

April 26, 2010

United Healthcare
Provider Appeals
P.O. Box 30559
Salt Lake City, UT 84130-0575

RE: Patient
Type of service: IVIg
Dates of service: To be determined (prior authorization)

Dear Sir or Madam:

I am writing on behalf of your insured, Patient, to request an appeal of United Healthcare's noncoverage decision of Intravenous Immunoglobulin (IVIg) to treat inclusion body myositis (IBM). My HIPAA release and authorization to represent Mr. Patient in this appeal is enclosed.

In sum, this is an older patient with progressive IBM. There is no other effective remedy. If it works, it will allow Mr. Patient to continue to live independently and productively despite his progressing and debilitating IBM.

United Healthcare takes the position that using IVIg to treat IBM is experimental. However, the use of IVIg in this case is supported by the medical literature. In fact, positive effects were noted in the very articles United Healthcare cites to deny IVIg. United Healthcare Drug Policy Immune Globulin (IVIg) Effective 11/19/2009. <https://www.unitedhealthcareonline.com/ccmcontent/ProviderII/UHC/en-US/Assets/ProviderStaticFiles/ProviderStaticFilesPdf/Tools%20and%20Resources/Policies%20and%20Protocols/Medical%20Policies/Drug%20Policies/IVIg_policy.pdf> (Last accessed 4/20/10). One of those articles concluded by saying, "**We suggest offering patients the chance of benefiting from IVIG on an individual trial basis.**" Walter, M., et al., "High-dose immunoglobulin therapy in sporadic inclusion body myositis: a double-blind, placebo-controlled study." *J Neurol*(2000) 247:22-28 (emphasis added).

United Healthcare has the discretion to cover IVIg in this case based on the medical literature submitted along with extensive clinical records. United Healthcare should exercise this discretion in this case, in which a heretofore independent man's life hangs in the balance, and no viable alternative treatments are available.

I. Mr. Patient Suffers Devastating Symptoms of IBM that Demand Treatment

On September 19, 2009, Mr. Patient was taken to Friendly Hospital due to injuries he sustained after falling on the stairs at the entrance to his workplace. During the intake interview, Mr. Patient stated that he had been feeling weaker over the previous two years. He got tired more easily when walking, and his grip was not nearly as strong as it used to be. Dr. Doctor performed an exam that showed Mr. Patient had difficulty rising from a chair and that his right foot dropped when walking. Dr. Doctor also found indications of atrophy in Mr. Patient's wrist, fingers and quadriceps. Mr. Patient could make a fist with his left hand, but could not close his fingers completely with the right.

Mr. Patient was admitted to the hospital to treat his injuries and to perform some tests. Doctor suspected Mr. Patient had a form of myositis. He ordered blood tests first. The results showed modestly elevated levels of serum creatine kinase. (See 9/20/2009 blood test results). To confirm the diagnosis of myositis, Dr. Doctor followed with a muscle biopsy of Patient's quadriceps. (See 9/21/2009 muscle pathology report). The results were typical for myositis showing the typical "rimmed vacuoles." These tests confirmed myositis.

Dr. Doctor then focused on isolating the type of myositis Mr. Patient suffered from. The lack of skin rash ruled out dermatomyositis. The weakness of wrists and fingers along with the only moderately elevated creatin kinase indicated inclusion body myositis (IBM) rather than polymyositis. Dr. Doctor ordered no treatment at that time because IBM does not respond well to steroids or other immunotherapy and sometimes stabilizes on its own. (See Sept. 22, 2009 Friendly Hospital discharge summary)

However, Patient's IBM continued to progress. At his check-up, Patient reported increased difficulty walking, frequent tripping, and low endurance. He was also beginning to have trouble swallowing. (See November 15, 2010 Doctor's notes).

The only treatment Doctor has recommended is IVIg. He cites research stating that IVIG is the only possible treatment for IBM and that high-dose steroids may actually have a negative effect on IBM. (See April 16, 2010 note by Dr. Doctor requesting authorization for IVIg therapy). Thus, we ask that UnitedHealthcare reverse its decision and permit Mr. Patient to undergo a trial of IVIg to see if his IBM responds as well as Dr. Doctor anticipates.

II. Use of IVIg Is Supported by the Medical Literature

United Healthcare has denied coverage of IVIg for IBM on the ground that it is experimental or investigational. In some sense, every treatment for IBM is experimental because there it is rare and there are not large enough cohorts to conduct large, long-term, randomized, double-blind studies. However, this is not an argument for denying all treatment. Lack of treatment can lead to serious consequences. "s-IBM¹ is the most common, progressive, debilitating muscle disease beginning in persons over age 50 years. . . . The progressive course of s-IBM leads slowly to severe disability Sudden falls,

¹ Sporadic inclusion body myositis is referred to as s-IBM. The medical literature treats the two interchangeably.

sometimes resulting in major injury to the skull or other bones, can occur Dysphagia can occur Respiratory-muscle weakness can sometimes eventuate." Engel W. and Askanas V., "Inclusion-body myositis: clinical diagnostic and pathologic aspects." *Neurology* 2006;66(Suppl 1):S20-S29. Patients with IBM also have been known to develop severe depression requiring hospitalization. Recher M., et al., "Treatment of inclusion body myositis: is low-dose intravenous immunoglobulin the solution?" *Rheumatol Int.* 2010 Jan 1 [Epub ahead of print]. Mukunda B.N., et al., "Long-lasting effectiveness of intravenous immunoglobulin in a patient with inclusion-body myositis." *Ann Intern Med.* 2001 Jun19;134(12):1156

A trial of IVIg is supported by the medical literature. Indeed, there are several physicians who believe that, "[a]t the moment intravenous immunoglobulins are the only therapeutic possibility." Pongratz D. "Therapeutic options in autoimmune inflammatory myopathies" *J Neurol*(2006) 253[Suppl5]:V/64-5. "In s-IBM, where there is significant muscle fiber atrophy, **high-dose steroids may be deleterious** by affecting the thick filaments of the already atrophic or myogenously denervated fibers. . . ." Dalakas, MD et al., "A controlled study of intravenous immunoglobulin combined with prednisone in the treatment of IBM." *Neurology* 2001;56;323-327 (emphasis added). Thus, IVIg not only is not experimental or investigational; it is the only safe and effective treatment available for Mr. Patient.

