# Health Economic Data on Burden of Hepatorenal Syndrome Published in Current Medical Research and Opinion

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**-- Long Hospital Stays, Frequent Medical Visits and Hospital Readmissions Drive Costs, Payer Burden --**

STAINES-UPON-THAMES, United Kingdom, June 23, 2017 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a leading global specialty pharmaceutical company, today announced new retrospective, claims-based health economic data that show hepatorenal syndrome (HRS), or the development of renal (kidney) failure in patients with advanced chronic liver disease,[1,2] imposes a significant economic burden on payers. HRS is a rare, life-threatening disease with an estimated prevalence of greater than 22,000 diagnosed in the U.S. each year.[3] The Mallinckrodt-sponsored study was recently published in *Current Medical Research and Opinion*. The intended audience of this study is population-based decision makers with knowledge and expertise in the area of healthcare economic analysis and its limitations.

"HRS-related hospital admissions have risen over the past decade and have led to increased inpatient costs, yet understanding of the overall economic burden of this serious condition has remained limited," said study investigator **Kevin Korenblat, M.D., Associate Professor of Medicine, Washington University School of Medicine.** "This study aimed to provide a comprehensive and current estimate of the costs involved with HRS in the U.S. from the payer perspective."

The retrospective study, titled "**The burden of hepatorenal syndrome among commercially insured and Medicare patients in the United States**," evaluated the characteristics, healthcare resource utilization (HCRU), and payer-related costs of HRS patients covered by commercial and Medicare insurance programs from 30 days prior to the "index date," defined as the date of the earliest inpatient admission with an HRS diagnosis, through 90 days post-diagnosis (outcome period). This includes inpatient resource utilization and costs to payers, longitudinal measures such as rates of readmissions, costs in a variety of non-inpatient settings such as outpatient and physician office, rates of transplants and dialysis and, as a secondary endpoint, mortality.

Anonymized claims from adults with HRS (18-64 years old) were identified from two HIPAA (the Health Insurance Portability and Accountability Act)-compliant claims databases of commercially insured patients (OptumHealth Care Solutions Inc., 18.5 million beneficiaries) between 1998–2014, and Medicare beneficiaries (aged 65 and older) between 2009–2013 (Standard Analytic Files, 5 percent of 4 million beneficiaries). Eligible patients were required to have continuous non-health maintenance organization coverage on the index date and meet the age criteria. Demographics, including age, gender, geographic region and clinical characteristics were summarized for commercially insured and Medicare patients during the 6-month baseline period and on the index date. Costs were then extrapolated using population statistics and information on rates of insurance coverage by payer to project the economic burden of HRS in the U.S.

The analysis suggests HRS poses a significant economic burden to payers estimated at $3.0–$3.8 billion in annual total direct medical costs. Additional findings include:

- A total of 784 commercially insured and 1061 Medicare HRS patients met the sample selection criteria.
  - Patients were disproportionately male (commercial: 63.0 percent; Medicare: 57.9 percent) with a mean age of 54.1 among commercially insured and 74.1 among Medicare patients.
- Average HCRU during the 90-day outcome period was substantial for both commercially insured and Medicare patients:
  - Within the first 30 days, the average hospital length of stay was 12.3 days among commercially insured and 10.8 days among Medicare patients.
  - Based on Kaplan–Meier analyses, 36 percent of commercially insured and 26 percent of Medicare patients were readmitted within the next 30 days.
  - Many patients received dialysis (commercial: 33.0 percent; Medicare: 22.1 percent) or liver transplant (commercial: 10.7 percent; Medicare: 1.6 percent) during follow up.
  - Median survival was 95 days among commercially insured patients and 33 days among Medicare patients.
- Per patient healthcare costs were substantial for both commercially insured and Medicare HRS patients during the 90-day outcome period:
  - Average costs were $157,665 for commercially insured and $48,322 for Medicare patients, with 68.3 percent and 78.3 percent of the costs incurred within the first 30 days.
  - The primary cost driver was inpatient visits (commercial: 90.3 percent of costs; Medicare: 83.1 percent of costs),

with differences between the subpopulations consistent with lower mortality, higher dialysis rates, and higher liver and kidney transplant rates among the commercially insured.

