APPENDIX A

Evidence Table

Author/Year	Study Design	Intervention	Demographics	Results	Methodological Comments
Neuwelt, Frenkel , Diehl, Vu, Rapoport , Hill; 1980	Case Series; a Phase I study	Mannitol	5 subjects included: all patients had either neoplasms metastatic to the central nervous system with defined histology, or they had a biopsy proven malignant glioma	4 of 5 subjects achieved good to excellent blood brain barrier disruption A single nontransient complication, a superficial wound infection at the burr hole in one subject. Reversible, transient osmotic barrier disruption was achieved 15 times in 5 subjects with additional toxicity	Small number of cases Case series No control group, no randomization
Neuwelt, Diehl, Vu, Hill, Michael, Frenkel; 1981	Case series	Mannitol used as BBBD, followed by MTX	6 subjects with primary malignant glial tumors	The six subjects underwent 33 disruptions Two subjects showed clinical improvement, one of whom had evidence of tumor regression by CT scan No significant or permanent adverse neurologic or systemic sequelae. Neuroradiologic evaluation with radiocontrast agent showed that materials in the tumor persisted longer after BBBD than without disruption, however MTX in spinal fluid did not correlate with the degree of barrier disruption	Case series Small number of cases No control group, no randomization Authors also do not reveal which tumor type had better outcomes

				measured by CT and radionuclide scan.	
Neuwelt, Balaban, Diehl, Hill, Frenkel; 1983	Case series	1 cased used Mannitol as a BBBD, and MTX/cy-clophosphamide/ leucovorin rescue/procarba-zine; 1 cased used Mannitol as BBBD, and MTX/cyclophos-sphamide as chemotherapuetic agent; and 1 case used Mannitol as a BBBD, and MTX/cyclo-phosphamide/ procarbazine;	3 subjects, ranging in age from 37 to 67	Complete regression of tumor in all cases, though in case #2, subject elected to stop chemotherapuetic treatment and use radiation treatment; Subject died 12 months after diagnosis	Case series Small number of cases No control group, no randomization
Neuwelt, Hill, Frenkel; 1984	Case series	All cases used mannitol as BBBD agent; 1 case used MTX, cytoxan, and procarbazine; another case used MTX; the 3 rd case only mentions the use of procarbazine and cyclophospho-mide	3 subjects ranging in age from 24 to 67. Metastatic breast cancer, PCNSL, and glioblastoma were identified	All had objective responses to combination chemotherapy in conjunction with BBB modification in those areas of the brain perfused. But each patient developed the occurrence or recurrence of CNS disease in areas not directly perfused by the chemotherapuetic agent.	Small number of case Case series No control group, no randomization
Neuwelt, Frenkel, Gumerlock, Braziel et al. 1986	Case series	All cases used mannitol as BBBD agent; cyclophospha-mide, MTX, leucovorin rescue, and procarbaizne used as	12 patients involved in study, all with PCNSL;	Initial complete response rate was 75%, and 1-year survival of 75%. BBBD/chemotherapuetic combination resulted in clinical response rate and survival that were at least as effective as	Small number of cases Case series No control group, no randomization

