

January 10, 2005

**From: Dr. Patrick M. Nemechek, D.O.
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**Regarding: Proposed Kansas Intravenous Immunoglobulin (IVIg) LCD
LCD Database ID Number: L2541 (Exhibit A)
Region VII, Midwest Consortium**

Introductory Statement

The practical effect of the proposed revisions to the IVIg LCD are to eliminate the availability of off-label immune globulin therapy to persons with illness arising out of secondary humoral immunodeficiencies. If the proposed revisions are permitted to become the controlling LCD, the LCD itself will create an excessive, irrelevant documentary burden that if not met 'with meticulous detail' will be used to demand refunds from honest, treating physicians. These documentary requirements combined with the carrier's pattern of punitive audits raises the specter of financial ruin for physicians to such a level that physicians will be hesitant to continue providing treatment to patients who require immune globulin therapy to maintain their health. Finally, the LCD changes will be used as an inappropriate means to deny reimbursement or demand refunds from physicians.

Our belief that the proposed LCD revisions will be detrimental to patients will be clearly illustrated by the misleading or patently erroneous clinical, laboratory and psychosocial criteria the Carrier has included or used as a basis for its proposed changes. I will highlight each area of physician/patient concern and provide peer-reviewed literature to support my concerns.

Thereafter, I will provide unmistakable evidence to show that the changes proposed in this LCD run contrary to the vast majority of established IVIg LCD's nationally. Both of these material failures to follow the Program Integrity Manual on the part of the carrier are fatal to the establishment of a new LCD.

I will conclude with a discussion about how the carrier, by and through its Medical Director, has wholly failed to follow the Medicare Program Integrity Manual as the manual relates to making revisions to LCD's. We will demonstrate that the carrier failed to demonstrate a need for an LCD change as is specifically required under the Program Integrity Manual.

Critique of Proposed Intravenous Immunoglobulin LCD

Issue 1

Draft Language:

‘To merit the label of recurrent infections there should be evidence of several infections, many confirmed by imaging changes and growth in cultures and most requiring antibiotics for resolution.’

Comment:

While useful and readily available in pulmonary disease such as Bronchiectasis, the requirement of radiographic image changes and growth in cultures obviously is impractical in the management and treatment of every case of acute sinusitis or otitis media. These 2 infectious complications account for upwards of 27% and 82%, respectively, of infectious complications in patients with CVID (Exhibit B; Cunningham-Rundles C. Common Variable Immunodeficiency. *Curr Allergy Asthma Rep* 2001; 1(5):421-9).

Culture specimens obtained from nasal swabs correlate poorly with sinus pathogens owing to contamination with resident flora. Cultures obtained from the ostiomeatal complex (OMC) require the assistance of ENT specialists. In addition, bacterial culture results in suspected cases of acute community-acquired sinusitis are positive in only 60% of cases. (Exhibit C; Gwaltney JM et al. *J Allergy Clin Immunol* 1992; 90s:457-61). It is simply improvident to require clinicians to obtain redundant cultures.

Additionally, its is nonsensical and cost prohibitive to require clinicians to show resolution of sinus radiographic abnormalities in spite of clear and generally accepted clinical evidence of said abnormalities. The diagnosis of sinusitis rests upon clinical history and is not dependent upon laboratory or radiographic confirmation in the vast majority of cases. Meeting the requirements of ‘evidence of several infections, many confirmed by imaging changes and growth in culture’ for acute or chronic sinusitis will require an unwarranted and costly number of CT scans and ENT consultations, and result in needless delays in treatment.

Documentation of an accurate and detailed history is important, given the non-specific nature of upper respiratory tract symptoms. In most cases, differentiation between infectious and non-infectious disease can be made by the clinical history and physical exam alone.

Issue 2

Draft Language:

‘Dosage Guidelines: IVIg loading dose of 200-400 mg/kg body weight and maintenance doses of approximately 400 mg/kg body weight administered approximately once per month by intravenous infusion. Infusions are usually given every 4 weeks, but the interval should be adjusted, depending on the serum trough IgG concentrations and the patient’s clinical condition.’

Comment:

The language in this section is particularly vague. For example, does ‘the statement ‘maintenance doses of *approximately* (emphasis added) 400 mg/kg body weight’ imply that doses may exceed this dosage if the clinical and laboratory evidence suggests that 400 mg/kg is inadequate? Likewise, does ‘*approximately* (emphasis added) once per month’ imply that if the patient continues to experience subjective chills and fatigue especially in the last week of their infusion cycle that the cycle is allowed to be shortened to every 3 weeks if clinically necessary?

Some guidance to the question of appropriate levels and timing for dosing can be found in the article by Dr. Lucy Parks (Exhibit D; Park, C L. Common Variable Immunodeficiency. <http://www.emedicine.com/ped/topic444.htm>. Last updated May 26, 2004.), as referenced in the Medical Review entitled, “Changes in Processing of Claims for Intravenous Immunoglobulin (IVIg)” (Exhibit E, which was posted to the www.kansasmedicare.com website on August 10, 2004, and interestingly, has been removed completely from the web site.). In this article, Dr. Park’s advice is to “Maintain trough serum IgG concentrations at 400-500 mg/dL in adults, a value close to the lower limit of normal. For most patients, a dose of 400-600 mg/kg every 3-4 weeks suffices to reduce frequency of infection.” She goes on to state, “Some patients with chronic lung disease require up to 600-800 mg/kg per month. The half-life of IgG is highly variable among patients with CVID, but it usually is longer than 18-23 days in healthy individuals.”

