Understanding Management Challenges with Immunoglobulin

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AMCP Market Insights Summary

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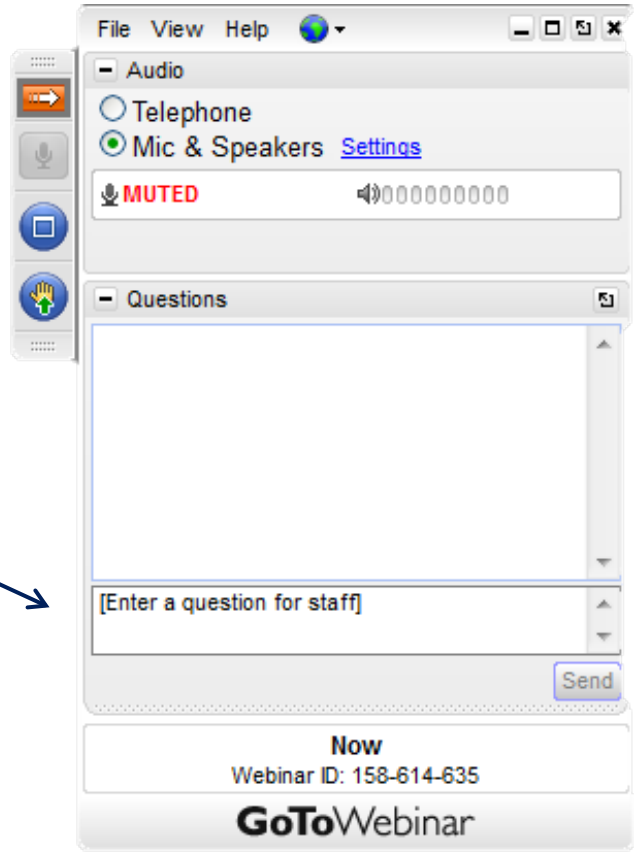

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AMCP Market Insights Overview

- **Association-led research** with AMCP members and non-members at regional and national plans
- **Blinded format** to allow participation and candid feedback
- **Topics are based upon category**, not product, to provide a holistic view of management
- Programs are **focus group meetings or virtual programs** with Clinical Key Opinion leader presentation
- **Current and future treatment options** are addressed to understand clinical and medical management utilization approaches

Michael Baldzicki

Executive Vice President, Growth & Strategy
AscellaHealth

Agenda

Guest Speakers:

Lorraine Anderson M.D.
UCLA, Health Assistant Professor

Mike Baldzicki
Executive Vice President, Growth & Strategy
AscellaHealth

Welcome & Setting the Stage for the Day
Clinical presentation: Immunoglobulin Clinical Considerations
Panel Questions
Discussion: Treatment Options
Distribution models and business considerations
Workshop & Discussion
Wrap-up and Closing Remarks

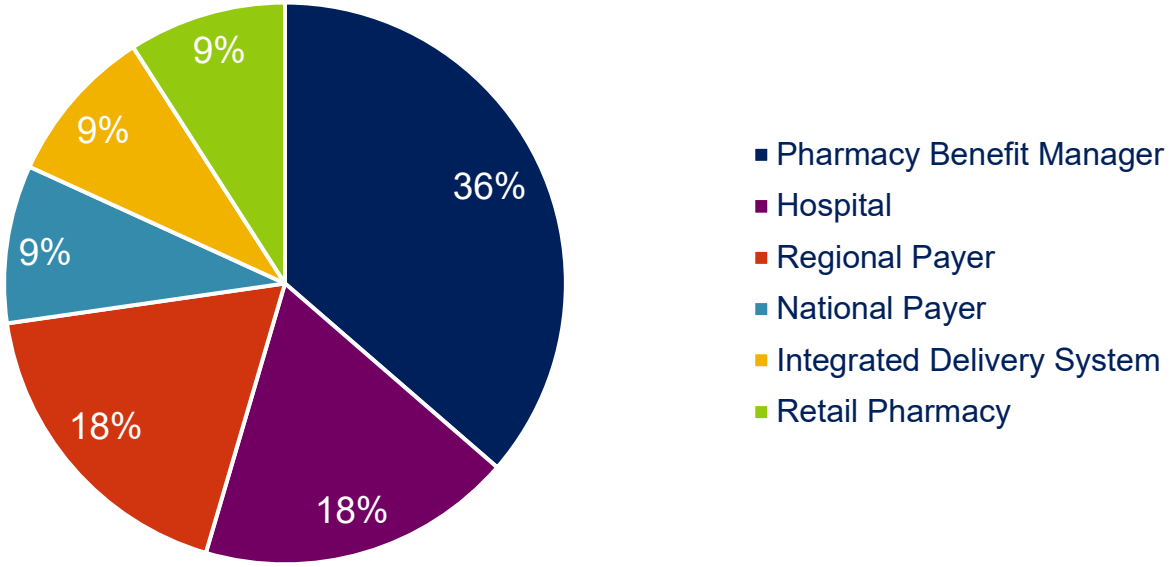
Objectives

- Understand participants understanding of the Immunoglobulin (IG) category
- Define current uses and treatment approaches with IG
- Identify challenges AMCP members face with IG management
- Garner recommendations for manufacturers in identifying partner opportunities