		chemotherapuetic agents		radiotherapy	
Neuwelt, Goldman, Dahlborg, Crossen, et al. 2000	Controlled study	BBBD with cyclophospha-mide, MTX, leucovorin rescue, and procarbaizne vs. cranial irradiation	N=30; 13 patients received cranial irradiation 1 to 9 months before referral (group 1), and 17 patients received initial BBBD followed by chemotherapy with subsequent radiation only for tumor progression or recurrence (group 2)	Median survival for group 1 (cranial irradiation) was 17.8 months, comparable with the 20 month median survival of the historical control series; median survival for group 2 (BBBD chemotherapuetic group) was 44.5 months. Study notes that improved survival was associated with preservation of cognitive function in six of seven non-irradiated complete responders observed over a 7 year period.	Small number of cases No randomization performed Study does not report number of patients with loss of cognitive function in the brain irradiation group Difficult to follow the numbers
Crossen, Goldman, Dahlborg, Neuwalt; 1992	Case series	BBBD with cyclophospha-mide, MTX, leucovorin rescue, and procarbaizne	N=8 patients with PCNSL who only received BBBD followed by chemotherapy without any cranial irradiation and achieved a complete response with no evidence of recurrence.	7 of the 8 participants had full-scale intelligence quotient which tended to remain stable, as did learning performance, memory scores, and other neurobehavioral variables. Trends of summary neuropsychological test indices were stable or improved for this group. Only one participant had lower test scores compared to baseline scores that was greater than one standard deviation on 3 variables.	Small number of cases No randomization performed No control group for comparison
Dahlborg, Henner, Crossen, Tableman, Petrillo et al.; 1996	Controlled study	Mannitol was used as the BBBD and MTX, leucovorin rescue, cyclophospha-mide,	N=58 consecutive patients with PCNSL were subdivided into 2 groups: those referred to medical center at tumor	The median survival from date of first BBBD for group 1 patients was 8.5 months, and for the group 2 patients 40 months (but	Small number of cases No randomization performed

		and procarbazine were used as chemotherapuetic agents.	regression or recurrence and after initial cranial radiation (n=19), and those referred after initial diagnosis, not receiving cranial irradiation (n=39). Subjects ages' ranged from 5 to 71, with 34% over age 60.	with the small sample size the difference did not reach statistical significance ($p<0.06$). In the neuropsycho-logic evaluation, none of the patients who received only chemotherapy with BBBD and who did not receive radiation therapy suffered significant global decline in neuropsychologic test results. Three of eight patients that received cranial radiation suffered declines in neuropsychologic testing.	Baseline demographic characteristics were obtained, but no attempt to perform statistical analysis (based on this assessment, a number of characteristics could explain difference between groups)
McAllister, Doolittle, Guastadisegni, Kraemer, Lacy, et al. 2000	Prospective study	Protocol 1-MTX, etoposide or cyclophospha-mide, procarbazine, leucovorin rescue Protocol 2- MTX, etoposide, cyclophospha-mide, granulocyte colony stimulating hormone, leucovorin rescue	111 consecutive patients with PCNSL enrolled, but 74 had no systemic lymphoma or did not receive cranial radiation	The estimated 5-year survival rate was 42% for this group, and the median survival time was 40.7 months. Complete remission occurred in 48 patients (65%), and 36 patients continued to show complete remission response after 1 year of BBBD-enhancing chemotherapy delivery. Of these 36 patients, none demonstrated any evidence of cognitive loss.	No controls for comparison No randomization
Tyson, Siegal, Doolittle, Lacy, Kraemer et al. 2003	Prospective study	Mannitol was used as the BBBD; carboplatin, etoposide, cyclphosphamide (either alone or in combination) were	37 patient with relapsing PCNSL, ranging in age from 22 to 77 (mean age 57.5); all were treated within 8 months after relapse (except 1), and 9 subjects had had previous radiotherapy.	The median time for survival after BBBD followed by chemotherapy was 6.8 months; however 18% of patients survived $\geq$ 27 months, 24% had complete radiographic response, 11% had partial radiographic response, 32% had	Small number of cases No randomization performed No control group for comparison

		used as chemotherapy agents		stable disease, while 27% had progressive disease. The median time for failure for patients with complete response and partial response was 9.1 months. Neuropsychologic evaluation was performed on 4 of 8 complete responders: 1 subject had no neuro-cognitive alterations, and in another patient there was significant improvement; Of the other 2, one developed a systemic disease and was too ill to perform the post-BBBD testing, and the other was in a stupor prior to treatment with BBBD, but completed post BBBD neuropsychologic testing.	No information provided on neuropsychologic testing of 4th complete responder
Neuwelt, Howieson, Frenkel, Specht et al 1986	3-arm controlled trial	Subjects in the experimental group received mannitol as a BBBD, and cyclophospha-mide, MTX, procarbazine as well as leucovorin rescue as chemotherapy agents.	3-arm study: experimental group consist of , 38 patients with glioblastoma previously treated with surgery and cranial radiation; group 1 consist of 14 patients treated with surgery and radiation; group 2 consisted of 8 patients with previous surgery, radiation, and systemic chemotherapy	An inverse relationship between age and survival time; A positive correlation between functional status and survival time No significant effects upon survival time in the 3 groups were demonstrated for necrosis Median survival for group 1 was 12.8 months, and 11.4 months for group 2; median survival for the experimental group was 17.5 months. This survival advantage was associated with a median KPS of 65% for those patients	No randomization Small sample size Limited information provided on historical control cases