The clinician should have the autonomy under this proposed LCD section to dose at a higher rate than indicated in the revision and time dosage based uniformly on a case by case patient clinical observation.

Issue 3

Draft Language:

‘If no clinical improvement occurs while receiving on-going infusions, then the infusions should not continue.’

Comment:

In order to meet the carrier’s demands for meticulous record keeping by the clinician, this language needs further clarification. A recommend time frame of 3-4 sequential treatments

of immune globulin (over 3- 4 months) is often adequate to determine clinical efficacy even in patients with several comorbid conditions. Therefore, the any revision should provide a definitive time frame within which to determine efficacy which, at a minimum, should permit a three to four month period.

Issue 4

Draft Language:

‘Once treatment is initiated, we expect meticulous documentation of progress. Some type of quantitative assessment to monitor the clinical course is required. There should be clinical evidence that the patient is benefiting from IVIg. Some suggested criteria for measurement include:

- 1. number of infections,**
- 2. frequency and duration of antibiotic use,**
- 3. number of febrile episodes,**
- 4. number of health provider visits,**
- 5. number of absences from work or school**
- 6. ADLs and/or other measures specific to the patient’s clinical condition.**

Subjective or experiential improvement alone is insufficient to either continue IVIg or to expect coverage.’

Comment:

Requiring documentation regarding the frequency, severity, and clinical impact of the recurrent infections is not necessarily difficult but asserts the question, “What do we do with the information?” Knowing the frequency, severity and duration of infectious complications prior to initiation of treatment with immune globulin is essential in determining the necessity of treatment to begin with. But after the patient has clinically stabilized, does the absence of frequent infections and an improvement in their ADL (Activities of Daily Living) score have any utility other than to confirm that the diagnosis is correct and the patient required treatment in the first place?

While ‘meticulous’ record keeping is required, the proposed LCD requires quantitative documentation of clinical progress. Data such as a reduction in the number prescriptions and interactions with the clinician required to treat infectious events is straight forward, however, the suggested criteria of absence from work or school is most likely an insensitive measure of clinical effectiveness. Many patients receiving reimbursement for immune globulin through the Medicare program are doing so because they have become physically disabled or are of retirement age. In either case, the measurement of missed school or work days would be a highly insensitive and prejudicial quantitative measure of clinical progress since most are so ill or old they can’t work nor go to school on any regular basis.

The criteria of a quantitative ADL score are also problematic. ADLs are commonly derived from Quality of Life (QOL) assessment instruments. No information as to which QOL scale is to be use is provided. No indication of whether to use general health or disease specific scales

is provided. General measures allow comparison across different disorders, severities of disease, and interventions, whereas disease-specific scales contain items most relevant to the condition under study and that are most likely to change with effective therapy. Moreover, as far as I can determine, no particular QOL assessment instrument has been standardized and shown to be clinically meaningful for patients with recurrent sinopulmonary disease from humoral immunodeficiency.

Finally, suggesting that ‘Subjective or experiential improvement alone is insufficient to either continue IVIg or to expect coverage’ is excessively restrictive and flies in the face of the medical concept of *patient care*. Many conditions in medicine are not readily quantifiable. The ‘subjective or experiential improvement’ is a critical and fundamental component of multiple measures a physician uses to determine the effectiveness of therapies for all illnesses.

As a certified specialist in Internal Medicine and HIV Medicine (Exhibit F) with 15 years of experience in managing thousands of persons with HIV infection including those with secondary humoral immunodeficiency (See conclusions of audit appeals concluding my medical use of immune globulin was medically necessary in every single instance; Exhibits G and H) I can say without hesitation that subjective or experiential improvement is one of the most important clinical indicators of successful therapeutic response to immune globulin.

Whereas ‘subjective or experiential improvement alone is insufficient’, the carrier also fails to recommend any ADL scales or other specific measures that have been standardized for immunodeficiencies. We are left to speculate as to which scale they find acceptable. The carrier seems to believe that patients with humoral immune deficiency are completely healthy when they get their regular IVIg infusions. On the contrary, the patients will report having more good days than bad but almost all of my patients report increasing fatigue the week prior to receiving their next infusion. They still have recurrent infections, just not as frequently nor as severe as before receiving immune globulin. Therefore, accurate documentation of the ‘subjective or experiential improvement’ (This information is documented in the chart by the physician with statements such as ‘The patient reports improved energy levels and fewer subjective chills and drenching night sweats since receiving immune globulin infusions.’) should be enough to warranted continued therapy.

