PATHFAST™

THE SEPSIS MARKER
PATHFAST™ PRESEPSIN

» Whole blood
» Early prognosis
» Risk stratification
» Patient monitoring
**What is PATHFAST™ Presepsin?**

**PATHFAST™ Presepsin** is a chemiluminescent enzyme immunoassay (CLEIA) for the quantitative measurement of the Presepsin concentration in whole blood or plasma. **PATHFAST™ Presepsin** improves the diagnosis and prognosis of sepsis defining its level of severity. It is a valid indicator of risk stratification in septic patients. Due to the fast analysis within 15 minutes and the high prognostic value even at patient’s admission, **PATHFAST™ Presepsin** is useful in laboratories, emergency- and intensive care units and neonatal departments. An early diagnosis with an excellent prognostic performance and its ability to respond rapidly to the variety of clinical conditions make **PATHFAST™ Presepsin** the ideal tool for monitoring treatment, selecting the correct antibiotic-dose or changing it if ineffective.

**Presepsin** is a reliable, specific and sensitive biomarker for sepsis and a valuable tool for the very early diagnosis of sepsis by **Gram-negative** and **Gram-positive** bacteria or fungi (1). Presepsin rises earlier than other biomarker and does not show unspcific increases (2). Presepsin values help to stratify the severity of the septic disease with excellent correlation to APACHE II-, GCS-, MEDS- and SOFA-score (3). Presepsin exceeds the prognostic power of other sepsis biomarkers and is specifically useful when combined with clinical risk scores like e.g. qSOFA (4).

**Why choose PATHFAST™ Presepsin?**

The time course of Presepsin can be used for monitoring: a decline demonstrates response to therapy and predicts a favorable outcome (5,6). Presepsin is an accurate biomarker in the diagnosis of neonatal sepsis with higher cut off values (7,8). In cardiac surgery elevated preoperative plasma Presepsin concentration is a strong predictor of postoperative mortality in cardiac surgery patients (9).

**Early marker of sepsis (Fig. 2)**

The Presepsin molecule is characterized by rapid kinetics: activation time is only 2 hours following a bacterial or fungal event, with a peak concentration after 3 hours. This characteristic makes the Presepsin molecule the fastest biomarker for sepsis in relation to procalcitonin (PCT) and C-Reactive Protein (CRP), which have activation times of 6-12 hours and 12-24 hours, respectively. The half life of the molecule in plasma is 4-5 hours, compared to 12-24 hours for PCT, allowing more effective and earlier management of the pharmacological treatment.

Presepsin (in orange) and other markers in post-traumatic patients following a serious burn were considered. It is well-known that Presepsin does not change after the trauma but there is an early increase in the values of Presepsin by day 2 following the occurrence of a bacterial infection confirmed by a positive blood culture of day 5. Effectiveness of antibiotic treatment is shown at day 13. Moreover, when patients were divided into an infection group and a non-infection group and ROC curves of each of the markers were plotted to compare Presepsin with other markers, the results showed that Presepsin was the best, followed by CRP, IL-6, and PCT (2).
The diagnostic validity of Presepsin has been evaluated in numerous clinical studies. Comparisons of different medical scores and relevant biomarkers in sepsis diagnosis revealed an important role for PATHFAST™ Presepsin.

**Improved 30 day mortality prediction (Fig. 3)**

Presepsin showed superior risk of 30 day mortality prediction at admission in septic patients compared to APACHE II, GCS, MEDS, SOFA and procalcitonin.

**Support of medical scores (Fig. 4A+B)**

Quick-SOFA (qSOFA) was defined by The Third International Consensus Definitions for Sepsis and Septic Shock in 2016 in order to provide a simplified version of SOFA without the need of laboratory tests. It can be directly assessed at patient admission. For discrimination between uncomplicated sepsis and severe sepsis or septic shock Presepsin showed superior discriminatory power compared to clinical scores and biomarkers. Additionally simultaneous assessment by combining Presepsin and qSOFA improved the diagnostic validity significantly. Combination of Presepsin and qSOFA showed a detection rate for non-survivors of 93% and 67% and for patients with severe sepsis/septic shock of 92% and 58% whereas qSOFA alone only reached 67% and 58%, respectively. Presepsin showed also a predictive superiority compared to lactate and procalcitonin (4).

**Presepsin and procalcitonin levels for mortality prediction (Fig. 5)**

Evolution of Presepsin levels over time in survivors was significantly different from that in deceased patients in the ICU. PCT levels decreased rapidly and similarly in survivors and non-survivors whereas Presepsin clearly differentiates already after 24 hours between the two cases. In comparison to survivors Presepsin levels in non-survivors stayed constantly high over the time period observed. Conversely, PCT levels fell rapidly and similarly from day 1 to 7 in survivors and non-survivors. Presepsin appears as an early marker of mortality with better prognostic performance than PCT and can be used as an aid in risk stratification strategies in septic patients (6).

