

# Immune Globulin

## Each Product Is Unique

By Ronale Tucker Rhodes, MS



While all IG products are comparably effective, they also have relevant differences that determine their tolerability by patients.

**THE CURRENT AVAILABILITY** of multiple immune globulin (IG) products gives providers many choices when prescribing this lifesaving therapy. The benefit of product choice, of course, is that it allows providers to match the best-suited product to the patient. And, this is extremely important because, while all products contain IgG (the most common protein in the body that helps ward off infections) and they all have comparable efficacy, they are not pharmaceutically equivalent. There are relevant differences between the current products on the market, considered third and fourth generation, that have evolved in terms of composition, resulting in decreased risk of infusion-related reactions and other adverse events. Product variations in sodium content, stabilizers, osmolality, osmolarity, IgA content, concentration and pH can affect the tolerability of a product for one patient versus another, based on both clinical conditions and comorbidities.<sup>1,2</sup>

When choosing an IG product based on the differences between each, the key factors a clinician considers are the patient's body type, weight, conditions presenting in addition to the one being treated with IG (such as diabetes, high blood

pressure or other heart disease), whether they are pregnant or postmenopausal, other medications taken, kidney function, and if there is patient history of blood clots or migraines. This information is particularly important for dosing recommendation and premedication selection, and it helps clinicians tailor patient-specific suggestions for tolerating therapy.<sup>3</sup>

Following is a review of the key differences among the products' stabilizers, osmolality, IgA content and concentration.

### Stabilizers

When intravenous IG (IVIg) was originally approved by the U.S. Food and Drug Administration in 1981, it contained no stabilizers, and patients often experienced undesirable side effects such as fever, chills, fatigue and chest, hip, joint and back pain, which were believed to be due to the formation of immunoglobulin aggregates. To resolve this issue, stabilizers were added, primarily sugars such as sucrose, maltose, glucose and sorbitol, and in some cases, glycine and albumin.<sup>4</sup>

The specific stabilizer used can play an important role in a product's tolerability.<sup>5</sup> Today, most IG products are no longer

stabilized with a sugar; however, a few still are, which can result in other adverse events. There is a strong association between renal failure and sucrose-containing products, rapid rates of infusion and diabetes. This is rare, and the cause of renal failure is unknown,<sup>6</sup> but it is believed that it could be due to the fact that sucrose has the highest osmotic activity of the stabilizers in IG products. In addition, since sucrose is metabolized by an enzyme, called sucrase, that is found only in the intestine, when administered intravenously, sucrose is eliminated unchanged in the urine, possibly resulting in osmotic nephrosis. And, while cautious use of IVIG is recommended in patients at increased risk for adverse renal events, including those with renal impairment, diabetes mellitus, age greater than 65 years, dehydration or hypovolemia, sepsis, paraproteinemia or concomitant use of nephrotoxic drugs, they are not contraindicated in patients with renal insufficiency.<sup>3</sup> In products stabilized with maltose, there is a possible interaction with strips that test for glucose in the blood. The maltose may cause an erroneous reading indicating glucose is high when it really isn't. However, most test strips have been modified to prevent these erroneous readings when maltose is present.<sup>6</sup>

## Osmolality

Osmolality is the solute concentration contained in the IG solution; thus, the higher the osmolality, the higher the concentration of the IG solution.<sup>6</sup> Higher osmolality solutions, also known as hyperosmolar, are typically seen with older lyophilized IVIG products. In contrast, today's fourth-generation products have a more physiologic osmolality comparable to that of individuals' blood because they have had amino acids glycine and L-proline added to them to help reduce the overall solute load, which can become elevated with sugars.<sup>5</sup>

Hyperosmolar solutions tend to cause more local venous irritation at the infusion site.<sup>5</sup> They also may be associated with an increased risk of thrombosis.<sup>6</sup> Dehydration also can cause the blood to become hyperosmolar, which is one of the reasons people receiving IG therapy are encouraged to drink a lot of water before, during and after the infusion.<sup>6</sup>

## IgA Content

All IG products contain varying amounts of IgA (one of the five classes of antibodies found in the blood). IgA is not problematic for most people.<sup>6</sup> However, in patients who are IgA deficient, IgA can cause the formation of anti-IgA antibodies that can cause anaphylactoid reactions upon infusion of

IVIG, which would result from the IgE development against IgA. While the risk of anaphylactoid reaction in IgA-deficient patients is anticipated, the incidence is low given the total number of reactions reported compared with the overall number of patients. In fact, screening for IgA deficiency prior to IVIG infusion is not routinely recommended.<sup>5</sup>

The amount of IgA in a given IG preparation may also influence the risk for common reactions that are milder such as fever, malaise, myalgia and headache.<sup>5</sup>

## Concentration

Today's IG products come in 5%, 10% and 20% solutions.<sup>6</sup> The solution percentage is the number of grams of IgG protein in an IG therapy solution. For instance, a 5% IG product contains 5 grams of IgG protein per 100 mL of solution, a 10% IG product contains 10 grams of IgG protein per 100 mL of solution, etc. The highest-concentration 20% solution can only be infused subcutaneously. Four of the higher-concentration 10% products can be infused subcutaneously, and all but one of them can be infused intravenously. The lowest-concentration 5% products are approved only for intravenous infusion.

Most of today's products are available as a ready-to-use liquid formulation.<sup>6</sup> However, there is one product that is lyophilized and requires reconstitution and pooling into an evacuated container for administration to the patient.<sup>2</sup>

## Highly Improved and Tolerated Products

With advances in manufacturing processes, today's IG products are safer than ever before. However, every IG product has different pharmaceutical characteristics, and there is even variation from batch to batch of each product. It's these differences that can influence patient tolerability. But with careful patient screening and understanding of the inherent differences in the products, clinicians can ensure that the most appropriate product is prescribed to the patient. ■

## Sources

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