Additionally, **none of the existing 66 national LCD/LMRP policies** addressing immune globulin require this level of documentation for physicians treating immunodeficiencies with immune globulin. (See following section entitled “Comparative Analysis of Local Coverage Determinations Nationally” for more detail.)

Dr. Mark Ballou (Exhibit I; Proposed LCD ref. #6, Ballou M. Primary immunodeficiency disorders: Antibody deficiency. *J Allergy Clin Immunol* 2002;109:581-91) states, “The clinical status of the patient is a critical and fundamental component of multiple measures a physician uses to determine the effectiveness of therapies for all illnesses”. To disregard the subjective and experiential improvement of a patient’s condition is to disregard the fact that the end result is not to try to quantify the carrier’s decision process to elements applicable to a spread sheet but rather to provide medically reasonable and necessary care which results in the improvement in the patient’s overall health and well-being.

Issue 5

Draft Language:

‘After a period of 1-2 years and at similar intervals thereafter, there must be an attempt made to wean or stop the IVIg infusion.’

Comment:

There is no scientific basis for this requirement and it will prove to be very harmful to patients whose lives depend on recurrent IVIg treatment. The majority of patients will tell you they slowly become more fatigued, experience subjective chills, or have increasing diarrhea the final week of their 4 week cycle before receiving their next infusion of immune globulin and that their general health fails more during lengthier dosing intervals. Under the proposed wording of this portion of the LCD we are left to wonder how long we need to try to wean a patient from IVIG before it will be considered necessary to restart at the risk of the contractor’s arbitrary refusal to cover one or more treatments.

None of the existing 66 national LCD/LMRP policies addressing immune globulin require physicians to withdraw immune globulin therapy when being it’s used for recurrent infections as a consequence of immune deficiency. This requirement to withdraw therapy is reckless and places patients at indescribable risk for serious infection, hospitalization and possible death. (See following section entitled “Comparative Analysis of Local Coverage Determinations Nationally” for more detail.)

No such LCD revision should be made in this regard as physician and patient observations are the only appropriate measure of whether continuation of immune globulin therapy for immunodeficiency is warranted.

Issue 6

Draft Language:

‘It is important to identify the specific immunochemical abnormality that led to the initial establishment of a diagnosis of primary immunodeficiency. This abnormality, be it serum IgG, subclass IgG or post-immunization changes, requires periodic monitoring to justify the need for continued infusion.’

Comment:

This LCD draft revisions is replete with vagaries such that a physician is left to guess about all of the following questions, among others. This language should be removed or revised in its entirety:

- How frequent do these measures need to be made?
- In the case of functional humoral deficiencies, does the patient need to be repeatedly vaccinated to demonstrate inadequate rise in post-vaccination antibody titers?

- If serum IgG levels are still subnormal in spite of reaching the maximum maintenance dose of 400 mg/kg monthly, is the clinician allowed to increase the monthly dosage above the limit of 400 mg/kg to reach normal trough levels if clinically the patient has demonstrated only a partial clinical response to treatment with 400 mg/kg?

Issue 7

Draft Language:

‘Low immunoglobulin levels or failure of antibodies to rise to an antigen challenge occurs sometimes in patients who do not have primary B-cell disorders. These changes may be the result of several systemic illnesses, malignancies, viral infections or drugs. In these disorders a state of secondary immunodeficiency exists. This state may also lead to recurrent infections and laboratory immunoglobulin abnormalities.

Secondary immunodeficiencies or hypogammaglobulinemia, in isolation, will not be covered unless the immunodeficiency is the result of chronic lymphocytic leukemia or childhood Human Immunodeficiency Virus (HIV) Infection.’

Comment:

The logic of this particular LCD revision is manifestly contradictory and is therefore inadequate to a physician trying to interpret said LCD as a whole. The first paragraph states that secondary immunodeficiencies exist, causes laboratory immunological abnormalities and can even lead to recurrent infections. But this is followed by a contradictory paragraph limiting immunoglobulin therapy in secondary immunodeficiency only to chronic lymphocytic leukemia or childhood Human Immunodeficiency Virus infection.

Why is this limited to only FDA-approved secondary immunodeficiencies? Since off-label uses of immune globulin are allowed for neurological disorders, it simply cannot be an argument of ‘FDA-approved usage vs. off-label usage’. The proposed LCD even goes so far as to state, “There are several "off-label" uses for IVIg, especially in neurological disorders.^{1,2} There is good scientific evidence that supports this use in a few of the disorders; in others, however, the evidence is either poor or lacking.” Therefore, this exclusion seems to be based on the fact that off-label use of immune globulin for secondary humoral immunodeficiencies is considered experimental and does not meet the standard of ‘Reasonable and Necessary’. Hence, a discussion of the issue of reasonable and necessary use must be considered.

I will approach the question of proper utilization of IVIg for secondary immunodeficiencies as is required pursuant to the provisions of ‘Reasonable and Necessary’ point-by-point as defined in the Medicare Program Integrity Manual, Section 13.5.1 (Exhibit J), which focuses on the following tests:

1. Safe and effective;
2. Not experimental or investigational; and

3. Appropriate including the duration and frequency that is considered appropriate for the service, in terms of whether it is:
 - a. Furnished in accordance with accepted standards of medical practice for diagnosis or treatment of patient's condition or to improve the function of a malformed body member;
 - b. Furnished in a setting appropriate to the patient's medical needs and condition;
 - c. Ordered and furnished by qualified personnel;
 - d. One that meets, but does not exceed, the patient's medical need; and
 - e. At least as beneficial as existing and available medically appropriate alternative.

