



## Growth in Demand for Intravenous Immune Globulin (IVIG) and Conservation Strategies

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Primary immune deficiency diseases (PIDDs) are genetic disorders, which, although uncommon, compromise the immune system and can place patients at risk for incapacitating chronic infections, which may increase the risk of cancer.<sup>1</sup> Based on data from the National Institute of Allergy and Infectious Diseases, there are over 200 different forms of PIDDs affecting approximately 500,000 people in the United States, with a prevalence that is on the rise.<sup>1,2</sup> With limited treatment options for these immunodeficiency disorders, the treatment of choice is IVIG, a blood product derived from plasma. IVIG is not only used for PIDDs but also for other neurologic, dermatologic, hematologic, and other disorders.<sup>3</sup> Consequently, there has been a dramatic increase in the demand for IVIG.<sup>2</sup>

The record growth of U.S. demand for IVIG is unprecedented and is continuing at an exceptional rate. According to Grand View Research, which [forecast IVIG use until 2022](#), the global IVIG market size “was estimated at 9.09 billion USD in 2016 and is anticipated to grow at a CAGR (compound annual growth rate) of 7.1% over the forecast period.” North America accounts for over 45% of the IVIG global market and is expected to maintain this high market share through 2022.<sup>2</sup> The key market drivers fueling this rising demand are the growing prevalence of PIDDs, increasing adoption of IVIG as a treatment option (including use for off-label indications), and the growing geriatric population, which is more prone to antibody deficiency disorders.<sup>2</sup>

In the United States, there are multiple IVIG products available, as depicted in the [Immune Deficiency Foundations IVIG comparison table](#).<sup>4</sup> However, the complexities of the IVIG manufacturing process make it challenging to keep up with the growing demand.<sup>5</sup> The raw material needed to develop IVIG is derived from human plasma, which is not in infinite supply and is more costly and complicated than manufacturing from non-living molecules.<sup>5,6</sup> To begin the

manufacture of IVIG, plasma, which is extracted from blood donations, is used as the raw material. Both IVIG and albumin are refined from the same plasma.<sup>6</sup> Thus, there is a delicate economic balance between IVIG and albumin production that must be maintained in order for manufacturers to invest in increasing the IVIG supply.<sup>6</sup>

As a result of this growing demand and the intricacies of increasing IVIG supply, hospitals may be experiencing difficulty acquiring IVIG.<sup>2,5,6</sup> A December 2018 Premier correspondence reported that over the prior 24 months, members may have experienced difficulty in obtaining their preferred brand, strength, or vial size of IVIG.<sup>6</sup> Premier predicted that this could continue until the first half of 2019.<sup>6</sup> The following strategies and resources are aimed at conserving IVIG during this time of supply strain.

### Ordering Practices

In its communication, Premier highlighted its efforts to increase the amount of IVIG in the U.S. market as well as the work of FFF Enterprises to help members get through times of limited availability.<sup>6</sup> Premier is working with all IVIG manufacturers to increase access.<sup>6</sup> The major IVIG manufacturers have reported their plans to increase IVIG supply to the U.S. market.<sup>6</sup> Premier noted the importance of incorporating flexibility in selecting and acquiring available vial sizes when purchasing as well as matching the preferred IVIG brand to the albumin manufacturer.<sup>6</sup>

### Strategies to Minimize IVIG Waste during Compounding

*Timing of Compounding* – Preparing IVIG once the patient is cleared to receive the dose can help ensure that a dose is not prepared only to be wasted.<sup>7</sup> Additionally, if IVIG administration is scheduled for multiple patients at the same time, batching can be used to make multiple doses simultaneously to decrease waste.<sup>7</sup>

*Dose Rounding* – Rounding IVIG doses to the closest vial size is another strategy to minimize waste. For example, in his 2010 article “[Safe Practices for IVIG Management](#),” Siegel J notes that the standard practice at many institutions is to round IVIG doses to the closest available vial size, staying within 10% of the prescriber order.<sup>7</sup> This is generally within 5 g of the ordered dose for adults and 1 g to 2.5 g for pediatrics.<sup>7</sup>

