

**IRO NOTICE OF DECISION TEMPLATE – HC**

---

**IRO Express Inc.**

An Independent Review Organization

835 E. Lamar Blvd. #394

Arlington, TX 76011

Fax: 817-549-0310

## Notice of Independent Review Decision

SENT TO: Texas Department of Insurance  
Health & Workers' Compensation Network Certification and QA  
Division (HWCN) MC 103-5A  
E-mail [IRODecisions@tdi.state.tx.us](mailto:IRODecisions@tdi.state.tx.us)

Jennifer Jaff  
Fax: 860-674-1378

Suzanne Gazda  
Fax: 210-692-9311

Guardian Life Insurance Co.  
Attn: Nancy Loveau  
Fax: 920-749-6229

Medical Review Institute of America  
Attn: Jeff Rollins  
Fax: 801-261-3189

March 18, 2008

RE: IRO Case #: 12515  
Name: ~~XXXXXXXXXX~~  
Type of Review: Health Care (non-workers' compensation)

IRO Express has been certified, certification number 5347, by the Texas Department of Insurance (TDI) as an Independent Review Organization (IRO). TDI has assigned this case to the IRO for independent review in accordance with the Texas Insurance Code and applicable regulations.

The IRO has performed an independent review of the proposed/rendered care to determine if the adverse determination was appropriate. In the performance of the review, the IRO reviewed the medical records and documentation provided to the IRO by involved parties.

This case was reviewed by a Neurologist. The reviewer has signed a certification statement stating that no known conflicts of interest exist between the reviewer and the patient, the patient's insurance carrier, the utilization review agent (URA), any of the treating physicians or health care providers who provided care to the patient, or the URA or insurance carrier health care providers who reviewed the case for a decision regarding medical necessity before referral to the IRO. In addition, the reviewer has certified that the review was performed without bias for or against any party to the dispute.

As an officer of IRO Express Inc., I certify that:

1. there is no known conflict between the reviewer, the IRO and/or any officer/ employee of the IRO with any person or entity that is a party to the dispute, and
2. a copy of this IRO decision was sent to all of the parties via U.S. Postal Service or otherwise transmitted in the manner indicated above on March 18, 2008.

Sincerely,  
IRO Express, Inc.



Reed Prejean  
President & Chief Resolutions Office

## **IRO REVIEWER REPORT TEMPLATE – HC**

---

**DATE OF REVIEW:** 03/16/08

**IRO CASE #:** 12515

**DESCRIPTION OF THE SERVICE OR SERVICES IN DISPUTE**

Intravenous immunoglobulin (IVIG)

**A DESCRIPTION OF THE QUALIFICATIONS FOR EACH PHYSICIAN OR OTHER HEALTH CARE PROVIDER WHO REVIEWED THE DECISION**

M.D., Board Certified Neurologist practicing full time, in practice since 1974, Fellow of the American Academy of Neurology and the American Academy of Disability Evaluating Physicians, having taken care of many kinds of neurologic disorders including many cases of multiple sclerosis

**REVIEW OUTCOME**

Upon independent review the reviewer finds that the previous adverse determination/adverse determinations should be:

- Upheld (Agree)
- Overturned (Disagree)
- Partially Overturned (Agree in part/Disagree in part)

**INFORMATION PROVIDED TO THE IRO FOR REVIEW**

Total Pages from URA 181 pages  
 Letter from Advocacy for Patients 3/10/08, 2/12/08  
 Medical Review Institute of America 2/19/08, 1/25/08  
 Letter from BCBS of TX No date  
 MRI, Lumbar and Thoracic Spines and Brain 7/22/04, 6/14/05, 12/27/05, 7/12/06, 12/20/07  
 Pathology Reference Lab and Dr. Munoz 4/5/07  
 Literature on IVig No Date  
 Medical Records from Garza 7/04 thru 1/08  
 Letter from Guardian 2/07 thru 7/07

**PATIENT CLINICAL HISTORY [SUMMARY]:**

1. The Reviewer reviewed records from Dr. Susan Gazda, which state she first saw the claimant on 07/21/04. In those records she stated the claimant has MRI scan findings

