

March 30, 2010

Customer Advocate Team
Wonting Insurance Co
100 Main St
Anywhere, USA 00000

RE: Patient
Provider: Dr. Surgeon
Service: IVIg
Date of service: Prior authorization for IVIg (proposed start date 3/24/2010)

Dear Sir or Madam:

I am writing on behalf of Patient to initiate an appeal of Wonting's denial of coverage of IVIg for treatment of Guillain-Barre syndrome (GBS). The appeal form, a release authorizing me to represent Mr. Patient in this appeal, and my HIPAA release is enclosed.

Wonting's initial denial was based on the fact that IVIg is an "off-label" use for GBS. However, there is a large amount of medical literature supporting the use of IVIg as a first-line treatment for GBS. Indeed, many other insurers cover IVIg for treating GBS.

Mr. Patient's medical records support Dr. Surgeon's clinical judgment that he is at risk of developing a more progressive form of the disease and, thus, that this treatment is called for **immediately**.

Thus, for these reasons, we ask that you reverse Wonting's noncoverage decision and allow this man to obtain the safe and effective treatment that his treating physician has prescribed.

I. IVIg IS MEDICALLY NECESSARY – INDEED, ESSENTIAL – IN THIS CASE

Patient is a 50 year old male who called Dr. Surgeon on March 20 because of concerns about his health over the previous weeks. He reported that he had finished a bout with gastrointestinal illness about a week earlier. He decided to return to his normal jogging routine that morning. When his legs felt weak and difficult to keep moving, he believed that it was merely due to the length of his layoff from running. However, a little later in the day, Patient started to feel prickling sensations and weakness in his hands and feet. Dr. Surgeon suggested that he come in the next day.

Dr. Surgeon examined Patient on the afternoon of March 21. By that time, the tingling had started working up both of his legs to about his knees. Patient also reported

some pain in his lower back. Dr. Surgeon asked Patient to walk to the end of the hall and noted some unsteadiness. A tendon reflex test on Patient's knees showed no response. Surgeon immediately ordered a lumbar puncture, electromyography (EMG) and a nerve conduction velocity (NCV) test. He also started Patient on a course of methylprednisone. (Patient records enclosed)

The test results dated March 23 showed prolonged distal latencies and conduction slowing. The lumbar puncture showed albumino-cytological dissociation with an elevated protein level (432 mg/dL), without an accompanying increased cell count (i.e., [pleocytosis](#)). All of these pointed to Surgeon making a diagnosis of GBS. (Lab results enclosed).

When Dr. Surgeon called with the results, Patient reported that he was having more trouble walking, tingling almost to his waist, more pain in his back, and considerable fatigue. Due to the rapid progression of symptoms, Dr. Surgeon admitted him to Hopeful Hospital immediately, stopped the methylprednisone, and requested IVIg treatment. (See March 24 note by Dr. Surgeon requesting authorization for IVIg therapy.) Subsequent to Wonting's coverage denial of IVIg, Patient's disease progressed further. He no longer can walk unaided and has difficulty breathing. (Hospital records enclosed).

Mr. Patient has tried all other available therapies. He has been treated with IV Solu-Medrol, as well as oral steroids, without lasting result. (See enclosed hospital records). Plasma exchange is not available in Hopeful Hospital, and it is unclear from the literature cited below that it would be preferable to IVIg. Further, Dr. Surgeon believes that moving Mr. Patient would be dangerous considering his condition. (See enclosed letter from Dr. Surgeon).

Thus, Mr. Patient's condition is worsening by the day. Steroids have been tried and failed to produce results, and plasmapheresis is not available. IVIg is absolutely necessary.

II. IVIg IS A WELL ACCEPTED THERAPY FOR GBS

As early as 2000, IVIg was considered, "the standard treatment for GBS in the United Kingdom and most neurology departments in Europe and the United States." Wiles, C.M., et al., "Intravenous immunoglobulin in neurological disease: a specialist review." *J Neuro Neurosurg Psychiatry* 2002;72:440-448.¹

The American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) and the European Federation of Neurological Societies (EFNS) both support treating GBS patients with IVIg due to the large amount of evidence from randomized,

¹ This article was published based on the results of a meeting of the authors in November 2000.

controlled clinical trials. Donofrio P.D., et al., "Consensus statement: the use of intravenous immunoglobulin in the treatment of neuromuscular conditions report of the AANEM ad hoc committee." *Muscle Nerve*. 2009;40(5):890-900. Elovaara, I., et al., "EFNS guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases: EFNS task force on the use of intravenous immunoglobulin in treatment of neurological diseases." *Eur J Neurol*. 2009 Sep;15(9):893-908.

Most insurance companies, including Aetna, Anthem and CIGNA, cover IVIg for treating GBS. Aetna Clinical Policy Bulletin no 0206. http://www.aetna.com/products/rxnonmedicare/data/INJ/IVIG_2007.html <last accessed 3/22/10>; CIGNA Coverage Policy Immune Globulin Intravenous (Human) (IGIV). Coverage Position 5026. http://www.cigna.com/customer_care/healthcare_professional/coverage_positions/pharmacy/ph_5026_coveragepositioncriteria_Immune_Globulin_Intravenous_IGIV.pdf. <last accessed 3/22/10>; Anthem Clinical UM Guideline IVIg. http://www.anthem.com/medicalpolicies/guidelines/gl_pw_a053678.htm. <last accessed 3/22/10>.

Many articles in the medical literature, including the respected Cochrane Database System Review, also support the use of IVIg for GBS. Hughes, R.A., et al., "Clinical applications of intravenous immunoglobulins in neurology." *Clin Exp Immunolo*. 2009 Dec; 158 Suppl 1:34-42.

