



**ACCESS TO IVIG BY SAFETY NET HOSPITALS
PARTICIPATING IN THE 340B DRUG DISCOUNT PROGRAM**

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Report and Survey by:



(A Coalition of the National Association of Public Hospitals and Health Systems)

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BACKGROUND ON THE PUBLIC HOSPITAL PHARMACY COALITION



The Public Hospital Pharmacy Coalition is an organization of over 350 public and private non-profit hospitals and health systems throughout the United States. The Coalition was formed to increase the affordability and accessibility of pharmaceutical care for the nation's low-income and underserved populations. PHPC monitors, educates, and serves as an advocate on federal legislative and regulatory issues related to drug pricing and other pharmacy matters affecting public and private non-profit hospitals and health systems that serve a large volume of uninsured and indigent patients. PHPC members participate in the Public Health Service 340B drug discount program. The Coalition is dedicated to preserving and enhancing the 340B program and creating new opportunities for members to save on pharmaceuticals. In addition to helping members maximize savings on pharmaceuticals, the Coalition provides assistance to its members to ensure compliance with various pharmacy-related laws.

A copy of PHPC's report can be found at www.phpcrx.org.

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ACCESS TO IVIG BY SAFETY NET HOSPITALS PARTICIPATING IN THE 340B DRUG DISCOUNT PROGRAM

EXECUTIVE SUMMARY

Access to adequate supplies of intravenous immunoglobulin (“IVIG” or alternatively “IGIV”) has been a problem for members of the Public Hospital Pharmacy Coalition (“PHPC”) for more than a decade. Access to IVIG at discounts required under the 340B drug discount program has been even more problematic. Member concerns have intensified over the past year, prompting PHPC to survey its members in an effort to measure the problem, identify the causes, and participate in a broader national dialogue about how to address these complex issues. This report represents PHPC’s preliminary effort to achieve these goals.

PHPC conducted its IVIG survey in February and March of 2006. In addition to disseminating a written questionnaire to its approximately 350 members, it interviewed selected representatives of the drug industry, wholesalers, specialty distributors, and the federal government. PHPC also followed up, as needed, with survey respondents to clarify or supplement their written answers. This report discusses and analyzes the information gathered by PHPC through these procedures, but does not purport to draw firm conclusions regarding the controversial question of whether there is an actual shortage of IVIG product or who bears primary responsibility for the difficulties patients and health care providers are generally experiencing in obtaining IVIG on today’s market. It does identify and discuss various factors and influences that may play a role in shaping current marketplace realities pertinent to IVIG supply and distribution, and that serve as a backdrop to the special problems encountered by 340B entities in that context.

Survey Results

PHPC hospitals report substantial difficulties in obtaining sufficient quantities of IVIG to treat their patients, although most have been able to obtain supplies of the product from wholesalers or other distributors and a slight majority of survey respondents reported being able to purchase adequate supply. Obstacles and problems in accessing IVIG products at 340B prices, however, are significantly more persistent and widespread than difficulties in finding supply, and strongly suggest that the frequent unavailability to covered entities of 340B pricing on IVIG products is not attributable to or directly associated with market supply limitations.

Key findings include the following:

- About half (50.66 %) of responding hospitals have been able to obtain enough IVIG product to fulfill their patients’ needs.
- A majority of responding hospitals (68.22 %) have been able to obtain at least some amount of IVIG product through their regular drug wholesalers or other drug distributors.

- A substantially smaller percentage of 340B hospitals, only 21.42 % or a little over one-fifth of responding PHPC members, have been able to obtain any amount of IVIG at 340B discount prices. Even those hospitals able to access some 340B pricing on IVIG generally have had to purchase additional product at above-ceiling prices in order to adequately fulfill their patients' needs.
- Hospitals reported that the financial impact of purchasing IVIG at above the 340B price was a serious concern.
- Some hospitals have been forced to delay or cancel IVIG infusions for patients due to supply limitations.
- Although, in oral communications with 340B providers, manufacturers and distributors commonly attribute the unavailability of 340B pricing on IVIG product to a "shortage" of supply, manufacturers and distributors have been unwilling to provide our survey respondents any explanations in writing for the lack of 340B prices. In fact, not one of the hospitals surveyed reported being able to obtain a written explanation as to why IVIG is unavailable at a 340B price.

Conclusions

The survey results confirm that 340B hospitals, like many other providers, are having great difficulty in obtaining enough IVIG product to care for their patients. The fact that obtaining IVIG at any price can be difficult and that supply of the product may be constricted, however, does not adequately explain the severely limited availability of 340B prices on IVIG drugs reported by our members. Although PHPC's survey indicates that only about one-fifth of its member hospitals have been able to procure any IVIG at 340B prices, a much higher percentage of survey respondents – approximately 50% – have been able to purchase enough IVIG to fulfill patient care needs, and almost 70% have been able to obtain at least some amount of IVIG from a wholesaler or other drug distributor. In other words, the incidence of unavailability of IVIG product at 340B pricing levels does not correspond with unavailability of product supply, and frequently IVIG is available for purchase, but just not at discounted, 340B prices.