- of a demyelinating plaque in the midthoracic region and has had three or four demyelinating lesions in the brain. She thinks this is diagnostic of multiple sclerosis, and she was recommending a course of IV Solu-Medrol.
2. The next recorded notes are 03/23/05. She states that the claimant is having stiffness and a feeling of heaviness in her legs while she was walking. She noticed increased fatigue and no numbness and tingling. Her examination at that visit showed her walking gait as totally balance and within normal limits. Her strength was normal. There was no weakness or heaviness. Dr. Gazda felt the claimant she was having signs and symptoms of relapse and recommended Baclofen tablets in the evening and increased to two tablets. The claimant also became tearful during that visit, and Dr. Gazda felt she was depressed and gave her Lexapro 10 mg a day.
  3. The claimant was seen on 05/18/05. She had started Baclofen for spasticity. The Baclofen seemed to help for a few weeks, but then she developed shortness of breath after reading about Baclofen. Dr. Gazda felt her legs were not probably spastic, but more fatigability. It was Dr. Gazda's opinion that the claimant had been on Copaxone and recommended a repeat MRI scan. The last sets of MRI scans were over a year ago. At that time her C-spine and T-spine were normal, and the brain had shown some scattered white matter lesions. She felt that the claimant's legs were predominantly due to fatigue and not spasticity. She stated they gave the claimant a course of IV Solu-Medrol, and she did not tolerate it. She felt extremely fatigued and wiped out after the Solu-Medrol. She felt the claimant was actually depressed and anxious.
  4. The claimant was seen again on 06/14/05. Dr. Gazda reviewed the results of the MRI scan. The brain and thoracic MRI scan was stable. The brain showed three white matter lesions, all in the same location. There was no evidence of enhancement. Her thoracic MRI scan showed scattered demyelination, unchanged from her original study a year ago. The MRI scan of the cervical spine showed patches areas of demyelination. Dr. Gazda felt, because of these MRI scan findings and based on the patient's symptoms with increased lower extremity weakness and fatigue, that she was showing some disease progression on Copaxone. She also felt that she may be having side effects related to Copaxone. Her opinion was that the claimant had relapsing and remitting MS with recent relapse, probably within the last few months, with MRI scan showing evidence of disease progression and side effects to Copaxone. She recommended that the claimant should begin Betaseron with a slow dose titration.
  5. The claimant was seen again on 12/21/05. She was doing well. She was having a little more droopiness involving the left eyelid. Her visual acuity was normal. She was having some stiffness. Her depression was also better. She was taking Lexapro at the time. Her neurologic exam showed slight droopiness of the left eye. All cranial nerves and extraocular movements were normal. There was no nystagmus. Motor and sensory were normal. Reflexes were normal. Her diagnosis was relaxing and remitting MS. The claimant was currently on Betaseron. Dr. Gazda stated in her note that she thought the claimant was tolerating Copaxone well a year ago but was still having problems about fatigue and spasm that would occur at night. She felt the reason she stopped the Copaxone was that the disease showed progression, and there were some side effects of the Copaxone. The claimant had reached a full dose of

