Corporate Medical Policy

Serum Testing for Evidence of Mild Traumatic Brain Injury AHS – G2151

File Name: serum_testing_for_evidence_of_mild_traumatic_brain_injury
Origination: 8/2019
Last Review: 7/2023

Description of Procedure or Service

Traumatic brain injury (TBI) is characterized by pathologic injuries to the brain resulting from external forces or trauma. A broad range of sequela of varying clinical severity include focal contusions and hematomas, diffuse axonal injury, cerebral edema and swelling, and a cascade of molecular injury mechanisms (Williamson & Rajajee, 2021).

Concussion refers to the trauma-induced alteration in mental status, which may or may not involve loss of consciousness, after a mild TBI (Evans & Whitlow, 2022). Measurement of blood and other fluid biomarkers has been proposed as a way of evaluating mild traumatic brain injury.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Serum testing for evidence of mild traumatic brain injury is considered investigational. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When serum testing for evidence of mild traumatic brain injury is covered

Not applicable

When serum testing for evidence of mild traumatic brain injury is not covered

The evaluation of mild traumatic brain injury, measurement of concussion markers (e.g., S100B, GFAP, and UCH-L1) in the blood, saliva, and/or cerebrospinal fluid (CSF), including proprietary biomarker panels (e.g., i-STAT TBI Plasma, Alinity® i TBI) is considered investigational.

Policy Guidelines

Traumatic brain injury (TBI) is a fairly common injury, with an incidence of 1.11 million and a prevalence of 2.35 million in the US in 2016 (Evans & Whitlow, 2022). According to the CDC, there were over 64,000 TBI-related deaths in the United States in 2020 (CDC, 2023). Although

approximately 75% of TBIs are mild, TBI can adversely affect a person's quality of life in numerous ways, including cognitive functioning, emotional functioning, and physical effects (CDC, 2015; Wright et al., 2013). As many as 1 in 5 TBI patients have symptoms persisting past 1 month (Silverberg et al., 2020).

Accurate diagnosis of TBI is critical to effective management and intervention but can be challenging due to the nonspecific and variable presentation (Mondello et al., 2017). Tools available to objectively diagnose injury and prognosticate recovery are limited (Mannix et al., 2014). Clinical assessment usually includes a neurological exam, followed by a computed tomography (CT) scan of the head to detect brain tissue damage that may require treatment (FDA, 2018). However, as most patients with mild TBI do not have detectable intracranial lesions, like epidural hematomas, on a CT scan (Evans & Whitlow, 2022), this assessment relies heavily on nonspecific symptoms that can vary widely and ignores the mechanistic heterogeneity of TBI (Williamson & Rajajee, 2021).

Brain damage in TBIs is initially caused by external mechanical forces being transferred to intracranial contents, generating shearing and strain forces which stretch and damage axons, and can result in contusions, hematomas, cerebral edema and swelling. Common mechanisms include direct impact, rapid acceleration/deceleration, penetrating injury, and blast waves. However, the pathophysiology of TBI is now understood to include not only the acute event, but also the resulting cascade of molecular injury mechanisms that are initiated at the time of initial trauma and continue for hours or days (Williamson & Rajajee, 2021). The pathophysiology of even mild TBI is complex and may include both focal and diffuse injury patterns. Neuropathological changes found after mild TBI indicate mild multifocal axonal injury, including altered circuit dysfunction and traumatic axonal injury (Truettner et al., 2018).

Cell death and the initiation of local metabolic and inflammatory processes resulting from TBI results in the release of a number of inflammatory mediators and damage-associated molecules that are able to cross a dysfunctional blood-brain barrier (Di Battista et al., 2015) or enter the circulation through the glymphatic pathway (Plog et al., 2015). Neurobiochemical marker levels in blood after TBI may reflect structural changes detected by neuroimaging (Mondello et al., 2017). Simpler, sensitive, and specific tests that provide early, quantitative information about the extent of brain tissue damage, identifying and stratifying TBI, would allow rapid and tailored diagnosis of TBI, while minimizing the time, risk, and cost associated with current standards (McMahon et al., 2015). No single ideal TBI biomarker exists (Halford et al., 2017). However, brain-specific markers of neuronal, glial, and axonal damage, identified in the peripheral blood, have shown potential clinical utility as diagnostic, prognostic, and monitoring adjuncts and have been investigated both individually and in combination (Di Battista et al., 2015; Mondello, Jeromin, et al., 2012). Acute-phase biomarkers, including S100 calcium-binding protein B (S100B), glial fibrillary acidic protein (GFAP), and ubiquitin C-terminal hydrolase-L1 (UCH-L1), have shown potential for use in initial screening of patients presenting with head trauma, the vast majority of whom will have normal brain CT findings (Evans & Whitlow, 2022; Maas et al., 2017).

