

The Economic Burden and Managed Care Implications of Chronic Inflammatory Demyelinating Polyneuropathy

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Although the clinical burden of chronic inflammatory demyelinating polyneuropathy (CIDP) has been well documented, its economic burden has been more difficult to estimate and address. Regarding direct costs of disease, limited information has been available on the hospitalization burden associated with CIDP. One study presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) in May 2016 by Suryavanshi and Khanna used data surrounding discharges of adult patients 18 years and older with CIDP identified from the 2010 pooled Healthcare Cost and Utilization Project National (Nationwide) Inpatient Sample (HCUP-NIS). Patients with CIDP-related hospitalizations were matched with 4 control hospitalizations based on gender and age. The study used survey formats to determine predictors of length of stay (LOS), total charges, predictors of death, and CIDP treatment (intravenous immunoglobulin [IVIg] vs plasmapheresis). There were 31,451 weighted records of CIDP hospitalization during the study period. Results reported that the estimated cost of hospitalizations for CIDP from 2010 to 2012 was \$2.1 billion in the United States alone. The mean cost of CIDP-related hospitalization was \$68,231 and related to 50% longer LOS and higher total charges than control patients without CIDP. Significant predictors of hospitalization outcomes included patient age, hospital bed size, location and teaching status, discharge to long-term care or skilled nursing facilities, presence of complications, administration of IVIg or plasmapheresis treatments, and higher diagnosis and procedures on record. The authors concluded that although CIDP is a rare disease, it still results in significant hospitalization costs and burden. Although these data were presented as noted at the ISPOR Congress, they have not yet been formally published.¹

Another important study was performed by Guptill et al to determine health plan–paid costs and healthcare resource usage of patients with CIDP who were enrolled in 9 commercial health plans in the United States and submitted claims during the 12-month period for the year 2011. The study assessed demographics, prevalence of comorbidities, prescribed drugs, place and service, and the mean annual healthcare costs paid for each patient. To be included, patients

ABSTRACT

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a symmetric demyelinating peripheral neuropathy with either a progressive or relapsing remitting course. CIDP is both debilitating and degenerative, leaving patients with functional impairment due to nerve damage in their extremities. Along with its medical burden, CIDP has a significant economic impact, with disease-related expenses and the often fairly high costs related to the immune therapies used to treat the disease. Costs for patients with this disorder often exceed those of other immune-mediated neuromuscular diseases. For these reasons, it is necessary for clinicians to better determine optimal long-term treatment strategies for patients with CIDP that are designed to address both the clinical and economic burden of its management and improve patient outcomes and quality of life.

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must have had at least 1 health insurance claim during the study period. Data were obtained from a variety of health plans, including commercial, Medicare, and Medicaid plans.² Patients included those with a CIDP diagnosis between January 1, 2011, and December 31, 2011, whose primary health insurance plan was considered eligible for the Accordant Health Services (AHS) care management program, a nationwide medical and pharmacy claims database.^{2,3}

Total costs were calculated per patient, and this amount was divided by total member-months and multiplied by 12 to determine per-patient per-year (PPPY) costs. Paid costs were categorized as either medical or pharmacy costs. Results demonstrated that mean health plan-paid costs for patients with CIDP during the study period were \$56,953 (\pm \$10,292). Medical costs were \$25,054 (\pm \$6840) and pharmacy costs were calculated at \$31,899 (\pm \$7375). Overall costs were lower for women (\$47,094 \pm \$15,560) versus men (\$64,648 \pm \$13,747). There was no evidence for a significant relationship between the health insurance–paid costs PPPY and either age or comorbidity burden. Pharmacy costs accounted for 57% of the total paid amounts from the health plans included. Health plan–paid costs that were incurred during hospitalization comprised 18% of total insurance paid amounts, with 16% of paid costs attributed to the outpatient hospital setting and 3% to physician offices. Approximately 90% of pharmacy costs were related to IVIg therapy, which was administered to 26% of patients included in the study. Overall costs and pharmacy costs were highly variable among the patient population studied. The distribution of total health care plan costs by place or service and/or claim category was divided as shown in the [Figure](#).²