Point 1 – Safe and Effective

Intravenous immunoglobulin therapy is a relatively safe therapy when administered by experienced medical personnel. In general, adverse reactions to IVIg therapy are usually minor and occur in not more than 10% of patients (Exhibit K; Dalakas M. The Use of Intravenous Immunoglobulin for Neurologic Diseases. *Neurology*, 51 suppl. 5: S1-S45:1998).

Point 2 – Not Experimental or Investigational

Determination of whether a medical therapy is experimental or investigational can be a rather ambiguous and multifaceted process and pursuant to guidance provided in the Medicare Program Integrity Manual must include a consideration of the following questions:

1. Are there other Medicare carriers that reimburse for treatment of secondary immunodeficiencies with immune globulin?
2. Are there scholarly articles or other outside documentation that this treatment is effective?
3. What are the opinions of immunologists familiar with the use of immune globulin in off-label secondary immunodeficiency?
4. What is the community experience with this treatment?

First, in a review of Local Coverage Determination policies from 66 different Medicare carriers and fiscal intermediaries (See following section entitled “Comparative Analysis of Local Coverage Determinations Nationally” for more detail.), the **majority** would allow off-label immune globulin therapy for diagnosis of hypogammaglobulinemia (non-specified), qualitative evidence of humoral immunodeficiency (i.e., IgG subclass deficiency) or quantitative evidence of humoral immunodeficiency i.e., (inadequate antibody response to pneumococcal vaccine challenge) humoral deficiencies or even simply diagnosis Acquired Immunodeficiency Syndrome alone. Additionally, **no other Medicare carriers or fiscal intermediaries limit secondary immunodeficiencies** only to the 2 FDA-approved indications, Pediatric HIV Infection and Chronic Lymphocytic Leukemia. This issue is outlined in greater detail below (see Issue 10).

Clearly, the overly restrictive limitations on immune globulin therapy in secondary immunodeficiency proposed in these guidelines runs contrary to the medical guidance put forth by the a large percentage of other carriers across the country. The fact that nearly half of Medicare carriers reviewed allow the use of immune globulin in secondary immunodeficiency, seems to underscore the fact that this treatment is not ‘experimental or investigational’ in the eyes of many other clinicians and researchers around the country.

Secondly, peer-reviewed articles citing the specific benefits of immune globulin therapy in off-label secondary immunodeficiencies have been written since the often-cited JAMA review of 1995 (Exhibit L; Ratko TA, Burnett DA, et al. Recommendation for Off-label Use of Intravenously Administered Immunoglobulin Preparations. University Hospital Consortium Expert Panel for Off-Label Use of Polyvalent Intravenously Administered Immunoglobulin Preparations. JAMA 273(23):1865-70). Limiting the recommendations of off-label use of immune globulin to the recommendations of the JAMA article and references specifically directed at neurological conditions doesn’t conclude that HIV Disease should not be considered for off-label use of immune globulin.

Specifically, most studies involving HIV up to that date were assessing the impact of immune globulin therapy on the *clinical course of HIV Disease per say* and not on the clinical impact of *sinopulmonary infections from humoral immunodeficiency secondary to HIV Disease*.

An excellent study examining the impact on infectious complications associated with humoral immunodeficiency in HIV infection was performed by Kiehl et al (Exhibit M, Kiehl MA et al. A Controlled Trial of Intravenous Immune Globulin for the Prevention of Serious Infections in Adults With Advanced Human Immunodeficiency Virus Infection. Arch Intern Med. 156:2545-2550, 1996). Kiehl performed a prospective, randomized outpatient clinical trial to determine the efficacy of IVIG in preventing infections, fever and hospitalizations in HIV-infected adults.

This study demonstrated a prolonged time until serious infections in IVIG treated individuals as well as a reduction in number and duration of hospitalizations, reduction in days with fever and a decrease in the frequency of diarrhea. The study even showed reduction in death that was close to reaching statistical significance (P=.06). Because of the overwhelming clinical benefit in patients assigned to be treated with immune globulin, ***the study was stopped prematurely by the local ethical board.***

Given Dr. Satya Murti’s economically intractable insistence that secondary immunodeficiencies should be excluded from IVIg coverage, we anticipate that he will attempt to argue that double-blinded, placebo-controlled studies of HIV-infected adults receiving immune globulin have not been performed, and this fact alone will be the basis for denying the use of immune globulin for HIV-related secondary immunodeficiency. His efforts in this regard must be rebutted in favor of the fact that once a controlled, clinical trial (Kiehl et al) has been prematurely stopped because outstanding treatment benefits were apparent midway in the trial, and continuation of the study is then considered unethical. Given this fact, there is a very low probability that further studies of immune globulin in

HIV-infected adults will ever be conducted involving a placebo control group. Hence, the lack of a fully blinded and controlled study should be considered in this instance as uncontroverted evidence that the field of medicine believes adequate research has been done to support its use.