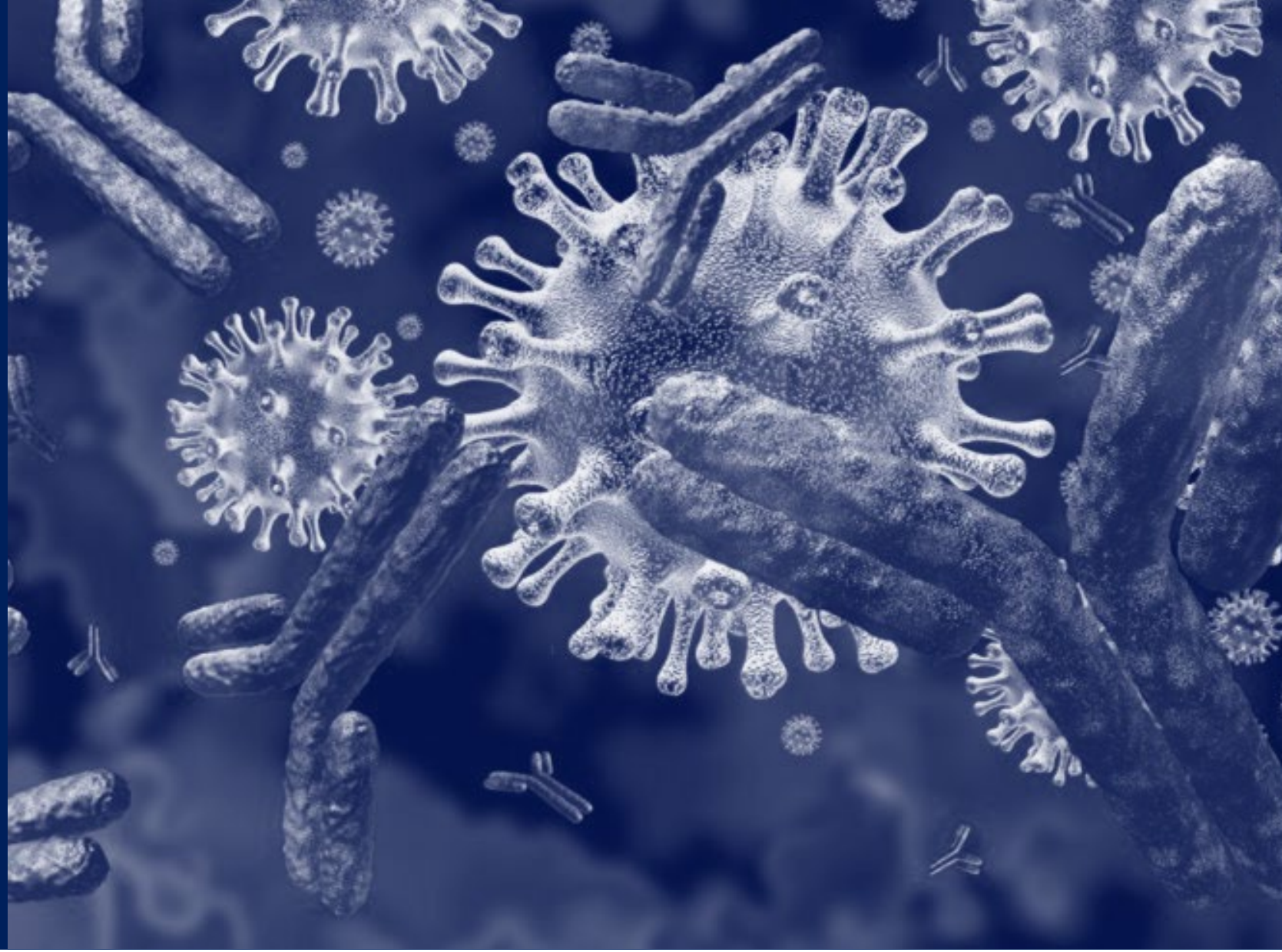
Methodology

- Six hour virtual meeting on October 28, 2020
- Roundtable format, with presentations and group discussion
- > 30 million lives covered

Market Insights Expert Panelist



Immunoglobulin Insights



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Plasma Components

Composed of many components; limitations on supply are based upon plasma donations and allocations of plasma

"The manufacturing and business model of a plasma manufacturer that uses human blood is dramatically different than a chemical-based pharmaceutical manufacturer…

