



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Adrenal-to-Brain and Fetal Mesencephalic Transplantation for Parkinson’s Disease

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Deep Brain Stimulation

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant’s particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant’s benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2008 CIGNA

Coverage Policy

CIGNA does not cover adrenal medullary-to-brain transplantation for Parkinson’s disease because it is considered experimental, investigational or unproven

CIGNA does not cover human or xenogeneic fetal mesencephalic transplantation for Parkinson’s disease because it is considered experimental, investigational or unproven.

General Background

Parkinson's disease (PD) is a slowly progressive neurodegenerative disorder caused by impaired dopamine neurons in the substantia nigra. The substantia nigra is part of the mesencephalon (i.e., mid-brain) that controls balance and coordinates muscle movement. Dopamine is a neurotransmitter, carrying information between neurons, allowing signals from the brain to reach the muscles. As the dopamine neurons degenerate, signals between the brain and the body become progressively weaker. Eventually, the brain is no longer able to direct or control muscle movement in a normal manner. The symptoms of PD include a shuffling gait, difficulty talking, tremors, rigid muscles and slow movement or the inability to move (National Institutes of Health [NIH], 2005).

According to the NIH (2008), at least 500,000 people in the United States are believed to suffer from PD, and about 50,000 new cases are reported annually. It is slightly more common in men than in women. The average age at diagnosis is 60.

There is no cure for PD (NIH, 2008). To date, treatment has been aimed at relief of symptoms and the increase of dopamine levels in affected neurons. Symptoms may be temporarily minimized with medication designed to replenish or mimic dopamine's actions by reducing muscle rigidity, improving speed and coordination of movement, and relieving tremor. The medications used include levodopa and the dopamine agonists ropinirole, pramipexole, and pergolide. Physical therapy and exercise may be an adjunct to medication. Deep brain stimulation may be an appropriate therapy for certain patients. Surgery, including pallidotomy and thalamotomy, may provide benefit to select patients.

Adrenal to Brain Transplantation

The transplantation of tissues from the adrenal medulla (autograft) and human fetal mesencephalon (allograft) to the striatum of patients with PD has been proposed as a source of dopaminergic neurons. The premise of adrenal medullary transplants is that adrenal cells, when transplanted into the brain of a patient with advanced PD, would survive and function as a new source of dopamine. Immunologic rejection can be avoided by taking the adrenal cells from the patient (i.e., autograft). This; however, results in two surgical procedures for the patient, increasing the risk of surgical complications.

Fetal Mesencephalic Transplantation

In this procedure, fetal brain cells (i.e., neurons) that produce dopamine are implanted in the putamen or head of the caudate area of the brain, which controls movement. In theory, the transplanted neurons can make up for the patient's loss of the normal dopamine-producing cells. Fetal cells may be human or xenogeneic. The patient remains awake throughout the procedure, allowing the surgeon to test speech and motor ability as the cells are implanted.

Literature Review

Adrenal to Brain Transplant

Scarce data exists in the published, peer-reviewed scientific literature regarding the current clinical use of this therapy in the treatment of Parkinson's disease in humans. In a review of the procedure and the documented literature, the American Academy of Neurology (AAN) Task Force on Surgery for Parkinson's Disease (Hallet and Litvan, 1999) found small, nonrandomized case studies which noted functional improvement in some patients; there was, however, an unacceptably high level of morbidity and mortality associated with the procedure. The AAN group also reviewed pathologic reports which found that few transplanted cells survived long term, suggesting that any benefit would be of short duration.

In a systematic review of the literature, the Agency for Healthcare Research and Quality (AHRQ) (2003) also notes that there is a lack of efficacy and substantial morbidity associated with the procedure, and concludes "adrenal medullary transplants are no longer performed to treat PD."

Based on these reviews, insufficient evidence exists to support improved outcomes with the use of adrenal medullary transplants for the treatment of Parkinson's disease and they are considered experimental, investigational and unproven.

Fetal Mesencephalic Transplant

There is ongoing research in animal and human models relative to the use of fetal mesencephalic transplantation for Parkinson's disease. Several recent studies reporting promising results in animals were found in the published, peer-reviewed scientific literature; although there are several clinical trials in progress, at this time scarce studies reporting outcomes in humans were found.