Moreover, The JAMA paper oft-cited by Dr. Satya-Murti as a basis to improperly preclude all but two off-label uses of IVIg buttresses our belief that further comparative trials should not and will not be performed in concluding, “Finally, for many of the debilitating or fatal off-label conditions in which IVIG has been used, it is highly improbable that randomized, comparative trials to evaluate IVIG therapy vs. conventional therapy will ever be performed in the U.S.” The article went on to state, “Approved label is not intended to set a standard of medical practice...rather, a drug should be used in a manner that is consistent with good medical practice and the patient’s best interest.”

The article cited by Dr. Satya-Murti in reference to his proposed LCD change (Exhibit N; Jaffe EF. Secondary Hypogammaglobulinemia. Immunol Allergy Clin North Am - 2001 Feb; 21(1); 141-163) is likewise inappropriately referenced as supportive evidence of the extreme restrictions on immune globulin therapy in secondary immune deficiency and is used in a patently misleading manner. This article primarily deals with evidence surrounding “disease in which IgG levels fall below normal because of hypercatabolism or accelerated protein loss or drugs that inhibit immunoglobulin (Ig) production through a variety of mechanisms.” ***This article provides no scientific support for the proposed LCD position*** that “Secondary immunodeficiencies or hypogammaglobulinemia, in isolation, will not be covered unless the immunodeficiency is the result of chronic lymphocytic leukemia or childhood Human Immunodeficiency Virus (HIV) Infection.”

A careful reading of the article actually provides evidence in support of the use of immune globulin in secondary immune deficiencies. In the discussion regarding secondary immunodeficiency arising out of HIV infection, the article states “depressed antibody responses to new and recall antigens are found, and recurrent infections with encapsulated bacteria occur frequently, all suggesting a B-cell defect.” The article additionally states in regards to secondary immune deficiency arising out of Epstein-Barr Virus infections (another disease state sometimes requiring off-label use of immune globulin for secondary immunodeficiency) that “Hypogammaglobulinemic patients usually require periodic infusions of immune globulin because of frequent bacterial infections.”

After being informed that her scientific work had been misappropriated under the proposed revision to the LCD, Dr. Jaffe offered to write a letter clarifying her position on secondary immune deficiencies as it relates to the proposed LCD. In her letter (Exhibit O), she unequivocally states that if patients “are unable to make functional antibody, they do have true immunodeficiency, and would greatly benefit greatly from IVIG.” She goes on further to add, “As stated in the summary on p. 157, immune function is best assessed by vaccination booster responses with diphtheria, tetanus, and pneumococcus. Lack of pneumococcus response, in isolation, can represent significant immunodeficiency. This is selective carbohydrate antibody deficiency, which can predispose to infection with

encapsulated organisms, such as pneumococcus. At least a trial use of IVIG is warranted if the clinical and laboratory evidence of immune deficiency is evident.”

Dr. Mark Ballow, M.D. another noted immunologist and author of cited reference #6 in the proposed LCD, stated to me in a phone conversation (December 30th, 2004) that he completely disagreed with the proposal that all secondary immune deficiencies except those with FDA-approval status be excluded from coverage for immune globulin. He had offered to provide a written critique of the proposed LCD but became extremely ill with Influenza and has been regretfully unable to fulfill his offer prior to the January 10, 2005 deadline for comments.

In addition to the foregoing it should be noted that many HIV physician specialists around the country use immune globulin in the treatment of secondary immunodeficiency related to HIV infection in adults. Testimony to this fact is a letter submitted in support by Dr. Robert Houghton (Exhibit P) that states, “I have had over 14 years experience as an HIV specialist along with other colleagues in southern California managing patients who have responded very favorably to gammaglobulin for secondary humoral immunodeficiency with sinopulmonary disease.”

In concluding this point, in reviewing the appropriateness of using IVIg for secondary immunodeficiencies we should give primary credence to the author of the only reference used by Dr. Satya-Murti that specifically addresses secondary immunodeficiencies wherein, Dr. Jaffe begs the question, “Having considered some of the causes of low immunoglobulin levels in patients who do not have primary B-cell disorders, how does one determine if low immunoglobulin is significant? The patient’s history of infections is the primary measure.”

Point 3 - Appropriate

This element is easily determined within generally agreeable parameters:

- Immune globulin should be furnished to individuals with humoral immunodeficiency who consistently demonstrates some of the clinical sequela associated immune deficiency such as sinopulmonary infections, bronchiectasis or pneumonia. These have been the logical and objective parameters within which this very carrier has determined IVIg to be medically necessary after two exhaustive audits of this physician’s practice alone;
- Furnished within a clinical setting that provides a safe and reliable atmosphere method of administration;
- Ordered and furnished by medical personnel familiar with the proper indication, dosing, administration and adverse effects immune associated with globulin therapy;
- The use of immune globulin should be used only after other less expensive and equally effective treatment modalities have reasonably failed to resolve the particular illness associated with the humoral immune deficiency.