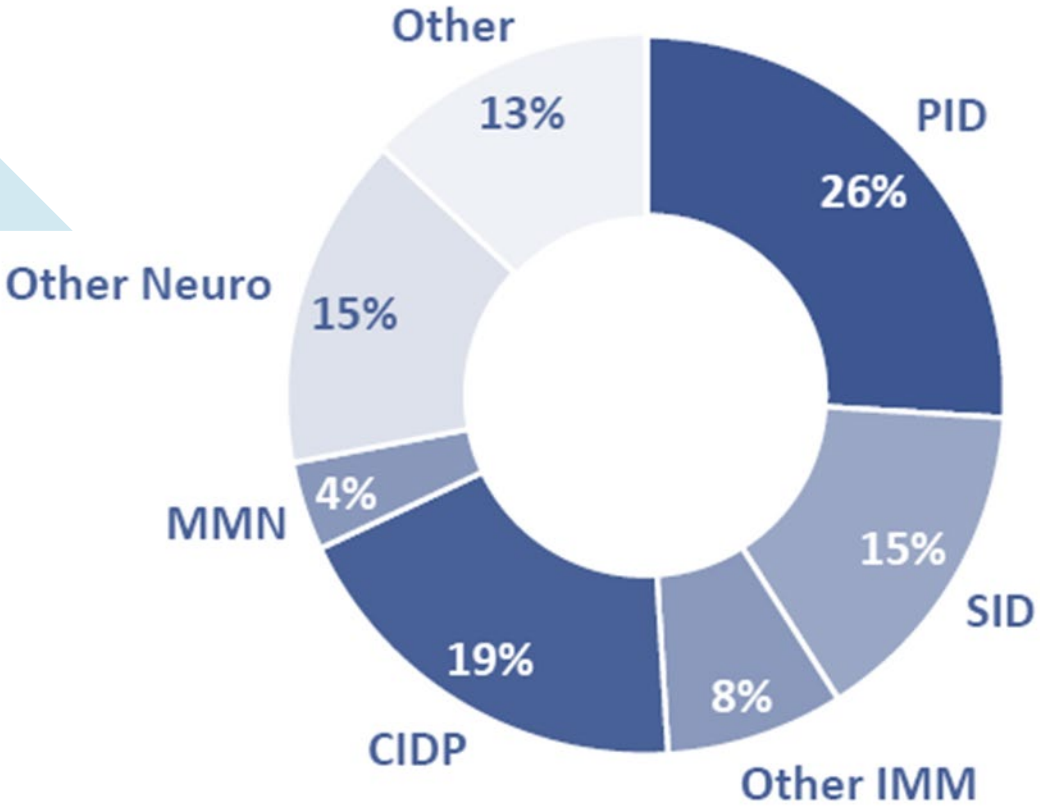
Raw material availability, safety and purification processes - can double manufacturing costs and extend total production time up to 12 months…

In order to cover the costs of production, at least three different medicines need to be produced and sold from a single donation."
- Specialty Pharmacy

Plasma proteins	Colloid osmotic pressure helps to maintain water balance between tissues and blood volume
Water	Liquid portion of blood. Suspends components of blood, transports, absorbs, releases heat
Albumin 25g	Produced by liver. Smallest, most numerous blood plasma protein. Maintains osmotic pressure, transports other proteins
Globulins 4g	Produced by liver and plasma cells which develop from B lymphocytes(B cells). Antibodies fight viruses and bacteria Alpha and beta globulins transport fat soluble vitamins, lipids and Fe
Fibrinogen, vonWillebrand and coagulation factors	Produced by liver. Essential in blood clotting

Use of IG is Increasing

PID, SID, & CIDP Composed of 60% of Total Usages of IG



"The use [of IG] is inconsistent and we struggle with the variety of indications being requested [for coverage]."
– Regional Health Plan

Primary immunodeficiency (PID), Secondary immunodeficiency (SID), Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Multifocal Motor Neuropathy (MMN)

Source: 2017 WW MRB Report

Food and Drug Administration Approved Indications

Disease	Goal of Therapy
B-cell Chronic Lymphocytic Leukemia (CLL)	Prevention of bacterial infections due to hypogammaglobinemia
Bone Marrow Transplantation	Prevention of infections, pneumonitis, and acute graft-versus-host disease (GVHD) following bone marrow transplantation
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)	To improve neuromuscular disability and impairment and for maintenance therapy to prevent relapse
HIV Infection	Reduction of serious bacterial infection in pediatric patients infected with HIV
Idiopathic Thrombocytopenic Purpura (ITP, CITP)	Increase platelet count in ITP to prevent or control bleeding
Kawasaki Disease	Preventing coronary artery aneurism associated with kawasaki disease
Multifocal Motor Neuropathy (MMN)	Modulating immune inflammatory condition, improve muscle strength and disability in adult patients
Primary Immunodeficiency Disease (PIDD)	To protect against frequent and/or severe infections (bacterial and viral)

"The goal of therapy is to provide protection against frequent and/or severe infections, bacterial and viral."
– Physician

"There is a lot of parity within the IG class among the majority of the disease states."
–Integrated Delivery System

(J Allergy Clin Immunol 2017;139:S1-46.)

Off Label Use of Immunoglobulin

Coverage policies are linked to the level of evidence and the evidence is ever changing; due to the many uses and varying level of evidence there is no consistency across payers for coverage criteria

Benefit	Indication	Evidence Category	Strength
Definitely beneficial	Graves ophthalmology	Ib	A
	Immune thrombocytopenic purpura	Ia	A
Probably beneficial	Dermatomyositis	IIa	B
	Birdshot Retinochoroidopathy	IIa	B
	Henoch-Schonlein purpura	IIb	B
May provide benefit	Juvenile idiopathic arthritis	Ia	A
	Anti-phospholipid antibody syndrome in pregnancy	Ib	B
	Severe RA	IIb	B
	Still disease	IIb	B
	Felty syndrome	IIb	B
	Macrophage activation syndrome	IIb	B
	Polyarteritis nodosa	IIb	B
	Post-transfusion purpura	III	C
	Thrombotic thrombocytopenic purpura	III	C
	ANCA syndromes	III	D
	Autoimmune neutropenia	III	D
	Autoimmune hemolytic anemia/Evan syndrome	III	D
	Autoimmune hemophilia	III	D
	SLE	III	D
	Neonatal alloimmune thrombocytopenia	III	D
	Neonatal isoimmune hemolytic jaundice	III	D

(J Allergy Clin Immunol 2017;139:S1-46.)

