Rapid molecular infectious disease testing for Group A Streptococcus

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Recent review date: 6/2026

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Policy contains: Group A Streptococcus, Group A beta-hemolytic Streptococcus, Streptococcus pyogenes, streptococcal pharyngitis, strep throat, rapid molecular testing, nucleic acid amplification testing, NAAT, amplified probe testing, rapid nucleic acid test, throat swab, rapid antigen detection test, RADT, throat culture, point-of-care testing, antimicrobial stewardship.

Coverage policy

Rapid molecular infectious disease testing for Group A Streptococcus, including nucleic acid amplification testing and amplified probe testing is investigational/not clinically proven and, therefore, not medically necessary for members with suspected streptococcal pharyngitis.

Limitations

No limitations were identified during the writing of this policy

Alternative covered services

No alternative covered services were identified during the writing of this policy.

Background

Rapid molecular infectious disease testing for Group A Streptococcus refers to assays that use nucleic acid amplification or amplified probe technology to detect organism-specific nucleic acid directly from throat swab

specimens. Group A Streptococcus, also called Group A beta-hemolytic Streptococcus or Streptococcus pyogenes, is a bacterial cause of acute pharyngitis. These assays are intended for symptomatic individuals with suspected streptococcal pharyngitis and should be interpreted in the clinical context, because detection of nucleic acid does not by itself establish that current symptoms are caused by active Group A Streptococcus infection (Dubois, 2021; FDA, 2018a; Fraser, 2020).

Specimens are collected from the tonsillar pillars and posterior pharynx, then processed on a point-of-care or laboratory-based platform. Methods described in the evidence include polymerase chain reaction, loop-mediated isothermal amplification, helicase-dependent amplification, nicking enzyme amplification reaction, and deoxyribonucleic acid probe technologies. Results are generally reported as positive or negative for Group A Streptococcus and are intended to inform diagnostic and treatment decisions during or near the clinical encounter (Dubois, 2021; Fraser, 2020; Thompson, 2020).

Clinical findings of streptococcal and viral pharyngitis overlap, so clinical judgment alone may not reliably distinguish individuals with Group A Streptococcus from those with viral illness in the absence of clear viral symptoms. Clinical scoring systems may be used to identify individuals with a low probability of Group A Streptococcus pharyngitis, for whom diagnostic testing is less likely to be useful. The Centers for Disease Control and Prevention states that patients with clear viral symptoms do not need Group A Streptococcus testing, that rapid antigen detection testing or throat culture can confirm Group A Streptococcus pharyngitis, and that symptomatic children older than 3 years should receive throat culture confirmation after a negative rapid antigen detection test. Standard diagnostic approaches include rapid antigen detection testing and throat culture. Rapid antigen detection testing provides results during the visit but has lower sensitivity than molecular testing in direct comparisons. Throat culture can identify viable organisms but generally requires an incubation period before results are available (CDC, 2025; Dubois, 2021; Linder, 2025; Panahandeh, 2024).

The proposed role of rapid molecular testing is to provide faster organism detection than culture and higher analytic sensitivity than rapid antigen detection testing. Molecular testing may be performed as a stand-alone test, as an adjunct to clinical scoring, or as a replacement for culture confirmation of negative rapid antigen detection tests in some clinical laboratory workflows. Current Procedural Terminology codes 87650, 87651, and 87652 describe direct probe, amplified probe, and quantification methods for Group A Streptococcus nucleic acid testing, respectively. U.S. Food and Drug Administration product classifications and decision summaries identify molecular Group A Streptococcus platforms, including Alere i Strep A 2 and Xpert Xpress Strep A, as prescription in vitro diagnostic tests intended to aid diagnosis in patients with signs and symptoms of pharyngitis. Regulatory clearance, Clinical Laboratory Improvement Amendments waiver status, or assignment of a Current Procedural Terminology code is distinct from evidence that a test improves clinical outcomes or meets plan medical necessity criteria (CMS, 2026; FDA, 2018a; FDA, 2018b; Fraser, 2020).