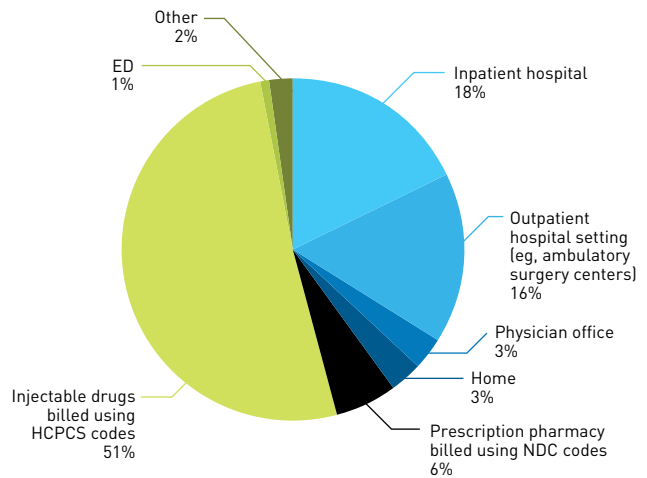
Overall, the investigators concluded that the mean annual health plan–paid costs for patients with CIDP were higher than those attributed to other recently studied immune-mediated neuromuscular diseases (eg, myasthenia gravis). Future studies are needed to better delineate optimal long-term treatment strategies for patients with CIDP, especially with attention to therapy use and cost.²

Cost Utility of Therapy for CIDP

CIDP was previously treated using corticosteroids and plasma exchange (PE); however, these therapies were limited by disease chronicity. Long-term use of steroids carried a substantial risk of serious adverse events (AEs), and the benefit from PE was usually transient, requiring access to specialized treatment centers and repeated vascular access.² The first IVIg agent was approved for use by the FDA in 2008; IVIg was widely used off label before FDA approval of the drug class, but it is now considered first-line treatment for CIDP.^{2,4,5}

Looking at the drug class in general, IVIg is used as therapy for more conditions than CIDP. Per a recent market analysis report, the World Health Organization identified more than 50 primary immunodeficiency diseases (PIDDs), including 176 rare hereditary disorders. The overall incidence of PIDDs is growing, which will

FIGURE. Total Healthcare Plan Costs



ED indicates emergency department; HCPCS, Healthcare Common Procedure Coding System; NDC, national drug code.

Reprinted from Guptill JT, Bromberg MB, Zhu L, et al. Patient demographics and health plan paid costs in chronic inflammatory demyelinating polyneuropathy. *Muscle Nerve*. 2014;50(1):47-51. doi: 10.1002/mus.24109, with permission from John Wiley & Sons.

likely increase demand for immunoglobulin therapies over the next several years. Results of market research data have estimated the global IVIg market size at \$9.09 billion (2016 USD), and this market is predicted to grow at a compound annual growth rate of 7.1% in the 10-year period from 2012 to 2022. Demand for IVIg in both PIDDs and acquired immunodeficiency disorders continues to rise as IVIg is the most effective and often the single available treatment option for these disorders. Recent marketing data show that the CIDP segment held the largest share of the IVIg market based on application, second only to hypogammaglobulinemia.⁶

Administration of IVIg constituted the greatest revenue share as of 2014, based on high usage of IVIg in a substantial range of indications and applications. The increasing number of intravenous (IV) product approvals and clinical trials for new applications will likely continue industry growth opportunities in this area. That said, subcutaneous (SC) administration of immunoglobulin is predicted to grow exponentially at a rate of 9.8% over the 2012-2022 forecast period. Growth potential of this segment of therapy is associated with the advantages of SC administration, which include the rapid action of the drug once administered, faster patient responses, and fewer AEs associated with these formulations.⁶ It also must be noted that the overall drug category of “inflammatory medications” is a significant cost driver in healthcare. A 2017 Express Scripts Drug Trend Report demonstrated that inflammatory agents remain the costliest category in terms of spending and is one of the highest in expected continued spending by trend. The anti-inflammatory category is dominated by specialty drugs and remains the leading pharmaceutical cost driver for health plans. However, treatments

for other diseases of aging, including cancer and diabetes, overtake anti-inflammatory drugs as patients age, as evidenced by anti-inflammatory drugs holding third place in this patient population.⁷

