Reimbursement Issues in IGIV Therapy

Faculty

Mark Ballow, MD
Jerry Siegel, PharmD
Howard M. Tag, JD

Nurse Reviewer

Brenda Reid, RN, MN

Target Audience

Immunologists, hematologists, oncologists, pharmacists, infusion nurses

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Reimbursement Issues in IGIV Therapy

Program Goal

To provide physicians, pharmacists, and nurses with information regarding IGIV reimbursement policies and procedures.

Learning Objectives

After reading the monograph, participants should be better able to:

- Discuss indications for the use of IGIV therapy.
- State the pros and cons of the various IGIV products available.
- Identify key policies and procedures related to IGIV reimbursement as they relate to the clinical setting (hospital, physician office, home care provider).

Faculty

Mark Ballow, MD
Acting Chair of Pediatrics
Chief, Division of Allergy/Immunology
and Pediatric Rheumatology
Women's and Children's Hospital of Buffalo
SUNY Buffalo School of Medicine
and Biomedical Sciences
Buffalo, New York

Jerry Siegel, PharmD
Senior Director, Pharmaceutical Services
The Ohio State University Medical Center
Clinical Associate Professor and Assistant Dean
The Ohio State University College of Pharmacy
Columbus, Ohio

Howard M. Tag, JD
President
Tag & Associates, PC
Alexandria, Virginia

Nurse Reviewer

Brenda Reid, RN, MN
Clinical Nurse Specialist
Division of Immunology/Allergy
The Hospital for Sick Children
Toronto, Ontario

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Dr Siegel: *consultant:* Talecris Biotherapeutics, Inc., ZLB Behring; *speakers bureau:* ZLB Behring.

Mr Tag: *consultant:* Talecris Biotherapeutics, Inc.

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Planning Committee Disclosure

Members of the planning committee include: Craig Borders, Christine Olsen, John Pryor, Kathy J. Johnston-Kavanagh, and Margaret Astrologo. Each member of the planning committee has disclosed that he/she has no financial relationships with the sponsor or any commercial entity related to this activity.

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Introduction

Reimbursement issues in the ever-changing healthcare environment represent a continuing challenge for physicians, pharmacists, and nurses. This is particularly true for immunoglobulin intravenous (IGIV) therapy. Reimbursement is not guaranteed for IGIV therapy, even though it is a life-saving treatment for patients with humoral deficiency. Barriers to reimbursement can have a substantial clinical impact on such patients if they are turned away from their regular site of care or forced to miss their scheduled appointments.

This monograph will review the critical issues involved with IGIV cost reimbursement as well as the clinical considerations. Beginning on page 1, Howard Tag presents practical information for navigating the IGIV reimbursement landscape. He reviews the major components of reimbursement, coverage and payment, as well as the new developments in the language of reimbursement (ie, coding) as they apply to IGIV therapy. He also provides up-to-date information about the changes occurring this year and in 2006. He then addresses reimbursement issues specific to government and private insurers, giving particular attention to Medicare reimbursement in the hospital outpatient, hospital inpatient, physician office, and home heathcare settings.

Beginning on page 9, Dr Jerry Siegel and I address the clinical considerations for patients receiving IGIV therapy. We examine the scope of medical indications for IGIV therapy, the range of product formulations available, and the importance of matching the IGIV product to patient risk factors. We also discuss what the clinical impact can be when patients are switched from one IGIV product to another because of reimbursement issues.

We hope that you will find the information presented in this monograph useful in your clinical practice.

Mark Ballow, MD

NAVIGATING THE REIMBURSEMENT LANDSCAPE

Howard M. Tag, JD

In the current healthcare environment, insurance reimbursement for emerging or innovative therapeutic regimens presents a challenge for patients, physicians, pharmacists, nurses, and administrative personnel. One regimen that involves special reimbursement consideration is immunoglobulin intravenous (IGIV) therapy for autoimmune and primary immunodeficiency (PI) disorders. This article will review the key issues involved with IGIV reimbursement, with special emphasis on Medicare, and present up-to-date, practical information for navigating the IGIV reimbursement landscape.

OVERVIEW OF IGIV REIMBURSEMENT

As with reimbursement for all medical technologies, reimbursement for the use of IGIV therapy has 2 components:

- Will the treatment be *covered* for a particular patient?
- Assuming it will be covered, how much will be *paid* for the IGIV and the clinical services to administer it?

It is important to examine each component separately with individual patients and their insurer(s), so that if there is a reimbursement problem or concern, the clinician has a clear understanding about its nature and whether it can be successfully resolved.

Coverage

IGIV is a life-saving therapy for patients who lack humoral immune responses, as it enables a normal host response to potential pathogens. There are currently 10 IGIV products licensed for marketing in the United States (Table 1), and all are approved by the Food and Drug Administration (FDA) for PI disorders. All the FDA-approved indications for IGIV products are listed in Table 2. However, not all IGIV products are FDA approved for all of these indications, and IGIV is frequently used off-label in a variety of clinical situations.

At this time, all government and nearly all private health insurers cover all IGIV labeled uses for all products, even though not every product is labeled for every use. For example, some IGIVs are labeled for Kawasaki syndrome. If a product without that indication on its label is used to treat Kawasaki syndrome, it is, strictly speaking, an off-label use. Nevertheless, insurers will not evaluate that use as off-label—for this coverage purpose, the labeled use on some IGIV products extends to all.

IGIV is gaining popularity in the treatment of autoimmune diseases and immune-mediated diseases, most of which are currently considered off-label indications for all IGIV products. Some of the off-label uses are well documented in the literature and are covered by most government and private payers. With other uses, there is more variation in coverage; however, the same policy described previously is applied: the choice of product will not affect the coverage decision.

Table 1.
Commercially Available IGIV Products*

- Carimune® NF
- Flebogamma® 5%
- Gammagard Liquid
- Gammagard S/D
- Gammar®-P I.V.
- Gamunex®
- Iveegam® EN
- Octagam®
- Panglobulin® NF
- Polygam® S/D

*As of September 2005. Consult with manufacturers regarding the availability of new products and formulations and for withdrawals of any currently existing products.

Table 2.
FDA-Approved Indications for IGIV Therapy

- Primary immunodeficiency
- Idiopathic thrombocytopenic purpura
- Kawasaki syndrome
- Chronic lymphocytic leukemia
- Pediatric human immunodeficiency virus infection*
- Bone marrow transplantation (allogeneic)*

FDA, Food and Drug Administration; IGIV, immunoglobulin intravenous. *IGIV S/D 10% (Gamimune® N S/D 10%), which is no longer manufactured, was the only IGIV product approved for this indication.

Payment

If the IGIV treatment is covered, how much will be paid? The answer differs from one payer to another and from one treatment setting to another—even with the same payer—and could change from one infusion cycle to the next. Payment variation and lack of predictability have been a source of significant frustration for clinicians, patients, suppliers, and manufacturers alike. The situation is not likely to improve in the near-term, but this article will provide information to help you anticipate when changes in payment are likely to happen and where to go for reliable information.

Coding

The language of reimbursement, coding is a shorthand way to categorize and describe a patient's diagnosis and the services and products that are included in his or her treatment. In theory, coding, coverage, and payment are discrete steps in the reimbursement process. Payers are quick to caution providers that the existence of a code for a product or service does not imply coverage or payment in a particular case. In addition, many will say the lack of a specific code for a unique technology does not prevent the technology from being reimbursed.

In practice, coding is a gateway to appropriate reimbursement. Incorrect coding by providers or the lack of codes that properly and completely describe a technology often results in reimbursement frustration. Correct use of codes that adequately distinguish one procedure from another will not create coverage, but it will ensure that, when coverage exists, the correct payment is received in the shortest time possible.

In 2005, IGIV products were assigned new codes in the Healthcare Common Procedure Coding System (HCPCS), and, in all probability, new codes will again be assigned for 2006. Until April 2005, all IGIV products, regardless of formulation, were billed using HCPCS code J1563 for units of 1 g and J1564 for units of 10 mg when a fraction of a gram was used. For example: To bill 37.5 g, the provider would file a claim for 37 units of J1563 and 50 units of J1564.

Beginning in April 2005, new codes were assigned to differentiate lyophilized and liquid (nonlyophilized) formulations. The new HCPCS codes for all lyophilized IGIV are Q9941 (for units of 1 g) and Q9942 (for units of 10 mg); the new codes for all nonlyophilized IGIV are Q9943 (for units of 1 g) and Q9944 (for units of 10 mg). Codes J1563 and J1564 are no longer used by Medicare and many other payers.