"This is a short list of all the off label uses for IG."
– Physician

"This is the challenge, having your PAs match the data…years ago we crossed that threshold where it is not just the label but level of evidence."
– National Payer

" We usually draw the line at IIb, for evidence levels."
– Hospital System

Preferred Product Considerations

The IV route has historically been the preferred route because of the larger volumes that could be administered

"Historical approach has been managing the indications, it is agnostic to [IG] product... they are viewed as clinically comparable."
–National Payer

"You want to have a preferred [IG] product, but also you want to have some secondary products."
– Integrated Delivery System

	IVIG	SCIg	SCIg^{FAC}
Administration	Intravenous Health care provided-administered	Subcutaneous Self-administered	Subcutaneous Self-administered two part infusion with hyaluronidase
Injection Site	1	4-30 (max 2 oz. per site)	1-2 (max 20 oz. per site)
Frequency	Every 3-4 weeks	Daily, every other day, weekly, biweekly	2-4 weeks
Infusion Time	2 – 4 hrs.	5 min – 2 hrs.	1-2 hrs.
Site of Care	Home infusion, in office, infusion center	Home or physician office or infusion center	Home or physician office or infusion center
Bioavailability	100%	62%	92%
Pre-medication	Required	Seldom needed	Seldom needed
Side effects	Systemic: headaches, malaise, muscle aches, flu like symptoms Local adverse reactions: rare	Systemic: rare Local reactions are common (redness, swelling, itching, discomfort) but decreases over time	Systemic: less than IVIG Local reactions similar to SCIg

Preferred Product Considerations

A variety factors are considered when selecting a preferred IG product; due to undifferentiated parity within the class contracting considerations dominate

Product

- Infusion time, volume
- Route of administration
- Side effects (SCIG < IVIG)
- Site of care
- Stabilizers
- Sucrose load, sodium content

"Some use glucose as a stabilizer and thus would not be recommended for diabetics. Others have high sodium content and would not good for patients with cardiac conditions."
– Physician

Contracting

- Exceptions for use of other IG agents during shortage or non-covered indications
- Carve-outs
- Supply guarantees during shortage
- Pricing per gram
- Purchase price for IDNs
- Rebates
- Value-based contracting - especially for an IDN where both the medical and pharmacy data is available

"It's all about contracting."
– Integrated Delivery System

Distribution

- Data collection for outcomes based contracts
- Open access vs. limited distribution
- Specialty pharmacy network

Preferred Product Considerations

Finding the “right match” for the patient is a high clinical concern

Clinical

- Evidence
- Expert consensus, key opinion leaders (KOLs)
- Indications
- Off-label uses
- Patient population (indication coverage)
- Safety

Financial

- Covered benefit (medical vs. pharmacy)
- Patient assistance programs

Patient

- Adherence
- Patient ability to self-administer

Utilization

- Current utilization and market share
- Limit switching for patients

“All IG products are *not* the same, matching the patient with the correct product improves patient outcomes.”
– Physician

“We would be interested in device innovation that would help IG administration and adherence.”
- Regional Payer

Preferred Product Considerations

SCIG is gaining popularity compared with IV administration but adherence concerns remain

No significant differences in total cost between SCIG and IVIG products for the patient or insurer.

"Sticking to one formulary agent drives accumulation to one NDC… over time there is less onboarding WAC expense… while there is a big effort to get the EMR order set built out, and around education and pharmacist time, the biggest impact is around reduced WAC onboarding expense.
- Integrated Delivery System

SCIG drugs may be more expensive per gram, however, there are different cost considerations related to the site of care, nurse and pharmacist time, product switching, and operational costs.

"What we hope to see is an onboarding expense less than 5% of total expense.
- Integrated Delivery System

"We would like to see more subcutaneous administration, as long as the physician supports it."
- Hospital

Medical supervision is required for IVIG, for SCIG there are no infusion nursing costs. IVIG patients receive infusions every two to four weeks, whereas SCIG patients infuse every week.

"We have concerns about adherence with SCIG."
– Regional Health Plan

Patients considerations focus on insurance coverage; interference with work and productivity; side effects; time required to order, prepare, and schedule infusions; and time required to travel to a medical facility.

Payers use a Variety of Approaches to Manage Cost and Use

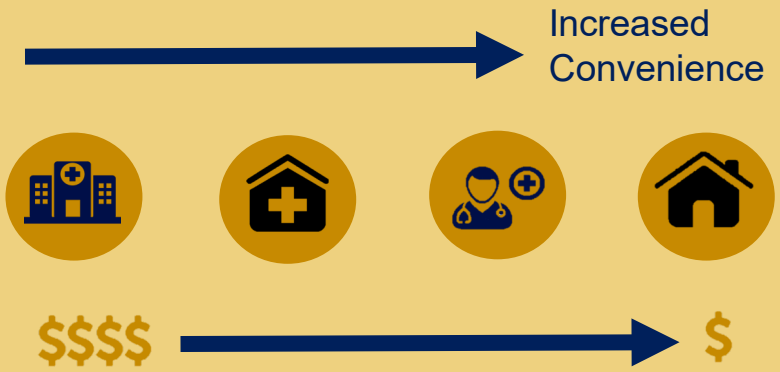
Interest in the shifting IG to the home setting due to cost and convenience

