



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 Disease

Effective Date 12/15/2010
Next Review Date.....12/15/2011
Coverage Policy Number0275

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Hyperlink to Related Coverage Policies

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 ©2010 CIGNA

Coverage Policy

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

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

General Background

Parkinson 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 that carries information between neurons and allows 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], 2010).

There is no cure for PD. 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 transplantation of tissues from the adrenal medulla (autograft) and human fetal mesencephalon (allograft) to the striatum of patients with Parkinson disease (PD) has been proposed as a source of dopaminergic neurons.

Adrenal-to-Brain Transplantation: The premise of adrenal-to-brain transplantation, also called adrenal medullary transplantation, is that adrenal cells will survive and function as a new source of dopamine when transplanted into the corpus striatum of the brain of an individual with advanced PD. It is thought that immunologic rejection can be avoided by taking the adrenal cells from the patient (i.e., autograft); however, this results in two surgical procedures for the patient, increasing the risk of surgical complications.

There are scarce data in the published, peer-reviewed scientific literature regarding the current clinical use of this therapy in the treatment of PD in humans. In a systematic review of the literature, the Agency for Healthcare Research and Quality ([AHRQ], 2003) noted that there is a lack of efficacy and substantial morbidity associated with the procedure. The AHRQ also concluded that adrenal medullary transplants are no longer performed to treat PD.

On behalf of the American Academy of Neurology (AAN) Task Force on Surgery for Parkinson Disease, Hallet and Litvan (1999) performed a review of the published literature. The authors determined that there were small, nonrandomized case studies which noted functional improvement in some patients; however, an unacceptably high level of morbidity and mortality was associated with the procedure. Review of pathologic reports found that few transplanted cells survived long term, suggesting that benefit of the procedure would be of short duration.

Summary for Adrenal-to-Brain Transplantation: At present there is insufficient evidence demonstrating the safety and effectiveness of adrenal medullary transplantation for the treatment of PD.

Fetal Mesencephalic Transplantation: There is ongoing research in animal and human models relative to the use of fetal mesencephalic transplantation for Parkinson disease. 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 is the area controlling movement. In theory, the transplanted neurons can replace the loss of normal dopamine-producing cells. These fetal cells may be human or xenogeneic.

Clinical improvement was demonstrated in small numbers of individuals with PD undergoing transplantation of fetal tissue in several nonrandomized studies; however, results have not been replicated in double-blind sham-surgery controlled clinical trials (Olanow, 2003; Freed, 2001). Transplantation of fetal substantia nigra into the striatum has failed to show significant efficacy and has been associated with the side effect of transplant-induced off-medication dyskinesias. More recently, implanted dopamine neurons have been found to contain Lewy bodies, suggesting that they are dysfunctional and may have been affected by the PD pathological process (Olanow, 2009).

A 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 Unified Parkinson Disease Rating Scale (UPRS). The researchers found no significant differences between groups. Based on these results, the researchers concluded that fetal nigral transplantation currently cannot be recommended as a therapy for Parkinson disease.

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 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.

On behalf of the AAN Task Force in Surgery for Parkinson Disease (PD) 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 studies in which a patient died from unrelated events, postmortem pathology reports documented healthy appearing graft tissue with large numbers of dopaminergic cells and extensive reinnervation. The summary notes 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.

There are scarce data regarding the use of xenogeneic fetal cells for transplantation in humans. Schumacher et al. (2000) reported results of a case series study of 12 individuals with PD who underwent unilateral implantation of embryonic porcine ventral mesencephalic tissue (Schumacher, 2000). In the medication-off state, total Unified Parkinson's Disease Rating Scale scores improved by 19% (p=.01). At the time of study publication there were no reported permanent complications. Limitations of the study include small size, uncontrolled study design, and short-term follow-up.

Summary for Fetal Mesencephalic Transplantation: Although some short-term treatment effects have been noted in individuals undergoing human or xenogeneic fetal mesencephalic transplantation, studies are limited by a lack of clear patient selection criteria, small patient populations, and short-term follow-up. Long-term safety and effectiveness has not been demonstrated. At this time the role of this therapy for the treatment of PD has not been established.

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

American Academy of Neurology (AAN): On behalf of the AAN, Hallet and Litvan (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. Regarding fetal mesencephalic transplantation the AAN (1999) notes that, while the procedure is promising, it remains experimental due to lack of controlled clinical trials.

The Agency for Healthcare Research and Quality (AHRQ): The AHRQ (2003) noted there is a lack of efficacy and substantial morbidity associated with adrenal-to-brain transplantation and that this procedure is no longer being studied.

Summary

Data are lacking regarding the safety and effectiveness of adrenal medullary-to-brain or fetal mesencephalic transplantation for the treatment of Parkinson disease (PD). The role of these therapies has not been established.

Coding/Billing Information

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

Experimental/Investigational/Unproven/Not Covered:

CPT [®] * Codes	Description
64999*	Unlisted procedure, nervous system

***Experimental, investigational, unproven and not covered when used to report human or xenogeneic fetal mesencephalic transplantation or adrenal medullary-to-brain transplantation for Parkinson disease.**

HCPCS Codes	Description
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S2103	Adrenal tissue transplant to brain
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ICD-9-CM Diagnosis Codes	Description
331.82	Dementia with Lewy bodies
332.0	Paralysis agitans
333.0	Other degenerative diseases of the basal ganglion

***Current Procedural Terminology (CPT®) © 2010 American Medical Association: Chicago, IL.**

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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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Connecticut General Life Insurance Company has acquired the business of Great-West Healthcare from Great-West Life & Annuity Insurance Company (GWLA). Certain products continue to be provided by GWLA (Life, Accident and Disability, and Excess Loss). GWLA is not licensed to do business in New York. In New York, these products are sold by GWLA's subsidiary, First Great-West Life & Annuity Insurance Company, White Plains, N.Y.