Findings

The evidence base for rapid molecular infectious disease testing for Group A Streptococcus includes diagnostic accuracy studies, evidence syntheses, health technology assessments, and limited clinical utility evidence. Molecular assays generally show high sensitivity and specificity compared with throat culture and greater sensitivity than rapid antigen detection testing, but molecular-specific evidence showing improved treatment decisions, antimicrobial stewardship, health care utilization, health outcomes, or cost-effectiveness compared with established standard testing pathways remains limited. Workflow, throughput, cost, and interpretation of

positive results in possible carriers remain important sources of uncertainty (Dubois, 2021; Fraser, 2020; Mägdefrau, 2025; Thompson, 2020).

Diagnostic accuracy

Dubois and colleagues (2021) systematically reviewed commercial rapid nucleic acid tests in individuals with pharyngitis, using throat culture as the reference standard. The review included 38 studies, 46 test evaluations, and 17,411 test results. Testing was most often performed in a laboratory rather than at the point of care. Summary sensitivity was 97.5% (95% confidence interval 96.2% to 98.3%), and summary specificity was 95.1% (95% confidence interval 93.6% to 96.3%). Sensitivity analyses restricted to studies with lower risk of bias or lower applicability concerns produced broadly similar estimates. The authors concluded that high diagnostic accuracy may allow rapid nucleic acid tests to be used as stand-alone tests to diagnose Group A Streptococcus pharyngitis, while also noting the need for additional point-of-care studies (Dubois, 2021).

Fraser and colleagues (2020) conducted a health technology assessment of rapid antigen detection and molecular tests in individuals age 5 years and older with acute sore throat in primary and secondary care settings. In the population of interest, defined by higher clinical scores, point estimates for point-of-care tests ranged from 0.829 to 0.946 for sensitivity and from 0.849 to 0.991 for specificity. The assessment reported substantial heterogeneity, sparse evidence for several test and setting combinations, and insufficient evidence to identify a single most accurate point-of-care test (Fraser, 2020).

Panahandeh and colleagues (2024) compared a nucleic acid amplification test, rapid antigen detection testing, and throat culture in 82 throat swab specimens from individuals with suspected bacterial pharyngitis in a Belgian clinical and reimbursement context. Culture identified Group A Streptococcus in 26 specimens. The nucleic acid amplification test had sensitivity of 100% and specificity of 96.42%, while rapid antigen detection testing had sensitivity of 80.76% and specificity of 100%. The study provides platform-specific data but has limited precision because of the small sample size and local practice context (Panahandeh, 2024).

Comparison with standard testing methods

Direct comparisons of molecular testing with rapid antigen detection testing show higher sensitivity for molecular assays and similar specificity. In 13 direct-comparison studies involving 4,224 participants, molecular testing had sensitivity of 96.8% (95% confidence interval 94.6% to 98.1%) compared with 82.3% (95% confidence interval 65.0% to 92.1%) for rapid antigen detection testing. Specificity was similar, at 97.0% (95% confidence interval 94.3% to 98.5%) for molecular testing and 97.2% (95% confidence interval 94.3% to 98.6%) for rapid antigen detection testing (Dubois, 2021).

Higher analytic detection may reduce false-negative results compared with rapid antigen detection testing, but a positive molecular result does not necessarily establish that current symptoms are caused by active Group A Streptococcus infection. Molecular assays can detect low organism burden, colonization, residual nucleic acid from recent infection, or nucleic acid from nonviable organisms. Culture remains distinct because it detects viable organisms and may support additional microbiologic assessment, while many molecular platforms detect only the targeted organism (Banerjee, 2018; Dubois, 2021; FDA, 2018b; Thompson, 2020).

Predictive values were less consistently synthesized than sensitivity and specificity. Predictive value depends on pretest probability, disease prevalence, clinical score selection, specimen quality, prior antimicrobial

exposure, and colonization rates. In the Belgian study, the nucleic acid amplification test had a positive predictive value of 92.86% and a negative predictive value of 100%, but those values reflect the study setting and prevalence and should not be generalized without considering population risk (Panahandeh, 2024).