### **Ideal or Adjusted Body Weight Dosing Strategies**

Traditionally, IVIG was dosed using actual body weight. However, growing pharmacokinetic data indicate that dosing based on ideal body weight (IBW) and adjusted body weight (ABW) may be appropriate given IVIG’s small volume of distribution.<sup>7-9</sup> For example, “[A Survey of Intravenous Immune Globulin \(IVIG\) Dosing Strategies](#)” (published in 2015) surveyed 92 hospitals about their IVIG dosing strategies.<sup>10</sup> The results of this survey indicated that in those hospitals that employ IBW or ABW dosing strategies, IBW was used unless the patient was obese (several methods used to define obesity), in which case ABW was used.<sup>10</sup> Some of the responses indicated that if the patient’s actual weight was less than their IBW, then actual body weight was used for dosing.<sup>10</sup> Certain hospitals also used actual body weight for certain patient populations, such as heart transplant, pediatric, and hematology-oncology patients.<sup>10</sup> Listed below are three studies that discuss dosing strategies based on IBW or ABW.

- [Comparison of Weight-Based Dosing Strategies for Intravenous Immunoglobulin in Patients with Hematologic Malignancies](#)
- [Initial intravenous immunoglobulin doses should be based on adjusted body weight in obese patients with primary immunodeficiency disorders](#)
- [Retrospective Evaluation of IVIG Use: Appropriateness and Potential Cost Savings from Body-Weight Dosing at a Northeastern Tertiary Hospital in the United States](#)

### **Ensuring Appropriate Use**

The American Academy of Allergy Asthma and Immunology has an online IVIG toolkit that includes a [position statement on the appropriate use of intravenously administered immunoglobulin](#).<sup>11,12</sup> Resources such as this position statement have been used by institutions to develop guidelines, protocols, and order sets to ensure the

appropriate use of IVIG.<sup>13</sup> Some hospitals even have pharmacy-driven immune globulin stewardship to ensure guideline compliance for appropriateness of indication and dose.<sup>13-15</sup> The May 2016 Acurity continuing education program highlighted [the role of pharmacists in the immune globulin stewardship program at Yale-New Haven Hospital](#).<sup>13</sup> As stewards, the pharmacists develop and monitor immune globulin protocols, ensure appropriate formulary product selection, educate patients, and contain costs by ensuring appropriate use.<sup>13</sup>

In 2017, an article titled “[Intravenous Immune Globulin Stewardship Program at a Tertiary Academic Medical Center](#)” was published, which describes a pharmacy-driven IVIG stewardship program for medication approval at Brigham and Women’s Hospital in Boston, Massachusetts.<sup>14,15</sup> The article concludes that a stewardship program that includes a pharmacy-driven approach can help ensure compliance with institution-specific prescribing guidelines.<sup>14,15</sup> Further examples of institutional IVIG guidelines and order sets that use some of the above-mentioned strategies (e.g., dose rounding, IBW dosing strategies) are provided below.

- UNC Healthcare Guideline. IVIG Clinical Guideline. Last updated August 2014. Available at: <http://news.unhealthcare.org/som-vital-signs/attachments/august-2014/ivig-guideline>. Accessed April 27, 2018.
- The University of Toledo. IVIG Dosing. October 2017. Available at: [https://www.utoledo.edu/policies/utmc/pharmacy\\_hsc/pdfs/3364-133-93.pdf](https://www.utoledo.edu/policies/utmc/pharmacy_hsc/pdfs/3364-133-93.pdf). Accessed April 27, 2018.
- University of Miami Hospital. Intravenous Immune Globulin (IVIG) Order Form. Last updated March 2014. Available at: <http://ugotabug.med.miami.edu/documents/IntravenousImmuneGlobulinOrders.pdf>. Accessed April 27, 2018.

The rapid growth in demand for IVIG paired with the complicated processes of increasing supply may be causing supply interruptions, forcing healthcare providers to devise strategies to conserve IVIG. Dose rounding, alternate dosing strategies using IBW and ABW, batching, developing and monitoring institution-specific IVIG guidelines, and initiating immune globulin stewardship programs to ensure appropriate use are examples of conservation strategies that pharmacists can employ to help prevent these supply strains from affecting patient care.

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