Under the old coding, payments for liquid and lyophilized products were typically the same because the same code was used for both. Under the new coding, 2005 payment by Medicare and some other insurers for IGIV administered in the physician's office or home healthcare (HHC) setting is lower for lyophilized than for liquid products, and the same will be true for IGIV administered in hospital outpatient departments in 2006.

The new "Q" codes are temporary codes that will be replaced by permanent "J" codes for 2006. Coding policy makers are considering whether the lyophilized-liquid differentiation should be kept as is for 2006 or made more inclusive to account for product differences in concentration, components, and excipients or method of viral inactivation (Table 3).

Table 3.
Changing HCPCS Codes for IGIV

2004 Codes		
All products:	For each gram unit	J1563
All products:	For each 10-mg unit	J1564
2005 Codes*		
Lyophilized products:	For each gram unit	Q9941
Lyophilized products:	For each 10-mg unit	Q9942
Nonlyophilized (liquid) products:	For each gram unit	Q9943
Nonlyophilized (liquid) products:	For each 10-mg unit	Q9944
2006 Codes†	New J codes to be assigned	

HCPCS, Healthcare Common Procedure Coding System; IGIV, immunoglobulin intravenous.
*Beginning in April 2005.
†Whether the new coding for 2006 will reflect product differentiation by lyophilized or liquid formulation or by other product characteristics has not yet been determined.

MEDICARE

Overview

Medicare provides healthcare benefits to persons who are age 65 or older or who qualify for Social Security disability payments. Although Medicare is not the largest payer (by category) for IGIV, it is the most influential. Therefore, special attention is given here to its coverage and payment policies. Medicare's influence is derived from the following:

- It is one payer rather than a collection of separate payers, as is the case with Medicaid and private insurers.
- Its policies are routinely adopted by Medicaid programs and private insurers.

Although Medicare is a national program financed entirely with federal dollars, it is administered on a local level. Medicare coverage and payment decisions are made by local contractors called *carriers* for claims filed by physician offices and *intermediaries* for claims filed by hospitals and HHC providers.

Much is being written about the new Medicare Part D prescription drug benefit that begins on January 1, 2006. Nothing about that benefit, however, applies to IGIV reimbursement, which occurs under a different Medicare benefit—Part B. What you read and hear about Part D should not affect your assumptions and conclusions about IGIV reimbursement under Part B.

Because Medicare reimbursement decisions are made locally by the contractors, there are variations in coverage from one state to another, especially for off-label uses. Check with the contractor for your location to determine the coverage policies that apply to your patients (Table 4).

Table 4.
IGIV Reimbursement Assistance and Information

To assist healthcare providers and patients with general information, claim filing, coding, and claim processing, government agencies, advocacy organizations, and IGIV manufacturers have established help lines or reimbursement resources on their Web sites including:

Centers for Medicare and Medicaid Services (CMS)

http://www.cms.hhs.gov/

For information on Medicare reimbursement by state:
http://www.cms.hhs.gov/medlearn/tollnums.asp.

For information on Medicare Part B Drugs Average Sales Price (ASP):
http://www.cms.hhs.gov/providers/drugs/asp.asp

For information on the Hospital Outpatient Prospective Payment System (HOPPS):
http://www.cms.hhs.gov/providers/hopps/

Manufacturers

- Baxter Healthcare Corporation
  http://www.baxter.com
  Reimbursement Hotline: (800) 548-4448
- Baxter International Inc
  http://www.immunedisease.com
  Insurance Reimbursement: (800) 548-4448
- Grifols
  http://www.grifols.com/
- Octapharma
  http://www.octapharma.com/
- Talecris Biotherapeutics
  http://www.talecris.com/
- ZLB Behring
  http://www.zlbbehring.com/
  Reimbursement: (800) 676-4266

Organizations

- Immune Deficiency Foundation
  http://www.primaryimmune.org/
- National Primary Immunodeficiency Resource Center
  http://www.info4pi.org/

Payment per gram (or fraction of a gram) for IGIV differs by treatment setting, but it is uniform throughout the country for a given setting, ie, all physician offices receive the same per-gram payment. Payment for the infusion service differs by locality because it is adjusted to reflect local wage rates. Your contractor's Web site should have specific local payment amounts.

Beginning in 2005, IGIV administered in hospital outpatient clinics and physicians' offices is being reimbursed according to a new formula, ASP plus 6%.

Hospital Inpatient Setting

There is no separate reimbursement for IGIV treatment given as part of an inpatient admission. As with almost all drugs and biologicals, reimbursement is incorporated into the fixed prospective payment made for the Diagnosis Related Group to which the case is assigned. With few exceptions, the payment is the same regardless of the length of stay or services provided during the admission.

Hospital Outpatient Setting

Outpatient treatment with IGIV is reimbursed under Medicare's Hospital Outpatient Prospective Payment System (HOPPS). IGIV is considered a "pass-through" biological, meaning there is separate reimbursement for the IGIV component under an IGIV Ambulatory Payment Classification (APC) group. There is also payment for the infusion and other services under different APCs for those services. As a "pass-through" biological, IGIV reimbursement is separate from, rather than incorporated into, the APCs for other services, a policy that has ensured that hospitals are reasonably reimbursed for IGIV treatment.

Congress and the Centers for Medicare and Medicaid Services (CMS) within the Department of Health and Human Services determine the reimbursement formula for pass-through drugs and biologicals. Through 2005, the formula has been pegged to the drug's or the biological's average wholesale price (AWP), a widely published reference price historically used by most payers.

For 2006 and beyond, Congress directed CMS to use a different formula, and CMS chose the average sales price (ASP) methodology, described below in the section on physician office reimbursement.[1,2] Hospital reimbursement for these drugs and biologicals, now referred to as "specified covered outpatient drugs" (SCODs), will be ASP plus 8%, a significant reduction from the 2005 reimbursement but a slightly higher payment than that for the same service in the physician office and HHC settings. The higher payment, compared to payment in other settings, results from a congressional directive to reimburse hospitals for pharmacy overhead. CMS decided to use the ASP plus 6% formula from the other settings and to increase it by 2% (ie, an increase to ASP plus 8%) to account for the pharmacy overhead factor.

Physician Office Setting

Beginning in 2005, IGIV administered in hospital outpatient clinics and physicians' offices is being reimbursed according to a new formula, ASP plus 6%. To establish reimbursement, CMS requires each manufacturer to report net selling price information on a quarterly basis. The reports take into account all forms of price reductions, including discounts and rebates, to all customers and the total number of grams of IGIV sold at each net price. CMS reviews the reports, audits them at its discretion, and, based on the reports, publishes the ASP plus 6% payment. Manufacturers are liable for steep fines for reporting errors; therefore, they pay close attention to the accuracy of the reported prices.

ASP data are grouped and payments are made by HCPCS code. Therefore, the payment for lyophilized IGIV, for example, will reflect the net selling prices and quantity of IGIV sold (number of grams) for all lyophilized products. The payments are the same for all, even though the provider's actual acquisition cost may not be the same for all. Staying informed about payments and acquisition prices is an important step in managing your facility's bottom line. You should update your information at least quarterly.

Manufacturers report net selling prices on a quarterly basis, and CMS revises its payments effective on the first day of January, April, July,

and October each year. New payment rates are posted by CMS around the middle of the month prior to the effective date of the change. Occasionally, in the interim, CMS will post a payment change that is retroactive to an earlier date. Checking for the new payments on the CMS Web site (Table 4) or with one of the manufacturer reimbursement hotlines near the end of December, March, June, and September should become part of your reimbursement routine.

Although the payments are adjusted quarterly, they do not necessarily reflect current prices and costs because there is a 6-month lag between the time the data are reported by manufacturers and when the ASP payments are posted by CMS. The lag is the result of the processing time needed by the manufacturers and CMS to collect, clean, analyze, and validate the data. If, during the 6-month period, selling prices have increased, providers will be under-reimbursed because the payments will be based on older, lower selling prices. Conversely, if prices fall during the lag time, reimbursement will be higher compared with current prices. Over time, the disparity is corrected by the quarterly updating of prices and payments, but during periods of volatile wholesale prices, as occurred in 2005, payments can be significantly below actual acquisition costs for some providers.