Clinical utility and antimicrobial stewardship

Molecular-specific evidence showing that nucleic acid amplification testing replacement of rapid antigen detection testing and/or throat culture improves patient outcomes, health care utilization, or cost-effectiveness remains limited. Fraser and colleagues (2020) found some randomized evidence that rapid antigen detection testing may reduce antimicrobial prescribing, but did not identify evidence on the prescribing impact of molecular technologies. The assessment also found no evidence on the number of appointments required per episode, morbidity, mortality, onward transmission, health-related quality of life, satisfaction with testing, or clinician satisfaction with testing (Fraser, 2020).

Banerjee and Ford (2018) reported mixed and largely indirect clinical utility evidence for rapid testing in a Canadian health technology review. One pragmatic randomized controlled trial found no clear advantage of rapid antigen detection testing over clinical scoring for symptom duration, symptom severity, or antibiotic use. An observational study reported fewer antibiotic prescribing decisions after rapid antigen detection testing, and a chart review suggested that some antibiotics prescribed at the visit were likely unnecessary after molecular or confirmatory results were considered. These findings do not establish that molecular testing improves outcomes compared with standard evaluation (Banerjee, 2018).

A 2025 systematic review and meta-analysis of randomized controlled trials by Mägdefrau and colleagues evaluated the impact of Group A Streptococcus point-of-care testing on antibiotic prescribing and patient health outcomes in outpatient care. The review included eight randomized controlled trials and found that point-of-care testing reduced antibiotic prescribing compared with standard care (risk ratio 0.62, 95% confidence interval 0.51 to 0.77). Follow-up health care visits, days until pain resolution, and days of school or work missed did not differ significantly in the limited trials reporting those outcomes. This evidence supports the clinical utility of Group A Streptococcus point-of-care testing as a broad diagnostic strategy, but it does not establish incremental net benefit of molecular testing over established rapid antigen detection testing and throat culture pathways (Mägdefrau, 2025).

Molecular testing may improve diagnostic certainty when the clinical decision depends on detection of Group A Streptococcus during the initial encounter. Diagnostic certainty does not necessarily translate into clinical utility. Because highly sensitive molecular assays may detect carriers or residual nucleic acid, the stewardship impact depends on appropriate pretest selection, interpretation of positive results in clinical context, and whether clinicians use results to avoid unnecessary antimicrobial treatment (Banerjee, 2018; Dubois, 2021; Linder, 2025; Thompson, 2020).

Workflow and economic considerations

Rapid molecular platforms may shorten time to laboratory result compared with throat culture, but operational performance varies by platform. Panahandeh and colleagues (2024) reported that rapid antigen detection testing required approximately seven minutes, while the evaluated nucleic acid amplification platform required approximately two minutes for specimen preparation plus about six minutes for analysis of negative results or less for positive results. The same study noted that the ID NOW instrument processed specimens sequentially,

which may limit throughput when multiple specimens arrive together. Culture required at least 24 hours of incubation before results were available. Other platform-specific studies and reviews similarly note that molecular platforms vary in hands-on time, batching capacity, contamination risk, and invalid or indeterminate result handling (Ferrieri, 2021; Panahandeh, 2024; Thompson, 2020).

Economic findings were context-specific and uncertain. In the Fraser and colleagues (2020) health technology assessment economic model, 14 of 21 scoped tests had sufficient accuracy and cost data for modeling. Under base-case assumptions in adults presenting in primary care, testing strategies were more costly and did not meet the cost-effectiveness thresholds used in that assessment. Key uncertainties included test acquisition cost, clinician time, culture confirmation for negative results, and assumptions about the harms and costs of unnecessary antibiotic use. In the Belgian study by Panahandeh and colleagues (2024), culture alone was the least costly approach in the local reimbursement context, followed by culture with rapid antigen detection testing. Nucleic acid amplification testing was not economically favorable without reimbursement adjustment (Fraser, 2020; Panahandeh, 2024).

Guideline recommendations

The 2025 Infectious Diseases Society of America Part 1 guideline update addressed risk assessment for Group A Streptococcus pharyngitis and the decision of who should undergo diagnostic testing by rapid antigen detection testing, molecular methods, or throat culture. The guideline suggested use of a clinical scoring system to determine who should be tested in children and adults with sore throat. The recommendation was conditional and based on very low certainty of evidence. The guideline emphasized that scoring systems are most useful for identifying individuals with low probability of Group A Streptococcus pharyngitis, in whom further diagnostic testing is unlikely to be helpful. The recommendation does not apply to children under three years of age, and high-risk individuals should be strongly considered for testing even if clinical scores are low (Linder, 2025).