However, recent reviews have noted concerns about a lack of specificity and unresolved issues with the use of mTBI blood biomarkers. While researchers note "impressive levels of sensitivity," they simultaneously acknowledge that correlations between blood biomarker levels and mTBI severity have been "disappointing to date." In particular, they state that it remains inconclusive whether biomarkers can predict recovery time, post-concussion syndrome, and/or return to sports activities (Hier et al., 2021).

S100 calcium-binding protein B (S100B)

S100B belongs to the calcium binding EF-hand protein group, and it has been associated with cytoskeleton structure, Ca2+ homeostasis, cell proliferation, protein phosphorylation and degradation (Chmielewska et al., 2018; Strathmann et al., 2014). S100B is expressed in the cytoplasm and the nucleus of astrocytes and is present in the bloodstream when the blood brain barrier is disrupted.

Several studies indicate that S100B measurement, either acutely or at several time points, can distinguish injured from non-injured patient (Strathmann et al., 2014) and guidelines intended to reduce the need for CT scan using S100B levels in the blood for the initial management of mild TBI have been published (Ingebrigtsen et al., 2000). These guidelines were recently validated in a large multicenter study where S100B was found to have a sensitivity of 97% and a specificity of 34% for the identification of intracranial hemorrhages confirmed by CT scans. The authors estimated CT scans would have been reduced by 32% with application of these guidelines (Unden et al., 2015). However, other investigators have failed to detect associations between S100B with CT abnormalities (Piazza et al., 2007). Additionally, it has limited utility in multiple trauma settings as it is not brain-specific. S100B can be found in non-neural cells, such as adipocytes, chondrocytes, and melanocytes (Chmielewska et al., 2018; Papa et al., 2014), and its levels are also elevated in trauma, specifically orthopedic, without head injury (Anderson et al., 2001; Wang et al., 2018). However, recent data highlight the inclusion of S100B in sets of markers that in combination could contribute to better diagnosis, monitoring, and treatment of CNS conditions (Chmielewska et al., 2018).

Glial Fibrillary Acidic Protein (GFAP)

GFAP is a filament protein that maintains cell shape and structure, coordinates cells' mobility and contributes to the transduction of molecular signals in astrocytes. It is released upon cellular disintegration and degradation of the astrocyte. Concentration of serum GFAP increases after neural trauma and TBI, either as the intact protein or as breakdown products (Chmielewska et al., 2018; Wang et al., 2018). GFAP measurements have provided promising data on injury pathway indication, focal versus diffuse injuries, and prediction of morbidity and mortality (Strathmann et al., 2014). GFAP level was increased in patients with CT-positive scans for intracranial lesions compared to CT-negative scans after mild TBI (Lei et al., 2015). Sensitivities have been reported between 67% and 100% while the specificities ranged from 0% and 89% (Mondello et al., 2017).

McMahon et al (2015) performed a multicenter trial to evaluate GFAP and its breakdown product GFAP-BDP in the diagnosis of intracranial injury. They found that "GFAP-BDP demonstrated very good predictive ability (area under the curve=0.87) and demonstrated significant discrimination of injury severity (odds ratio, 1.45; 95% confidence interval, 1.29-1.64)". The authors concluded that "use of GFAP-BDP yielded a net benefit above clinical screening alone and a net reduction in unnecessary scans by 12-30%" (McMahon et al., 2015).