This suggests that the ostensible product "shortage" often cited by manufacturer representatives and distributors to explain above-ceiling pricing, is in fact not the actual reason 340B prices are usually unavailable. In a significant percentage of situations, it is only the discounted 340B price, and not the product itself, that is inaccessible. Accordingly, it appears likely that something beyond limited supply of IVIG is at the root of the pricing problem currently encountered by 340B hospitals, and that the ostensible "shortage" of IVIG and the currently pervasive failure of manufacturers and distributors to offer 340B pricing on these products may spring from a distinct set of underlying causes.

ACCESS TO IVIG BY SAFETY NET HOSPITALS PARTICIPATING IN THE 340B DRUG DISCOUNT PROGRAM

I. BACKGROUND

PHPC has received numerous reports from its members that, not only have they had difficulty procuring sufficient amounts of IVIG to meet the needs of their patients, but even when they can locate and obtain an adequate amount of IVIG, it is only available at prices that are higher than the statutory ceiling price to which the hospitals are entitled under the 340B drug discount program. This is an issue of serious concern for PHPC's member hospitals, as the discounts they receive on 340B drugs are often essential to their continued capacity to provide outpatient pharmaceutical treatment and other services to their large volume of indigent and uninsured patients. This is especially true with regard to expensive specialty drugs (like IVIG products) that may comprise a disproportionately large segment of a hospital's outpatient pharmacy expense. In an attempt to gain a more comprehensive and accurate understanding of the specific IVIG problems 340B hospitals are facing today, PHPC conducted a survey of its members with the objective of quantifying and assessing the frequency with which member hospitals experience difficulty in procuring IVIG products and obtaining proper pricing under the 340B program.

A. Federal 340B Drug Discount Program

The federal 340B drug discount program was established in 1992 and is an outgrowth of the Medicaid rebate program. Under the Medicaid rebate program, pharmaceutical manufacturers, as a precondition to coverage of their outpatient drugs by Medicaid or Medicare Part B, are required to enter into an agreement with the Secretary of the Department of Health and Human Services ("HHS") to pay statutorily defined rebates to State Medicaid agencies on covered outpatient drugs dispensed to Medicaid recipients.¹ Section 340B of the Public Health Service Act ("PHS Act"), in tandem with related provisions of the Medicaid statute, requires those same manufacturers to agree to provide a discount on covered drugs purchased by any health care provider that qualifies as a "covered entity" under that statutory provision or under §1927(a)(5) of the Social Security Act.² The 340B discount is provided at the time of purchase rather than through a post-payment rebate mechanism.

Covered entities enumerated in the 340B statute include various categories of "safety net" health care providers. Most 340B providers are federal grantees or other facilities owned by,

¹ The Medicare Prescription Drug Improvement and Modernization Act of 2003 ("MMA") amended the Medicaid statute to include payment of Medicaid rebates and 340B participation as a condition of coverage of a manufacturer's outpatient drugs under Medicare Part B as well as Medicaid. See Social Security Act §1927(a)(1), 42 U.S.C. §1396r-8(a)(1) and (5). Previously the law only conditioned coverage of a manufacturer's outpatient drugs by Medicaid upon 340B and Medicaid rebate program participation.

² Pursuant to recent amendments to the Medicaid statute enacted through the Deficit Reduction Act of 2005 ("DRA"), pharmaceutical manufacturers of Part B Medicare and Medicaid-covered drugs are now required to agree to afford 340B-level discounts on outpatient drug purchases to qualifying children's hospitals as well as the various covered entities identified in the 340B statute itself. See §1927(a)(5) of the Social Security Act, 42 U.S.C. §1396r-8(a)(5) as amended by DRA §6004.

under contract with, or funded at least in part by state or local governments, and serve large numbers of indigent, uninsured, or underserved patients. Covered entities include, for example, non-profit hospitals that have a high disproportionate share (“DSH”) adjustment percentage, community health centers, AIDS clinics, and hemophilia treatment centers. A discounted price, sometimes referred to as the “340B ceiling price,” is calculated for each covered drug subject to the program, according to a formula defined in the statute. Each manufacturer of Medicare Part B or Medicaid-covered outpatient drugs is required to execute a pharmaceutical pricing agreement (“PPA”) with HHS obligating the manufacturer to offer covered drugs for purchase by 340B covered entities at or below the applicable 340B ceiling price.

B. IVIG Infusion Therapy

Over the past few years, health care providers, and hospitals in particular, have found it increasingly difficult to procure IVIG (referring to any of various intravenous immunoglobulin products). Immunoglobulin is a sterile preparation of concentrated antibodies (immunoglobulins) recovered from pooled human plasma of healthy donors. This “plasma product” is used to manage serious conditions, including immune system disorders and related illnesses. Production of IVIG involves a complex manufacturing process that uses antibodies taken from one thousand or more blood donors to make one batch of product. Due to the resource-intensive collection and processing activities involved in IVIG production, the drugs are typically very expensive. There are, moreover, practical limits on the amount of IVIG that can be produced, primarily determined by the available supply of blood plasma and the number of manufacturing facilities capable of processing IVIG.

IVIG is an infusion product administered directly into the bloodstream, and thus the product cannot be self-administered. For patients in need of these drugs, access to IVIG infusion therapy may mean the difference between relative good health and a severely compromised medical condition or even death. It is, therefore, critical that hospitals and physicians have access to an adequate supply of IVIG product to ensure that patients receive the treatment that is most appropriate for their specific conditions.

