Test Specific Guidelines

Immunohistochemistry (IHC)

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Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

Procedures addressed by this guideline	Procedure codes
Immunohistochemistry or immunocytochemistry, per specimen; each additional single antibody stain procedure (List separately in addition to code for primary procedure)	88341
Immunohistochemistry or immunocytochemistry, per specimen; initial single antibody stain procedure	88342
Immunohistochemistry or immunocytochemistry, per specimen; each multiplex antibody stain procedure	88344

What Is Immunohistochemistry?

Definition

Immunohistochemistry (IHC) is a method used to determine the expression of biomarkers in tissue. Antibodies that detect specific antigens (proteins, biomarkers) are applied to tissue and attach to their target antigen. The antibodies are tagged with a visible label that allows the pattern or distribution of the antigen in the tissue to be directly visualized microscopically.

Test Information

Immunohistochemistry is used widely in pathology for diagnosis, sub-typing, and increasingly to identify therapeutic targets. It has also dramatically changed the approach to evaluating cancer of unknown primary. There are numerous other applications and some of the most common are outlined below:[1-3]

Diagnostic

Initial detection of malignancy, tumor classification (including cancers of unknown origin), and sub-typing

Identification of infections (e.g. CMV infection)

Neurodegenerative disorder classification

Therapy Selection/Management

Identification of specific therapeutic targets (e.g., HER2/neu)

Further characterization of prognosis to gauge treatment aggressiveness

Genetic Disorder Evaluation

Altered gene expression predictive of an underlying genetic disorder (e.g., loss of expression of the mismatch repair genes associated with Lynch syndrome)

Skeletal muscle biopsy protein abnormalities that help establish a specific muscular dystrophy diagnosis

Criteria

This guideline addresses common issues in billing for immunohistochemistry-based tests using CPT codes 88341-88344. It is not intended to encompass immunohistochemistry-based tests billed using more specific CPT codes (e.g., 88360, 88361).

Medical Necessity Requirements

Given the numerous applications of IHC, it is not practical or desirable to create policy to address the specific use of stains in various settings. That said, it is possible to determine a maximum number of stains that should be reasonable for the vast majority of applications, and an approximate frequency by which the maximum threshold would be reached.

Several studies have included data on the average number of immunohistochemical (IHC) stains used per case in various settings. In a cost-effectiveness of IHC study, Raab (2000) modeled the analysis on a 5-antibody panel, which was the average number of antibodies ordered per case in that hospital system. No data was provided on the upper and lower limits of that range.[5]

A study published by Shah, et al. (2012) looked at the use of IHC stains among different pathology practice settings, which included academic, private and commercial practices. The study concluded that regardless of where IHC was performed, the average number of stains ordered per case was similar among all groups although ranges varied considerably. Pathologists from private groups performed an average of 4 stains (range 1-13), whereas those in commercial

laboratories used an average of 3 stains per case (range 1-7 for both). When broken down by organ system, the highest average was 6 stains per case for head and neck tissue.[6]

The National Comprehensive Cancer Network (NCCN) Guidelines for Treatment of Cancer by Site provide detailed guidelines on the use of individual IHC stains in the diagnosis and management of each cancer type addressed.[7]

National Comprehensive Cancer Network (NCCN, 2018) Guidelines on Occult Primary (Cancer of Unknown Primary [CUP]) state the following: "In patients with occult primary tumors, immunohistochemical studies are useful for the characterization of poorly differentiated or undifferentiated tumors and for cell-type determination and pathologic diagnosis. However, exhaustive IHC studies (in excess of 10-12 stains) have not been shown to increase the diagnostic accuracy in identifying the putative primary sites." NCCN recommends a tiered approach as follows: first tier determines tissue lineage, second tier can suggest putative primary sites, and an optional third tier to identify therapeutic targets in select patients.[8]

Based on these findings, most immunohistochemistry applications should rarely require more than 13 IHC stains per unique specimen. Therefore the following criteria will be applied when processing claims for IHC procedures:

In addition to the first stain billed with one unit of 88342, reimbursement will routinely be limited to 13 units of CPT 88341 per specimen.

Any claim for IHC, regardless of the number of units billed, may be subject to post-service medical necessity review if excess units are suggested based on the available clinical information.

Billing and Reimbursement Considerations

There are currently three codes for reporting qualitative IHC stains: 88341, 88342, and 88344. IHC stains are now reported per unique specimen instead of per block (paraffin-embedded tissue). Examples of unique specimens that may be evaluated on the same date of service are separate colon polyps or skin biopsies from different lesions.

Current codes:

Codes 88342 and 88341 are reported for a single antibody stain procedure.

Code 88344 is used to report a multiplex staining procedure* (e.g., PIN-4, ADH-5, Uro-3 triple stain).

Retired codes:

Code 88343 was deleted in 2015.

The HCPCS codes G0461 and G0462 are also no longer reportable.

***Multiplex staining refers to the use of two or more different antibodies mixed together ("cocktails") that demonstrate different staining characteristics on a single slide. Multiplex does not refer to antibody cocktails such as Cytokeratin AE1/AE3 that do not show distinct color changes between antibodies. There are a limited, although expanding, number of multiplex stains with PIN4 being among the most frequently utilized (evaluation of prostate biopsies).[4]**

Therefore, the following limitations will be applied when processing claims for IHC procedures:

Qualitative immunohistochemistry procedure codes 88341-88344 should only be used when other, more specific, procedure codes are not available to describe the performed test, AND

For single antibody stains:

One unit of 88342 should be used for the first single antibody applied to a unique specimen. Additional stains applied to that same specimen are billed with one unit of 88341 per stain to an allowable maximum (see Allowable Units policy below). 88341 should therefore not be billed without 88342 on the same date of service, and

It is generally unnecessary to test more than three separate specimens on the same date of service. Therefore, no more than three units of 88342 are routinely reimbursable on a single date of service, and

When more than one specimen is studied, the units of 88341 applicable to each unique specimen should be entered separately on the claim and each entry should have a corresponding unit of 88342 billed, OR

For multiplex antibody stains:

One unit of 88344 may be used for a multiplex stain applied to a unique specimen. A multiplex stain is defined as a combination of antibodies that yield separately identifiable staining characteristics on a single slide, and

No more than one multiplex stain on one specimen should be necessary on a single date of service, AND

Modifiers 26 and TC can be used to split codes 88341, 88342, and 88344 into their technical and professional components. When split, one unit of the technical component of a code and one unit of the professional component of a code will be viewed as the equivalent of one unit when calculating maximum allowable units for any code. Alternatively, the sum of units billed with the same modifier (e.g. TC) can fulfill the maximum allowable units regardless of whether the units for the other modifier (e.g., 26) are ever billed.

References

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