Payers are most likely to use

1. Prior authorization (PA)
2. Preferred product formulary status
3. Limit prescribing to certain medical specialties

   Allergy, Immunology, Oncology, Neurology

Payers have introduced site-of-care policies



"We have had a lot of success in offering home site-of-care whenever it is appropriate. And we have looking for more opportunities to move IG to the home."
- Regional Payer

"However, it is important to keep in mind that there are multiple reimbursement scenarios (e.g. capitation) in each site of care, which may vary based on the payer and the route of administration."
- Hospital

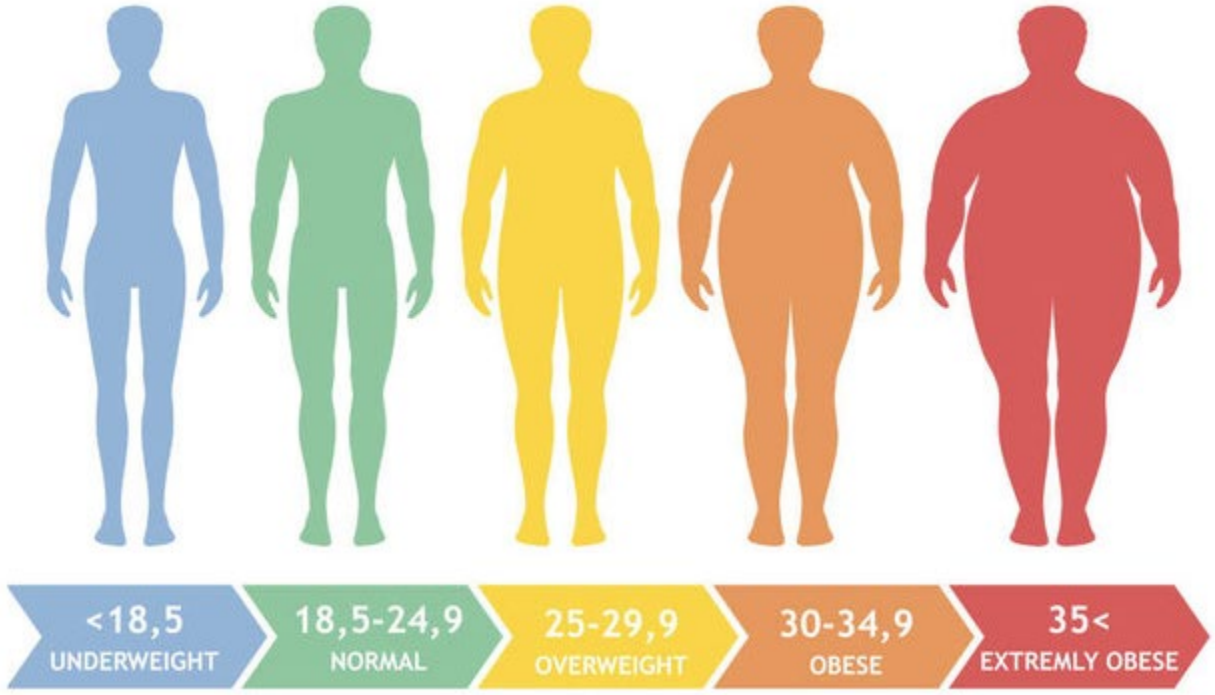
While home infusion offers the lowest cost per unit, the majority of patients are treated in the most costly place of service. There is good evidence that patients much prefer infusions in the home environment.

Site-of-Care Considerations

	Infusion Center	Homecare
Advantages	Safety – Trained staff and equipment available if patient has negative reaction Reassuring – Controlled environment makes nervous patients feel better	Convenient for the patient Comfortable for the patient Less risk of infection
Patient Types	Patients prone to adverse reactions Patients whose home environment is not conducive to administering therapy	Young, active patients Elderly or homebound patients Patients who live far away from infusion centers

Growing Priority for Dose-Optimization Programs

Traditionally dosed on actual body weight



Looking for RWE on value of dose-optimization programs, including trough-based dosing

Dosing based on ideal body weight or adjusted body weight following evidence that overweight patients were being overdosed. Studies show no differences in infection rate and IG-level response when weight based dose-optimization strategy used.

"We know that ideal body weight is just as effective as actual body weight for IG dosing, we were able to use IBW to decrease consumption and costs by approximately 5%."
– Specialty Pharmacy