Competitive Acquisition Program

IGIV will likely be excluded from the new Medicare Competitive Acquisition Program (CAP) that is expected to begin sometime during the third quarter of 2006. CAP would allow physicians, at their option, to give up the "buying and billing" function for selected drugs and biologicals and instead contract with a CMS-approved vendor who will take over that function. The vendor will deliver patient-specific doses of IGIV to the physicians' office, bill Medicare for its 80% portion of the drug payment, and bill patients for their 20% coinsurance. Physicians will continue to bill Medicare in the usual way for their professional services (eg, the infusion) but will not be at economic risk for the IGIV itself. The sole purpose of CAP is to reduce Medicare's expenditure for the Part B drugs administered in physician offices.

IGIV and selected other drugs and biologicals were exempted from CAP by CMS because it believes patients who need certain treatments like IGIV would not have adequate access under the CAP system. Final rules have not been issued, but when they are, the IGIV exemption is expected to be included.

Home Healthcare

Home infusion of IGIV is covered by Medicare only for patients with PI disorders, and only for the IGIV itself, not for the professional services or supplies necessary to administer it. Payment for the IGIV in HHC is under the same ASP plus 6% formula as it is in physician offices.

MEDICAID

Although Medicaid programs are jointly funded by the federal government and the states, coverage and payment policies are made exclusively by each state for its own program. Policies vary widely from one state to another, with many changes expected in the near future as states continue to struggle with burgeoning Medicaid spending. Clinicians are encouraged to check with their local Medicaid provider relations office or one of the manufacturer hotlines for current state-specific information.

Home infusion of IGIV is covered by Medicare only for patients with PI disorders, and only for the IGIV itself, not for the professional services or supplies necessary to administer it.

PRIVATE INSURERS

Because hundreds of private insurance plans are offered by employers and purchased individually by patients, only broad generalizations can be made about their approaches to reimbursement for IGIV. Private insurers typically have contracts with hospital and physician providers ("participating," "member," or "network" providers), and the IGIV coverage and payment rules are governed by those contracts. On the whole, private insurers are similar to Medicare in their scope of coverage for off-label

uses, although there can be dramatic differences among insurers.

Private insurer payment is markedly better than Medicare's, but that will likely change in 2006. In a recent survey of 15 large private insurers covering almost 100 million lives, payment for IGIV averaged AWP minus 15%, with a range of AWP minus 5% to AWP minus 20%.[3] More than one third of medical and pharmacy directors interviewed for the survey, however, reported that they were planning to switch to an ASP-based formula in 2006 or would reduce the discount from AWP. One half of the payers interviewed are studying similar changes.

In 2006, payments in the physician office and HHC settings are likely to be more stable than in past years because the current ASP-based formula continues unchanged.

CURRENT ISSUES

Unpredictable and Widely Fluctuating Medicare Payments

During the past 2 years, Medicare hospital and physician office payment for IGIV has fluctuated from a low of $38 per gram to a high of $80 per gram. Reimbursement rates changed because of sweeping changes in Medicare law, targeted changes affecting only IGIV, and data analysis mistakes that were retroactively corrected by CMS. The combination of factors created confusion and uncertainty about IGIV reimbursement that still lingers with some providers.

In 2006, payments in the physician office and HHC settings are likely to be more stable than in past years because the current ASP-based formula continues unchanged. In the hospital outpatient setting, however, the formula is changing from AWP-based to ASP-based. Pharmacy directors will see a 50% drop in payment for lyophilized products and a 30% drop for liquid products, adding further to the sense of uncertainty about the adequacy of IGIV reimbursement.

Two-Tiered Medicare Payment

Historically, hospital and physician office Medicare payments have been based on different formulas, which created very different payments. For most of 2005, for example, hospital payment for all IGIVs was in the $80 range, while in physician offices it was in the $40 range for lyophilized IGIV and the mid-$50 range for liquid IGIV. This somewhat irrational disparity will be narrowed in 2006, when hospital payment moves to an ASP-based formula.

Inadequate Reimbursement for Infusion Procedure

Payments for infusion services are affected by the complexity of the drug or biological being infused and the length of infusion time. Cancer chemotherapy and biologic response modifiers (BRMs) have higher payments than other drugs and biologicals.

IGIV is not currently classified as a BRM, although some pharmacologists maintain that IGIV treatment satisfies the definition of BRM therapy, and the intensity or resources required to infuse IGIV are comparable to those for other BRMs. Reclassifying IGIV as a BRM would increase infusion fees by approximately 20%.

Coverage for Off-Label Uses

IGIV is routinely used for off-label indications. Most insurers cover off-label uses that are supported by publications in the medical literature or by consensus findings of specialists who practice at academic medical centers (Figure 1).

Payer frustration over rising healthcare costs has led to tighter controls on off-label uses of all drugs and biologicals. Thus far, payers overall have been reasonable and appropriately cautious in how they implement changes in IGIV coverage policy. As economic pressures intensify on all segments of the healthcare system, it will be important to monitor for changes in IGIV coverage that could prevent seriously ill people from having access to medically necessary treatments.

Link Between Reimbursement and Product Supply

Over the years, there have been times when the demand for plasma-derived products, including IGIV, has outpaced supply. The reasons for that are

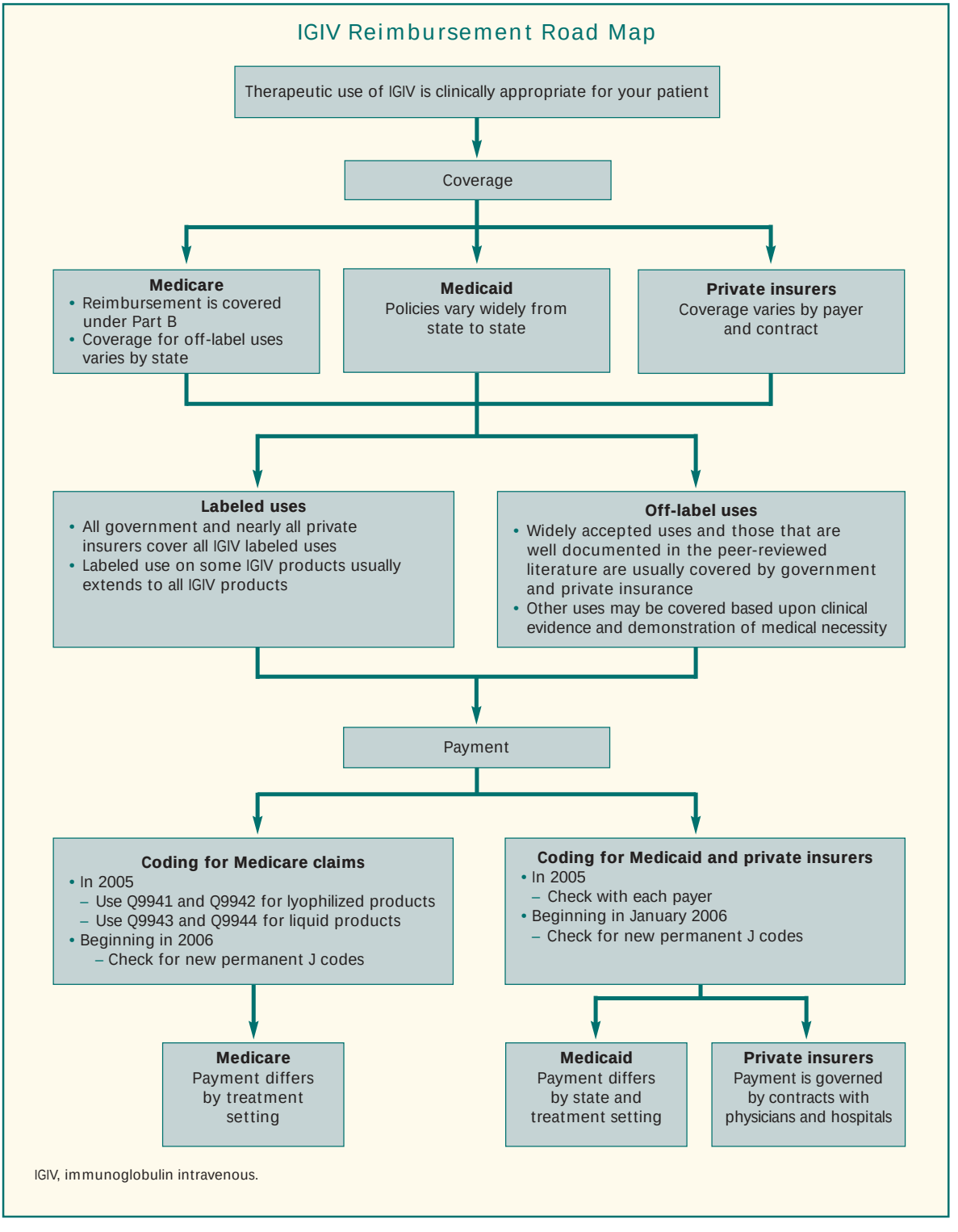

Figure 1. **Key steps in navigating the IGIV reimbursement landscape** are summarized here.

complex and include the long lead times needed for manufacturing and processing of plasma products. For example, manufacturers must plan purchase commitments for raw plasma at least 1 to 2 years prior to its delivery for use in IGIV production. As a result, when demand for IGIV increases above projections, it can take several months before additional product reaches the market.