II. THE IVIG MARKET AND SUPPLY

The current state of the IVIG market and the factors affecting product availability are subjects of considerable debate and many issues merit further inquiry and investigation. Certain aspects of the problem are quite clear: (1) the price of IVIG products is rising substantially each year; and (2) the expense and seemingly limited availability of the product is causing concern for providers and patients alike. However, there is disagreement within the health care community as to whether there is an actual shortage of IVIG product or if one or more other market factors are responsible for procurement difficulties currently facing hospitals and other providers.

A. Product Shortage and Market Distortion

According to informational materials posted on the website of the Food and Drug Administration (“FDA”), a federal agency that, among its many other functions, tracks biological

product shortages, there is no clear evidence of a current IVIG product shortage.³ Also, some manufacturers currently producing IVIG products and their representatives maintain that there is adequate supply to fulfill market needs.⁴ While IVIG production contracted somewhat in 2004, it increased again in 2005;⁵ and the trade association for IVIG manufacturers reported “record amounts” of product being distributed in the U.S. in 2005 with even higher distribution levels in the first six months of 2006.⁶

Yet despite the at least superficially encouraging manufacturer data relating to product distribution levels, there have been continuing reports of health care providers experiencing difficulties in obtaining IVIG products on a sufficiently consistent basis to meet patient needs,⁷ and patient complaints of problems in obtaining needed IVIG treatments are legion.⁸ As of August 3, 2006, the American Society of Health-System Pharmacists (“ASHP”) included IVIG in its listing of “Current Drug Product Shortage Bulletins,” although noting that manufacturers “will not provide a reason” for the shortage, and that the FDA has not found “clear evidence” that a shortage exists.⁹

At the same time, IVIG manufacturers have almost uniformly put products “on allocation,” meaning that providers are only permitted to buy an amount of product that is pre-allocated to them, usually based on historical purchasing of IVIG dating back a number of years.¹⁰ The rigidity with which these allocation limits are being imposed naturally gives rise to an inference that the practice is a means of managing a shortage situation. Also, field representatives for drug companies, even if not their more high-ranking corporate officers, often

³ See Center for Biologics Evaluation and Research, Biological Product Shortages listing at <http://www.fda.gov/cber/shortage/shortage.htm> (last visited Sept. 15, 2006).

⁴ The trade association for IVIG manufacturers and other products of plasma-based and recombinant biological therapeutics, the Plasma Protein Therapeutics Association (“PPTA”), represents on its website that inventory levels of IVIG are at a 2-5 week supply level and remain “adequate.” See PPTA Data Center at <http://www.pptaglobal.org> (last visited Sept. 15, 2006).

⁵ See Testimony of July 13, 2006, by Herb Kuhn, CMS Director of Medicare Management, on Payment for Medicare Part B Drugs, before the House Subcommittee on Health of the Committee on Ways and Means.

⁶ 2006 Brochure of PPTA entitled “Plasma protein therapies save and improve lives.”

⁷ Letter of March 27, 2006 to Arthur Bracey, M.D., Chair of the Advisory Committee on Blood Safety and Availability from John O. Agwunobi, Assistant Secretary for Health, U.S. Department of Health and Human Services, Response to September 2005 recommendations available at <http://www.hhs.gov/bloodsafety/resolutions/html> (last visited Sep. 15, 2006).

⁸ According to the President of the Immune Deficiency Foundation in recent testimony before the House Ways and Means Subcommittee on Health, that organization has received thousands of calls, e-mails and letters from Medicare patients and their physicians, reporting that they have been unable to obtain IVIG infusions at various sites, including physician’s offices, outpatient infusion suites, home care settings, and hospitals. Reported in Washington Outlook, a newsletter published by Premier, Inc., July 21, 2006, available on-line at <http://www.premierinc.com/advocacy/publications/outlook/06/jul-21.jsp> (last visited Sept. 15, 2006).

⁹ See ASHP Drug Product Shortage Management Resource Center, Current Drug Product Shortage Bulletins, at <http://www.ashp.org/shortage/index.cfm> (last visited Sept. 15, 2006).

¹⁰ This manufacturer practice has been widespread in the IVIG marketplace for sometime. See commentary by CMS published at 70 Federal Register 70216 (November 21, 2005), acknowledging that “[most] brands of IVIG have been put on allocation by manufacturers...”

cite product shortage to providers as an explanation for manufacturers' allocation policies, and those policies certainly suggest, even if they do not prove, a shortage situation. Another significant point often cited as a contributing factor to an IVIG shortage scenario is the fact that the number of IVIG manufacturers declined during the first half of this decade.¹¹

Notwithstanding these observations, however, federal officials have continued to accept the premise that product supply is adequate, and what is occurring in the IVIG market is not a true shortage but a situation of considerably greater complexity, shaped by a wide range of diverse forces.¹² There are in fact considerable grounds for skepticism as to whether current IVIG procurement problems are the result of an actual product shortage, or of external factors such as Medicare reimbursement policy, flawed or discriminatory distribution practices, and possible market manipulations in the interests of higher profits.

B. Influence of Medicare Reimbursement

One possible cause of IVIG procurement problems frequently cited by industry observers is inappropriate reimbursement policy for IVIG treatment in federal health care programs and the private insurance sector. In particular, because of its size and consequently vast influence on all payment policies for health care payors, the federal Medicare program and its policies play a critical role in shaping the operation of the IVIG market and often drive the behavior of treatment providers and suppliers of health care products. Many industry commentators believe that problems faced by providers seeking to obtain IVIG, especially hospitals, are the direct result of flawed Medicare reimbursement policies for IVIG products.