				surviving 24 months.	
Dahlborg, Petrillo, Crossen, Roman-Goldstein et al. 1998	Prospective study	Mannitol was used as BBBD. Protocol 1-MTX, cyclophospha-mide, procarbazine, and etoposide Protocol 2-carboplatin, etoposide, and cyclophospha-mide (protocol 2).	Thirty-four patients with histologically confirmed germ cell tumor (n=9), PCNSL (n=9), or primitive neuroectodermal tumor (n=16) were included in the study. Participant's age's ranged from 1 to 30.	82% had an objective response to treatment (62% with complete response, 20% with partial response). The authors note that for most patients, cognitive functioning was maintained or improved at follow up	Small number of cases No control group for comparison Findings not generalizable to Medicare population
Hall, Doolittle, Daman, Bruns, et al. 2005	Prospective study	BBBD and MTX, cyclophospha-mide, etoposide, or carboplatin, cyclophospha-mide and etoposide.	8 patients with diffuse pontine gliomas, ranging in age from 2 to 44.	MR imaging revealed partial response in 2 patients, stable disease in 5, and progression of disease in one. Median time to tumor progression was 15 months (ranging from <1 month to 40 months). Median survival form the first BBBD treatment was 16.5 months (ranging from 5 to 59 months).	Small number of cases No randomization or controls Findings not generalizable to Medicare population
Neuwelt, William, Mickey, Frenkel, Henner 1994	Prospective study	All patients received chemotherapy in a 2-stage regimen. Patients received initial treatment of cisplatin and etoposide, then consolidated therapy consisting of etoposide with carboplatin in conjunction with BBBD.	4 consecutive patients with disseminated CNS germinoma Participants ranged in age from 14 to 29.	Complete response was noted in all 4 subjects, and at the time of publication, 3 participants were tumor free without radiotherapy 24 to 40 months from diagnosis The 3 patients that remained tumor free at the end of the study did not develop cognitive deterioration	Small number of cases No randomization or controls Time period between 2 regimens not stated-its possible that first regimen could have achieved observed results Findings not generalizable to Medicare population

Neuwelt, Specht, Barnett, Dahlborg, et al. 1987	Prospective study	Week 1-iodinated anit-melanoma nonspecific Fab 48.7 or 96.5; Week 2-iodinated nonspecific Fab 1.4; Week 3-iodinated Fab 48.7 or 96.5 after osmotic opening with BBBD.	3 patients with melanoma metastatic to the central nervous system	Increased uptake in the blood brain barrier modified areas in all three subjects when radiolabeled tumor-specific MAb was administered in conjunction with osmotic BBB opening.	Small number of cases No controls or randomization No information provided on age of participants (unable to say if study is generalizable to Medicare population)
Tyson, Kraemer, Hunt, Muldoon, Orbay, et al. 2006	Retrospective study	Chemotherapy consisted of MTX, cyclophospho-mide and etoposide. Ten patients were treated with this regimen. After 1994, IA carboplatin was used with BBBD, and 10 patients received IA carboplatin cyclophospha-mide and etoposide. 7 patients received trastuzumab	25 patients with central nervous system metastases; ages ranged from 25 to 65; 10 subjects had metastasis only to the brain, while the other 15 had brain and systemic involvement.	Median overall survival was 45.5 weeks. Of those patients evaluable for response, 4 had objective responses (either complete or partial) for a response rate of 16%, 15 had stable disease (60%), while the other 6 had progressive disease (24%). Median time to progression was 4.13 months, the 6 month progression-free survival was 32% and the 12-month progression-free survival was 12%. The authors noted that with just 7 patients receiving trastuzumab, response and survival could not be assessed.	Small number of cases No randomization No information provided survival amongst patients taking trastuzumab
Neuwelt, Dahlborg 1987	Case series	Mannitol was used as BBBD, used in combination with MTX, procarbazine,	Seven patients with intra-cranial metastasis Patients ranged in age from 24	Based on follow up radionuclide studies, good to excellent disruption were documented in 50% of procedures, and in only 3	Small number of cases No control or randomization