Although IVIg has demonstrated significant clinical improvement for patients with CIDP, it remains a considerably more expensive therapy than standard corticosteroids. Because of this, the predicted cost-utility of IVIg drugs must be taken into consideration along with their clinical efficacy. One analysis in this area was performed by Blackhouse et al and compared the cost-utility of these drugs versus corticosteroids in a Canadian patient population with CIDP. This study was performed using a Markov model and drawn from the perspective of a publicly funded healthcare system in Canada, noting that the costs of IVIg were paid by public health payers as part of their payment to Canadian Blood Services (CBS). Effectiveness was measured in quality-adjusted life-years (QALYs). The time model was 5 years in the basecase analysis, and alternative time models were assumed in the sensitivity analysis. Costs and effects were also discounted at a rate of 5% per year. Basecase results demonstrated that the total costs of IVIg over the 5-year period were \$124,065 (3.962 QALYs) versus \$2196 for corticosteroids (3.785 QALYs). This represented an incremental cost for IVIg of \$121,869 compared with corticosteroids. The cost-utility ratio of IVIg compared with corticosteroids was calculated at \$687,287 per QALY gained. The data suggested that, based on common willingness-to-pay thresholds, the use of IVIg drugs in CIDP would be considered cost-effective. However, the investigators acknowledged limitations to the study, including that a public health payer perspective was used and, because of this, indirect costs were not included in the analysis. If an actual societal perspective had been considered, the cost-utility of IVIg use may have shown more encouraging results. The investigators noted that IVIg remains a popular therapy due to its potential for more optimal patient outcomes versus less expensive, standard therapies.⁴

In the more recent Guptill study published in 2014, a total of 179 health insurance claims were paid among patients with CIDP who received IVIg. In this analysis, the majority of the IVIg infusions were done in the home setting (72%), with 16% administered in a physician's office and 12% administered in either an outpatient hospital or other point-of-service (POS) setting (11% and 1%, respectively). The mean PPPY cost for patients treated with IVIg was \$108,016 (\pm \$118,437; range, \$4998-\$248,938), and the paid amount per IVIg infusion was \$8598 (\pm \$476; range, \$950-\$24,458). Per-infusion costs were almost the same in the home setting ($\$9720 \pm \561) compared with the outpatient setting ($\$9718 \pm \951). Total paid costs for IVIg infusions administered in the clinic setting were \$2610 (\pm \$118). As noted earlier, the chronic management of CIDP with IVIg leads to considerable long-term treatment costs. However, given the proven efficacy of IVIg in this disease, studies need to be performed to determine long-term management strategies using these agents, especially in terms of dosing, dose intervals, and tapering, to both

maximize treatment efficacy and justify the high costs of therapy over the long term.²

Reducing Costs of IVIg Therapy

Considering the high costs associated with immunoglobulin therapy, opportunities for cost containment must be explored and potentially implemented. Hadden et al performed a study to assess both clinical outcomes and patient satisfaction in patients with CIDP or multifocal motor neuropathy (MMN) who were switched from IVIg to an SC formulation of the drug (SCIg). The patients, half with CIDP, were already receiving long-term hospital-based IVIg treatment and were switched to SCiG. Results demonstrated that the majority of patients studied had a smooth transition from IV to SC administration and were highly satisfied with the SCiG formulation. They had good outcomes, including fewer AEs, increased therapy convenience, and no wear-off effect. Importantly, the cost of IVIg treatment was compared with the cost of SCiG therapy. While accounting for the limitation that patients who received SCiG in the study used less product as a condition of participation, the investigators found only small differences in cost between the 2 modes of administration. This analysis included considerations for the costs of home delivery and medical equipment and a slightly more expensive cost of the SC product offset by the cost of outpatient hospital admission, including staff costs and the patients' loss of a workday for IV infusion. In the end, the cost difference between the 2 formulations was considered small and it was not actually clear which cost less.⁸