Randomised [sic] trials in severe disease show that intravenous immunoglobulin started within two weeks from onset hastens recovery as much as plasma exchange, which is known to be more effective than supportive care. Treatment with intravenous immunoglobulin is significantly more likely to be completed than plasma exchange.

Hughes, R.A., et al., "Intravenous immunoglobulin for Guillain-Barre syndrome." *Cochrane Database Syst Rev*. 2006 Jan 25;(1):CD002063.

In fact, "Intravenous **immunoglobulin (IVIg) is the first choice treatment for Guillain-Barre syndrome (GBS).**" (Emphasis added). Kuitwaard K., et al., "Pharmacokinetics of intravenous immunoglobulin and outcome in Guillain-Barre syndrome." *Ann Neurol*. 2009 Nov;66(5):597-603. IVIG has even been found to be "safe and effective treatment for childhood GBS, which shortens the time to recovery." Yata, J., et al., "High-dose immunoglobulin therapy for Guillain-Barre syndrome in Japanese children." *Pediatr Int*. 2003 Oct;45(5):543-9.

Perhaps Harel and Schoenfeld have summarized it best:

A number of randomized, controlled studies have shown IVIg to be at least as effective as PE in the treatment of GBS, and in some cases superior. Moreover, IVIg has been found to be safer than PE, having a lower frequency of multiple

complications. IVIg has also been found to be both effective and safe in the treatment of pediatric patients with GBS. Thus, its efficacy, safety, and availability make IVIg the treatment of choice in many patients with GBS.

Harel, M., Shoenfeld, Y., "Intravenous immunoglobulin and Guillain-Barre syndrome." *Clin Rev Allergy Immunolo.* 2005 Dec;20(3):281-7.

Thus, the medical literature overwhelmingly supports the use of IVIg in treating GBS.

Indeed, it is urgent that Patient receive this treatment immediately. "Despite medical treatment, GBS often remains a severe disease; 3-10% of patients die and 20% are still unable to walk after 6 months. In addition, many patients have pain and fatigue that can persist for months or years." Van Doorn, P.A., et al., "Clinical features, pathogenesis and treatment of Guillain-Barre syndrome." *Lancet Neurol.* 2008 Oct;7(10): 939-50. GBS can cause total paralysis and is life-threatening. It can cause the patient to stop breathing and interfere with heart-rate. National Institute of Neurological Disorders and Stroke. "Guillain-Barre Syndrome Fact Sheet." http://www.ninds.nih.gov/disorders/gbs/detail_gbs.htm <last accessed March 16, 2010>.

It should also be noted that the older a patient is, the worse the prognosis (vanDoorn, *supra*) and that "the sooner appropriate treatment is started, the better the chance of a good outcome." Mayo Clinic, "Guillain Barre syndrome." <http://www.mayoclinic.com/health/guillain-barre-syndrome/DS00413/DSECTION=coping-and-support> <last accessed March 16, 2010>. "Recovery occurred faster in the group randomized for early treatment." Korinthenberg R, et al. "Intravenously administered immunoglobulin in the treatment of childhood Guillain-Barre syndrome: a randomized trial." *Pediatrics.* 2005 Jul;116(1):8-14.

There is no treatment available to Mr. Patient that carries with it the same promise of safety and efficacy as IVIg. As explained above, corticosteroids have shown no improvement. In fact, "oral corticosteroids given for two or more weeks significantly slowed recovery [in GBS]." Hughes R.A., et al., "Immunotherapy for Guillain-Barre syndrome: a systematic review." *Brain.* 2007 Sep;130(Pt9):2245-57. Plasmapheresis is both available and unwise. There are many possible complications from plasma exchange treatment including "venous access, risk of pneumothorax and bleeding, sepsis, hypotension from labile blood pressure and cardiac arrhythmias associated with autonomic instability." Lindenbaum Y., et al., "Treatment approaches for Guillain-Barre syndrome and chronic inflammatory demyelinating polyradiculoneuropathy." *Neurol Clin.* 2001 Feb;19(10):187-204. Lindenbaum goes on to say that IVIg is attractive because of the ease of administration, especially in the ICU setting, and due to its possible protection against sepsis.

Therefore, IVIg is the best option for this gentleman whose health and mobility are deteriorating rapidly. The medical literature supports this use of IVIg as a safe and effective medication for treating GBS. In fact, “the efficacy, safety and relative availability of IVIg compared with PE has made it the treatment of choice in GBS today.” Harel and Shoenfeld, *supra*.

III. CONCLUSION

There is ample medical literature upon which to base the use of IVIg for GBS. All alternatives present significant risks that are not present with IVIg. This is a previously healthy 50 year old man whose physical condition is slipping away. His doctor believes that he should be treated with IVIg immediately. Dr. Surgeon fears that Mr. Patient could develop total paralysis or need to be placed on a respirator without treatment. Corticosteroids are not helping. There is no plasma exchange available at Hopeful Hospital and Mr. Patient is too sick to move. The earlier the treatment is started the more effective it will be. Therefore, the safest alternative is immediate induction with IVIg. Without effective treatment, Mr. Patient’s medical bills for a respirator, rehabilitation, physical therapy, and other needs will skyrocket far beyond the cost of IVIg. Thus, it is in both Wonting’s interest and Mr. Patient’s to try IVIg therapy.

For all of these reasons, we urge you to reverse Wonting’s noncoverage decision and give this man a chance at the safe and effective treatment that his treating physician deems most appropriate.

Of course, if you would like any additional information, please do not hesitate to contact me. Thank you.

Sincerely,

Representative of Patient