Issue 8

Draft Language:

‘Determination of to what constitutes (i) failure of conventional therapy, (ii) contraindications to conventional therapy and, (iii) the duration of short-term therapy are subject to review by the contractor, pre or post-payment.’

Comment:

If the carrier believes it is necessary for them to have the final and lasting “determination of what constitutes (i) failure of conventional therapy, (ii) contraindications to conventional to conventional therapy and, (iii) the duration of short-term therapy”, then the carrier is obligated to clearly provide these criteria to physicians within the LCD guidelines. The carrier may find this demand of them as excessive, but it is no more excessive than the administrative burden effected by the proposed revised LCD, especially when reviewing the LCD’s impact of completely abrogating the physician-patient relationship, and the joint clinical decision-making process which arises out of the nuances of that relationship.

Issue 9

Draft Language:

‘279.00 Hypogammaglobulinemia, unspecified (Do not use 279.00 as a stand-alone diagnosis. Instead use it as a secondary diagnosis when describing secondary hypogammaglobulinemia of Chronic Lymphocytic Leukemia (204.10 or 204.11.))’

Comment:

It is my medical opinion and the opinion of Dr. Jaffe and other practitioners in the field that ‘279.00 Hypogammaglobulinemia, unspecified’ should be maintained as an allowable diagnostic code to account for the treatment of clinically meaningful secondary immunodeficiencies in which qualitative or quantitative immune deficiency are present. Moreover, there are no specific indicators or medical opinions that indicate a need for such a radical change in LCD policy.

Issue 10

Comparative Analysis of Local Coverage Determinations Nationally

A thorough comparative analysis of all existing Local Coverage Determinations was performed utilizing the Medicare Coverage Database (www.cms.hhs.gov/mcd/search.asp? Exhibit Q), the results of which are attached (Exhibit R). Copies of each LMRP/LCD are provided in tabulated for in the adjoining binder entitled (Compendium of IVIg LMRP/LCD). A hyperlinked version of this material is also included on compact disk of similar name.

As stated previously, one of the key indices for determination as to whether a medical therapy is considered ‘reasonable and necessary’ is the frequency the therapy is accepted and utilized by other health care providers. Unlike the carrier whose duty it is to make relevant inquiry, I have

performed a rather exhaustive analysis of all LMRP/LCD policies concerning immune globulin published by Medicare carriers and fiscal intermediaries.

A total of 66 policies were analyzed for specific common elements regarding immune globulin use in immune deficiency which include:

1. Specific coverage for disease states when the listing cites the full name of the disease as compared to listing of ICD-9-CM codes (e.g., Hypogammaglobulinemia);
2. Specific coverage for disease states when the listing cites the ICD-9-CM for the disease as compared to citing the full name only (e.g., 279.00);
3. Requirement of extensive documentation;
4. Requirement to stop or wean immune globulin therapy; and
5. The specific exclusion of all off-label use of immune globulin for secondary immunodeficiency.

The initial analysis showed a majority (57%) of the nation's Medicare carrier or financial intermediary policies would allow off-label immune globulin therapy for diagnosis of hypogammaglobulinemia (non-specified), qualitative evidence of humoral immunodeficiency (i.e., IgG subclass deficiency) or quantitative evidence of humoral immunodeficiency i.e., (inadequate antibody response to pneumococcal vaccine challenge) humoral deficiencies or even simply diagnosis Acquired Immunodeficiency Syndrome alone. Collectively, these diagnoses are utilized when a physician is requiring to treat a patient with immune globulin but the patient fails to meet the diagnostic criteria of one of the primary immune deficiencies (congenital agammaglobulinemia common variable immunodeficiency, X-linked immunodeficiency with hyperimmunoglobulin M, severe combined immunodeficiency, and Wiskott-Aldrich syndrome).

Secondly, when analyzing the specific ICD-9-CM codes listed within the policy section entitled "ICD-9 Codes that Support Medical Necessity" an overwhelming majority of the carriers and fiscal intermediaries (FI) include codes commonly used for secondary immunodeficiency (Primary immunodeficiencies have their own specific codes: 279.04, 279.05, 279.06, 279.09, 279.12 and 279.2). The frequency of the ICD-9-CM codes that 'support of medical necessity' secondary immunodeficiencies are as follows: 279.00 (hypogammaglobulinemia, non-specified) is allowed by 80% of the carriers or FI, 279.03 (Other Selective Immunoglobulin Deficiencies; commonly used to identify qualitative or quantitative immunodeficiencies) is allowed by 83% of the carriers or FI, and 042 (HIV Infection or Acquired Immunodeficiency Syndrome) without an age limitation is allowed by 73% of the carriers or FI.

Thirdly, **none** of the 66 policies reviewed levied any requirement that the physician must attempt to wean or stop immune globulin therapy when being successfully used for immunodeficiency states.

Most notably, the newly proposed Kansas Immune Globulin LCD was **the only** policy in the entire country to specifically preclude the use of immune globulin for all secondary immunodeficiency states with the exception of the only 2 FDA-approved diseases, Pediatric AIDS and Chronic Lymphocytic Leukemia.