More recently, Le Masson et al performed a cost-minimization analysis to determine whether home-based IVIg treatment in MMN and CIDP and its variant, Lewis-Sumner syndrome (LSS), was effective, safe, and less costly than hospital-administered IVIg. The primary end point of the study was the cost of treatment, which was estimated from a payer perspective from Social Health Insurance in France. Data were collected for the hospital-based treatment from medical records and the hospital's claims database. Data for home-based infusion were collected prospectively over 9 months, and the total costs were estimated over the hospital-based and home-based infusion periods adjusted to a 12-month time frame. Results demonstrated that the 9-month total costs (extrapolated to the 12 months of therapy) were €48,189 (\pm €26,105) (US\$63,755 \pm US\$34,537) for home-based therapy compared with €91,798 (\pm €51,125) (US\$121,448 \pm US\$67,638) for in-hospital treatment. Improved tolerability and absence of AEs were the key drivers in patients choosing home-based therapy, along with appropriate understanding of the advantages and drawbacks of home-based infusion. Overall, the study demonstrated that total annual costs of IVIg therapy were divided almost in half with the use of home-based administration, with consistent savings noted for patients with all 3 disorders. Cost savings were achieved based on fewer hospital admissions and, to a smaller extent, fewer commutes for

therapy. The investigators concluded that switching from hospital-based to home-based treatment represented significant savings in disease management of CIDP, LSS, and MMN.⁹

Payer Concerns for Therapy Costs in CIDP

Along with patient needs surrounding immunoglobulin therapy, payer needs surrounding health economics and costs concerns with these agents and their appropriate use must be taken into consideration. Brogan et al performed a study to determine US payers' needs for health economics and outcomes research (HEOR) data from immunoglobulin use in treating immune dysfunctions and to better delineate payer rationale for use of these agents. This study utilized 9 payer one-on-one interviews with US medical and pharmacy directors (6 and 3, respectively) to assess their use of immunoglobulin products for treatment of CIDP and PIDDs. Results showed the following¹⁰:

- US payers indicated that immunoglobulin products are typically managed with a prior authorization (PA) based on indication. Payers emphasized that correct diagnosis is a critical component for a PA.
- When the various immunoglobulin agents have different FDA-approved indications, PA does not differentiate agents based on variable indications or routes of administration.
- 56% of participants indicated that failure of oral immunosuppressants and/or corticosteroids was required before they would switch to an immunoglobulin product.
- Those whose health plan did not require prior treatment failure indicated that immunoglobulin is usually not the primary treatment of choice by their patients. In these cases, there is not a strong perceived need to have treatment failure requirements for disease management with immunoglobulin products.
- Immunoglobulin products are primarily handled as part of medical benefits instead of pharmacy benefits; however, some participants noted that management of therapy by specialty pharmacies could provide some degree of cost savings through bulk purchasing power and minimizing "buy-and-bill" locally for these drugs.
- When asked specifically about coverage status and tier placement of specific agents, payers stated that immunoglobulin products were covered on the highest tier because of the actual drug costs for both CIDP and PIDDs, with minimal preference for any specific agent.
- The payers overwhelmingly considered these drugs to be interchangeable therapeutic equivalents from a health plan perspective.
- There was strong concern about the site of administration and its relationship to cost, with preference given to infusion at a health clinic, infusion center under the health plan, or at home.

- Specific concerns cited by payers relating to management of these drugs included:
 - » Drug price
 - » Off-label or questionable use
 - » Correct diagnosis
 - » Complexities and differences making contracting more difficult
 - » Difficulties associated with switching to home-based administration
- Payers agreed that outcomes data would be considered valuable for decision making, especially surrounding collection of resource usage, cost-impacting care variations, and head-to-head agent comparisons.