More specifically, a Medicare reimbursement change effective in 2005 that substantially reduced the payment rate for physicians who administer IVIG treatments may have been especially significant in generating IVIG procurement difficulties for hospitals. The Medicare statute as amended in late 2003 by the Medicare Prescription Drug Improvement and Modernization Act of 2003 ("MMA"), now provides for reimbursement to physicians for IVIG administered in their offices at the rate of 106 percent of average sales price ("ASP").¹³ Prior to 2005, the law provided for reimbursement costs of IVIG and other injectable or intravenous drugs administered incident to physicians' services at a rate of 95 percent of the drug's Average Wholesale Price ("AWP") as reflected in published compendia.¹⁴

¹¹ Aventis Behring was purchased by ZLB and was consolidated into ZLB-Behring. One brand of IVIG previously manufactured by Alpha Therapeutics, Venoglobulin, was purchased by Grifols Biologicals and then phased out. The Bayer Healthcare Biological plasma products group was purchased by Cerberus, a venture capital group, and became Talecris Biotherapeutics. Also, in 2005, the American Red Cross sold its fractionation business to Baxter. See Formulary Considerations for IVIG Products, Tom Schleis, MS, RPh. and Jerry Siegal, PharmD, FASHP, published April 1, 2005 in U.S. Pharmacist, available at <http://www.uspharmacist.com> (last visited Sept 15, 2006).

¹² Letter of August 8, 2005 from John O. Agwunobi to Mark Brecher, M.D., Chair, Advisory Committee on Blood Safety and Availability. See "Response to May 2005 Recommendations" available at <http://www.hhs.gov/bloodsafety/resolutions/html> (last visited Sept. 15, 2006).

¹³ Social Security Act § 1842(o)(1)(E), 1847A; 42 U.S.C. §§1395U(o)(1)(E), 1395w-3a. For a single source drug, the statute specifies reimbursement at 106 percent of the lesser of the drug's ASP or wholesale acquisition cost ("WAC"). See §1847A(b)(4), 42 U.S.C. §1395w-3a(b)(4).

¹⁴ See former Social Security Act §1842(o)(1), prior to amendment by the MMA.

According to some sources, this reimbursement change made it impossible for physicians to provide their patients' IVIG treatments without financial loss to the physicians.¹⁵ Although CMS, in response to the concerns expressed by providers and beneficiary groups, made some effort to ameliorate the situation by refining IVIG payment rates in regulatory issuances,¹⁶ many of the services that were once provided in physician offices are now being shifted to hospital settings, presumably because physicians no longer regard IVIG administration as a financially viable part of their practice. The increased demand for IVIG treatments in hospitals requires them to procure a larger volume of IVIG products than before, which is difficult because of finite market supply, and rendered virtually impossible by manufacturer allocation policies. This factor further exacerbates the perception in the hospital community that there is a severe product shortage, even though it is possible that the actual deficiency may lie more in market allocation and product distribution than total supply.

However, while this reimbursement change certainly increases the difficulty hospitals have in meeting the IVIG needs of their patients, misdirected distribution systems and unrealistic allocations may play more of a role in the problem than an actual drug shortage. Logically, a mere shift in treatment settings should not increase overall product demand, but instead should simply require a shift in distribution patterns for IVIG products. Since many IVIG manufacturers are determining allocations for providers based on their purchases in 2004, a major source of IVIG access problems may be that the distribution structure has not adjusted to the shift in IVIG demand in different treatment settings resulting from reimbursement changes that began to affect the marketplace in 2005.

C. Rise of Specialty Distributors

Yet another factor contributing to IVIG procurement problems may be the increased use of specialty distributors as a means of dispensing products to health care providers. Specialty distributors are alternative drug distribution organizations that generally function in a role similar to that of a pharmaceutical wholesaler. Typically, these organizations distribute a small number of products that may require special handling or to which other special considerations pertain. Specialty distributors usually purchase the products they distribute directly from a manufacturer and then resell them to customers on the open market, most often health care providers. Currently, a large volume of IVIG product is being distributed through the use of specialty distributors, and a high percentage of IVIG produced by manufacturers is contractually pre-allocated for sale to these distributors.

¹⁵ See PPTA materials referenced at note 6. A Lewin Group study, in fact, concluded that physicians lose almost \$400 per IVIG infusion as a consequence of present Medicare reimbursement methodology. See *Assessing the Cost of IVIG Infusion Services in Physician Offices and Hospital Pharmacy Departments*, The Lewin Group, March, 2006.

¹⁶ Though regulatory issuances, CMS established separate payment rates for liquid and powder IVIG beginning April 2005, and allowed special pre-administration handling fees of about \$72 per infusion service for physicians. See July 13, 2006 Testimony of Herb Kuhn before the House Subcommittee on Health of the Committee on Ways and Means. See also Final Rule: Revisions to Payment Policies Under the Physician Fee Schedule for Calendar Year 2006 and Certain Provisions Related to the Competitive Acquisition Program of Outpatient Drugs and Biologicals Under Part B; 70 Federal Register 70116 (November 21, 2005), especially discussion at 70219-21. The recently issued proposed Physician Fee Schedule for Calendar Year 2007 contains no reference to a continuation of the add-on payment for pre-administration expense, and it appears this supplemental payment will be discontinued in the coming year.

