400 dialyzer HDF with latest generation high-flux dialyzer for HDF
Q_b = 400 mL/min – Treatment Time = 4.4 h – Volume = 24 L (Mean) – n = 20

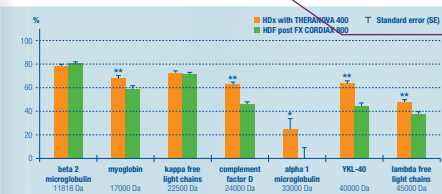
*p < 0.01 vs. HDF
**p < 0.001 vs. HDF



REDUCTION RATIO HDx vs. HDF²⁵

HDx with THERANOVA 400 dialyzer HDF with latest generation high-flux dialyzer for HDF
Q_b = 400 mL/min – Treatment Time = 4.4 h – Volume = 24 L (Mean) – n = 20

*p < 0.01 vs. HDF
**p < 0.001 vs. HDF



FLUID QUALITY

It is recommended to run the HDx therapy solution with high quality dialysis fluid. However, the unique structure of the THERANOVA dialyzer membrane, providing high adsorption capacity to bacterial products, presents an effective barrier to endotoxins²⁶ and enables the HDx therapy to remain to be compatible with standard-quality dialysis fluid (ISO 11663 or AAMI R90C).



MONITOR

Thanks to the standard design and operating mode of the THERANOVA dialyzer, the HDx therapy solution can be easily implemented on any HD monitor (provided it is equipped with an accurate volumetric UF control system). The compatibility has been verified on a large sample of HD monitors during extensive field tests.²⁷

CONVERSATION STARTER:

Help your customers grasp the outstanding performance of **Theranova** in HD mode, in terms of middle molecule removal, and understand the potential benefits of the HDx therapy using clinical data.

Typical questions:

- > What are the expected clinical benefits of a significantly higher middle molecule removal?
- > How appealing is the HDx therapy, providing HDF performance and beyond in the removal of large middle molecules, with regular hemodialysis equipment and protocol?

2. TO HDF PERFORMANCE (AND BEYOND FOR LARGE MIDDLE MOLECULES)

- > Similar, to greater removal in comparison to high-volume HDF
- > Albumin removal limited to between 1 and 4 grams

MARKETING VALUE PROPOSITION

HDx THERAPY: HDF PERFORMANCE AND BEYOND AS SIMPLE AS HD

KEY MESSAGES TO CONVEY FROM THIS SPREAD

The HDx therapy may allow clinics to save costs by providing HDF performance and beyond in the removal of large middle molecules without the infrastructure of HDF therapy.

1. HDF PERFORMANCE AND BEYOND

Equivalent performance to high-volume HDF, possibly greater for large middle molecules when it comes to clearance and intradialytic reduction ratio.

HDx THERAPY

HDF was born on the need to increase middle molecule removal, at a time when the permeability of high-flux dialysis membranes was more limited. By applying high convective volume, HDF can significantly increase solute clearance within the size range defined by high-flux membrane permeability.

HDx can achieve a similar solute removal and beyond in the removal of middle and larger middle molecules, when used on any dialysis machine in standard HD mode, removing the need for the more complex equipment required for convective therapies. The **THERANOVA** membrane is optimized for trans-membrane transport of large solutes and does not require additional HDF type connection.

Do not use **THERANOVA** dialyzers for HDF or HF due to higher permeability of larger molecular weight proteins such as albumin.

HDF PERFORMANCE AND BEYOND...

Equivalent removal of small and conventional middle molecules

Greater removal is possible for large middle molecules

Applicable to any patient requiring higher clearance of large uremic toxins

AS SIMPLE AS HD

HD infrastructure: no need for HDF capable monitors and specific water quality and fluid quality assurance measures^{2,14}

Avoiding HDF additional running costs: no disposable infusion line, fewer ultrafilters, less dialysis water and less concentrates

Avoiding requirement for specialist training and extensive monitoring during therapy delivery²⁵

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



CONVERSATION STARTER:

Get your customers thinking about the value of the HDx therapy, providing HDF performance and beyond (for large middle molecules) in HD set-up, thus may help reduce the costs and complexity associated with high-volume HDF.

Typical questions:

- > What is the share of patients on HDF in your clinic, and are you aiming at increasing this share?
- > What are the greatest roadblocks to high-volume HDF standardization: infrastructural requirements, higher cost per treatment, patient tolerance and eligibility, complexity of the therapy delivery for the staff?
- > How can HDx complement HD and HDF as a new dialysis modality?

2. AS SIMPLE AS HD

The **Theranova** dialyzer may allow clinics to save costs compared with the HDF treatment modality by:

- > Not having to purchase special disposables required for the HDF treatment modality
- > Not having to invest in additional special equipment required for the HDF treatment modality
- > Not having to train staff on the HDF treatment modality
- > Not having to perform the dedicated microbiology tests required for HDF treatment
- > Not having to maintain/upgrade and monitor a dialysate purification system to deliver the HDF treatment modality

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