Reimbursement can indirectly affect product supply. If inadequate or unreliable reimbursement discourages providers from ordering as much IGIV as the medical needs of their patients actually require, manufacturers may interpret that as a decline in demand and adjust their manufacturing plans accordingly. Then, if demand increases because reimbursement has stabilized or improved, a shortage in available product may occur.

Even though the amount of IGIV produced has increased over the years (eg, from 15,000 kg in 1998 to 27,000 kg in 2004[4]), the recent uncertainty surrounding reimbursement may have discouraged some manufacturers from producing as much as they might have in a more stable reimbursement climate.

Failure of HCPCS Codes to Differentiate Dissimilar Products

For decades, all IGIVs were lumped together under the same HCPCS code, regardless of their formulation, method of viral inactivation, or other clinically relevant product components. Coding policymakers are beginning to better understand that 2 IGIV products with the same active ingredient, immunoglobulin G, can have significant differences. Taking a step in that direction, CMS assigned new codes to IGIV in 2005 to distinguish lyophilized (Q9941, Q9942) from liquid (Q9943, Q9944) formulations. However, there are reasons to assign additional codes that go further in their recognition of product differences. Codes might be expanded to recognize other IGIV components that result in significant pharmaceutical distinctions among IGIV products, such as concentration, sodium content, sugar content, osmolality/osmolarity, and pH. Depending on dose and patient risk profile, such product characteristics can yield significant, clinically relevant differences.

CONCLUSION

Steps for navigating the IGIV reimbursement landscape are summarized in Figure 1. Insurance reimbursement for IGIV therapy is challenging for clinicians because the landscape is continually changing. This situation is not likely to improve in the near-term. Staying informed about changes in IGIV therapy coverage, payment policies, and coding is the best way to anticipate problems in reimbursement and to find a path to resolution.

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CLINICAL PERSPECTIVES IN IGIV THERAPY

Mark Ballow, MD and Jerry Siegel, PharmD

Immunoglobulin intravenous (IGIV) is a life-saving therapy used to treat a variety of diseases and conditions, both as a means of antibody replacement and for modulating the immune system (Figure 1). It is the mainstay of therapy for patients who have PI disease. These patients are unable to produce specific immunoglobulin G (IgG) antibodies as a primary defense against infections. As a result, patients with PI are at increased risk of infection, particularly sinopulmonary, gastrointestinal, and dermatologic infections.[1-3] IGIV contains a broad range of specific antibodies against pathogens and foreign antigens, critical for replacement therapy in patients with PI. About 50,000 Americans suffer from PI and about 70% rely on IGIV to keep them alive.[4] Other clinical uses of IGIV are listed in Table 1.

Barriers to reimbursement can have a substantial clinical impact on patients with PI or other conditions that require IGIV therapy. Policymakers need to understand that these patients require reliable and consistent IGIV treatment. They cannot be turned away from physician offices and miss their scheduled treatments or be denied home care because of reimbursement issues. Although referral to a hospital

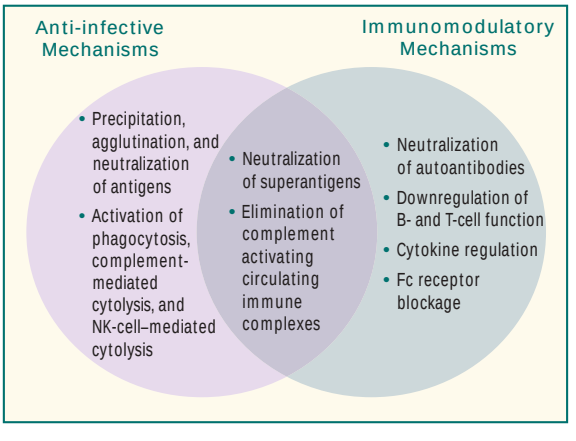

Figure 1. **Anti-infective, anti-inflammatory, and immunomodulatory actions are exerted by IGIV.** The proposed mechanisms for these effects overlap, as shown here.

Table 1.
Clinical Uses of IGIV Therapy

Replacement Therapy in Primary Immunodeficiency
- Agamma/hypogammaglobulinemia
  - Bruton's disease/infantile X-linked agammaglobulinemia
  - Common variable immunodeficiencies
- Hyper IgM syndromes
- Specific antibody deficiency
- Combined T- and B-cell deficiencies
  - Severe combined immunodeficiency diseases
  - Wiskott-Aldrich syndrome
  - Ataxia/telangiectasia

Adjunct or Passive Immunotherapy
- Chronic lymphocytic leukemia
- Recurrent infections in children with AIDS
- Bone marrow transplantation
  - Cytomegalovirus pneumonia
- Parvovirus B19 infection–related diseases
- Prophylaxis or treatment of sepsis in the preterm infant
- Disorders related to staphylococcal or streptococcal exotoxins
  - Toxic shock syndrome
  - Kawasaki disease

Autoimmune Disorders
- Immune cytopenias
  - Idiopathic thrombocytopenic purpura
  - Neutropenia
- Immune coagulopathies
- Neurologic and neuromuscular diseases
  - Chronic inflammatory demyelinating polyneuropathy
  - Guillain-Barré syndrome
  - Multifocal motor neuropathy
  - Inflammatory myopathies
  - Dermatomyositis
  - Myasthenia gravis (Lambert-Eaton)
  - Stiff Man syndrome
  - Relapsing-remitting multiple sclerosis

IGIV, immunoglobulin intravenous; AIDS, acquired immunodeficiency syndrome.

Table 2.
Comparing Currently Available IGIV Preparations

	Carimune® NF§	Flebogamma® 5%	Gammagard Liquid	Gammagard S/D
Form	Lyophilized	Liquid	Liquid	Lyophilized
Available sizes	1, 3, 6, 12 g	10 mL (0.5 g), 50 mL (2.5 g), 100 mL (5 g), 200 mL (10 g)	10 mL (1 g), 25 mL (2.5 g), 50 mL (5 g), 100 mL (10 g), 200 mL (20 g)	2.5, 5, 10 g
Storage	<30°C (86°F)	2°-25°C (36°-77°F)	36 months at 2°-8°C (36°-46°F) 9 months (within first 24 months of manufacturing date) at 25°C (77°F)	Not to exceed 25°C (77°F)
Concentration options	3%, 6%, 9%, 12%	5%	10%	5% or 10%
Reconstitution fluid	0.9% NaCl 5% Dextrose Sterile water	N/A	N/A	Sterile water for injection
FDA-approved indications†	PID, ITP	PID	PID	PID, ITP, CLL, KS
pH	6.6 ± 0.2	5-6	4.6-5.1	6.8 ± 0.4 (5% concentration)
IgA content	Trace	<0.05 mg/mL	37 µg/mL	≤2.2 µg/mL (5% concentration)
Sugar content	Sucrose, 1.67 g per gram of protein	D-Sorbitol, 50 mg/mL	None (stabilized with glycine)	Glucose, 20 mg/mL (5% concentration)
Osmolarity/ osmolality	mOsm/kg: In sterile water: 192 (3%), 384 (6%), 576 (9%), 768 (12%) In 0.9% NaCl: 498 (3%), 690 (6%), 882 (9%), 1074 (12%) In 5% dextrose: 444 (3%), 636 (6%), 828 (9%), 1020 (12%)	240-350 mOsm/L	240-300 mOsm/kg	Not specified in PI
Compatibility‡	Infuse by separate IV line. Do not mix with other medications or fluids	Infuse by separate IV line. Do not dilute with other IV fluids. Do not add any medications or IV fluids	Administer separately from other drugs or medications. Do not use saline as a diluent	Administer separately from other drugs or medications
Filtration	Not required. If used, pore sizes ≥15 µ less likely to slow infusion. Antibacterial filters (0.2 µ) may be used	Optional. Filter with a pore size of 15-20 µ may be used. Antibacterial filters (0.2 µ) may be used but may slow infusion	Use of in-line filter optional	Product-administration set includes mandatory 15 µ filter
Initial infusion rate	Use 3% solution for PID patients. Start at 10-20 drops (0.5-1.0 mL) per minute	0.01 mL/kg/min (0.5 mg/kg/min)	0.5 mL/kg/h (0.8 mg/kg/min)	0.5 mL/kg/h of 5% solution

*All IGIV preparations are contraindicated in patients with IgA deficiency.
†Gamimune® N, which is no longer manufactured, was the only IGIV product FDA-approved for pediatric HIV infection and bone marrow transplantation (allogeneic).
‡IGIV products of different formulations or from different manufacturers should not be mixed.
§The manufacturing process for this product provides reasonable assurance that prions associated with transmissible spongiform encephalopathy (TSE) would be removed if present in donated plasma.
¶Lighter text indicates that ZLB Behring will discontinue the manufacture of Gammar®-P I.V. and Panglobulin® NF at the end of 2005.