The AAN (Hallet and Litvan, 1999) reviewed the documented studies of fetal mesencephalic transplantation. The studies were small and nonrandomized. There was variation between the studies in the techniques utilized, the site of transplantation, the number of mesencephalons used and the immuno-suppressive regimen provided. In all of the studies, some of the patients demonstrated improvement in motor function. In two of the studies, a patient died from unrelated events, and pathology reports documented healthy appearing graft tissue with large numbers of dopaminergic cells and extensive reinnervation. The summary concludes that, while the procedure is promising because it appears effective and has low morbidity and mortality, it is considered experimental because of the absence of controlled studies.

Subsequent to the AAN review, Freed et al. (2001) conducted a prospective, double-blind, placebo-controlled trial in which 40 patients with PD were randomized to receive either embryonic tissue implants or a placebo operation. The participants were evaluated at 12 months after surgery for functional improvement with the use of the Unified Parkinson's Disease Rating Scale (UPDRS). There was statistically significant improvement in patients under the age of 60 who underwent transplantation. At one year after surgery, there was no difference in outcome between those who received transplant surgery and those who received sham surgery in patients over age 60. The researchers continued to follow the patients after the study concluded and found five patients who underwent transplantation who developed dystonia and dyskinesia more than one year after the surgery, leading the researchers to the conclusion that the surgical technique should be refined.

Another prospective, 24-month, double-blind, placebo-controlled trial of human fetal nigral transplantation was conducted by Olanow et al. (2003). Thirty-four patients were randomized to undergo bilateral transplantation with one or four donors per side for a placebo procedure. Outcomes evaluated were change in baseline and final visits in the motor component of the UPDRS. The researchers found no significant difference between groups. Based on these results, the researchers concluded that fetal nigral transplantation currently cannot be recommended as a therapy for Parkinson's disease.

The only identified study using xenogeneic fetal cells for transplantation was a case series study of 12 patients conducted by Schumacher et al. (2000). Patients were followed for 12 months, and demonstrated significant improvement in UPDRS scores. There were no permanent complications. While promising, this study is limited by its small size and lack of blinding and controls.

Although there appears to be some treatment effect in maintaining or improving motor function, there is a lack of clear patient selection criteria and demonstration of long-term safety and efficacy. Based on the small patient populations, and the lack of long-term improved outcomes noted in these studies, at this time fetal mesencephalic transplantation for Parkinson's disease is considered experimental, investigational and unproven.

U.S. Food and Drug Administration (FDA)

The FDA Center for Biologics and Research regulates the transplantation of fetal/embryonic cells. Companies supplying cell and tissue-based products must register and list their products with the FDA.

Professional Societies/Organizations

The AAN (1999) recommended that adrenal-to-brain transplantation not be performed because of unacceptable risk to the patient. They further noted that the procedure was no longer being studied.

The AHRQ (2003) stated that there was a lack of efficacy and substantial morbidity associated with adrenal-to-brain transplants and that this procedure is no longer being studied.

Regarding fetal mesencephalic transplantation the AAN (1999) notes that, while the procedure is promising, it remains experimental due to lack of controlled clinical trials.

Summary

The premise of adrenal medullary transplantation is the use of adrenal medullary cells as a new source of dopamine production in the brain. Studies are small and uncontrolled, and safety is a concern with this procedure. Evidence in the available published peer-reviewed scientific literature is insufficient to support the use of this therapy for Parkinson's disease (PD). The use of fetal mesencephalic cell transplantation is also based on the premise that cells transplanted into the brain of patients with PD can develop into dopamine-producing cells. While results are more promising, studies are also uncontrolled, compromised by small size, and lack of long-term follow-up. Although this therapy remains a focus of research, scarce peer-reviewed, published literature relative to the use of fetal mesencephalic transplantation in humans with PD was found. At this time the role of this therapy has not been established; the published, peer-reviewed scientific evidence is insufficient to support the use of this therapy for the treatment of PD.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Experimental/Investigational/Unproven/Not Covered:

HCPCS Codes	Description
S2103	Adrenal tissue transplant to brain

ICD-9-CM Diagnosis Codes	Description
332.0	Paralysis agitans
	Multiple/varied

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	12/07/2008	0275	Adrenal-to-Brain and Fetal Mesencephalic Transplantation for Parkinson's Disease

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