- Betaseron by 08/10/05, which began in June 2005, and was doing well. The MRI scan of the brain and thoracic MRI scan were stable.
6. The claimant was seen on 12/21/05. She thought the droopy eyelid was perhaps due to another symptom of MS. She did see an ophthalmologist who did not see any pupillary abnormalities to suggest Horner's syndrome, and she was not sure of the cause of the droopy lid. Acetylcholine receptor antibody studies were normal. She felt the claimant's disease was under good control at that time.
  7. Dr. Gazda reviewed the case and stated the claimant initially had presented in April 2004 with numbness and tingling below the waist, and she had a full workup by another physician, a neurologist, with a negative MRI scan of the thoracic spine on 05/04/04. Also, EMG studies, B12, RPR, and sed rate were normal. Dr. Gazda took over the case when the claimant saw her, and a repeat MRI scan of the spine showed some demyelinating plaques in the midthoracic region and some in the brain. Apparently she was given at the time Solu-Medrol and responded well. The claimant was having other symptoms at this current visit in December 2005 including some sexual dysfunction, which was felt to be secondary to Lexapro, but her depression and anxiety were normal. Dr. Gazda felt Copaxone was causing shortness of breath, which had resolved when it was discontinued.
  8. The claimant was seen again on 03/01/06. Overall, she was doing well. She did not develop any new symptoms. The ophthalmologist had seen her, and there was no evidence of eye disease. The claimant was taking Betaseron and was doing better and felt it was helping better than Copaxone. She was not developing any new symptoms. She had repeated the MRI scan, which showed some disease stability in the cervical spine and in the brain.
  9. The patient was seen on 03/21/06. Dr. Gazda felt the patient was having a relapse because there was increased lower extremity weakness, low back pain, which was radiating into her legs, which she stated were identical to the initial symptoms she had upon presentation. Dr. Gazda gave her a round of oral prednisone. She felt she was better but was still complaining of some symptoms and worsening fatigue. She apparently did not tolerate IV Solu-Medrol. As a result, Dr. Gazda considered that the patient had an acute relapse and recommended a course of IVIG. She felt that she will have to stop working because of these symptoms.
  10. Dr. Gazda wrote a letter "To Whom It May Concern" on 03/29/06 that the claimant had relapsing and remitting MS with intermittent attacks with fatigue, motor weakness, and gait imbalance and had failed therapy with her drugs. As a result, she recommended IVIG at 2 g/kg.
  11. The patient was seen again on 05/22/06 after her dose of IVIG. She was doing great, felt better, and back pain and leg symptoms had resolved. She was working full time. She had more energy. Her clinical impression was that because she was feeling better that she did not have to take the Provigil that was given to her for fatigue. She was to remain on Betaseron, which she had been placed on in June 2005.
  12. The patient was seen again on 07/12/06. IVIG was helping. Fatigue was better. Back pain was much better. Numbness was still present intermittently. Dr. Gazda's impression of that visit was that she was improving. She was going to repeat neutralizing antibody level and CBC liver function tests. Repeat MRI scan of the brain showed disease was stable. She felt that the depression was mild, and she was

- now off all medication. She recommended continued IVIG treatment once a month for the next three months.
13. Dr. Gazda spoke to the patient on 09/18/06. She was having back pain and leg numbness again, which started over the weekend. Her dose of IVIG had been reduced to 1 g/kg a few months prior to these new symptoms. Dr. Gazda felt that the reduction of the dose from 2 g to 1 g may not have been sufficient during her IVIG treatment.
  14. The patient was seen on 10/12/06. She had been out of town on vacation. She did hiking. Her fatigue was much better, and back pain had resolved. She was scheduled to have another IVIG 2 g/kg.
  15. Dr. Gazda went about summarizing the entire case as it started in May 2004. Dr. Gazda stated that the most recent MRI scan of the cervical spine that was done on 07/12/06 showed no cord abnormalities. Her brain MRI scan showed a single nonspecific increased area in the left frontal periventricular area and midcentral white matter in the right frontal area. The brain MRI scan definitely showed improvement. The thoracic MRI scan showed no cord abnormalities. She felt there was improvement of the MRI scan since the Betaseron and IVIG were given. She stated that on 12/27/05 the cervical MRI scan and brain MRI scan showed more lesions when the patient was only taking Betaseron. She felt that fatigue was definitely better without even using Provigil. She still had the droopiness of the left eye of unknown cause. The antibodies to the acetylcholine receptor were negative. She also had checked the lumbar MRI scan, which only showed some mild disc bulge and was not the cause of the back pain. She recommended continued IVIG 2 g/kg every month for two months then slowly taper.
  16. The patient called Dr. Gazda on 12/21/06 and told her she had gotten worse with the dose reduction of IVIG down to 1 g/kg, and she was going to go up to 2 g/kg.
  17. The patient had called Dr. Gazda on 03/07/07. She was having a lot more problem with back pain and lower extremity weakness. She had not received any further IVIG because of denial, and she seemed to be having more symptoms.
  18. Dr. Gazda saw the patient on 03/20/07. On the visit of 03/20/07 the patient was doing poorly. She had developed increased weakness in her lower limbs, significant back pain, and was having trouble swallowing and severe pain. Her fatigue was very bad. She still was not getting IVIG due to the denial of her treatment. Her examination showed normal speech and language. There was some nystagmus with end gaze on the left and nonsustained, motor strength 5/5 in both upper and lower extremities, reflexes were brisk throughout, and gait was wide-based. She had a positive Romberg and was unable to do heel-to-toe tandem walking. It was Dr. Gazda's opinion that the patient had a relapsing remitting MS, and the IVIG absence was giving her some relapse. Her EDSS score had gone from 0 to 3. Dr. Gazda did not believe there were any other treatment options. She did not want to put her at risk with Tysabri, which can develop progressive multifocal leukoencephalopathy. She did not believe Novantrone would be as effective as IVIG, and she did not believe Copaxone was helpful in the long term. Betaseron alone was not controlling her disease. She believed that Solu-Medrol caused her to have more weakness and side effects.