		and cytoxan	to 65. Cancers included breast cancer, lung cancer, CNS lymphomas, testicular cancer, and small cell lung cancer.	procedures (8%) was there no evidence of disruption.	
Roman-Goldstein, Mitchell, Crossen, Williams, et al. 1995	Prospective study	Mannitol was used as BBBD-Two different chemotherapuetic regimens were used: cyclophospha-mide, MTX, and procarbazine or etoposide and carboplatin.	15 consecutive patients with metastasis to the brain; Patients involved in the study had PCNSL, germinomas, astrocytomas, or neuroectodermal tumor; Ages ranged from 6 to 66.	10 patients (67%) had no new abnormalities on repeat MR imaging, while recurrent tumor occurred in 5 patients (33%). Also no patient showed a decline in global cognitive function, and 5 patients showed improved global scores.	Small number of cases No control or randomization
Williams, Henner, Roman-Goldstein, Dahlborg, Brummett, et al. 1995.	Prospective study	Two different chemotherapuetic regimens were used: cyclophospha-mide, MTX, and procarbazine or etoposide and carboplatin.	34 patients; different types of cancers of the brain (glioblastoma multiforme, malignant astrocytoma, malignant astrocytoma-oligodendroglioma, primitive neuroectodermal tumor, disseminated CNS germ cell tumor, PCNSL, metastatic breast cancer, metastatic lung cancer); Patient's ages ranged from 7 to 72.	10 patients (67%) had no new abnormalities on repeat MR imaging, while recurrent tumor occurred in 5 patients (33%); No patient showed a decline in global cognitive function, and 5 patients showed improved global scores.	Small number of cases No control or randomization
Doolittle, Miner, Hall, Siegal, Hanson, et al. 2000	Prospective multi-center study	2 different chemotherapy regimens were used: carboplatin, cyclophospha-mide, etoposide (protocol 1), or MTX, cyclophospha-mide,	221 patients from 5 university centers; Patients ranged in age from 18 to 75 Patients had either primary brain cancers (e.g., PCNSL,	Results of the study revealed that, of the evaluable patients PCNSL, 75% achieved complete response; all evaluable patients with primary neuroectodermal tumor (n=17), metastatic disease (n=12), or germ cell tumor (n=4) achieved stable disease or better;	No control or randomization Unable to generalize to Medicare population because numbers of patients >65 not reported

		etoposide, leucovorin rescue (protocol 2). Both regimens used mannitol as BBBD, and granulocyte-colony stimulating factor.	germ tumors, primitive neuroectodermal tumor), or metastatic tumors (e.g., breast cancer).	and of the 57 evaluable patients with glioblastoma multiforme, 79% achieved stable disease or better.	May not be able to generalize finding from multi-center study to Medicare setting

APPENDIX B

General Methodological Principles of Study Design

(Section VI of the Decision Memorandum)

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.

Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.

Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.

Larger sample sizes in studies to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.

Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias).

Co-interventions or provision of care apart from the intervention under evaluation (performance bias).

Differential assessment of outcome (detection bias).

Occurrence and reporting of patients who do not complete the study (attrition bias).

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, in general, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The design, conduct and analysis of trials are important factors as well. For example, a well designed and conducted observational study with a large sample size may provide stronger evidence than a poorly designed and conducted randomized controlled trial with a small sample size. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

Randomized controlled trials

Non-randomized controlled trials
Prospective cohort studies
Retrospective case control studies
Cross-sectional studies
Surveillance studies (e.g., using registries or surveys)
Consecutive case series
Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess and consider the evidence.

Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage determinations for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. One of the goals of our determination process is to assess health outcomes. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived. Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

APPENDIX C

WHO Classification of CNS tumors

This classification is based on the World Health Organization (WHO) classification of nervous system tumors. The WHO approach incorporates and interrelates morphology, cytogenetics, molecular genetics, and immunologic markers in an attempt to construct a cellular classification that is universally applicable and prognostically valid. Earlier attempts to develop a TNM-based classification were dropped: tumor size (T) is less relevant than tumor histology and location, nodal status (N) does not apply because the brain and spinal cord have no lymphatics, and metastatic spread (M) rarely applies because most patients with central nervous system (CNS) neoplasms do not live long enough to develop metastatic disease.

The WHO grading of CNS tumors establishes a malignancy scale based on histologic features of the tumor. The histologic grades are as follows:

WHO grade I includes lesions with low proliferative potential, a frequently discrete nature, and the possibility of cure following surgical resection alone.

WHO grade II includes lesions that are generally infiltrating and low in mitotic activity but recur. Some tumor types tend to progress to higher grades of malignancy.

WHO grade III includes lesions with histologic evidence of malignancy, generally in the form of mitotic activity, clearly expressed infiltrative capabilities, and anaplasia.

WHO grade IV includes lesions that are mitotically active, necrosis-prone, and generally associated with a rapid preoperative and postoperative evolution of disease.

The following outline has been adapted from the WHO classification. Tumors of glial origin are grouped under a common heading, and tumors limited to the peripheral nervous system have been excluded. Some rare or exclusively pediatric tumors are listed below for purposes of classification, but they are not discussed in the text that follows.

Neuroepithelial tumors.
Glial tumors.
- Astrocytic tumors.
  - Pilocytic astrocytoma.
  - Diffuse astrocytoma (including fibrillary, protoplasmic, and gemistocytic).
  - Anaplastic astrocytoma.
  - Glioblastoma (including giant cell glioblastoma, and gliosarcoma).
  - Pleomorphic xanthoastrocytoma.
  - Subependymal giant cell astrocytoma.
- Oligodendroglial tumors.
  - Oligodendroglioma.
  - Anaplastic oligodendroglioma.
- Mixed gliomas.
  - Oligoastrocytoma.
  - Anaplastic oligoastrocytoma.
- Ependymal tumors.
  - Myxopapillary ependymoma.
  - Subependymoma.
  - Ependymoma (including cellular, papillary, clear cell, and tanycytic).
  - Anaplastic ependymoma.
- Neuroepithelial tumors of uncertain origin.
  - Astroblastoma.
  - Chordoid glioma of the third ventricle.
  - Gliomatosis cerebri.

Neuronal and mixed neuronal-glial tumors (some glial component may be present).

- Gangliocytoma.
- Ganglioglioma.

Desmoplastic infantile astrocytoma/ganglioglioma.
Dysembryoplastic neuroepithelial tumor.
Central neurocytoma.
Cerebellar liponeurocytoma.
Paraganglioma.

Nonglial tumors.

Embryonal tumors.
Ependymoblastoma.
Medulloblastoma.
Supratentorial primitive neuroectodermal tumor (PNET).

Choroid plexus tumors.
Choroid plexus papilloma.
Choroid plexus carcinoma.

Pineal parenchymal tumors.
Pineoblastoma.
Pineocytoma.
Pineal parenchymal tumor of intermediate differentiation.

Meningeal tumors.

Meningioma.
Hemangiopericytoma.
Melanocytic lesion.

Germ cell tumors.

Germinoma.
Embryonal carcinoma.
Yolk-sac tumor (endodermal-sinus tumor).

Choriocarcinoma.
Teratoma.
Mixed germ cell tumor.

Tumors of the sellar region.

Pituitary adenoma. (Refer to the PDQ summary on Pituitary Tumor Treatment for more information.)
Pituitary carcinoma.
Craniopharyngioma.

Tumors of uncertain histogenesis.

Capillary hemangioblastoma.

Primary CNS lymphoma. (Refer to the PDQ summary on Primary CNS Lymphoma Treatment for more information.)

Tumors of peripheral nerves that affect the CNS.

Schwannoma.

Metastatic tumors.