United Healthcare's own policy guidelines cite several studies that show improvement for patients with IBM when treated with IVIg. For instance, in an open-label trial, four patients treated with IVIg showed improved or normalized muscle strength that lasted 2 to 4 months in 3 of 4 patients. United Healthcare, *supra*. The 1997 study by Dalakas and others showed that "the drug induced functionally important improvement in 6 (28%) of the 19 patients." Dalakas, M.D., et al., "Treatment of inclusion-body myositis with IVIG: A double-blind, placebo-controlled study," *Neurology* 1997;48:712-716.

A 2000 study by Walter produced even better results. "Overall there was no progression of the disease in 90% of patients, unlike that which might have been expected in untreated patients. A mild and significant improvement (11%) in clinical symptoms was found. . . . Activities of daily life as evaluated by NSS showed a stabilization in the treated group and a trend to a decline in the untreated group." Walter concluded by saying:

Therapy with IVIG promises stabilization of disease as well as moderate improvement in the activities of daily life for many but not all s-IBM patients. . . . Slowing of disease progression or moderate improvement for a limited time may give s-IBM patients additional years of acceptable quality of life by maintaining reasonable strength and activity. . . . We suggest offering patients the chance of benefiting from IVIg on an individual trial basis.

Walter, *supra*. Thus, Mr. Patient should at least be given a trial of IVIg to see if it will stop his steady decline.

United Healthcare describes the 2001 study by Dalakas, et al., as showing that "[n]o significant change in QMT [Quantitative Muscle Strength] and MRC [Medical Research Council scores] was noted from baseline at each month after treatment between the two groups." United Healthcare, *supra*. However, UnitedHealthcare's discussion does not mention that Dr. Dalakas noted several problems with the study's design – the patients' age, the concomitant use of steroids that may actually have had a negative effect, and the

length of the study – that may have contributed to the less-than-hoped-for results. Dalakas, et al., A controlled study of intravenous immunoglobulin combined with prednisone in the treatment of IBM, *Neurology* 2001;56;323-327 2001.

United Healthcare also failed to report more recent research has shown promise in treating IBM with low dose IVIg. Recher, et al., present “a case of a 70-year-old woman with diagnosed inclusion body myositis that showed progressive muscle weakness without treatment and following immuno-suppressive treatment with corticosteroids and azathioprine. . . . The patient responded rapidly to low dose IVIG treatment with amelioration of muscle strength and normalization of CK serum activities. . . . Elevated muscle enzymes normalized within 1 month and since then without exception stay within normal range for now 12 months after initiation of IVIG therapy. Control MRI scans of the leg muscles now failed to detect active myositis.” They consider the possibility that previous experiments with high doses of IVIg were actually counterproductive to showing significant improvement “because of temporarily increased blood viscosity and/or direct toxic effects of immunoglobulins on the already abnormal myocytes in IBM.” Recher, *supra*.

Recher, et al. support this proposition with the incredible results reached by Mukunda, et al., achieved with low-dose IVIg. Mukunda, et al., treated a 63-year-old woman with IBM who became wheel chair bound and was so severely depressed that she had been admitted to an inpatient psychiatric hospital. “She was given intravenous immunoglobulin . . . 24 g every 2 weeks for 12 doses. Her muscle strength improved, and **she was able to walk independently in 3 months. She maintains her activity level after 2 years.**” Mukunda, *supra* (emphasis added). IVIg has done nothing short of giving this and other patients their lives back.

Time is very much of the essence for treating Mr. Patient. Mr. Patient’s case is now progressing with symptoms – weakness in legs and hands, tripping, and dysphagia – that have become increasingly severe and disabling. Since the only possible treatment Doctor suggests is IVIg, UnitedHealthcare should allow a trial of IVIg in an effort to stem the progression of this disease.

Without the IVIg, we know that his condition will worsen. As is the case in IBM patients who are not treated, he could fall again and break bones. His dysphagia could worsen to the point of needing a feeding tube. He could even have trouble breathing and develop depression severe enough to require hospitalization. In short, the literal application of UnitedHealthcare’s policy regarding IVIg would mean denying Mr. Patient any treatment at all. This is unacceptable. Mr. Patient is 60 years old. If IVIg were to work, he would retain his ability to work and live independently. Without it, he is condemned to a shortened life in pain, with feeding tubes and oxygen, and repeated hospitalizations.

In sum, there is ample medical literature to support the use of IVIg in treating IBM. Therefore, the noncoverage decision should be reversed.

III. Conclusion

IVIg should be covered. Without effective treatment, Mr. Patient's medical bills for hospitalization, rehabilitation, physical therapy, and other needs will skyrocket far beyond the cost of IVIg. Thus, it is in both UnitedHealthcare's interest and Mr. Patient's to try IVIg therapy. Of course, if you would like any additional information, please do not hesitate to contact me. Thank you.

Sincerely,

Patient Advocate