Although the specific terms of the sales contracts between manufacturers and specialty distributors are not publicly available, it does appear that costs of drugs purchased from specialty distributors frequently exceed the costs of purchasing the same drugs from non-specialty wholesalers. Some observers therefore theorize that specialty distributors apply significantly greater price mark-ups to products than regular wholesalers when selling drugs to a provider or other end-user. However, specialty distributors assert that much of the product they receive is already allocated by manufacturers for sale to specific providers or categories of providers at pre-determined price levels, and the distributor has no discretion to adjust the selling price. Because so much IVIG product is contractually committed for initial sale to specialty distributors, end-user purchasers have narrowly restricted options to obtain the products. Many providers report that when they have contacted manufacturers directly in an effort to obtain IVIG, they have been told that there is no product available for direct purchase and have been encouraged to seek supply from specialty distributors that have received large contractually established allocations of IVIG product, available for purchase only at above 340B ceiling prices.

D. Off-Label Uses

Another factor that is often identified as adding to the strain on available IVIG supply is the increased utilization of the product for off-label uses. Indeed, according to CMS, while IVIG therapy was initially reserved for FDA-approved indications, in recent years off-label uses of the product have grown so substantially that they exceed on-label uses by a significant margin,¹⁷ even though IVIG infusions have not been demonstrated to be of significant therapeutic value for some of the conditions for which they are being used.¹⁸ The Department of Health and Human Services, therefore, has expressed the view that one means to alleviate increasing pressure on IVIG suppliers is for physicians and providers to insure that priority is given to IVIG treatment for FDA labeled uses and diseases or clinical conditions which there is evidence of IVIG safety and efficacy.

It is important to recognize, however, that off-label uses for which there is evidence IVIG can have a real benefit include treatment of a number of extremely serious and in some instances potentially fatal disorders.¹⁹ Thus there appears to be room for debate as to whether the growing practice of off-label IVIG use is more accurately seen as one factor increasing legitimate demand for scarce IVIG resources, or as a problem that should be controlled to alleviate a present “shortage” of product for approved medical indications.

¹⁷ See Responses to Comments on Physician Fee Schedule at 70 Federal Register 70219 (November 21, 2005).

¹⁸ Letter of August 8, 2005 from Christina V. Beato, M.D., Acting Assistant Secretary for Health to Mark Brecher, M.D.

¹⁹ See *Use of intravenous immunoglobulin in human disease: A Review of Evidence by Members of the Primary Immunodeficiency Committee of the American Academies of Allergy, Asthma and Immunology*, Orange, Jordan S., *et al.* (J Allergy Clin Immunology 2006; 117: 5525-53), discussing evidence to support use of IVIG in treatment of conditions to include rheumatoid arthritis, Guillan-Barré syndrome, multiple sclerosis, myasthenia gravis, Kawasaki disease, sepsis, septic shock, toxic shock syndrome, and potentially fatal dermatologic diseases.

III. SURVEY DESIGN AND RESULTS

In late February 2006, PHPC distributed to its members a survey designed to elicit information needed to assess how much IVIG product the hospitals were able to obtain over the course of a three month period, and how much product is needed to meet the demands of their patients.²⁰ Survey respondents were also asked to identify from what sources PHPC member hospitals most frequently purchased IVIG products and whether the products were available for purchase at 340B prices. Hospitals reporting that they were unable to obtain IVIG product at 340B prices were asked to relay the reasons given by wholesalers and/or manufacturers for the lack of 340B pricing. The survey also asked members to describe how the unavailability or limited availability of IVIG products is affecting hospitals and their patients.

Some of the more significant results of the survey are set forth in summary form in the chart below, and are discussed in the succeeding pages.

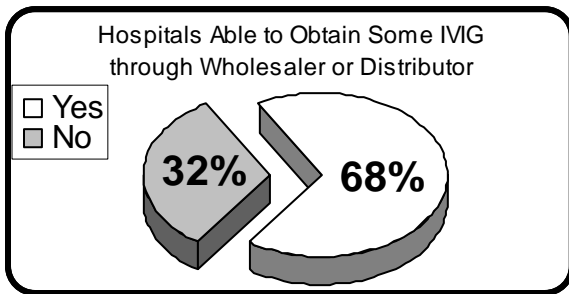
IVIG Procurement Summary					
Survey Question	Number of Responses (out of 137)	Yes	No	% Yes	% No
Able to obtain IVIG from Wholesaler or Distributor	107	73	34	68.22%	31.77%
Able to obtain some amount of IVIG at 340B Price	98	21	77	21.42%	78.5%
Able to obtain enough IVIG to fulfill Hospital's patients needs	75	38	37	50.66%	49.33%
Able to obtain a written explanation as to why IVIG is unavailable at 340B price from Manufacturer or Distributor	64 (Manufacturer)	0	64	0%	100%
	69 (Distributor)	0	69	0%	100%

Results of the survey indicate: (1) that 340B hospitals are experiencing serious difficulties in securing adequate amounts of IVIG product to meet patients' needs; (2) that relatively few PHPC members are able to obtain IVIG products at 340B prices; and (3) that many hospitals perceive the limited availability of IVIG product as a factor that hinders them from providing critical care to their patients. Of the 335 hospitals that received the survey, 134 responded, representing a 40% response rate. Not all survey respondents provided answers to each question on the survey form. Therefore, percentages of respondents cited in connection with particular questions reflect the percentage of respondents to each individual question, not a percentage based on total survey respondents.