Overall, cost remains an overriding factor for payers and must be considered along with clinical benefits of these agents.¹⁰ Importantly, in cases of CIDP, clinicians must adhere to a majority, preferably all, of the clinical and laboratory criteria as determined by specialty societies, including the American Academy of Neurology and the European Federation of Neurological Associations.¹¹⁻¹³ Otherwise, a payer may consider the use of IVIg unproven in patients who do not meet diagnostic criteria for CIDP. After treatment is initiated, it is critical for clinicians to document progress meticulously. If there is clinical improvement in a given patient and continued therapy is needed, quantitative assessment to monitor progress is paramount. While a clear diagnosis of CIDP may provide coverage for immunoglobulin agents, the duration, frequency, and dosage of treatment are more likely to be culprits in a denial of coverage or any payer-provider discussions and disagreement about the need for immunoglobulin therapy.¹³

Different payers may set specific rules and criteria for coverage of immunoglobulin agents for patients with CIDP and other immune disorders. As an example, a sample policy from Independence Blue Cross on the use of IVIg and SCIG stated that use of IVIg therapy, with specific covered brand name drugs listed, is considered medically necessary and covered for the specific indications within the dosing and frequency requirements and criteria outlined in the policy. For CIDP, the policy states that objective clinical evidence to support the diagnosis of CIDP must be provided. Examples of evidence cited include slowing of nerve conduction velocity on nerve conduction studies. CIDP was not listed as an indication for SCIG in this particular policy bulletin.¹⁴

In addition, the policy bulletin stated that once treatment of CIDP with immunoglobulin is initiated for any approved indication, documentation of patient progress is required. If improvement is noted and continued treatment is still necessary, objective clinical assessment to monitor patient progress is required. Objective monitoring may be accomplished by approved clinical methods, such

as the Medical Research Council scale, Rankin score, activities of daily living scores, and/or objective findings on patient physical examinations. Documentation must outline any changes in these measures and identify any relationship between the measure change and usage of immunoglobulin. Clinical monitoring is considered to take precedence over laboratory monitoring, and evidence for clinical improvement portends no need for laboratory monitoring.¹⁴

Maximizing Opportunities for Optimal Patient Management in CIDP

It must be kept in mind that CIDP is a heterogeneous entity that can have atypical forms, and coexisting comorbidities, such as diabetes, can significantly complicate management of patients with this disorder. The rarity of CIDP may inhibit clinical investigation into optimal therapies in appropriately sized studies. Overall, therapeutic decision making for use of immunoglobulin agents in patients with CIDP must be individualized, considering each patient's circumstances. Disease subtype and severity, age, and comorbidities all play a significant part in the decision-making process.¹⁵

Shared decision making (SDM) can be an integral part of the decision pathway for the management of patients with CIDP. Patients are known to want to participate more actively in their healthcare overall. Goals of SDM include ensuring that patients understand their disease and encouraging patients to increase the roles they assume in their own disorder and its management. This means collaborating with them to be more aware of their symptoms and the AEs of therapy, essentially promoting optimal interaction between patients and clinicians. In SDM, the patients' participation is actively sought to help them explore and compare treatment choices and options, assess their values and preferences, and help them come to a therapy decision and assess that decision. Instead of just telling the patient what to do, the clinician truly works with the patient to make and evaluate the decision together and ensure it is the optimal one for the individual patient.² The overall task of tailoring CIDP therapy and management for each patient is crucial and has long-term implications. The best decision may not be easy, but it is critical to maximize the patient's chances of remission while offering the most justifiable and appropriate option.¹⁵

Conclusions

Accurate diagnosis and treatment of CIDP are critical to successful patient outcomes. However, the cost burden of CIDP and optimal disease treatment must also be addressed and managed by healthcare systems overseeing these patients. The high costs of immunoglobulin agents for therapy must be considered in terms of both clinical

effectiveness and cost-utility, and future data are needed to better determine long-term use strategies for these drugs, including best practices for dosing, tapering, routes of administration, and available options. Finally, active patient participation in CIDP management is crucial, including using SDM to better individualize treatment strategies for every patient and provide meaningful and interpretable measures of patient progress, assessment of the effectiveness of treatments, and overall management. ■

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