

11 July 2006

Steve Phurrough, M. D., M. P. A.
Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Blvd.
Baltimore, MD 21244

Dear Dr. Phurrough,

I would like to submit a formal request for a National Coverage Determination (NCD) for Medicare non-coverage for Blood Brain Barrier Disruption (BBBD) chemotherapy.

The **benefit category** for BBBD chemotherapy includes inpatient hospital services and both inpatient and outpatient physician services.

BBBD Chemotherapy is used in the Medicare population in the treatment of both primary and metastatic central nervous system cancers of multiple types. It is also used both as primary therapy and as secondary therapy following other types of cancer treatment including chemotherapy and radiation therapy.

A **detailed description of the therapy** follows. BBBD Chemotherapy requires the use of multiple modalities including, but not limited to, the following:

- (1) Hospital admission and preoperative evaluation, including blood work and brain imaging studies by CT or MRI, on first hospital day
- (2) Preoperative intravenous hydration therapy on first or second hospital day
- (3) General endotracheal anesthesia on second hospital day
- (4) Transfemoral catheterization and cannulation of femoral artery and internal carotid artery on a single side while under general anesthesia on second hospital day
- (5) Intra-arterial injections of Mannitol followed by intra-arterial injections of chemotherapeutic agent(s) on second hospital day
- (6) Repeat of steps (2), (3), (4), and (5) on the opposite side of the body on third hospital day
- (7) Brain imaging with MRI or CT following each single course of therapy and prior to hospital discharge
- (8) Total hospitalization of four days if no complications occur, or longer than four days when complications occur for each single course of therapy
- (9) Repeat monthly courses of therapy [repeat of steps (1) through (8)] for one year
- (10) Frequent outpatient examinations during the year long course of therapy

Despite over twenty years of repeated use of this technique, the long-term effects of BBBD remain unknown and there are no randomized, controlled trial data to establish the superiority of BBBD with chemotherapy over conventional chemotherapy. Multiple

clinical trials have been utilized and many are ongoing, but no definitive conclusions have been reached regarding the efficacy of this therapy.

In addition to comparing potential risks against potential benefits from this procedure, the costs to the Medicare program to both Part A and Part B Medicare are significant and may be in the range of \$500,000 for each beneficiary who is so treated.

Trailblazer Enterprises LLC (Medicare Part B Contractor) has incorporated a non-coverage policy for this procedure in a Local Coverage Decision (LCD) while Noridian Administrative Services currently has a draft LCD for non-coverage of this procedure. All other Part A and Part B contractors have no BBBD Chemotherapy LCDs and are, therefore, currently paying for this procedure.

The Blood Brain Barrier (BBB) of the Central Nervous System (CNS) prevents toxic substances (including circulating drugs) from entering the brain. The blood brain barrier in some brain tumors is more permeable to circulating drugs so the importance of the BBBD in limiting drug delivery is unclear. BBBD using hyperosmolar agents to temporarily shrink the endothelial cells that form the barrier theoretically may increase the concentration of chemotherapy drugs delivered to the tumor and may prolong the drug-tumor contact time.

Conventional treatments for brain tumor include corticosteroid therapy, operative procedures, radiation therapy and standard chemotherapy.

Osmotic BBBD is an aggressive approach that can be potentially dangerous. Increasing the permeability in regions of normal brain may produce fluid overload that may lead to side effects such as seizures and increased intracranial pressure with risk of obtundation, focal neurologic deficits, cerebral herniation and death. Other risks include vascular injury resulting in stroke in addition to side effects of the chemotherapy agents themselves. The long term effects of repeated BBBD procedures are unknown.

In summary, BBBD Chemotherapy has a higher risk of complications and is considerably more expensive when compared to conventional chemotherapy. Despite over twenty years of repeated use of this technique, the long-term effects of BBBD remain unknown and there are no randomized, controlled trial data to establish the superiority of BBBD with chemotherapy over conventional chemotherapy. Blood Brain Barrier Disruption Chemotherapy does not meet reasonable and necessary criteria for the general Medicare population and, therefore, I am requesting that this be determined a non-covered service for Medicare beneficiaries.

Supporting documentation:

(1) Institute for Clinical Systems Improvement; Technical Assessment Report; Blood Brain Barrier Disruption Chemotherapy; TA#59, November 2001

“ICSI Medical Brief...With regard to blood brain barrier disruption chemotherapy the ICSI Technology Assessment Committee finds...”

<http://www.icsi.org/index.asp>

<http://www.icsi.org/knowledge/detail.asp?catID=107&itemID=268>

(2) Kaal PhD et al; Therapeutic management of brain metastases; The Lancet Neurology; Volume 4, Number 5, May 2005

“...others argue that the BBB has already been disrupted if the brain metastases are detectable.⁵³ **The importance of the BBB for chemotherapeutic drugs has been questioned.** For example, the presence of a contrast-enhancing lesion on imaging indicates a disrupted BBB, implying that brain metastases may be equally sensitive to chemotherapy as metastases elsewhere in the body.”

(3) TrailBlazer Health Enterprises, LLC

LCD for Non-covered Services - Z-14B-R19 (L13344)

Not Medically Necessary...

”64999 Note:Use CPT code 64999 to identify: 1) blood brain barrier disruption...”

Yours truly,

George Waldmann, M. D.
Noridian Medicare Part B Contractor Medical Director
1800 SW First Avenue-Suite 380
Portland, OR 97201
Phone 503-944-8810
Fax 503-944-8814
Email george.waldmann@noridian.com

Enclosures:

(1) Institute for Clinical Systems Improvement; Technical Assessment Report; Blood Brain Barrier Disruption Chemotherapy

(2) Kaal PhD et al; Therapeutic management of brain metastases; The Lancet Neurology; Volume 4, Number 5, May 2005

(3) TrailBlazer Health Enterprises, LLC
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