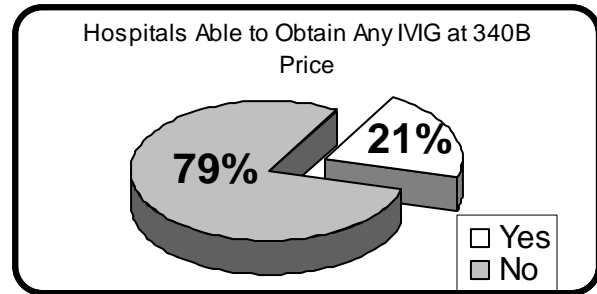
²⁰ A copy of the survey in its entirety is included at Tab 1.

A. Procurement of IVIG by 340B Hospitals

As the graphs below indicate, seventy-three hospitals, 68% of the responding hospitals, indicated that they were able to obtain some amount of IVIG product through their regular wholesaler distribution channels during the time period of November 2005 through February 2006, while thirty-four hospitals, 32% of the responding hospitals, did not receive any IVIG product from their regular wholesalers.²¹ However, seventy-seven hospitals, about 79% of the hospitals responding to the question, reported that they could not find any IVIG product available for purchase at a 340B price. The other 21% of responding hospitals stated that they were able to obtain some amount of IVIG product at a 340B price from their regular wholesalers, but in many of these cases only a relatively small amount of product was offered at a 340B price.



Data Taken from PHPC Survey



Data Taken from PHPC Survey

Based upon the IVIG procurement data provided by survey respondents for the three month period through February 2006, the top three sources for IVIG products included both regular wholesalers and a particular specialty distributor. Amerisource Bergen, a general wholesaler, was the source from which the responding hospitals obtained IVIG product most frequently, followed by specialty distributor FFF Enterprises and wholesaler Cardinal Health.

B. Adequacy of IVIG Supply and Impact on Patients

Based upon the survey data submitted by PHPC members, the conditions most frequently treated with IVIG products were primary immunodeficiencies, generally the most prevalent indications treated with IVIG. The drugs were also frequently used to treat idiopathic thrombocytopenia purpura ("ITP"), an FDA-approved indication for the use of IVIG, and to facilitate bone marrow transplants, a usage supported by some, but not all of current IVIG treatment research.²² Thirty-eight PHPC member hospitals, 51% of hospitals responding to the question, stated that they were able to obtain an amount of IVIG that was adequate to fulfill the needs of their patients. However, during the period covered by the survey, thirty-seven hospitals, 49% of those responding, reported that the total amount of IVIG they were able to obtain was *not*

²¹ Many respondents identified specialty distributors as their regular wholesaler for IVIG products.

²² Orange, Jordan S. et al, *Use of intravenous immunoglobulin in human disease: A review of evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology*. *Journal of Allergy and Clinical Immunology*. 117-4. p. S531, S536.

adequate to fulfill patient treatment needs. Many of these hospitals also reported that the lack of adequate IVIG supply had forced them to delay or cancel important IVIG infusions for patients. Several hospitals indicated that they were forced to ration IVIG products through the use of strict priority protocols that reserved IVIG products for patients most in need, and still more hospitals indicated that in instances when the preferred IVIG product for treatment of a patient was unavailable, another IVIG drug had been substituted to avoid cancellation of the patient's treatment. A number of hospitals were concerned about whether such substitution adversely affected the quality of care they provided and whether patients might thereby be put at risk. However, only one hospital reported a specific instance of a patient having an adverse reaction to IVIG drug substitution.

Member hospitals also generally indicated that the financial impact of having to purchase IVIG products at above-ceiling prices was a serious concern from the perspective of their overall pharmacy budgets. Many reported, in addition, that staff had to dedicate a substantial amount of time to contacting multiple distribution sources – on a weekly or even daily basis – in order to obtain adequate IVIG product supply to meet patient treatment needs.²³

C. Industry Explanations for Unavailability of 340B Discounts

Thirty-three hospitals, or 43% of hospitals responding to the question, stated that they had discussed IVIG procurement directly with manufacturer personnel. All of these hospitals indicated that when a manufacturer representative or officer sought to explain why IVIG drugs were not available at 340B prices, the reason typically cited was short supply of the drug or unavailability of additional allocations. Similarly, wholesalers and other distributors also generally cited an inadequate supply of IVIG or other market factors as the reason they did not offer 340B pricing on IVIG products. Interestingly, no hospital reported being able to obtain these explanations in writing from a manufacturer or distributor. Indeed, some hospitals have reported to PHPC that certain manufacturers refuse to either accept or respond to orders or requests for IVIG product in written form, insisting instead on purely oral communications regarding the amount of product sought and the amount provided.

²³ That hospitals must expend extra resources to locate and obtain adequate IVIG product in today's market is a point that has been recognized by federal officials, and was one of the reasons CMS supplemented Medicare payments to hospital outpatient departments for IVIG treatments in fiscal year 2006 with an approximately \$75 add-on for preadministration-related services. See March 27, 2006 letter to Arthur Bracey, M.D. from HHS Assistant Secretary for Health John O. Agwunobi (cited above at note 7). Also see Medicare Program; Changes to the Hospital Outpatient Prospective Payment System and Calendar Year 2006 Payment Rates; Final Rule, 70 Fed. Reg. 68516 (November 10, 2005).