"Liver transplant is the only definitive treatment for HRS, but not feasible in most cases due to organ availability and eligibility issues. Yet at present there are no approved drug therapies for HRS type 1 in the U.S. or Canada," said **Steven Romano, M.D., Chief Scientific Officer and Executive Vice President at Mallinckrodt**. "This analysis provides important insights into the economic burden of HRS, and reinforces our commitment to evaluating terlipressin as a potential treatment option for patients with HRS type 1 in these countries."

Terlipressin is being investigated in a Phase 3 clinical trial for the treatment of HRS type 1, an acute form of the condition. The safety and effectiveness of terlipressin has not been established with the U.S. Food and Drug Administration or Health Canada. Terlipressin is approved for use in countries outside the U.S., including several in Europe.[4,5,6,7]

**Limitations of the Study**

- Limitations of the study include its reliance on the accuracy of diagnosis codes to identify patients with HRS, to evaluate their comorbidity profiles at baseline, and their HCRU during the outcome period.
- Diagnosis codes do not differentiate between HRS type 1 and HRS type 2, and accuracy of all codes may vary.
- The HCRU and cost findings may not be generalizable to other patients, such as those enrolled in Medicaid.
- The economic burden of HRS is likely underestimated as this study did not assess the longer- term economic burden of HRS, and cost estimates were not inflation adjusted over the study periods (1998-2014 for commercial and 2009-2013 for Medicare cohort).

The *Current Medical Research and Opinion* study may be accessed here: http://dx.doi.org/10.1080/03007995.2017.1331211

**About Hepatorenal Syndrome**
HRS is characterized by rapid, progressive functional renal failure and has a very poor prognosis, with >80 percent mortality within three months. HRS is a rare syndrome of marked renal dysfunction in patients with cirrhosis, decompensated liver disease and portal hypertension. At present, there are no approved drug therapies for HRS type 1 in the U.S. or Canada. The only curative treatment for HRS type 1 and the underlying end-stage cirrhosis is liver transplantation. However, more patients will not survive long enough to receive a liver transplant.

**About Terlipressin**
Terlipressin is a synthetic vasopressin analogue being investigated for the treatment of HRS type 1 in the U.S. and Canada. Safety and efficacy has not been established with nor has approval been granted by regulatory authorities in either country.

**ABOUT MALLINCKRODT**
Mallinckrodt is a global business that develops, manufactures, markets and distributes specialty pharmaceutical products and therapies. Areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, nephrology, pulmonology and ophthalmology; immunotherapy and neonatal respiratory critical care therapies; and analgesics and hemostasis products. The company's core strengths include the acquisition and management of highly regulated raw materials and specialized chemistry, formulation and manufacturing capabilities. The company's Specialty Brands segment includes branded medicines and its Specialty Generics segment includes specialty generic drugs, active pharmaceutical ingredients and external manufacturing. To learn more about Mallinckrodt, visit www.mallinckrodt.com.

Mallinckrodt uses its website as a channel of distribution of important company information, such as press releases, investor presentations and other financial information. It also uses its website to expedite public access to time-critical information regarding the company in advance of or in lieu of distributing a press release or a filing with the U.S. Securities and Exchange Commission (SEC) disclosing the same information. Therefore, investors should look to the Investor Relations page of the website for important and time-critical information. Visitors to the website can also register to receive automatic e-mail and other notifications alerting them when new information is made available on the Investor Relations page of the website.

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[1] Arroyo V, Gines P, Gerbes AL, et al. Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. International

Ascites Club. Hepatology 1996;23:164-76.

[2] Betrosian AP, Agarwal B, Douzinas EE. Acute renal dysfunction in liver diseases. World J Gastroenterol 2007;13:5552-9.

[3] Do A, Ezaz G. Increasing incidence and cost, but decreasing mortality in patients with hepatorenal syndrome: a study of the National Inpatient Sample 2005-2011. Hepatology 2015;62(21 Supplement):abstract no. 283.

[4] Nadim, M., et al. Management of the critically ill patient with cirrhosis: A multidisciplinary perspective. Journal of Hepatology. 2016, vol. 64, 717–735.

[5] Angeli, P., et al. Diagnosis and management of acute kidney injury in patients with cirrhosis: Revised consensus recommendations of the International Club of Ascites. Journal of Hepatology. 2015, vol. 62, 968–974.

[6] 4 Nadim, M., et al. Hepatorenal syndrome: the 8th international consensus conference of the Acute Dialysis Quality Initiative (ADQI) Group. Critical Care 2012 16:R23.

[7] 5 European Association for the Study of the Liver clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. Journal of Hepatology. 2010, vol. 53, 397–417.

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