Patients with decreasing levels of Presepsin over 7 days in ICU were more likely to have received an early appropriate first-line empirical antibiotic therapy on day 1 than those with increasing levels (5).
**Negative Predictive Value and cut off values (Fig. 6)**

An important diagnostic factor is the high Negative Predictive Value (NPV) of Presepsin. In fact for healthy individuals, not affected by a clear bacterial outbreak, the values of Presepsin are below 200 pg/mL. A Presepsin cut off value of 1.622pg/ml excludes 30 day mortality by a Negative Predictive Value (NPV) of 98.5% (3). Presepsin concentration is already related to the severity of the disease at the time of first presentation and may be useful in the differential diagnosis in patients presenting with clinical signs of SIRS and sepsis in the emergency department. In summary, based on the Presepsin values measured in the study patients with different disease severity degrees (SIRS, sepsis, severe sepsis or septic shock) and the close relationship between Presepsin and outcome decision thresholds for risk stratification could be established (1,10).

**Evaluation of Severity**

Presepsin correlates significantly with the degree of severity of the infection as its quantitative results increase proportionally. In fact, the studies reveal maximum correlation with the SOFA score values (clinical scoring used most frequently to evaluate organ failure). Higher values on the first day of monitoring are closely associated with a higher incidence of new organ failure and hemodynamic instability in the first 24 hours.

All together, Presepsin concentration increased with the SOFA score, the number of prevalent organ dysfunctions or failures, and the incidence of new failures of the respiratory, coagulation, liver, and kidney systems, therefore Presepsin is an early predictor of host response and mortality in septic patients. Changes in concentrations over time seem to reflect the appropriateness of antibiotic therapy (5).

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**Fig. 6: Decision thresholds of PSEP for early risk stratification in patients with sepsis**

<table>
<thead>
<tr>
<th>Presepsin (pg/ml)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 200</td>
<td>Exclusion of sepsis</td>
</tr>
<tr>
<td>&lt; 300</td>
<td>Systemic infection not probable</td>
</tr>
<tr>
<td>&lt; 500</td>
<td>Systemic infection (sepsis) possible</td>
</tr>
<tr>
<td>&lt; 1000</td>
<td>Significant risk of the systemic infection progression (severe sepsis), increasing risk of unfavorable outcome</td>
</tr>
<tr>
<td>≥ 1000</td>
<td>High risk of the systemic infection progression (severe sepsis/septic shock). High risk for mortality after 30 day comparable with a SOFA score ≥ 8</td>
</tr>
</tbody>
</table>

Mod. from Carpio et al., 2015 and C. Chenevier-Gabeaux et al., 2015

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**Evaluation of Severity**

- **Pathfast**
  - Results in 15 minutes
  - Fast kinetics (2/3 hours after onset of the infectious event) (1)
  - Short half-life: 4/5h (11)

- **Practicality**
  - Whole blood or plasma (100 μL)
  - Up to 6 tests in parallel (all in 15 min)
  - Ideal for Emergency Units

- **Sensitivity**
  - Chemiluminescent enzyme immunoassay
  - No interference
  - “All-in-one” single use cartridges

- **Reliability**
  - High Negative Predictive Values
  - No unspecific results
  - Excellent correlation with medical scores
**PATHFAST™ Test Principle**

**IMMUNOREACTION**
- Magnetic particles coated with antibody
- ALP labelled antibody
- Target molecule

**SEPARATION**
- Sample (whole blood, plasma)
- Magnet

**ENZYME REACTION**
- Chemiluminescent substrate

**DETECTION**
- Photomultiplier
- Measurement of light emission

**PATHFAST™ Technical Specifications**

<table>
<thead>
<tr>
<th>Specification</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instrument type</td>
<td>Desktop Immunoassay Analyzer</td>
</tr>
<tr>
<td>Throughput</td>
<td>Up to 6 samples or parameters per run</td>
</tr>
<tr>
<td>Measuring time</td>
<td>15 minutes for 6 samples using emergency markers or PATHFAST™ Presepsin</td>
</tr>
<tr>
<td>Sampling material</td>
<td>Whole blood, plasma, serum</td>
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<tr>
<td>Measuring principle</td>
<td>Chemiluminescence enzyme immunoassay technology (CLEIA) and Magtration® technology.</td>
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<tr>
<td>Reaction temperature</td>
<td>37 °C</td>
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<tr>
<td>Sample volume</td>
<td>100 µl</td>
</tr>
<tr>
<td>Data storage</td>
<td>Patient data: 1000, QC data: 1800, CAL data: 300</td>
</tr>
<tr>
<td>Datatransfer</td>
<td>ASTM and Fixed standard</td>
</tr>
<tr>
<td>Weight</td>
<td>28 kg</td>
</tr>
<tr>
<td>EL requirements</td>
<td>100 - 240 V AC (50/60 Hz)</td>
</tr>
<tr>
<td>Power consumption</td>
<td>360 VA</td>
</tr>
<tr>
<td>Monitor/keyboard</td>
<td>LCD touch-screen</td>
</tr>
<tr>
<td>Printer</td>
<td>Integrated</td>
</tr>
<tr>
<td>PC</td>
<td>Integrated, Handheld Barcodereader included</td>
</tr>
<tr>
<td>Interface</td>
<td>RS-232C and Ethernet Port</td>
</tr>
<tr>
<td>Calibration</td>
<td>Factory calibration, 2-point calibration every 4 weeks</td>
</tr>
<tr>
<td>24-h operation (stand-by)</td>
<td>Recommended</td>
</tr>
</tbody>
</table>