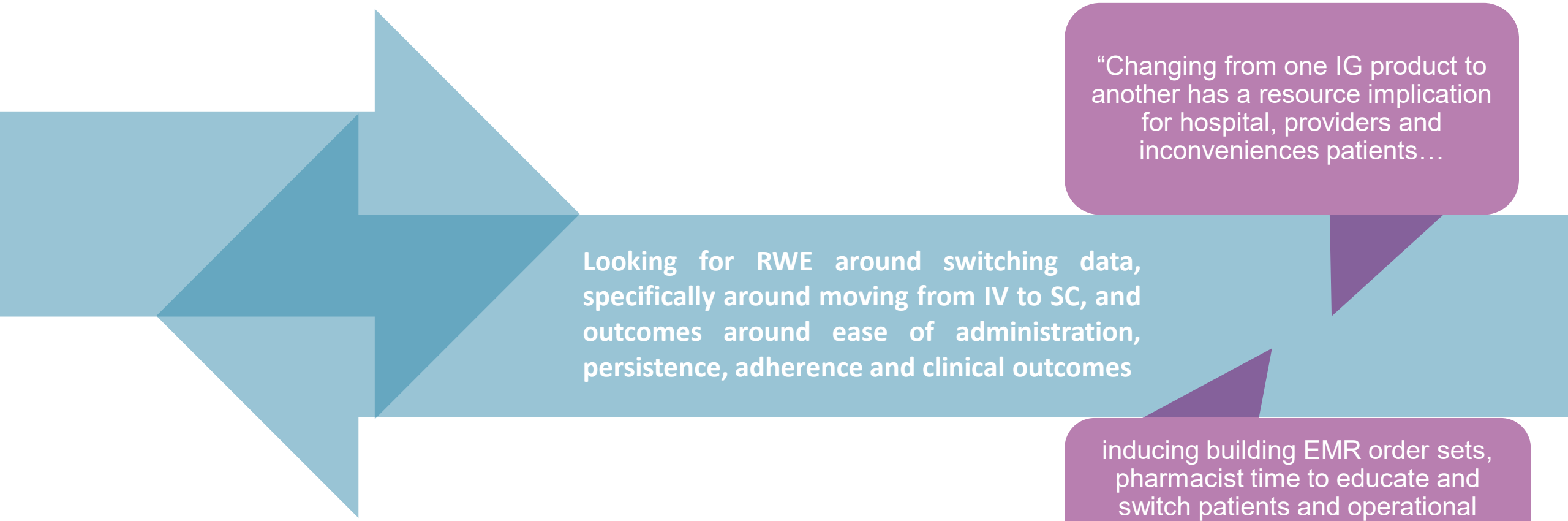
Trough level doing of IG is an area of interest given the inverse relationship between trough IG levels and pneumonia in patients with PIDD.

"Dosing and adjustments of IG should be based upon clinical response to the product. Trough levels only apply to subsets of and not all PID patients."
– Physician

Orange J.S. , et. al. clin Immunol 2010, 137;21-30

Considerable Resource Investment Required to Run IG Product Switching Programs

Grandfathering Reduces Administrative Burden and Protects Patients



Non-branded IG Prescriptions are on the Decrease

Brand and preferred agent prescribing is driven primarily by payer policies

1. Payer coverage policies
2. Utilization management programs
3. Specific patient needs including, indication and risk factors
4. IG product differences and dosing

Mixed Contracting Strategies

Risk-sharing, adherence-based or flat/percent discounts are preferred IG contracting options

Lack of head-to-head comparison studies for immunoglobulins means that VBC could be an important tool for expanding access.

VBC are best used in clinical areas where there are questions of efficacy, safety or value. And since immunoglobulins have a strong evidence base to support their efficacy and safety across multiple disease states, risk-sharing, adherence-based, or flat/percent discounts are preferred contracting options.

Looking for innovations in ancillary devices and products to improve the delivery of immunoglobulin to support improved adherence and ease of use for patients.

"Real world outcomes are huge to us, especially as the future is going to be with value-based contracts."
- Integrated Delivery System

"The collaborative effort inherent in VBC agreements was seen as promising, as it demonstrates the willingness of health care stakeholders to engage in innovative approaches."
- Regional Health Plan

"A capitated arrangement based on utilization may also be of interest for some payers and could be presented as a reasonable option during negotiations."
- National Health Plan

Mixed Contracting Strategies

Growth of hospital-owned specialty pharmacies and 340B contract pharmacies are factors in contract negotiations

"The 340B drug pricing program often presents significant cost saving opportunities and IG is a good example where savings can be obtained."
- *Hospital*

When establishing a contract for IVIG acquisition, the purchase route is also considered as it varies among manufacturers.

Purchases can be made directly from the manufacturer, via a group purchasing organization (GPO), and/or through special pharmacy distribution networks. The chosen method of purchase can have a significant impact on pharmacy budgets.

If a payer or hospital has more than one product on formulary, the purchasing method may be different for each product depending on the manufacturer.

Patient Support

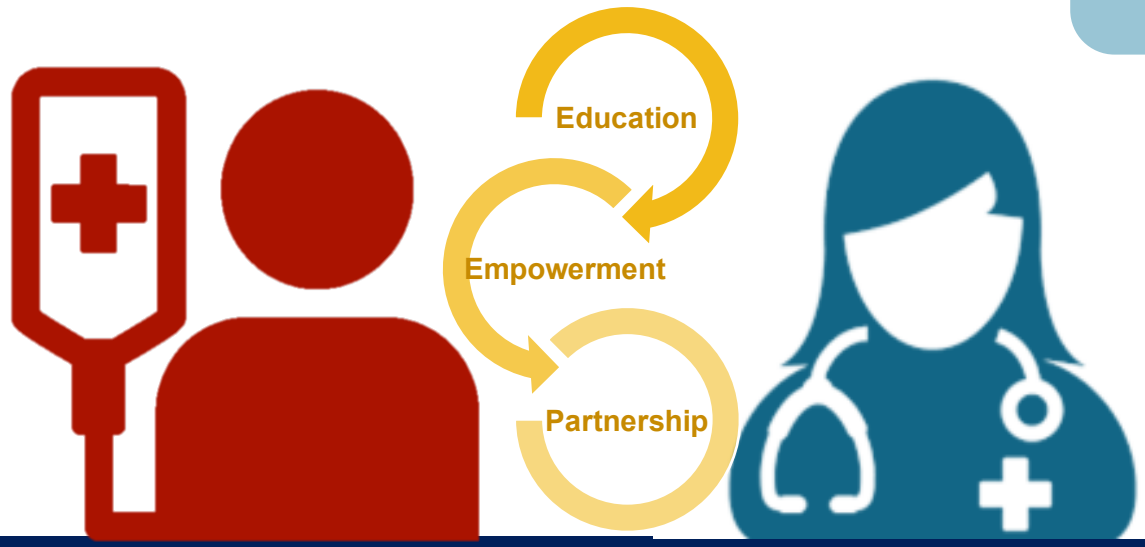
Digital tools and advocacy groups have a role in helping patients and providers understand IG treatment preferences

