INTRAVENOUS IMMUNE GLOBULIN (IVIG) UTILIZATION AUDIT

March 2009

This summary was prepared to share high level information from the Final Report submitted March 31, 2009, to the Ministry of Health and Long Term Care Blood Programs Coordinating Office.
**Executive Summary**

In order to address the utilization management of IVIG in Ontario, the Ontario Regional Blood Coordinating Network (ORBCoN) was directed by the Blood Programs Coordinating Office (BPCO) to design and conduct a project to collect baseline data on IVIG use. The purpose of this audit was to collect baseline data on utilization practices for the product Intravenous Immune Globulin (IVIG) for the top users of the product in Ontario hospitals.

Canadian Blood Services (CBS) shipment data indicate that, at the time this audit was conducted, 20 hospitals used 70% of the IVIG in Ontario. Most of those 20 hospitals were involved in this data collection audit. Prior to this data collection, investigators were unable to discern to what extent the current uses in Ontario are clinically appropriate ones, supported by evidence-based literature. Over the three-month period of the audit, approximately $11,964,336 worth of IVIG was consumed at the 25 participating hospitals (66% of total use in Ontario during that time period). Note: Use of IVIG for a typical 70 kg adult, using a dose of 1 g/kg, was reported in 2007 as approximately $4,000 per single infusion.

To keep the supply of blood sustainable for the Canadian population, there are a number of strategies that are being put in place by the various provinces and territories. Implementation of clinical guidelines for proper use of certain products like IVIG is one of those strategies. Several provinces served by Canadian Blood Services, including Nova Scotia and British Columbia, are using clinical guidelines and monitoring their provincial utilization of IVIG at every hospital in their province that uses the product. At the time of this audit, the 2002 BC Guidelines have also been used as the norm for instituting province-wide, or institution-specific, clinical guidelines used in many Canadian hospitals.

**Milestones of the Ontario IVIG Audit**

- Video conference with top 20 users: February 2007
- Protocol design, ethics approval: March 2007
- Steering group formed: May 2007
- Pilot at 3 sites: June 2007
- 25 participating sites identified: August 2007
- Data entry complete: February 2008
- Data validation complete: April 2008
- Preliminary analysis shared with OBAC*: April 2008
- Analysis shared with participating sites: February 2009
- Final Report: March 2009

*Ontario Blood Advisory Committee*
The Ontario IVIG Planning Group (members from across Ontario) identified the data variables to be collected in this study and a web-based data collection system was designed as a tool to capture the data. Data collection was pilot tested for two weeks in June 2007. The pilot was intended to establish best practice in terms of the training of data collection staff and the details of the process of data collection.

This audit sought to collect a standardized set of information to obtain baseline data on IVIG utilization practices in Ontario hospitals. In some institutions, a data collection form was issued with the IVIG product at the time that the product was issued to the clinical area. The data elements listed below were captured on the form for all participating hospitals. The data were then entered into the web-based system.

The following data elements were collected:

- Hospital site (by code number)
- Patient care area (specialty)
- Date of infusion
- Patient identification by study code number
- Patient weight
- Primary Diagnosis
- Indication for IVIG infusion
- Dose of IVIG ordered
- Ordering physician specialty
- Volume of product issued
- Total volume infused yes/no
- If total volume not infused, indication of reason why not infused
- Hospitals were also asked to record the time required for data entry

Verification and validation procedures took place during the data collection and entry period (October 2007) and at the end of the final data entry period (March 2008). For the verification process, staff reviewed 10% of hard copy and checked them against what was entered into the database itself, to confirm a match between hardcopy and database.

As illustrated in Figure 1 below, the hospitals represented were predominately teaching and community hospitals.
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In this audit, 1,345 patients received 4,234 infusions of IVIG. The total dose of IVIG administered was 199,405.6 grams. Of the total patients treated with IVIG, 1,181 were adult patients; 549 males and 632 females. Pediatric patients constituted 141 of the total number of patients, and 23 neonates were treated with IVIG during the audit.

Clinical indications were assessed in two (2) ways. First, the list of indications was reviewed to identify which were ‘labelled’ indications and which were ‘unlabelled’. Unlabeled indications were further categorized into ‘unlabeled, potentially indicated’, and ‘unlabeled, not indicated or indeterminate’. (see Table 1). Second, all indications were compared to the 2008 BC Guidelines, to establish whether they conformed to a recognized provincial guideline for administering IVIG (see Figure 4).

Thirty-seven point one (37.1 %) of the IVIG was used for conditions having labeled (licensed by Health Canada) indications. An additional 50.4 % was categorized as unlabeled but potentially indicated. IVIG use categorized as “no apparent indication” accounted for 10.5% and 2% was listed for ‘unknown’ indications. 10.5% and 2% was listed for ‘unknown’ indications. Table 1 summarizes this information.

Table 1: IVIG Utilization by Labeled and Unlabeled Indications (source: IVIG Consensus Conference, 2000 and Manufacturers' Monographs, 2007)

<table>
<thead>
<tr>
<th>Labeled/Unlabeled Use Categories</th>
<th>Amount of IVIG (g)</th>
<th>% of Total IVIG Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labeled</td>
<td>74,022.8</td>
<td>37.1</td>
</tr>
<tr>
<td>Unlabeled, potentially indicated</td>
<td>100,464.1</td>
<td>50.4</td>
</tr>
<tr>
<td>Unlabeled, not indicated</td>
<td>20,984</td>
<td>10.5</td>
</tr>
<tr>
<td>Indication reported ‘unknown’</td>
<td>3,934.7</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Figure 1: Distribution of the 25 Participating Hospitals by Small, Community, Teaching
The patients were categorized into nine specialties: Hematology, Immunology, Neurology, Rheumatology, Dermatology, Obstetrics/Gynecology, Infectious Disease, Solid Organ Transplant and Miscellaneous/Other. The “unknown” indication category represents 32 patients, 2.4% of the total. In total, 477 different indications were originally reported. In order to clarify whether there were clinical differences between the indications listed by the data collectors; the investigators asked two hematologists to review the indications list. This resulted in many of the indications being categorized as a single entity (different wording; however, not a different clinical indication). At the end of the review, the number of indications, including the category ‘unknown’ counting as one, was 81.