Gammar®-P I.V.¶	Gamunex®§	Iveegam EN	Octagam®	Panglobulin® NF¶	Polygam® S/D
Lyophilized	Liquid	Lyophilized	Liquid	Lyophilized	Lyophilized
5, 10 g	10 mL (1 g), 25 mL (2.5 g), 50 mL (5 g), 100 mL (10 g), 200 mL (20 g)	500, 1000, 2500, 5000 mg	1, 2.5, 5, 10 g	6, 12 g	5, 10 g
Not to exceed 25°C (77°F)	2°-8°C (36°-46°F)	2°-8°C (35°-46°F)	24 months at 2°-8°C (36°-46°F) 18 months from manufacturing date at ≤25°C (77°F)	Do not exceed 30°C (86°F)	Do not exceed 25°C (77°F)
5%	10%	5%	5%	3%, 6%, 9%, 12%	5% or 10%
Sterile water for injection	N/A	Sterile water for injection	N/A	0.9% NaCl 5% Dextrose Sterile water	Sterile water for injection
PID	PID, ITP	KS, PID	PID	PID, ITP	PID, ITP, CLL, KS
6.8 ± 0.4	4.0-4.3	Not specified in PI	5.1-6.0	6.6 ± 0.2	6.8 ± 0.4 (5% solution)
Not specified in PI	0.046 mg/mL	Trace amounts	≤0.1 mg/mL	Trace	≤2.2 µg/mL (5% solution)
Sucrose/5%	None (stabilized with glycine)	Glucose, 50 mg/mL	Maltose, 100 mg/mL	Sucrose, 1.67 g per gram of protein	Glucose, 20 mg/mL (5% solution)
Not specified in PI	258 mOsm/kg	Not specified in PI	310-380 mOsm/kg	mOsm/kg: In sterile water: 192 (3%), 384 (6%), 576 (9%), 768 (12%) In 0.9% NaCl: 498 (3%), 690 (6%), 882 (9%), 1074 (12%) In 5% dextrose: 444 (3%), 636 (6%), 828 (9%), 1020 (12%)	Not specified in PI
Administer by separate infusion line without admixture with other drugs or medications	Infuse by separate IV line. Do not mix with other IV fluids or medications. *Not compatible with saline*	Not evaluated	Administer separately from other drugs or medications	Infuse by separate IV line. Do not mix with other medications or fluids	Administer separately from other drugs or medications
Not required. If used, pore sizes ≥15 µ less likely to slow infusion	Not required	Product-administration set includes filter needle/ filter	Optional. If used, filter size must be 0.2-200 µ	Not required. If used, pore sizes ≥15 µ less likely to slow infusion	Product-administration set includes mandatory 15 µ filter
0.01 mL/kg/min	0.01 mL/kg/min (1 mg/kg/min)	1-2 mL/min	30 mg/kg/h (0.01 mL/kg/min)	Use 3% solution for PID patients. Start at 0.5-1.0 mL/min	0.5 mL/kg/h of 5% solution

FDA, Food and Drug Administration; IgA, immune globulin A; PID, primary immunodeficiency disorder; ITP, idiopathic thrombocytopenic purpura; IV, intravenous; N/A, not applicable; CLL, chronic lymphocytic leukemia; KS, Kawasaki disease; PI, prescribing information; HIV, human immunodeficiency virus.

is an option for patients with PI, it may take time to find a suitable hospital and to schedule appointments. Meanwhile, patients may miss their life-saving treatments.

There is a common misconception that all IGIV products are pharmacologically equivalent and may be used interchangeably. However, IGIV products differ in concentration (and osmolarity), pH, and composition (eg, in IgA and sugar content) (Table 2). Such product differences can impact tolerability, especially for patients with risk factors, and they can potentially affect the efficacy of IGIV treatment. Both tolerability and efficacy may ultimately affect cost-effectiveness of therapy and patients' quality of life. These issues may also become important when patients are switched from one infusion site to another (and thus perhaps from one IGIV product to another) because of reimbursement issues. This article will examine the range of IGIV product formulations available and the clinical considerations in matching a particular IGIV product to a patient's individual risk profile.

IGIV PRODUCT DIFFERENCES

Tolerability

The incidence and types of adverse events associated with IGIV products vary significantly. Depending on the particular disease and patient population studied, the incidence of adverse events ranges from about 2% to 25%.[5] Pyrexia, myalgia, arthralgia, and headache are commonly reported adverse events associated with IGIV therapy (Table 3). IGIV product composition, concentration, and rate of infusion may dramatically affect tolerability.

Table 3.
Common Adverse Events* After IGIV Therapy

- Pyrexia
- Myalgia
- Arthralgia
- Headache
- Rigors/shivering
- Renal failure/acute/anuria/renal tubular necrosis
- Dyspnea
- Increase in blood creatine

*Listed in descending order of frequency

Adapted from Pierce LR et al. *Transfusion Med Rev.* 2003.[5]

Sodium, sugars, and other proteins present in IGIV preparations contribute to the osmolarity of the preparation. Each of these components, in turn, can also affect tolerability.

Osmolarity

The osmolarity of IGIV preparations ranges from physiologic osmolarity (275-295 mOsm/kg H_2O) to greater than 1000 mOsm/kg (Table 2). Lyophilized products reconstituted at higher concentrations will result in hyperosmolar solutions. Renal and thromboembolic complications have been associated with the use of hyperosmolar IGIV products.[6-8] These preparations should, therefore, be avoided in patients with diabetes, congestive heart failure (CHF), and/or renal dysfunction. Neonates and elderly patients also may be particularly vulnerable to hyperosmotic preparations.

Sodium, sugars, and other proteins present in IGIV preparations contribute to the osmolarity of the preparation. Each of these components, in turn, can also affect tolerability.

Sodium content

The sodium content of currently available IGIV products ranges from trace amounts to 1.7%.[9] Infusion of an IGIV product with a high sodium concentration may upset fluid and electrolyte balance. Patients with CHF, hypertension, or renal impairment, as well as neonates, have a very fragile electrolyte balance. In these patients, the sodium content of an IGIV product will be an important consideration.[8]

Sugar content

All current IGIV preparations, with 2 exceptions, contain sugars in the form of sorbitol, maltose, glucose, or sucrose (Table 2). Sugars are added to IGIV preparations to stabilize IgG monomers and

to prevent IgG aggregate formation at the near physiologic pH at which most IGIV preparations are kept. The other 2 products are stabilized with glycine, a naturally occurring amino acid. Adverse renal events have been associated with the sugars present in IGIV preparations.

The use of sucrose-containing products has resulted in 90% of IGIV-associated adverse renal events in the United States, while 8% of renal events have occurred with glucose-containing IGIV products.[10] Extra precaution should be exercised when administering sucrose-containing IGIV products to patients who are older than 65 years, who have any pre-existing renal condition (eg, elevated BUN or creatinine levels), who have diabetes, or who are receiving nephrotoxic medications concomitantly with any carbohydrate-containing product. Both the rate of infusion and concentration of the product may need to be adjusted in patients with renal risks.

Volume load

The concentration of IGIV preparations ranges from 3% to 12% (Table 2). Preparations that are administered at a higher concentration would reduce the volume load. For example, an 80-kg patient who is given an infusion of IGIV at a dosage of 1 g/kg would receive 800 mL of a 10% solution, compared with 1600 mL of a 5% solution. In patients with CHF, hypertension, renal dysfunction, or vascular disease, volume load is an important consideration. Neonates and the very elderly are also vulnerable to fluid overload.