19. The claimant had received a course of IVIG in April, and Dr. Gazda wrote a note on 05/21/07. Prior to this dose, she was functioning at work, but now she was having weakness, overwhelming fatigue, and progressive swallowing difficulty. Full GI workup suggested her swallowing problem was due to a central neurologic disorder. Neurologic examination showed unsteadiness, slight tremor, and some vibration loss in the lower extremities. Her EDSS score was 2.
20. The claimant was seen on 08/28/07. She had her second course of IVIG since July 2007. She had a dramatic improvement of her symptoms with improved swallowing. She had developed painful burning in her feet, which improved after the IVIG. Her balance also improved. Fatigue was still an issue but was better following IVIG. No new symptoms were noted. Her neurologic examination was essentially normal with an EDSS score of 0. Her diagnosis was still relapsing and remitting MS with improvement in stability on IVIG. Dr. Gazda was going to put the Betaseron on hold for a month or two and see if she was able to maintain the stability just on IVIG treatment.
21. The patient was seen on 10/24/07. She was feeling very well with dramatic benefit of IVIG, which is her fourth dose. She was able to go on vacation and keep up with her activities. Her fatigue level was much better, and her balance was much better. EDSS was normal. The plan was to continue IVIG 2 g/kg a month. She was going to monitor the MRI scan changes before her next visit.
22. On 12/20/07 MRI scan of the cervical spine did not show any spinal cord abnormalities. The MRI scan of the thoracic spine on the same date showed a few small areas of signal in the central spinal cord at T5 and T8. The note by the radiologist is that these areas of signal that were seen were new and more readily apparent as compared to the previous study of 07/12/06.
23. Dr. Gazda reviewed the MRI scan reports that were done in December 2007. She stated that in June 2005 the claimant did have a signal abnormality in the cervical cord, which now is not present. The thoracic area that was done in that year showed abnormalities at four levels, and now there were only two areas.
24. Dr. Gazda saw the patient again on 01/16/08. She was stable with very little complaints and was swallowing normally. Dr. Gazda felt that the MRI scan showed improvement from the prior study overall. EDSS score was 0.
25. Other records available for review were all the MRI reports that had been done in this case, and the Reviewer had already reviewed them individually as the Reviewer went through the history of Dr. Gazda's medical records.
26. The Reviewer also reviewed letters from an advocacy group for the patient and guardian.
27. The other area of review was the report from the previous physician dated 02/19/08 who had reviewed this case and denied further IVIG. The reviewer stated that IVIG had not been approved by the FDA as a modifying therapy in MS, and he had reviewed the therapies for MS that are currently available, which include Copaxone, Avonex, Rebif, Betaseron, Tysabri, and Novantrone. He also stated that the efficacy of IVIG treatment was currently most convincing in relapsing remitting MS, but it is not as good as the other treatments. The dosage was also not clearly established. He also stated the EDSS scores improved compared to placebo, and relapses were reduced, but chronic deficits were not reversed or improved by long-term IVIG treatment. He stated also in

