



BlueCross BlueShield
of Alabama

Name of Policy:

Antineoplaston Cancer Therapy

Policy #: 280

Category: Medicine

Latest Review Date: June 2010

Policy Grade: **Active Policy but no
longer scheduled for
regular literature
reviews and updates.**

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

- 1. The technology must have final approval from the appropriate government regulatory bodies;*
- 2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
- 3. The technology must improve the net health outcome;*
- 4. The technology must be as beneficial as any established alternatives;*
- 5. The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

- 1. In accordance with generally accepted standards of medical practice; and*
- 2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
- 3. Not primarily for the convenience of the patient, physician or other health care provider; and*
- 4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Antineoplastons are a group of medium and small size synthetic peptides and amino acid derivatives that are thought to be components of a biochemical defense system that functions by inducing differentiation in neoplastic cells. Two main groups of antineoplastons have been isolated. One includes compounds with broad spectrum activity in many different cell lines and the other includes compounds with a narrow spectrum of activity against single cell lines. Five of the broad spectrum antineoplastons have been isolated from normal human urine: A1, A2, A3, A4, and A5. Antineoplaston A10 was the first active ingredient that has been reproduced synthetically. Antineoplaston AS2-1 and AS2-5 are metabolites of antineoplaston A10 that have also been synthesized. Antineoplastons A10 and AS2-1 have been most commonly researched as a treatment of a wide variety of malignancies and HIV infections.

Sodium phenylbutyrate (Buphenyl) taken orally is metabolized in the liver into a combination of phenylacetylglutamine and phenylacetate, which then enter the bloodstream. These two chemicals are the prime ingredients of antineoplaston AS2-1.

Policy:

Antineoplaston therapy, including, but not limited to, antineoplaston A10 and AS2-1, **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational** for all conditions, including, but not limited to any malignancy and HIV infection.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

Antineoplastons are a group of synthetic compounds that were originally isolated from human blood and urine by Stanislaw Burzynski, M.D., Ph.D. in Houston, Texas. Dr. Burzynski has used antineoplastons to treat patients with a variety of cancers. In 1991, the National Cancer Institute (NCI) conducted a review to evaluate the clinical responses in a group of patients treated with antineoplastons at the Burzynski Research Institute in Houston.

The medical records of seven brain tumor patients who were thought to have benefitted from treatment with antineoplastons were reviewed by NCI. This did not constitute a clinical trial but, rather, was a retrospective review of medical records, called a "best case series". The reviewers of this series found evidence of antitumor activity and NCI proposed that formal clinical trials be conducted to further evaluate the response rate and toxicity of antineoplastons in adults with advanced brain tumors.

Investigators at several cancer centers developed protocols for two phase II clinical trials with review and input from NCI and Dr. Burzynski. These NCI-sponsored studies began in 1993 at the Memorial Sloan-Kettering Cancer Center, the Mayo Clinic, and the Warren Grant Magnuson Clinical Center at the National Institutes of Health. Patient enrollment in these studies was slow, and by August 1995, only 9 patients had entered the trials. Attempts to reach a consensus on proposed changes to increase accrual could not be reached by Dr. Burzynski, NCI Staff, and investigators. On August 18, 1995, the studies were closed prior to completion. Because of the small number of patients in these trials, the NCI concluded that no definitive conclusions can be drawn about the effectiveness of treatment with antineoplastons.

At present, the Burzynski Research Institute is conducting trials using antineoplastons for a variety of cancers. Information about these trials is available from the Cancer Information Service or the NCI's web site: <http://www.cancer.gov> or http://www.cancer.gov/clinical_trials.

A recent search of the literature identified some case reports, case series, and data from single institution phase II trials. Dr. Burzynski is the author of many of these reports. Two of the more recently published reports are summarized below.

In a Phase II clinical trial, Burzynski, et al (2005), studied the effect of antineoplaston (ANP) therapy in 13 children with primitive neuroectodermal tumors (PNETs) (median age 5 7/12 years, range 1-11 years) with either recurrent disease or high risk. The diagnoses included medulloblastoma (n = 8), pineoblastoma (n = 3), and other PNET (n = 2). Prior therapies included surgery (n = 12), chemotherapy (n = 6), or radiation therapy (n = 6). Six patients had not received chemotherapy or radiation. The treatment consisted of IV infusions of 2 formulations of ANP, A10 and AS2-1, for an average of 20 months. The results showed complete response in 23%, partial response in 8%, stable disease in 31%, and progressive disease in 38%. Six patients (46%) survived more than 5 years from the initiation of ANP; 5 were not treated earlier with radiation therapy or chemotherapy. The serious side effects included single occurrences of fever, granulocytopenia, and anemia. The study is ongoing and accruing additional patients. The authors noted that the percentage of patients' response is lower than for standard treatment of favorable PNET, but long-term survival in poor-risk cases and reduced toxicity makes ANP therapy promising for very young children, patients at high risk of complication of standard therapy, and patients with recurrent tumors.

In another published report, Burzynski, et al (2006), reported on 18 patients with brainstem glioma (4 with glioblastoma, 14 with anaplastic high-grade pathology) treated with antineoplastons in 4 phase 2 trials. Patients were treated with IV ANP (A10 and AS2-1) for a median duration of 5 months. The results showed overall survival was 39% at 2 years and 22% at 5 years. Complete response was achieved in 11%, partial response in 11%, stable disease in 39%, and progressive disease in 39% of patients. The authors concluded that ANP did contribute to survival in these patients, but this was a small study group.

Antineoplaston therapy is not FDA approved for any indication, and there are no controlled, peer-reviewed clinical trials to validate the effectiveness of antineoplaston therapy for any indication. In summary, there is inadequate published data to permit scientific conclusions regarding the efficacy of antineoplaston therapy.

June 2008 Update

There continues to be no new peer-reviewed clinical trials to validate the effectiveness of antineoplaston therapy for any indication.

June 2010 Update

A recent literature search was performed and no new peer-reviewed published articles were identified that would alter the coverage statement.

Key Words:

Antineoplaston cancer therapy, antineoplastons (ANP), A10, AS2-1

Approved by Governing Bodies:

Sodium phenylbutyrate was FDA approved April 30, 1996 for the treatment of urea cycle disorders.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply

FEP contracts: Special benefit consideration may apply. Refer to member's benefit plan. FEP does not consider investigational if FDA approved. Will be reviewed for medical necessity.

Pre-certification requirements: Not applicable

Current Coding:

CPT Codes: There are no specific codes to identify this treatment

References:

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18. Ogata Y, et al. *Long-term survival following treatment with antineoplastons for colon cancer with unresectable multiple liver metastases: Report of a case*. Surgery Today 2003; 33(6): 448-453.
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20. Tsuda H, et al. *A novel strategy for remission induction and maintenance in cancer therapy*. Oncology Reports 2002; 9(1): 65-68.
21. Vickers A. *Alternative cancer cures: "Unproven" or "disproven"?* CA: A Cancer Journal for Clinicians, March 2004; 54(2): 110-118.

Policy History:

Medical Policy Group, June 2006 (3)

Medical Policy Administration Committee, July 2006

Available for comment July 18-August 31, 2006

Medical Policy Group, June 2008 (1)

Medical Policy Group, June 2010 (1) Policy update performed, no change in coverage

Medical Policy Group, September 2012 (3): Effective September 14, 2012 this policy is no longer scheduled for regular literature reviews and updates.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.