Ubiquitin C-terminal Hydrolase-L1 protein (UCH-L1)

UCH-L1 is a cytoplasmic enzyme, highly enriched and specifically expressed in neurons, involved in the ubiquitinoylation of abnormal proteins destined for proteasomal degradation (Halford et al., 2017). It is also an important element of axonal transport and, by a strong interaction with cytoskeleton proteins, plays an important role in the axon's integrity (Chmielewska et al., 2018). UCH-L1 has been shown to increase after TBI in serum and CSF as well as correlate with TBI severity and abnormal CT findings (Diaz-Arrastia et al., 2014; Wang et al., 2018). UCH-L1 has also been shown to be significantly elevated in serum among athletes after concussions (Wang et al., 2018). High prognostic value of poor outcome was found at both 3-months (Diaz-Arrastia et al., 2014) and 6-months intervals (Mondello, Akinyi, et al., 2012). Two recent studies report the same sensitivity of 100% and specificities of 21% and 39% (Mondello et al., 2017).

Clinical Utility and Validity

Welch et al (2016) evaluated three serum biomarkers' (glial fibrillary acidic protein [GFAP], ubiquitin C-terminal hydrolase-L1 [UCH-L1] and S100B measured within 6 h of injury) ability to differentiate CT-negative and CT-positive findings. They found that "UCH-L1 was 100% sensitive and 39% specific at a cutoff value >40 pg/mL. To retain 100% sensitivity, GFAP was 0% specific (cutoff value 0 pg/mL)

and S100B had a specificity of only 2% (cutoff value 30 pg/mL). All three biomarkers had similar values for areas under the receiver operator characteristic curve: 0.79 for GFAP, 0.80 for UCH-L1, and 0.75 for S100B. Neither GFAP nor UCH-L1 curve values differed significantly from S100B. In our patient cohort, UCH-L1 outperformed GFAP and S100B when the goal was to reduce CT use without sacrificing sensitivity. UCH-L1 values <40 pg/mL could potentially have aided in eliminating 83 of the 215 negative CT scans" (Welch et al., 2016). However, the authors note that further research is needed.

Wang et al. (2018) reported on the usage of TBI serum and CSF biomarkers as prognostic tools in the ED, neurointensive care unit, and out-of-hospital settings. In the case of mTBI, the researchers stated the similar biomarkers could aid in predicting any development of persistent post-concussive syndrome, including S100B, GFAP, and UCH-L1. Within 12-36 hours from TBI in neurointensive care units, it was found that serum levels of 100B correlate with patient outcomes, and S100B serum levels > 0.7ng/mL correlate with 100% mortality. GFAP modestly correlates with poor outcomes, and "serum GFAP levels were also significantly higher in patients who died or had an unfavorable outcome and have predicted neurological outcome at 6 months." It was also shown in other studies that GFAP and UCHL-1 proteins outperformed S100B in predicting poor outcomes, and the two together "predicate the recovery and unfavorable outcome by distinguishing patients with GOS [Glasgow Outcome Score] 1-3 from patients with GOS 4-5" (Mondello et al., 2016; Takala et al., 2016; Wang et al., 2018).

Gan et al. (2019) evaluated TBI serum biomarkers for four clinical situations: "detecting concussion, predicting intracranial damage after mild TBI (mTBI), predicting delayed recovery after mTBI, and predicting adverse outcome after severe TBI (sTBI)". A total of 200 publications (61722 "observations") were included. For concussion detection, 9 unique publications addressing 15 biomarkers and 946 observations were identified. Four panels ("copeptin, galectin-3, and MMP-9; GFAP and UCH-L1; 10 metabolites; and 17 metabolites") were found to have areas under the curve (AUC) of over 0.9. For evaluation of necessity of CT scan after TBI, 56 publications, 24 biomarkers, and 23316 observations were identified. S-100B (30 publications, 8464 observations) was found to have an AUC of 0.723 and GFAP/GFAP-BDP (16 publications, 2040 observations) was found to have an AUC of 0.831. For evaluation of delayed recovery after mTBI, 44 publications, 29 biomarkers, and 13291 observations were identified. S-100B (24 publications, 2800 observations) had an AUC of 0.691; GFAP's AUC was 0.716 (17 publications, 1959 observations). Finally, for evaluation of poor outcome after sTBI, S-100B (25 publications, 3712 observations) was rated at AUC of 0.762, and GFAP (10 publications, 2448 observations) was rated at AUC of 0.749. Neuron-specific enolase (9 publications, 911 observations) was rated at AUC of 0.715 (Gan et al., 2019).