Volume load can also impact infusion time. The ability to deliver higher amounts of IgG in smaller volumes could be an important consideration in patients who are intolerant of large fluid volumes or long infusion times.

IgA content

All IGIV products have at least trace amounts of IgA and, thus, are contraindicated in patients with selective IgA deficiency. These patients may be at risk for developing IgE- or IgG-type anti-IgA response to the IgA present in IGIV products. The presence of IgE antibodies to IgA could lead to severe and immediate hypersensitivity reactions, including anaphylaxis.[11] True anaphylactic reactions are extremely rare with the use of IGIV products. However, if the IgA content is an issue for a patient, a product with the lowest IgA content should be considered.

pH

The pH of currently available IGIV products ranges from 4.0 to 7.2, although most have a pH that is close to neutral (pH 6.0 to 7.5) (Table 2). A neutral pH is desirable because it reduces local injection site reactions, but at this pH the IgG monomers are unstable. Therefore, the optimal pH for IGIV in solution is from 4.0 to 4.5.[12] At this pH range the active IgG monomer content is maintained, and the formation of IgG aggregates is limited. To stabilize the IgG monomer content, sugars are added to IGIV preparations that have pH in the neutral range. IGIV-caprylate/chromatography (IGIV-C) is currently the only IGIV product in the market with a pH optimal for maintaining IgG in the monomeric form. A low pH product, however, prompts 2 concerns. First, it may increase the risk of phlebitis; second, the low pH may not be tolerated by neonates and patients with renal dysfunction.[13] However, clinical experience to date has not indicated that pH is an important clinical issue for most patients.

In patients with CHF, hypertension, renal dysfunction, or vascular disease, volume load is an important consideration. Neonates and the very elderly are also vulnerable to fluid overload.

Safety

The safety differences among IGIV products are an inadvertent consequence of the production processes adopted by manufacturers to ensure product purity and pathogen safety. The latter is of particular concern with IGIV products because they are processed from human blood and, hence, potentially can transmit a variety of blood-borne pathogens from the donor to the recipient. Manufacturers of IGIV products have therefore introduced steps to ensure pathogen inactivation and clearance from IGIV products.

Pathogen inactivation is normally achieved by physical (heat and pasteurization) or chemical (acidic or solvent/detergent treatment) processes. Some of these processes, such as viral inactivation with caprylate (a natural plant substance), are environmentally friendly; others can impact the usage of natural resources. For example, large amounts of water are needed to remove solvent/detergent treatments from the final product. Other trade-offs may also pertain. For instance, pasteurization can denature proteins, which could contribute to an increased risk of adverse effects.

The safety differences among IGIV products are an inadvertent consequence of the production processes adopted by manufacturers to ensure product purity and pathogen safety.

Viral removal is accomplished via precipitation, chromatography, or nanofiltration. Although all current IGIV products have excellent safety records against bacteria and viruses, the abnormal pathogenic prion proteins associated with transmissible spongiform encephalopathies (TSEs), such as variant Creutzfeldt-Jacob disease (vCJD), remain an emergent threat. The introduction of an innovative caprylate/chromatography process[14] in the production of IGIV has been shown to provide a reasonable assurance of a significantly reduced risk from pathogenic prions. These agents have been demonstrated to be removed by several individual steps within the caprylate/chromatography production process, which includes cloth filtration and depth filtration. The manufacturing process of one nanofiltered IGIV preparation, which includes precipitation and depth filtrations as well as nanofiltration, also provides reasonable assurance that prions associated with TSE would be removed if present in the donated plasma (Table 2).

For patients, product safety is an important criterion when selecting an IGIV product, as revealed by a national survey of patients with PI. In this survey, 75% of patients identified safety as an essential characteristic of an IGIV product and expressed concerns about the theoretical risks of viral disease transmission via IGIV therapy.[15]

Efficacy

IGIV products differ in the percentage of IgG, the percentage of IgG monomers, circulating half-life, and the percentage of IgG subclass distribution. These differences may lead to efficacy differences among IGIV products.[9] In the IGIV-C versus IGIV-solvent/detergent-treated (IGIV-SD) treatment for idiopathic thrombocytopenic purpura study, a trend toward a more pronounced, sustained response and less frequent use of post-treatment emergent care therapies in patients treated with IGIV-C compared with those treated with IGIV-SD was seen, although the difference was not statistically significant (per protocol efficacy analysis).[16] Another study that compared the same 2 IGIV products, but in patients with PI, reported a significant decrease in the rate of validated infections in IGIV-C–treated patients versus IGIV-SD–treated patients (Figure 2).[17] These 2 studies suggest that not all IGIV products are clinically equivalent.

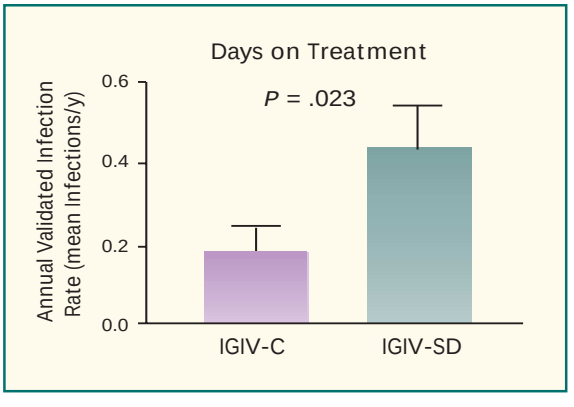

Figure 2. **The annual rate of validated infections** (mean rate of infections per year) was significantly lower among patients with primary immunodeficiency who were treated with IGIV-C (0.18) compared with those treated with IGIV-SD (0.43), according to the results of a randomized double-blind efficacy trial. (From Roifman CM et al. *Int Immunopharmacol.* 2003.[17])

CLINICAL CONSIDERATIONS

Matching the IGIV Product Profile With the Patient Profile

Each IGIV product has a unique profile. The selection of one IGIV product over another should be dictated by tolerability, safety, and coexisting risk factors—not solely by the price of the product. Matching the appropriate IGIV product with the patient profile (Table 4) is critical. An appropriate match will lead to improved outcomes and may result in cost efficiencies as unnecessary adverse event management is avoided. An example of how one can match an appropriate IGIV product with a particular patient profile is provided in a representative case study (Case Study 1).

Matching the appropriate IGIV product with the patient profile is critical. An appropriate match will lead to improved outcomes and may result in cost efficiencies as unnecessary adverse event management is avoided.

IGIV Infusion Rate vs Tolerability

As noted earlier in "Navigating the Reimbursement Landscape" (page 6), payment for infusion services is affected by the complexity of the drug or biological being infused and the length of infusion time. Because IGIV is classified as a low-complexity product, physician administration fees for IGIV have been decreased. However, it can be argued that IGIV should not be classified as a low-complexity administration product because of the preparation requirements and the risks of infusion-related adverse reactions of some IGIV products. Additionally, infusions, on average, take from 3 to 5 hours, with some infusions lasting more than 8 hours in patients with autoimmune disorders (Figure 3).[15] If IGIV were reclassified as a BRM therapy, physicians would be allowed to bill IGIV under the chemotherapy administration code and increase administration fees. The United States National Library of Medicine defines BRM therapy as a treatment intended to stimulate or restore the ability of the immune system to fight infection and disease.