Value in supporting shared decision making around IG products, but questioned how the patient data would be used within digital tools.

> "We would require better visibility in to the tool algorithms if it was to be used by our patients and providers."
> *- Integrated Delivery System*

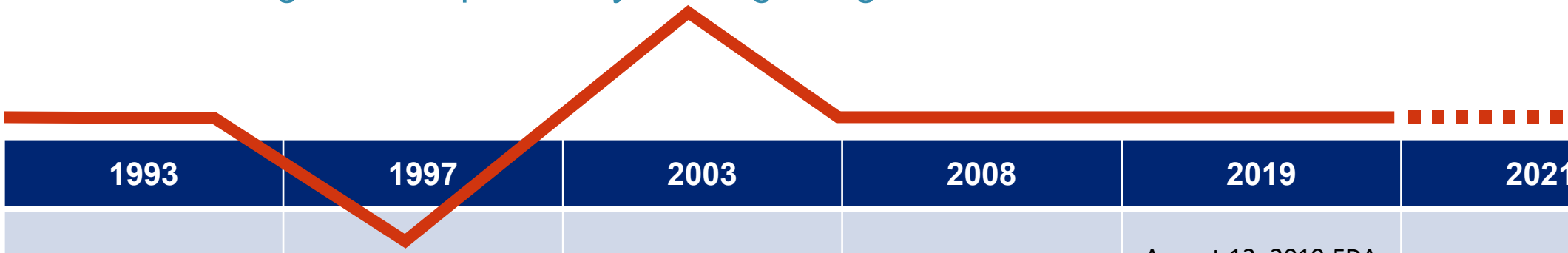
Patient advocacy groups, e.g. Immune Deficiency Foundation (IDF) and Jeffrey Modell Foundation (JMF) are recognized as valuable resources for patients and physicians.

> "We do not have experience working directly with advocacy groups on pipeline information or utilization management programs."
> *- Regional Payer*



IG Supply And Demand is Complicated and Unpredictable

Supply and demand for plasma-derived medicinal products will need to be addressed, otherwise shortages are expected by the beginning of 2021



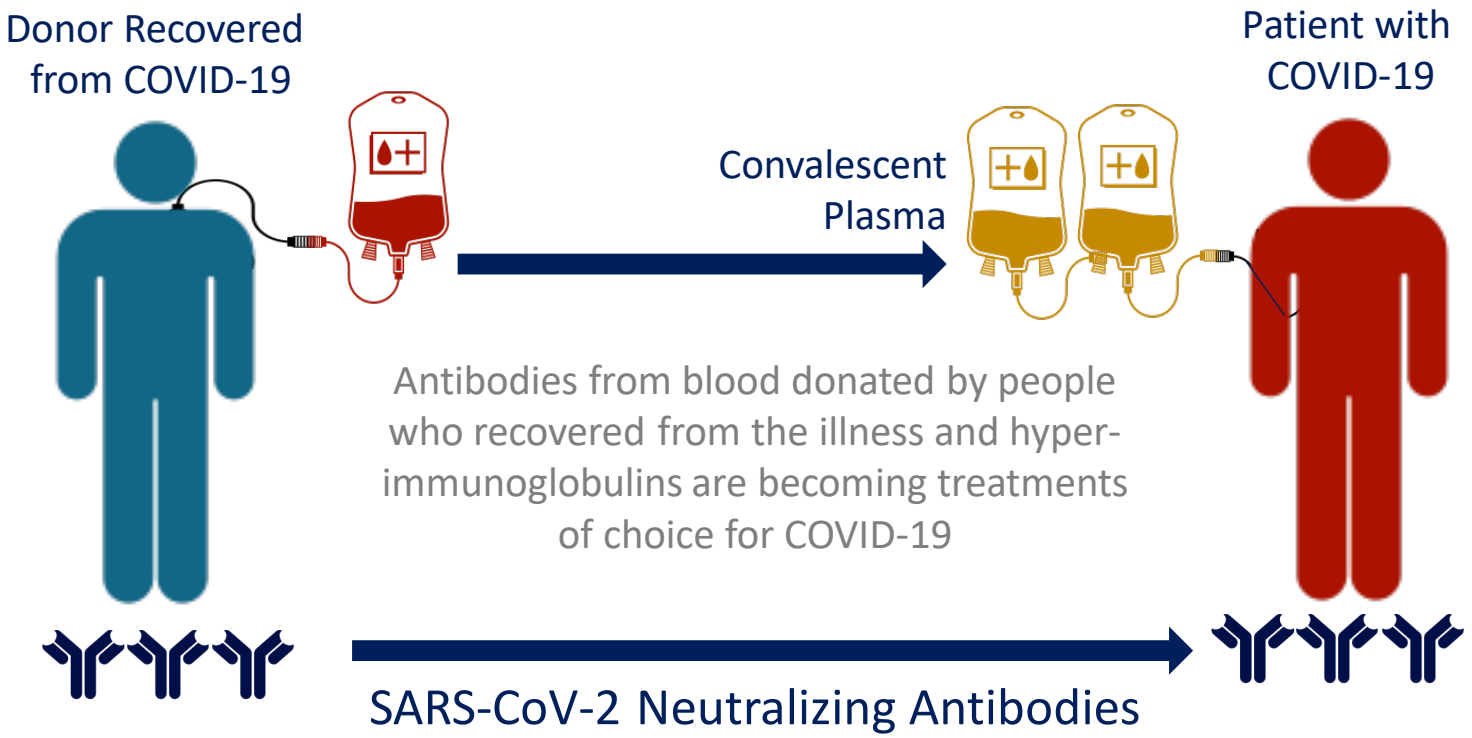
1993	1997	2003	2008	2019	2021
4 major fractionators operating in the United States	FDA closed 2 fractionators causing supply shortage Product allocation ensued	IG supply exceeded demand	Supply/demand equilibrium achieved in developed markets	August 12, 2019 FDA announced the demand for immunoglobulin products has increased resulting in an ongoing shortage of IVIG and SCIG	IG supply disruptions are expected to become apparent by early 2021