Korley et al. (2022) investigated the prognostic value of glial fibrillary acidic protein (GFAP) and ubiquitin C-terminal hydrolase L1 (UCH-L1) in traumatic brain injuries in a study called TRACK-BTI. The prognostic accuracy of the two biomarkers was studied amongst 2552 participants. Participants were 17 years and older and had been evaluated for TBI. All patients were given a head CT during evaluation. Participants had plasma samples taken on the day of injury (for measurement of GFAP and UCH-L1). In the results, of the 1696 participants with brain injury (data available at baseline and at 6 months), 120 (7.1%) died, 235 (13.9%) had unfavorable outcomes, and 561 (33.1%) recovered fully. The area under the curve of GFAP for predicting death at 6 months in all patients was .87 (95% CI 0.83-0.91), for unfavorable out come was 0.86 (0.83-0.89), and for incomplete recovery was 0.62 (0.59-0.64). The AUC for UHC-L1 was 0.89 (95% CI 0.86-0.92) for prediction of death, 0.86 (0.84-0.89) for unfavorable outcome, and 0.61 (0.59-0.64) for incomplete recovery at 6 months. Additionally, "Among participants with GCS [Glasgow Coma Scale] score of 3–12 (n=353), adding GFAP and UCH-L1 (alone or combined) to each of the three International Mission for Prognosis and Analysis of Clinical Trials in traumatic brain injury models significantly increased their AUCs for predicting death (AUC range 0·90–0·94) and unfavourable outcome (AUC range 0·83–0·89). The authors concluded, "GFAP and UCH-L1 plasma concentrations have good to excellent prognostic value for predicting death and unfavourable outcome, but not for predicting incomplete recovery at 6 months" (Korley et al., 2022).

In January 2021, Abbott Laboratories received FDA 510(K) clearance for the i-STAT™ Alinity™ handheld device, which would help evaluate mTBIs. It simultaneously measures UCH-L1 and GFAP in blood and produces results in 15 minutes once a plasma sample is inserted. It has a sensitivity of 95.8% and a >99% negative predictive value. Abbott Laboratories states that this blood test's availability "could help eliminate wait time in the emergency room and could reduce the number of unnecessary CT scans by up to 40%." The company is also working on a whole blood test, and has received breakthrough designation to create a TBI test that runs "on its Alinity™ and ARCHITECT® core laboratory instruments" (Abbott Laboratories, 2021).

In March 2023, Abbott Laboratories received FDA clearance for the Alinity® i TBI test that measures two biomarkers in the blood— C-terminal hydrolase L1 (UCH-L1) and glial fibrillary acidic protein. Like the i-STAT™ Alinity™, this test is intended for use in adults who are suspected of having mild traumatic brain injury, such as adults who present to the hospital within 12-hours of a concussion or suspected mTBI. Initial studies show the test provides results with 96.7% sensitivity and 99.4% negative predictive value. After a blood draw, results are available within 18 minutes and the test is run on Abbott's Alinity™ i platform (MPR, 2023).

Guidelines and Recommendations

American College of Emergency Physicians recommended consideration could be given to not performing a CT (Level C) in mild TBI patients without significant extracranial injuries and a serum S100β of level less than 0.1μg/L measured within 4 h of injury (Jagoda et al., 2009).

Centers for Disease Control (CDC, 2016) reaffirmed the 2008 ACEP recommendation in 2016. However, in 2018, the CDC remarked that "Health care professionals should not use biomarkers outside of a research setting for the diagnosis of children with mTBI", noting that there is insufficient evidence to recommend any of the studied biomarkers for mTBI diagnosis in children. The CDC identified S100B, tau protein, autoantibodies against glutamate receptors and oxide metabolites, neuronal ubiquitin C-terminal hydrolase-L1, and glial fibrillary acidic protein biomarker levels as biomarkers that have been studied for concussion evaluation (Lumba-Brown et al., 2018).