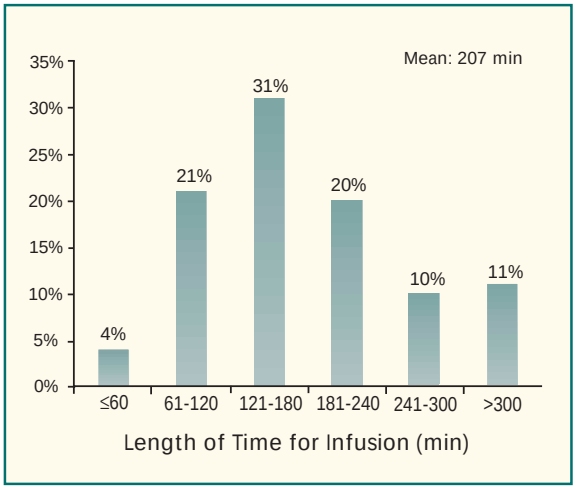

Figure 3. **Infusion times for IGIV therapy can vary markedly,** from 1 hour or less to more than 5 hours. Shown here are the treatment experiences in patients with primary immunodeficiency. (From Immune Deficiency Foundation. First national survey. 2003.[15])

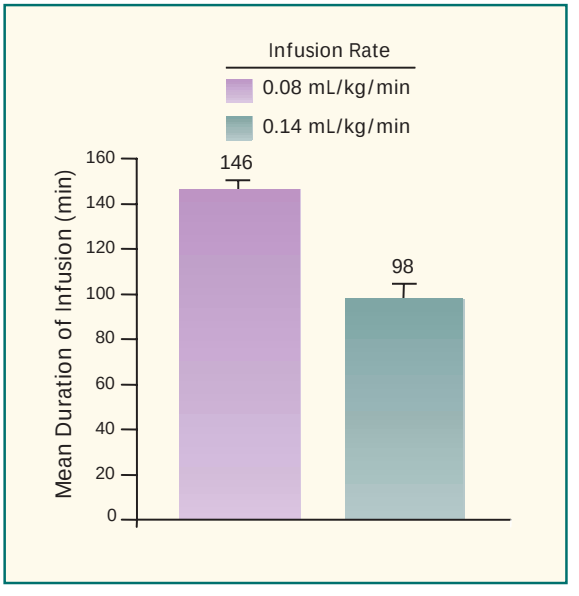

Figure 4. **Infusion times at the standard and maximum infusion rates of IGIV-C, 10%** in patients with idiopathic thrombocytopenic purpura are compared here. Infusion at the maximum rate resulted in a time savings of 48 minutes, approximately one third of the total infusion time at the standard rate. (Data from Bussel JB et al. *Blood.* 2004.[20])

Table 4.
Matching IGIV Profile With Patient Profile

PATIENT RISK FACTORS	IGIV RISK FACTORS					
	Volume Load	Sugar Content	Sodium Content	Osmolality	pH	IgA
Cardiac impairment	•		•	•		
Renal dysfunction	•	•	•	•		
Anti-IgA antibodies						•
Thromboembolic risk	•		•	•		
(Pre)diabetes		•				
Elderly patients	•	•	•	•		
Neonates/pediatrics	•		•	•	•	

CASE STUDY 1

Presenting profile: A 70-year-old man presented with a history of gum and nose bleeds and a tendency to bruise easily.

Findings: Physical and laboratory findings included blood pressure, 155/90 mm Hg; and fasting glucose, 120 mg/dL. Laboratory results also showed a platelet count of 2000/L. Bone marrow analysis revealed an increased number of megakaryocytes.

Diagnosis: The patient was diagnosed with chronic idiopathic thrombocytopenic purpura.

Initial treatment: After achieving only a partial response with prednisone and vincristine, the patient was referred for IGIV therapy. He was given a lyophilized IGIV product reconstituted to a 10% formulation. Halfway through the infusion, the patient experienced shortness of breath and chest pain. Physical examination revealed rales in his chest and edema of the feet. X-ray films indicated congestive heart failure (CHF). The IGIV therapy was discontinued.

Risk factor profile: The patient's risk factor profile was notable for CHF, hypertension, and prediabetes.

Relevant IGIV product characteristics: Volume load, osmolarity, and sodium content are important concerns for this patient because of his history of CHF and hypertension. As the patient was also prediabetic, the sucrose content of the IGIV product selected may not impact insulin requirements but may be an additional concern because of potential renal risks (Table 4). The sodium content and the osmolarity of the 10% product initially given may have exacerbated the underlying CHF. Additionally, because a reconstituted lyophilized product was used, reconstitution may have also increased the sodium content and osmolarity of the preparation, depending on the final volume of the formulation.

Outcome: A concentrated, sucrose-free, non-lyophilized IGIV product with physiologic osmolarity and low sodium content was eventually selected for this patient and resulted in a positive outcome.

CASE STUDY 2

A 66-year-old man with PI has been treated monthly with IGIV for years at his immunologist's office. He has a regular routine of receiving his infusion the last Wednesday of each month. He drives 2 miles to the office, parks in the physician's parking lot, is seen by the nurse for laboratory work, and receives a 2-hour infusion of IGIV. He then heads off to his part-time job as a sales associate at a local department store.

On this visit, he is informed that next month his immunologist will no longer be providing his IGIV infusion because of constant supply shortages, increased costs, and reduced reimbursement. From 2004 to 2005, the infusion reimbursement for this case dropped by more than 35%, while product and labor costs continued to rise.

The patient is concerned about the out-of-pocket expenses for home infusion and is not confident about doing self-infusion, which is not covered by Medicare. He decides to make the 85-mile trip to the closest outpatient hospital facility but is concerned about driving home if he experiences an adverse reaction. When he schedules his appointment, he is told he must be at the facility by 8:00 AM since the average infusion time at the center is 4 to 5 hours. Because of the early arrival time, he decides to travel the night before his appointment. He is concerned about parking, an overnight stay at a motel, and losing contact with his immunologist.

The patient's IGIV order is for 40 g. He had been receiving a 10% liquid product that contained no sodium chloride and was isotonic. He required no premedications and only had occasional mild headaches. The new center does not carry the 10% liquid product but instead uses a 10% lyophilized product. This patient has hypertension, but it has been controlled, and he has no history of renal disease or diabetes.

Halfway through the infusion with the new formulation, the patient complains of headache. His blood pressure is 188/100 mm Hg. The infusion is stopped, and the physician is reluctant to continue it. The patient remains in the center until his blood pressure returns to normal, but he then needs to spend a second night in the motel because he still does not feel well. The center would like him to return the following day but can't squeeze him in until 2:00 PM. The patient is concerned about having another adverse reaction and having to stay in a motel for a third night, so he schedules an appointment for a week later.

The new IGIV formulation contained nearly 2% sodium chloride at the 10% concentration and was hyperosmolar at more than 1000 mOsm/L. The inability to complete the infusion might compromise the effectiveness of the treatment and might also pose risks to the patient.

As IGIV restores the ability of the immune system to fight infection and disease, it arguably should be reclassified as a BRM.

An approach that would lead to more convenience for patients as well as improved efficiency for practitioners would be to reduce IGIV infusion time. Reduction in infusion time can be achieved by increasing infusion rates or by using products of higher concentrations. Each IGIV preparation has a recommended infusion rate, which varies from 0.03 to 0.13 mL/kg/min. Tolerability is both product- and patient-dependent. Increasing the infusion rate beyond the recommended rate may lead to serious adverse events, including thromboembolic events.[18,19] However, not all IGIV products have this tendency. Studies that compared standard (0.08 mL/kg/min) versus maximum (0.14 mL/kg/min) infusion of IGIV-C 10% reported that the most common adverse event was headache.[20,21] In one randomized, single-center, open-label, crossover study, 8 patients with ITP received IGIV-C at the standard infusion rate during

the first month of treatment. Patients were then crossed over to receive the maximum infusion rate of the IGIV product during the second month of treatment. Both infusion rates were given at a dose of 1.0 g/kg body weight. The faster infusion rate resulted in a time savings of 48 minutes (Figure 4) without serious consequences.[20]

Using an IGIV preparation that is more concentrated, such as a 10% formulation, will reduce the infusion time more than using a less concentrated preparation, such as a 5% formulation. Alternatively, reconstituting lyophilized products in a smaller volume will also reduce the infusion time. However, other product characteristics, such as osmolarity, sodium content, and sugar content of the lyophilized reconstituted preparations could pose serious problems, depending on the patient.

Using an IGIV preparation that is more concentrated, such as a 10% formulation, will reduce the infusion time more than using a less concentrated preparation, such as a 5% formulation.

Convenience of Care

Patients with PI need to be given an infusion of IGIV every 3 to 4 weeks, with each infusion lasting on average 3 to 5 hours.[15] IGIV therapy, therefore, consumes a substantial portion of a patient's and, in some cases, a caregiver's time. Time lost for therapy equates to time lost from school or work. Ideally, the infusion site should be conveniently located so that patients do not spend an excessive amount of time on transportation. Transferring patients to hospitals or other sites distant from their homes because of reimbursement issues may inconvenience them further in terms of lost work time and travel costs (Case Study 2).

CONCLUSION

The misperception that all IGIV products are pharmaceutically equivalent and can be used interchangeably can have serious clinical implications. Product differences can impact tolerability, particularly in high-risk patients. Barriers to reimbursement that require patients to be switched from one infusion site to another (and thus perhaps from one IGIV product to another) can have adverse clinical consequences. Careful consideration should be given to matching the product choice to patient needs, so as to provide the best possible quality of care.