his review that approaches to breakthrough disease include increasing the dose of Interferon, which already has been used, or switching to Copaxone, and that patients who failed this approach should be initiated on the mitoxantrone. Also, Tysabri can be used as monotherapy for those who have had inadequate response to other disease-modulating agents. Comments were also made that the episodes of acute neurologic symptoms were not substantiated by the changes on the MRI scan. She had never had any enhancing lesions, and the neurologic exam did not show any specific findings when the claimant was switched from Copaxone to Betaseron. He also felt there was no objective documentation on the examination, only symptoms of back pain, leg weakness, and fatigue. The reviewer stated that the claimant was taking Betaseron and IVIG until 08/28/07, and when they reduced the IVIG, this caused further symptoms. These symptoms remained until the IVIG was given. He also stated there was no literature showing the IVIG improves the acute or chronic signs and symptoms of relapsing remitting MS or lowering of the dose will cause temporary related signs or symptoms. The reviewer felt that IVIG was not medically necessary for this claimant because the records have not shown definitive failure of Betaseron as evidenced by lack of enhancing MRI lesions or a definite increase in the number of exacerbations. The temporal relationship between IVIG and her symptoms appearance and disappearance could not be documented in the literature for the diagnosis of MS. He also felt that if the patient had failed on Copaxone and Betaseron, she should have been treated with Novantrone or Tysabri, which are both FDA approved.

**ANALYSIS AND EXPLANATION OF THE DECISION INCLUDE CLINICAL BASIS, FINDINGS AND CONCLUSIONS USED TO SUPPORT THE DECISION.**

After a careful review of all medical records and literature regarding IVIG, the Reviewer's medical assessment is that this claimant should continue to be treated with intravenous gamma globulin for her multiple sclerosis disorder. From the standpoint of the clinical picture, the Reviewer's medical assessment is that this claimant, in all medical probability, had relapsing and remitting multiple sclerosis. It would have been of some value for this patient to have lumbar puncture for further evaluation of oligoclonal bands and IGG abnormalities that are often seen in this disorder, but the nature of the history, the MRI scan lesions, and the course of the claimant's symptoms are certainly compatible with the diagnosis of multiple sclerosis. The Reviewer also believes that there is evidence in the medical records that the lesions seen on MRI scan had fluctuated with the treatment and seemed to recur at the time that the claimant's symptoms were most severe. Granted, the claimant's symptoms were predominantly fatigue, pain, numbness, and balance difficulties with very little objective neurological signs, but this is not unusual in many cases with multiple sclerosis. There appeared to be evidence of side effects of Copaxone and also evidence of recurrence of symptoms and some new lesions while the patient was on Copaxone and some improvement with Betaseron. However, there had been dramatic improvement with IVIG in many of the followup visits with the patient. We do know that fatigue is a major factor along with poor balance and numbness and tingling in this disorder, and these symptoms tended to disappear when IVIG was administered and maintained even when Betaseron was discontinued. The Reviewer realizes that in individual cases it can be difficult to find

objective changes on neurologic examination when the symptoms of fatigue, balance, and numbness are also highly subjective symptoms. One also has a tendency to believe that many of these treatments can have a placebo effect, but this is always the difficulty in a disease like multiple sclerosis. It appears that the claimant's best improved symptoms have been with IVIG without any side effects and continue to remain for longer periods of time during the IVIG treatments with a tendency to relapse when the IVIG dose was discontinued or when the dose was decreased to half the amount.