The Veterans Administration and Department of Defense Practice Guideline for the Management of Concussion – mild Traumatic Brain Injury states that:

"Excluding patients with indicators for immediate referral, for patients identified by post-deployment screening or who present to care with symptoms or complaints potentially related to brain injury, we suggest against using the following tests to establish the diagnosis of mTBI or direct the care of patients with a history of mTBI:

a. Neuroimaging
b. Serum biomarkers, including S100 calcium-binding protein B (S100-B), glial fibrillary acidic protein (GFAP), ubiquitin carboxyl-terminal esterase L1 (UCH-L1), neuron specific enolase (NSE), and α-amino-3-hydroxy-5- methyl-4-isoxazolepropionic acid receptor (AMPAR) peptide
c. Electroencephalogram (EEG)" (VA/DoD, 2021).

The consensus statement **from American College of Sports Medicine (ACSM), American Academy of Family Physicians (AAFP), American Academy of Orthopedic Surgeons (AAOS), American Medical Society for Sports Medicine (AMSSM), American Orthopedic Society for Sports Medicine (AOSSM), and the American Osteopathic Academy of Sports Medicine (AOASM)** (Herring et al., 2011) states that: "Investigation in the area of biomarkers (e.g., S-100 proteins, neuron specific enolase, tau protein) is inconclusive for identifying individuals with concussion and represents research that may one day be clinically applicable."

The **American Academy of Pediatrics (AAP)** acknowledges that biomarkers such as "S100β, glial fibrillary acidic protein, neuron-specific enolase, τ, neurofilament light protein, amyloid β, brain-derived neurotrophic factor, creatine kinase and heart-type fatty acid binding protein, prolactin, cortisol, and albumin" have all been investigated in concussion evaluation, but none of these biomarkers have been used in clinical settings (AAP, 2018; Halstead et al., 2018).

The **National Institute for Health and Care Excellence (NICE)** guidelines regarding "assessment and early management of head injury in children, young people and adults" do not mention any serum biomarkers for evaluation of head injuries (NICE, 2019).

The **American Medical Society for Sports Medicine** notes that fluid biomarkers (blood, saliva, and cerebrospinal fluid) in diagnosis of sports-related concussion is under active investigation, but states that overall evidence level is "low". The Society writes that more studies are needed to determine their clinical utility. The Society also acknowledges the FDA approval of the "two-protein brain trauma indicator with glial fibrillary acidic protein and ubiquitin carboxy-terminal hydrolase L1 (UCHL1), and clinical use of S100 calcium-binding protein b (s100b) in Europe," but remark that neither of these tests have a role in diagnosis or management of a sports-related concussion (Harmon et al., 2019).

The **American Congress of Rehabilitation Medicine Brain Injury Interdisciplinary Special Interest Group Mild TBI Task Force** published a synthesis of practice guidelines for "Management of Concussion and Mild Traumatic Brain Injury." In it, they note that the Scandinavian Neurotrauma Committee guidelines recommend that "S100B values of <0.10 mg/L, if sampled within 6 hours of injury, can help rule out the need for CT in patients younger than 65 years with a Glasgow Coma Scale score of 14 or a Glasgow Coma Scale score of 15 with loss of consciousness or repeated vomiting". However, they also remark that neither GFAP nor C-terminal hydrolase-L1 have been incorporated into any published clinical practice guidelines. Further, the task force notes that the biomarkers' incremental value over established clinical decision rules (such as the Canadian CT head rule) is unknown.

The task force also states that "At present, there is no objective biomarker to determine mTBI resolution" (Silverberg et al., 2020).

The **International Traumatic Brain Injury Research (InTBIR) Initiative** states that there "remains a critical need for more accurate diagnostic and prognostic tools in TBI. The development and validation of genomic, proteomic, and imaging biomarkers will be essential for tackling TBI heterogeneity and moving towards precision medicine. The heterogeneous nature of traumatic brain injury presents a major challenge to biomarker identification, validation, and clinical application."

In a statement on genomic screening, they note that a genome-scale wide approach hasn't gained traction over identifying single candidate biomarkers, and that "regardless of the method by which a candidate biomarker is identified, appropriate testing and validation is crucial to accurately assess a biomarker's predictive/diagnostic potential."