Collectively, this analysis clearly demonstrates that the overwhelming majority of Medicare LMRP/LCD policies allow use of immune globulin for immunodeficiency states which cannot be

accurately classified as a Primary Immunodeficiency and are therefore classified as secondary regardless of whether the originating cause of the immune deficiency is an FDA-approved entity or not.

Current Proposal of LCD Revisions Plainly Fails to Follow PIM/LCD Revision Guidelines.

The Medicare Program Integrity Manual (PIM) is designed to prevent contractors from inventing or varying the terms of coverage determinations for particular services without adequate procedural precautions being taken. The PIM's term "integrity" within its very title is telling. A careful reading of the PIM leads to the irrefutable conclusion that the proposed LCD lacks integrity at both the procedural and substantive level. Given the manifest weaknesses in the proposed LCD it should not be allowed to see the light of day. As drafted, this LCD would place providers in an untenable position of being required to balance compliance with a nonsensical and economic-driven LCD against the health and indeed the very lives of patients. The remainder of this submission will detail some of the PIM procedural and substantive failings of the contractor in its revision of the IVIg LCD proposal that should result in its rejection.

The recently proposed LCD for Intravenous Immunoglobulin (IVIg) is a classic example of what the PIM refers to as a Contractor purposefully failing to "ensure that LCD's present and maintain a positive statement and do *not malign any segment of the medical community*".¹ Dr. Satya-Murti's proposed policy change is the product of a longstanding effort to **malign** Dr. Nemechek and his practice by targeting patients with a co-existing diagnosis of common variable immunodeficiency or hypogammaglobulinemia (unspecified) and HIV; marking them with an unjustifiable badge of ineligibility for IVIg treatment. The PIM manual provisions clearly envisioned this type of wrongful conduct by a contractor and the PIM contains specific directives to ensure integrity in the process of revisions.

Contractors are permitted to revise an LCD *only* on condition that (1) a validated widespread problem demonstrates a widespread risk to the Medicaid trust funds; (2) a LCD is needed to assure beneficiary access to care; (3) A contractor has assumed the LCD development workload of another contractor and is undertaking an initiative to create uniform LCD's across its jurisdiction; (4) frequent denials are issued following routine or complex review or frequent denials are anticipated. See: §13.4 B of PIM 13. Dr. Satya-Murti and the Blue Cross intermediary who authored the pending LCD change have not adequately demonstrated that any of the above conditions have been met or are even the purpose of the proposed LCD changes.

We are left to assume from our conversations with Dr. Satya-Murti, however, that the contractor is alleging that a validated widespread problem is perceived to exist for which the LCD change has been proposed. Neither at the point of the first audit of this office, nor at any later time has a "**validated widespread problem**" been demonstrated to exist. In all correspondence published by the contractor, only "preliminary statistical data suggesting an increase in immune globulin usage" has ever been alleged as a basis for concerns regarding IVIg usage. Investigation of the increased utilization was effected by the contractor and usage was determined to be proper and explainable in two exhaustive audits of our practice alone.

¹ See: Medicare Program Integrity Manual (Chapter 13 – Local Coverage Determinations) (Rev. 71, 04-09-04) (hereafter referred to generally as PIM 13).

Notwithstanding the forgoing, issuance of newly proposed LCD regulation on October 27, 2004 was effected by Dr. Satya-Murti a little more than 8 weeks (62 days to be exact) after issuing an audit letter to providers of immune globulin (Exhibit S, Medicare Audit Notification Letter to Dr. Nemechek, August 26th, 2004) under the guise of continued concern over “preliminary statistical data suggesting an increase in immune globulin usage”.² It would have been physically impossible for the contractor to conclude that there was a “**validated widespread problem**” from the results of the audit undertaken at that time because the audit was being done on patients who had not even yet been treated by the physicians who were the subject of the audit. During the mere 62 days between when the audit began and the LCD change was published, patients would have been treated for upwards of 30-45 days from the date the audit letter was issued. Medicare was then required to issue a letter to the provider (7 day turnaround time) regarding the patients subject to the audit, and the provider was thereafter allowed 45 days to respond with appropriate documentation for purposes of the audit to proceed. Given these time constraints, Dr. Murti and his staff could not have even begun to analyze the data from providers for at least 97 days (December 1, 2004) after the issuance of the initial audit letters to targeted IVIg user physicians. Certainly, the contractor could not have determined there was a “**validated widespread problem**” 35 days in advance of the end of the preliminary data collection period absent its sophomoric ploy to manufacture the impression that an audit had been conducted to justify the revision of the LCD!

The proposed IVIg LCD was pre-determined prior to any effective analysis that could possibly have drawn a conclusion that there was a “**validated widespread problem**” with immune globulin usage. Interestingly, the only fact that is alleged to exist as a basis to audit physicians, such as the third proposed audit of my practice, is the misleading assertion that the utilization rates in our area are higher as compared to the overall rates in Kansas, and Nebraska and US as a whole. Dr. Satya-Murti’s staff didn’t have the foresight or were simply not interested in using comparative data on cities with copasetic per capita testing pools to that of Kansas City such as may be found in cities like Indianapolis or even St. Louis. Hence, the contractor had to stretch the use of its own statistics to even conduct the audit whose preconceived “audit results” formed the alleged basis for the most recent LCD revisions in the first place.