There is an excellent review article on the current status of intravenous gamma globulin in multiple sclerosis by Per Solberg Sorenson published in "Neurodegenerative Diseases, 2008, Volume 5," page 815. This article, which basically reviews all the articles prior to this article, covers all the positive and negative trials in this disorder. In the discussion and conclusion of this article, it states that all the published randomized studies in relapsing remitting MS have shown evidence of a beneficial effect of IVIG, which is based primarily on relapses and MRI changes. It has also been difficult to compare the IVIG benefits with the approved therapies that are currently present today, particularly the Betaseron and the Copaxones. It appears that IVIG is probably equivalent to help reduce the relapse rates as these other current therapies. It also suggests that the effect on the disease itself and MRI scan changes may not be quite as robust as in the other immunological treatments. The conclusion reached in the article is that IVIG can be considered an alternative to established therapies in relapsing and remitting MS, but the ideal dose is still not totally clear. The majority of these studies have used doses of 0.2 g/kg to 0.4 g/kg, and other studies have used higher doses of 1 g/kg to 2 g/kg. The important point also is that very few side effects and any long-term complications have essentially not been reported.

The summary of all of the articles suggests that IVIG can be considered as second line therapy in this disorder in people particularly who do not respond to Copaxone or Betaseron products or have contraindication to other approved therapies. It is certainly not recommended for first line treatment, but in this case it is being used as a second line of treatment based, in my opinion, on adequate reasons to change the treatment program. We also have to take into account that each case still has to be taken as an individual case. The Reviewer's medical assessment is that since this patient had made fairly dramatic improvements with some MRI scan changes to show less disease, this is important in making a decision on the benefits of this treatment. The Reviewer does not believe that the improvement is based on a placebo response. It is true that other treatments such as Tysabri and Novantrone have been approved for multiple sclerosis, but The Reviewer also would concur with Dr. Gazda's comments that there is a risk of developing progressive multifocal leukoencephalopathy, which is a devastating disorder, despite the fact that it is infrequent. Novantrone also is a difficult medication to use and has many more side effect problems and drug monitoring difficulties than IVIG.

Therefore, the Reviewer's would approve the use of IVIG in this patient's disease based on the dramatic clinical response of marked improvement in fatigue and pain, numbness, and balance, and the fact that she is able to return to her normal activities, which is a major plus in this therapy. The Reviewer also would concur with her treating physician

that the other FDA approved medications have much high risk of complications and side effects to warrant their use in this case, particularly since IVIG has been used and appears to be effective in her disorder. The real question is how long this treatment should be given, and this is still unclear. A number of trials have given this treatment for six months and up to a year. The Reviewer would support the use of this medication for at least twelve months.

**A DESCRIPTION AND THE SOURCE OF THE SCREENING CRITERIA OR OTHER CLINICAL BASIS USED TO MAKE THE DECISION:**

- ACOEM- AMERICAN COLLEGE OF OCCUPATIONAL & ENVIRONMENTAL MEDICINE UM KNOWLEDGEBASE
- AHCPR- AGENCY FOR HEALTHCARE RESEARCH & QUALITY GUIDELINES
- DWC- DIVISION OF WORKERS COMPENSATION POLICIES OR GUIDELINES
- EUROPEAN GUIDELINES FOR MANAGEMENT OF CHRONIC LOW BACK PAIN
- INTERQUAL CRITERIA
- MEDICAL JUDGEMENT, CLINICAL EXPERIENCE AND EXPERTISE IN ACCORDANCE WITH ACCEPTED MEDICAL STANDARDS
- MERCY CENTER CONSENSUS CONFERENCE GUIDELINES
- MILLIMAN CARE GUIDELINES
- ODG- OFFICIAL DISABILITY GUIDELINES & TREATMENT GUIDELINES
- PRESSLEY REED, THE MEDICAL DISABILITY ADVISOR
- TEXAS GUIDELINES FOR CHIROPRACTIC QUALITY ASSURANCE & PRACTICE PARAMETERS
- TEXAS TACADA GUIDELINES
- TMF SCREENING CRITERIA MANUAL
- PEER REVIEWED NATIONALLY ACCEPTED MEDICAL LITERATURE
- "Neurodegenerative Diseases, 2008, Volume 5," page 815
- OTHER EVIDENCE BASED, SCIENTIFICALLY VALID, OUTCOME FOCUSED GUIDELINES (PROVIDE A DESCRIPTION)