"Supply challenges is currently one of the largest challenges in managing the [IG] category."
– Integrated Delivery Network

"There's likely going to be some hoarding of IG supply as patients recall their difficulties with previous shortages."
– Integrated Delivery Network

Pipeline

Collections of blood plasma have fallen sharply because of the coronavirus pandemic & convalescent plasma and hyperimmune globulin is further stressing the plasma supply



"We need to see [IG] supply guarantees and preferred product flexibility due to ongoing shortages"
- Integrated Delivery System

On August 23, 2020, FDA issued an emergency use authorization (EUA) for COVID-19 convalescent plasma for the treatment of hospitalized patients with COVID-19. Convalescent plasma is not routinely available, nor is it a licensed FDA product; it has been made available for specific pathogens at times of disease epidemics or pandemics.

Payer Key Insights

- Large number of products, various doses, formulations, and indications makes it one of the most complex classes for payers to manage
- Payers believe the immunoglobulin class is manageable, and they are looking for collaborative partnerships
- Growing geriatric population, rising prevalence of immunodeficiency diseases, increasing adoption, and rising indications are the key drivers of utilization and cost trends
- Payers have numerous options to ensure that IG is used appropriately for the right patient in the right setting
- Better channel management, dose optimization, supply guarantees and preferred product flexibility are needed due to ongoing shortages
- Challenges remain around structuring VBC, payers are seeking risk-based, adherence based or flat/percentage discount contracts

Opportunities for Improved Positioning

Leverage

1. The collaborative partnerships for innovative contracting arrangements, and be flexible around supply guarantees and additional channel management opportunities
2. The innovations in device and delivery systems to improve patient adherence
3. The value of RWE to demonstrate safety, efficacy and cost savings of shifting IVIG to the home setting, shifting patients from IVIG to SCIG, channel management and dose optimization programs
4. Multiple strategies based on the specific payer (e.g., commercial, Medicare) and contracts type (e.g., VBC, capitated, adherence-based)

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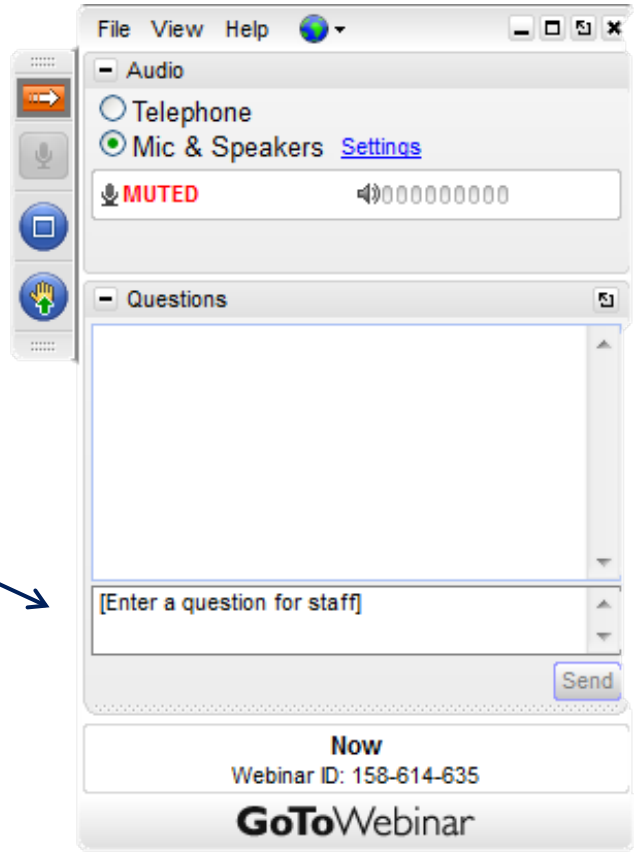

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