**PATHFAST™ Dimensions**

- **Dimensions**
  - Width: 343 mm
  - Height: 569 mm
  - Depth: 475 mm

**References**

1. Presepsin (sCD14-ST), an innate immune response marker in sepsis.
   Chenevier-Gobeaux C, Borderie D, Weiss N, Mallet-Coste T, Claessens YE

2. Usefulness of presepsin (sCD14-ST) measurements as a marker for the diagnosis and severity of sepsis that satisfied diagnostic criteria of systemic inflammatory response syndrome.
   Shozushima T, Takahashi G, Matsumoto N, Kojika M, Okamura Y, Endo S

3. Diagnostic and prognostic value of Presepsin (soluble CD14 subtype) in emergency patients with early sepsis using the new assay PATHFAST Presepsin.
   Spanuth E, Ebelt H, Ivandic B, Werdan K
   21st International Congress of Clinical Chemistry and Laboratory Medicine, IFCC-World Lab-EuroMedLab, Berlin, 15-19 May 2011

4. qSOFA (quick SOFA) score, presepsin and procalcitonin for severity assessment in initial sepsis.
   Spanuth E, Ebelt H, Ivandic B, Thomas H, Werdan K
   ISICEM 2017 – 37th International symposium on Intensive Care and Emergency Medicine, Brussels, March 21-24, 2017

5. Circulating presepsin (soluble CD14 subtype) as a marker of host response in patients with severe sepsis or septic shock: data from the multicenter, randomized ALBIOS trial.
   Crit Care. 18 (2014) R6

6. Presepsin (soluble CD14 subtype) and procalcitonin levels for mortality prediction in sepsis: data from the Albumin Italian Outcome Sepsis trial.
   Crit Care. 18 (2014) R6

   Pugni L, Pintorasant C, Milani S, Vener C, Ronchi A, Falbo M, Arghitu M, Mosca F

8. Presepsin for the detection of late-onset sepsis in preterm newborns.
   Poggi C, Bianconi T, Gozzini E, Generoso M, Dani C

9. Presepsin (sCD14-ST) Is a Novel Marker for Risk Stratification in Cardiac Surgery Patients.
   Bomberg H, Klingele M, Wagenpfel S, Spanuth E, Volk T, Sessler DI, Schäfers HJ, Goeresdonk HV
   Anesthesiology. 126 (2017):631–42

10. Utility of presepsin (sCD14-ST) as a diagnostic and prognostic marker of sepsis in the emergency department.
    Carpio R, Zapata J, Spanuth E, Hess G

11. Early elevation of plasma soluble CD14 subtype, a novel biomarker for sepsis, in a rabbit cecal ligation and puncture model.
    Nakamura M, Takeuchi T, Naito K, Shirakawa K, Hosaka Y, Yamasaki F, Furuhashi S
## Product List

**PATHFAST™ for critical care and sepsis diagnostics**

### SYSTEM

**PATHFAST™ Immunoanalyzer**  
Analyzer for the detection of cardiac and other emergency parameters and sepsis  
Item number: 1114-0000  
Pack size: 1 x 1

### CONSUMABLES AND ACCESSORIES

**PATHFAST™ pipette tips**  
Item number: 1114-1000  
Pack size: 5 x 42 units

**PATHFAST™ waste box**  
Item number: 1114-1001  
Pack size: 10 units

### REAGENT KITS FOR CRITICAL CARE DIAGNOSTICS

**PATHFAST™ cTnl**  
Item number: 1110-2000  
Pack size: 60 tests

**PATHFAST™ Myoglobin**  
Item number: 1110-2001  
Pack size: 60 tests

**PATHFAST™ CK-MB**  
Item number: 1110-2002  
Pack size: 60 tests

**PATHFAST™ D-Dimer**  
Item number: 1110-2003  
Pack size: 60 tests

**PATHFAST™ NT-proBNP**  
Item number: 1110-2004  
Pack size: 60 tests

**PATHFAST™ hsCRP**  
Item number: 1110-2005  
Pack size: 60 tests

**PATHFAST™ HCG**  
Item number: 1110-2009  
Pack size: 60 tests

**PATHFAST™ HCG control set**  
Item number: 1110-2010  
Pack size: 4 x 1 ml

### REAGENT KITS FOR SEPSIS DIAGNOSTICS

**PATHFAST™ Presepsin**  
Item number: 1110-4000  
Pack size: 60 tests

**PATHFAST™ Presepsin control set**  
Item number: 1110-4001  
Pack size: 4 x 1 ml