While this add-on payment has undoubtedly been helpful to hospitals, it may nevertheless still have been inadequate to counterbalance the effect of MMA provisions that amended the law to specify the same reduction of IVIG reimbursement for hospitals beginning in 2006 as became effective for physicians in 2005 (*i.e.*, to ASP + 6%). See Social Security Act § 1833(t)(14)(A)(iii), 42 U.S.C. § 13951(t)(14)(A)(iii). Moreover, it does not appear that this supplemental payment – effectuated through a temporary, separate payment code for hospital IVIG services in 2006 – is likely to continue to be available in 2007. Instead, recently issued proposed rules for the Hospital Outpatient Prospective Payment System in 2007 provide for specific payment for each hour of IVIG infusion, but indicate the CMS belief that “separate payment for preadministration-related services specific to IVIG infusions would not be necessary in CY 2007 to ensure Medicare beneficiary access to IVIG.” See preamble to proposed rule published August 23, 2006, at 71 Federal Register 49604.

D. Hospital Response to Restricted Product Supply

In order to better understand how hospitals are utilizing IVIG products in the face of limited supplies, PHPC included a survey question seeking to determine how many respondents had a prescription protocol in place for IVIG drugs with criteria established by medical staff. Forty-eight percent (48%) of hospitals responding to this question indicated they did have protocols in place, while 8% indicated that they have established some limited protocols, and 44% reported that they have no such protocols yet. Finally, when asked whether they thought the availability and procurement issues surrounding IVIG would improve or worsen in the coming year, 46% of hospital respondents stated that they believe the situation will worsen and 19% reported an expectation that the situation will improve over the next year. Another 20% of responding hospitals anticipate that the situation will remain static and the remaining 15% of hospitals answering the question did not feel they could predict future market conditions.

IV. DISCUSSION

The survey results indicate that PHPC member hospitals are generally experiencing significant problems in obtaining IVIG products for their patients and that relatively few hospitals are receiving pricing on these drugs at or below the applicable statutory 340B ceiling price. Roughly four out of every five hospitals responding to the survey were not able to obtain any IVIG products at a 340B price, and less than one in five members responding to the survey reported being able to obtain all of their IVIG product supply at the appropriate 340B prices. Plainly this is a serious problem for 340B hospitals, and the data strongly suggests that IVIG manufacturers and/or suppliers are not complying with their obligations to provide discounted 340B pricing to qualified hospitals. The survey results and follow-up interviews also suggest that the unavailability of 340B pricing is related to a tightly controlled market in which a significant amount of the product is allocated to specific third-parties, such as specialty distribution companies. These entities have contractual relationships with manufacturers that are being accorded higher priority than manufacturers' statutory obligations to provide discounted pricing to 340B covered entities, and their participation in the IVIG distribution chain creates a secondary market through which 340B providers can purchase IVIG, but not at 340B prices.

Ostensibly, 340B hospitals are being denied 340B pricing because of an inadequate supply of product in the marketplace. However, based on the high percentage of hospitals reporting that they were able to purchase IVIG products from their wholesalers (68%) in comparison with a much lower percentage of hospitals reporting that they were able to purchase IVIG products at the appropriate 340B price (21%), it appears that unavailability of 340B pricing is substantially more frequent than unavailability of the product, and may not be attributable (or may not be entirely attributable) to a shortage of supply.

It is noteworthy that some information concerning the IVIG supply seems contradictory. The website of the Plasma Protein Therapeutics Association ("PPTA"), the trade association that represents manufacturers of IVIG products, reflects that the group monitors market supply of IVIG and analyzes industry data to determine the adequacy of supply.²⁴ In recent months the website has consistently described the supply of IVIG products as "adequate," and indicated that

²⁴ See <http://www.pptaglobal.org> (last visited Sept. 15, 2006).

the amount of product inventory on-hand is relatively equal to the 12 month average for product demand.²⁵ Nevertheless, when asked what explanations are given by manufacturers that refuse to provide IVIG products at a 340B price, all hospitals responding to the question on PHPC's survey reported that they have been told that a shortage of supply on the market necessitates strict product allocation and is the reason for IVIG product not being available at a 340B price.

This suggests that manufacturers may believe they are only obligated to furnish products at a 340B discount when there is abundant supply and unlimited opportunities to sell the product more profitably at a significantly higher price. Yet neither the governing federal statutes nor the pharmaceutical pricing agreements between HHS and drug manufacturers contain any such proviso, and a refusal to offer discounted pricing likely violates manufacturer obligations under the 340B program. Furthermore, where a manufacturer sells a large portion of its IVIG inventory to a specialty distributor (from which providers may purchase IVIG, but only at above-340B ceiling prices) and then claims that it has no product left to sell covered entities at a 340B price, the question arises whether this practice is an impermissible end-run around 340B program requirements, and circumvents both the intent of the 340B statute and the terms of the manufacturer's PPA with the Secretary of HHS.

Aside from the matter of limited IVIG product availability at 340B prices, the survey data also reveals that almost half of responding hospitals have been unable to obtain a supply of IVIG at any price adequate to meet the needs of their patients. Further, some hospitals reported that substantial staff resources had to be regularly devoted to calling many sources of IVIG supply in an effort to piece together an adequate supply of product by purchasing multiple small amounts available from various sources.