Regarding specific biomarkers, they state, "Proteins highly specific to astroglial overexpression and injury, S100B and glial fibrillary acidic protein (GFAP) are logical choices for investigation. S100B is a calcium-binding protein found in astrocytes, the levels of which are elevated in response to neural injury or inflammation. A number of clinical studies have shown that elevated serum levels of S100B correlate with poor outcome after TBI, but S100B has also been shown to be elevated in response to other inflammatory/traumatic processes in the absence of TBI." Furthermore, "In the case of S100B, although it has been shown to be highly sensitive to brain trauma, it lacks specificity for TBI because it is also released from extracerebral tissue and can be elevated in response to numerous other non-CNS injuries."

Regarding GFAP, they note it has been "suggested that it may serve as a marker of focal lesions and intracranial bleeding, but may not be adequately sensitive to axonal injury. Unlike GFAP, the protease ubiquitin C-terminal hydrolase-L1 (UCH-L1) has been shown to be suggestive of diffuse injuries, and appears to be a promising TBI biomarker candidate in its own right. Taken together, these observations suggest that simultaneous assessment of biomarkers reflecting different pathophysiological mechanisms and injury types would provide complementary information and might increase diagnostic and prognostic accuracy, hence enabling clinicians to stratify risk more effectively among TBI patients"(Huie et al., 2021).

Food and Drug Administration (FDA)

On Jan 8, 2021, with 510(K) clearance, the FDA approved marketing ofi-STAT TBI Plasma Cartridge with the i-STAT™ Alinity™ System from Abbott Laboratories. This brain trauma assessment test is intended for in vitro diagnostic use to aid in evaluating patients, 18 years of age or older, with suspected mTBI (Glasgow Coma Scale score 13-15) within 12 hours of injury with other clinical information to assess the need for radiologic imaging (CT, MRI). A result from this test is associated with the absence or presence of acute traumatic intracranial lesions seen on a head CT scan, but is not intended for use in point of care settings (FDA, 2021). In March 2023, the FDA approved Abbott's Alinity® i TBI lab test as a complement to the i-STAT™ Alinity™ System. According to Abbott, the test measures ubiquitin C-terminal hydrolase L1 (UCH-L1) and glial fibrillary acidic protein; the test assesses whether there are elevated concentrations of these biomarkers in the blood. While the i-STAT™ Alinity™ System is the first rapid hand-held test that measures biomarkers in plasma, the Alinity® i TBI test is a blood test run on Abbott's Alinity® i instrument (MPR, 2023).

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 83516, 84999

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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Medical Director Review- 7/2023

Policy Implementation/Update Information

8/27/19 New policy developed. BCBSNC will not provide coverage for serum testing for evidence of mild traumatic brain injury because it is considered to be investigational. BCBSNC does not provide coverage for investigational services. Medical Director review 8/20/2019. Policy noticed 8/27/2019 for effective date 10/29/2019. (sk)

9/10/19 Codes 81479 and 84999 added to Billing/Coding section. Policy remains on notice until 10/29/2019. (sk)

6/23/20 Specialty Matched Consultant Advisory Panel review 5/20/2020. (sk)

7/28/20 Reviewed by Avalon 2nd Quarter 2020 CAB. When not covered section updated, no change to policy statement. Policy Guidelines updated. References updated. Medical Director review 7/2020. (bb)

6/15/21 Specialty Matched Consultant Advisory Panel review 5/19/2021. (sk)

8/24/21 Reviewed by Avalon 2nd Quarter 2021 CAB. Policy Guidelines updated. References updated. Federal Regulations updated. Medical Director review 7/2021. (sk)

9/13/22 Reviewed by Avalon 2nd Quarter 2022 CAB. Table of Terminology added. Medical Director review 8/2022. (sk)

8/15/23 Reviewed by Avalon 2nd Quarter 2023 CAB. Description, Policy Guidelines, and References updated. CPT Code 83516 added to Billing/Coding section, and CPT code 81479 deleted from Billing/Coding section. When Not Covered section reworded to provide clarity. No change to policy statement. Medical Director review 7/2023. (ldh)