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SELF-ASSESSMENT QUESTIONS

1. Two components of reimbursement for IGIV (or for any other medical technology) that should be examined with individual patients and their insurers are:
   a. Coverage and coding.
   b. Payment and coding.
   c. Coverage and payment.
   d. Coding and denial management.

2. In 2005, new Healthcare Common Procedure Coding System (HCPCS) codes were assigned to differentiate IGIV products based on:
   a. Labeled and off-label uses.
   b. Lyophilized and liquid formulations.
   c. Sugar content.
   d. Sodium content.

3. In 2006, Medicare reimbursement for IGIV therapy in the hospital outpatient setting will be based on:
   a. Average sales price (ASP) plus 8%.
   b. Average sales price (ASP) plus 6%.
   c. Average wholesale price (AWP) plus 8%.
   d. Average wholesale price (AWP) plus 6%.

4. Beginning in 2005, Medicare reimbursement for IGIV therapy in the physician office setting is based on:
   a. Average sales price (ASP) plus 8%.
   b. Average sales price (ASP) plus 6%.
   c. Average wholesale price (AWP) plus 8%.
   d. Average wholesale price (AWP) plus 6%.

5. Home infusion of IGIV is covered by Medicare:
   a. Only for patients with primary immunodeficiency disorders.
   b. Only for the IGIV itself and not for professional services or supplies for administering it.
   c. At the rate of average sales price (ASP) plus 6%.
   d. All of the above

6. A commonly reported adverse event associated with IGIV therapy is:
   a. Anaphylaxis.
   b. Headache.
   c. Thrombosis.
   d. None of the above

7. Which of the following statements is **TRUE**?
   a. Lyophilized products reconstituted at higher concentrations result in hyperosmolar solutions.
   b. Hyperosmolar IGIV preparations have been associated with renal or thromboembolic complications.
   c. Both of the above
   d. None of the above

8. An 80-kg patient prescribed IGIV at 1 g/kg would receive:
   a. 1600 mL of a 5% solution or 800 mL of a 10% solution.
   b. 800 mL of a 5% solution or 1600 mL of a 10% solution.
   c. 1600 mL of a 5% solution or 1600 mL of a 10% solution.
   d. 800 mL of a 5% solution or 800 mL of a 10% solution.

9. The caprylate/chromatography and precipitation/depth filtration/nanofiltration production processes have been shown to provide reasonable assurance of a significantly reduced risk from pathogenic prions associated with transmissible spongiform encephalopathies.
   a. True
   b. False

10. Which IGIV product characteristic(s) is(are) important to consider before prescribing IGIV for a patient with a history of congestive heart failure and hypertension?
    a. Volume load
    b. Osmolarity
    c. Sodium content
    d. All of the above

EVALUATION FORM FOR PHYSICIANS

Photocopy and mail evaluation form to New York Medical College, Office of Continuing Medical Education, Vosburgh Pavilion, Room 230, Valhalla, NY 10595, prior to September 30, 2006.

Please print legibly. This form will be used to generate and mail your certificate of credit.

First Name ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ Middle Initial ☐

Last Name ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ Degree(s) ☐☐☐☐☐☐☐☐

Address ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

City ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ State ☐☐ ZIP Code ☐☐☐☐☐

Phone ☐☐☐ – ☐☐☐ – ☐☐☐☐ Fax ☐☐☐ – ☐☐☐ – ☐☐☐☐

E-mail ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Specialty: ☐ Immunology ☐ Hematology ☐ Oncology ☐ Other: _____

Activity Title: *Reimbursement Issues in IGIV Therapy*

Target Audience: Immunologists, hematologists, oncologists **CME No.** 7502 **Designated Credit(s):** 1.5

Learning Objectives: Discuss indications for the use of IGIV therapy • State the pros and cons of the various IGIV products available • Identify key policies and procedures related to IGIV reimbursement as they relate to the clinical setting (hospital, physician office, home care provider)

Please provide us with your candid evaluation. We thank you for your comments and appreciate your suggestions for future activities.

After participating in this activity, do you feel that:	Yes	No	Somewhat
1. The content was free of commercial bias?	☐	☐	☐
2. The content was not affected by any faculty conflict of interest?	☐	☐	☐
3. The learning objectives were met?	☐	☐	☐
4. Your skills have been improved?	☐	☐	☐
5. The activity was effective in meeting identified needs?	☐	☐	☐
6. You were satisfied with the activity content?	☐	☐	☐
7. The information gained applies to your practice?	☐	☐	☐
8. The information gained will assist in improving the health of your patients?	☐	☐	☐

Would you recommend this activity to a colleague? ☐ Yes ☐ No ☐ Maybe

Suggestions for future activities: _____

_____

_____

Comments: _____

_____

I certify that I have completed this activity and the actual time I spent was:

☐ 1.00 h ☐ 1.25 h ☐ 1.50 h

Signature _____ Date _____

ANSWER GRID (please circle 1 answer per question)

1.	a	b	c	d	6.	a	b	c	d
2.	a	b	c	d	7.	a	b	c	d
3.	a	b	c	d	8.	a	b	c	d
4.	a	b	c	d	9.	a	b		
5.	a	b	c	d	10.	a	b	c	d

Please address questions regarding this activity to the Continuing Education Alliance at inquiries@cealliance.org.

CTE28905

NOTES

EVALUATION FORM FOR NURSES

Photocopy and fax evaluation form to 402.559.6379 or mail it to University of Nebraska Medical Center, College of Nursing Continuing Nursing Education, 985330 Nebraska Medical Center, Omaha, NE 68198-5330, prior to September 30, 2006.

Please print legibly. This form will be used to generate and mail your certificate within 4 to 6 weeks.

First Name ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ Middle Initial ☐

Last Name ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ Degree(s) ☐☐☐☐☐☐☐☐

Address ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

City ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐ State ☐☐ ZIP Code ☐☐☐☐☐

Phone ☐☐☐ – ☐☐☐ – ☐☐☐☐ Fax ☐☐☐ – ☐☐☐ – ☐☐☐☐

E-mail ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Activity Title: *Reimbursement Issues in IGIV Therapy*

Target Audience: Infusion nurses

Designated Contact Hour(s): 1.8 (with 70% or more correct)

Goal: To provide physicians, pharmacists, and nurses with information regarding IGIV reimbursement policies and procedures.

We would like your opinion regarding this educational activity. Please complete the evaluation form, including the self-assessment answers, and return it to the address or fax number indicated above.

	Yes	No	Somewhat
1. As a result of completing this learning activity are you now better able to:			
a. Discuss indications for the use of IGIV therapy?	☐	☐	☐
b. State the pros and cons of the various IGIV products available?	☐	☐	☐
c. Identify key policies and procedures related to IGIV reimbursement as they relate to the clinical setting (hospital, physician office, home care provider)?	☐	☐	☐
2. Were the objectives of this learning activity as stated in item #1 above related to its overall goal?	☐	☐	☐
3. Was the content of this learning activity clear.	☐	☐	☐
4. Was the content scientifically rigorous?	☐	☐	☐
5. Was the content of this activity free of commercial bias?	☐	☐	☐
6. Was the information/content relevant to your clinical practice?	☐	☐	☐
7. Did the format of this activity promote learning?	☐	☐	☐

If you answered NO or SOMEWHAT to any items above, please explain: _____

_____

Comments/suggestions for future activities: _____

I certify that I have completed this activity and the actual time I spent was:

☐ 60 min ☐ 75 min ☐ 90 min ☐ 105 min ☐ Other (fill in number of minutes: _____)

Signature _____ Date _____

ANSWER GRID (please circle 1 answer per question)

1.	a	b	c	d	6.	a	b	c	d
2.	a	b	c	d	7.	a	b	c	d
3.	a	b	c	d	8.	a	b	c	d
4.	a	b	c	d	9.	a	b		
5.	a	b	c	d	10.	a	b	c	d

Please address questions regarding this activity to the Continuing Education Alliance at inquiries@cealliance.org.

CTE28905

NOTES

Pharmacists may take the self-assessment test and
submit the evaluation form
online by accessing the Web site:
http://www.cealliance.org/igiv/cpe.

If Internet access is not available, please fax
a request for an evaluation form to 203.422.6120
(please include return fax number) or
e-mail sbuckingham@cealliance.org.

Continuing Education Alliance
One Sound Shore Drive, Suite 210
Greenwich, CT 06830

Reimbursement Issues in IGIV Therapy