It is possible that part of this "supply problem" is attributable to the recent change in Medicare physician reimbursement for IVIG treatments and the market's failure to shift product distribution accordingly. As physicians send their patients to hospitals for IVIG treatments (because physicians feel they are no longer adequately reimbursed for IVIG products), hospital demand for IVIG naturally increases, while the historic allocation data used by distribution sources to supply their customers continues to be based upon a market preceding this significant shift in medical service demand and delivery. Thus hospitals may be experiencing the supply pinch more than other providers in the IVIG marketplace. Meanwhile, restricted market distribution inevitably results in a financial pinch as well. As some hospitals indicated in their responses, the scarcity of IVIG for purchase, at either 340B or non-340B prices, has raised the cost of IVIG drugs for 340B providers substantially. This puts strain on hospital pharmacy budgets and requires them to cut back on services in other areas to compensate for additional pharmaceutical expense.

The impact of the IVIG situation on PHPC member hospitals' patients is of course another area of critical importance. As the survey data illustrates, the lack of an adequate supply of IVIG products can result in delay or cancellation of IVIG treatments for patients who are in dire need of the drugs. Autoimmune deficiencies, the condition for which hospitals reported IVIG treatments were most frequently sought, are serious, life-threatening illnesses that must be managed with a high degree of care. Furthermore, a number of hospitals indicated that they were unable consistently to procure the same brand or type of IVIG, and therefore often had to switch the drug used by individual patients based upon the availability of particular IVIG products at the time treatments were rendered. Although such product substitutions theoretically should not

²⁵ See http://www.pptaglobal.org/docs/supplydata_3.pdf (last visited Sept. 15, 2006).

cause significant complications or medically adverse effects, many survey respondents expressed concern that these drug substitutions compromised the quality of patient care.

V. CONCLUSIONS

The current condition of the IVIG market is an area of serious concern for PHPC and its members. Not only is there very limited availability of IVIG products at the 340B price, but the procurement of IVIG products in general has become increasingly difficult and expensive for hospitals and their patients. Possible causes of these problems are many and varied, and include such factors as limited product supply, low manufacturing profit margins, Medicare reimbursement changes affecting the distribution of IVIG demand in different treatment settings, manufacturers' growing use of specialty distribution channels, increased demand for IVIG for off-label uses, and manufacturers' unduly rigid or otherwise skewed allocation and contracting policies. While there is little agreement and much debate concerning what is at the root of IVIG procurement problems, it seems likely that the present state of affairs is actually attributable to some combination of these factors (and possibly other unidentified factors).

It is important to acknowledge that difficulty in obtaining IVIG drug products is not a problem exclusively affecting 340B hospitals. Finding and buying adequate supplies of IVIG is a problem that plagues health care providers and patients in many sectors of the health care community and, for this reason, the problem has been highly publicized. The emphasis in this report on the challenges facing 340B providers and their patients should not be misconstrued as suggesting that only 340B providers and their indigent patients have a genuine need for IVIG products and deserve increased access to these drugs through changes to the current IVIG drug manufacturing and distribution systems. Nevertheless, consistent with PHPC's mission as an advocate and representative of the interests and concerns of hospitals participating in the federal 340B drug discount program, our principal focus is on how IVIG market factors and IVIG-related pricing and distribution arrangements affect 340B hospitals. Based on the survey results, it is clear that health care providers participating in the 340B program (and presumably other federal drug discount programs as well) face special challenges in obtaining IVIG, because the products are increasingly unavailable at the discounted prices on which these providers rely in order to adequately serve indigent patient populations, and suppliers are allocating much of the available IVIG to other purchasers with contracts in place for higher prices.

Many PHPC hospitals report that they have prescription protocols in place to assure that the IVIG product they are able to obtain is reserved for the patients in the greatest need, and increased use of such protocols may be one constructive step in addressing current product supply problems. This would be especially true to the extent protocols might more effectively restrict utilization of limited IVIG supplies for off-label uses in the treatment of conditions posing no significant threat to patients' health or safety. However, rationing product through selective protocols is unlikely to offer a comprehensive solution to the existing IVIG crisis, since IVIG is an important therapy for numerous extremely serious disorders and even a rational and evidence-based prioritization of patients' needs for IVIG treatment may leave some patients without access to appropriate treatment.

PHPC therefore strongly encourages further inquiry and investigation by both private and governmental entities into the current IVIG distribution structure, the existing demand for IVIG

products, the cause of the IVIG supply shortage for hospitals,²⁶ and the minimal availability of IVIG product at statutorily mandated discount prices. In particular, PHPC urges HHS, through the Health Resources and Services Administration and the Office of Pharmacy Affairs, to take affirmative steps to assure that 340B providers are able to purchase IVIG products for their patients at the discounted prices to which those providers are entitled, and that pharmaceutical manufacturers and distributors are not allowed to circumvent 340B program requirements in the name of an unverifiable product “shortage.”

²⁶ It should be noted that the HHS Office of the Inspector General is reportedly conducting a study on the availability and pricing of IVIG drugs, and a report of the results of that study is expected to be issued in the near future. We are further informed that the Office of the HHS Assistant Secretary for Planning and Evaluation (“ASPE”) is also conducting a study of IVIG access and availability issues.