Hence, Dr. Satya-Murti, as scrivener of the proposed LCD, and on behalf of the contractor, had no right to make a revision in the LCD pursuant to §13.4(B) of PIM 13 but forged ahead in any event. As is specifically set forth in §13.7 of PIM 13, when the contractor validates a need for a new or revised LCD (which the contractor did not do in this instance), the contractor must then “*Adopt or adapt an existing LCD, if possible; or Develop a policy if no policy exists or an existing policy cannot be adapted to the specific situation.*” If it were not enough that Dr. Satya-Murti improperly effected an LCD revision under the PIM in the first place, Dr. Satya-Murti has also wholly failed to effect revisions under this clear PIM guideline as well.

In fact, after a lengthily review of all Medicare LCD’s covering IVIg (See preceding section entitled “Comparative Analysis of Local Coverage Determinations Nationally” for more detail.), our offices have discovered that most every other contractor in the nation has an existing IVIg

² It should be noted that the changes to the LCD were carefully constructed to eliminate coverage of secondary immunodeficiencies such that the proposed LCD would have been in the works for months, if not years before the conclusion of the audit.

policy which bears on the issues raised by Dr. Satya-Murti in the present LCD. In a review of LCD policies from 66 different Medicare carriers, a majority specifically allow off-label immune globulin therapy for diagnosis of non-specified hypogammaglobulinemia (ICD-9-CM 279.00), other selective immunoglobulin deficiencies such as qualitative (IgG subclass deficiency) or quantitative (inadequate antibody response to pneumococcal vaccine challenge) humoral deficiencies (ICD-9-CM 279.03) or even simply Acquired Immunodeficiency Syndrome (ICD-9-CM 042). Additionally, and most tellingly, ***not a single other Medicare intermediary in the entire country*** has attempted to limit secondary immunodeficiencies only to the 2 FDA-approved indications, (Pediatric HIV Infection and Chronic Lymphocytic Leukemia), as has been the effect of Dr. Satya-Murti's proposed revision. The over-reaching application of the new LCD will have a devastating impact on patients who have long been recognized as being appropriate candidates for IVIg in the face of no change in the medical literature, medical science, or any test or audit results which would warrant such drastic LCD conversion.

Moreover, the stringent limitations on immune globulin therapy in secondary immunodeficiency suggested in the proposed LCD runs contrary to the medical guidance put forth by the a large percentage of other carriers across the country. The fact that nearly half of Medicare carriers reviewed allow the use of immune globulin in secondary immunodeficiency, clearly underscores the fact that this treatment is not 'experimental or investigational' in the eyes of the majority of other clinicians and researchers around the country. It is readily apparent that Dr. Satya-Murti and his staff did not even attempt to "adopt or adapt an existing LCD", but rather, set off on their own reckless course of developing radical policy for the sole purpose of denying reimbursement for immune globulin in secondary humoral immune deficiency. The proposed LCD change is wholly inconsistent with the authority of a carrier to make a policy or guideline change and reflects the bad faith nature of the proposed LCD change by Dr. Satya-Murti and his staff as was more fully outlined in our letter to Dana Edwards dated September 27, 2004 and the exhibits thereto, all of which are attached hereto as Exhibit T.

The indisputable reason that the contractor has formulated a proposed LCD aimed at the elimination of IVIg coverage for certain HIV patients was brought to light during the legal discovery process which was the product of defending my practice and my patients the first time this very contractor (through Dr. Satya-Murti and his staff) audited my practice nearly 5 years ago. Medicare turned over an internal memorandum to my legal counsel, a copy of which is attached hereto as Exhibit U that reveals, in pertinent part, the true purpose and intent of Dr. Satya-Murti's long-standing effort to remove coverage for a service that Medicare's own appellate nursing staff have found to be reasonable and necessary in two concurrent and exhaustive audits. The memo read in pertinent part:

"J1562 is aberrant over threshold for specialty 11 family practice in KC. This code was also selected because the carrier % of change was 125.54. This means basically that our usage of this procedure code has increased 125%..."

Dr. Murti is in the process of rewriting the Immune Globulin policy and we will nab that as the corrective action. I would preliminarily like to suggest looking at least one provider Nemechek E56236 as he is driving the aberrancy." Emphasis added.

In summary, Dr. Satya-Murti, on behalf of the carrier has ignored those aspects of the PIM aimed at curbing a rogue carrier from deviating from the standards of care owing the patients and physicians who work within the Medicare program. If contractors are permitted to invent reasons to modify LCD's it will only be a matter of time before contractors restrict coverage of unpopular claims at will. If this LCD is permitted to become the relevant authority in Kansas and Nebraska, the core purposes of the Medicare Integrity Manual will have been subverted.

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