Figure 2 below summarizes the number of audited patients within each specialty and the proportion of patients included in the audit by specialty.

Figure 2: Summary of the Patients Using IVIG by Specialty (n = 1,345)
Figure 3 that follows shows each of the specialties encountered in this audit, with the total grams of IVIG used in each specialty during the 3 month audit.

![Figure 3: IVIG Use in Grams by Specialty](image)

Specialty
- Neur = Neurology
- Imm = Immunology
- Hemat = Hematology
- Derm = Dermatology
- Rheum = Rheumatology
- ID = Infectious Diseases
- SOT = Solid Organ Transplant
- OBG = Obs/Gyn

As indicated earlier, eighty-one (81) indications were reported for IVIG use in this audit (80 different indications; and one ‘unknown category’ which accounts for 2.4% of all indications) and these indications were compared to the indications approved as per the 2008 BC IVIG Utilization management guidelines. The top indications were: Primary Immune Deficiency (22.8%), Secondary Immune Deficiency (12.9%), CIDP (9.3%), ITP (9.1%), and Allogeneic Stem Cell or Bone Marrow Transplant (5.8%). The six (6) other indications with >1% of total were Guillain-Barre Syndrome (3.2%), Dermatomyositis (2.9%), Multifocal Motor Neuropathy (3.0%), Myasthenia Gravis including Lambert Eaton Myasthenic Syndrome (4.5%), Pemphigus Vulgaris (2.8%), and Polymyositis (1.5%). All of these except Allogeneic Stem Cell or Bone Marrow Transplant are approved in the 2008 BC Guidelines. However, Allogeneic Stem Cell or Bone Marrow Transplant is a Health Canada labeled indication.

Figure 4 that follows shows the top 15 clinical indications reported in this audit, and depicts by colour coding which are approved medical conditions for receiving IVIG according to the 2008 British Columbia IVIG Utilization Management Guidelines (and which are not approved).
Figure 4: Summary of the IVIG Use in Top 15 Clinical Indications (approved or not approved as per the 2008 BC Guidelines)
Upon reviewing this report, the following recommendations were made by the Ontario IVIG Planning Group:

**Recommendation 1**
A provincial guideline for use of IVIG in Ontario must be created and adopted.

This guideline would be based on the 2008 IVIG Utilization Management Guidelines from British Columbia, which references the 2007 Canadian Guidelines for the Use of IVIG for Hematologic and Neurologic Conditions. The 2009 IVIG Canadian Guidelines for the Use of IVIG in Solid Organ Transplant and in Immunology indications would also be made part of an Ontario IVIG guideline.

**Recommendation 2**
A blood administration guideline, outlining the best practices for proper infusion of IVIG, should be prepared with input from nurses, transfusion safety officers, and physicians.

**Recommendation 3**
Results of this report should be shared with the participating sites as soon as possible.

**Recommendation 4**
Results of this report should be shared with the National Advisory Committee, specifically to recommend that national guidelines be prepared for Rheumatology and Dermatology specialties.

**Recommendation 5**
Specific, assigned clinician support must be available to the ORBCoN staff working on the IVIG utilization project. This would be a budget item in the proposal for continued work in this utilization project. An example of duties for the clinician would be to monitor for new appropriate and potentially inappropriate uses of IVIG which appear in the literature and/or in practice.

**Recommendation 6**
An IVIG toolkit, including Ontario IVIG guidelines once developed, and other resources related to IVIG utilization, should be developed and introduced at an appropriate provincial education forum event.

**Recommendation 7**
Specific best practice information to be included in the Ontario IVIG guidelines and toolkit:

i. Indications where IVIG should be used, and where it should not be used

ii. Product should not be dispensed without a clinical indication available (no orders filled for ‘unknown’ clinical indication)
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iii. Doses appropriate for those indications and recommended duration of use
iv. Best practice for infusion of IVIG
v. New orders for IVIG should be checked prospectively at the site where the order is made, preferably through an SOP applied through the blood transfusion service or pharmacy, where the IVIG orders are received and product is dispensed
vi. Regular monitoring of patient’s weight for patients who use IVIG over a period of time
vii. Recommended monitoring of platelet counts in ITP patients using IVIG
viii. Recommended regular testing of patients to detect hemolysis arising from use of IVIG
ix. Clear direction on the practice of ‘rounding up’ and ‘rounding down’ of IVIG doses
x. Collection of specific information on wastage of IVIG product
xi. Request that manufacturers consider producing smaller size vials and larger size vials
xii. Specific direction on maximum doses of IVIG for patients >100 kg
xiii. Pre IgG levels for Primary and Secondary Immune Deficiency patients (baseline and trough)

**Recommendation 8**

An information package including the 2008 IVIG Utilization Management Guidelines from British Columbia, and the draft National Advisory Committee Guidelines for Immunology and Solid Organ Transplantation, should be circulated to clinicians in Ontario hospitals as soon as possible as an awareness campaign. In addition, information on the costs associated with IVIG use should be included in the package.

Next steps in the IVIG Utilization project will focus on implementation of these recommendations.

NOTE: This version of the report contains only the Executive summary. Please contact Kate Gagliardi for a full version of the report contents.