The 2025 Infectious Diseases Society of America Part 1 update did not establish molecular testing as the preferred routine diagnostic strategy. It noted that clinical scoring systems were developed when throat culture was the main comparator, while contemporary practice often uses rapid antigen detection testing or nucleic acid amplification testing. It also highlighted limited evidence on how established scoring systems perform within current diagnostic workflows and recommended risk-stratified testing rather than unselected testing of all individuals with sore throat (Linder, 2025).

Current Centers for Disease Control and Prevention clinical guidance similarly supports selective testing. The Centers for Disease Control and Prevention states that patients with clear viral symptoms do not need testing for Group A Streptococcus, that rapid antigen detection testing or throat culture can confirm Group A Streptococcus pharyngitis, and that symptomatic children older than 3 years should have a negative rapid antigen detection test confirmed with throat culture. The guidance does not identify molecular testing as the preferred routine diagnostic strategy (CDC, 2025).

References

On 5/19/2026, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, the Centers for Medicare & Medicaid Services, the Centers for Disease Control and Prevention, the U.S. Food and Drug Administration, and relevant professional society sources. Search terms were: ("Group A Streptococcus" OR "Streptococcus pyogenes" OR "group A beta-hemolytic Streptococcus") AND (pharyngitis OR "sore throat" OR

"strep throat") AND ("rapid molecular testing" OR "nucleic acid amplification" OR NAAT OR PCR OR "amplified probe" OR "rapid nucleic acid test" OR "point-of-care testing") AND ("rapid antigen detection test" OR RADT OR "throat culture" OR "diagnostic accuracy" OR "antimicrobial stewardship"). We included the best available evidence according to established evidence hierarchies, including systematic reviews, meta-analyses, full economic analyses, regulatory materials, coding sources, and professional guidelines based on such evidence and clinical expertise.

Banerjee S, Ford C. Rapid Tests for the Diagnosis of Group A Streptococcal Infection: A Review of Diagnostic Test Accuracy, Clinical Utility, Safety, and Cost-Effectiveness. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health; 2018. CADTH Rapid Response Report: Peer-reviewed summary with critical appraisal.

Dubois C, Smeesters PR, Refes Y, Levy C, Bidet P, Cohen R, Chalumeau M, Toubiana J, Cohen JF. Diagnostic accuracy of rapid nucleic acid tests for group A streptococcal pharyngitis: systematic review and meta-analysis. Clin Microbiol Infect. 2021;27(12):1736-1745. Doi: 10.1016/j.cmi.2021.04.021

Fraser H, Gallacher D, Achana F, Court R, Taylor-Phillips S, Nduka C, Stinton C, Willans R, Gill P, Mistry H. Rapid antigen detection and molecular tests for group A streptococcal infections for acute sore throat: systematic reviews and economic evaluation. Health Technol Assess. 2020;24(31):1-264. Doi: 10.3310/hta24310

Linder JA, Watson ME Jr, Wessels MR, Carter DM, Cohen AL, Dien Bard J, Erdem G, Gregory CJ, Kourtis AP, Martin JM, Mochon AB, Shapiro DJ, Stevens RW, Kaur D, Barshak MB. 2025 Clinical Practice Guideline Update by the Infectious Diseases Society of America on Group A Streptococcal (GAS) Pharyngitis: Risk assessment using clinical scoring systems in children and adults. Clin Infect Dis. 2025;ciaf668. Online ahead of print. Doi:10.1093/cid/ciaf668

Panahandeh MH, Soleimani R, Nezzar Y, Rodriguez-Villalobos H, Kabamba-Mukadi B, Grimmelprez A, Schatt P. Molecular Diagnostics for Group A Streptococcal Pharyngitis: Clinical and Economic Benefits in the Belgian Healthcare Context. J Clin Med. 2024;13(21):6627. Doi:10.3390/jcm13216627

Centers for Disease Control and Prevention. Clinical Guidance for Group A Streptococcal Pharyngitis. Updated 2025. https://www.cdc.gov/group-a-strep/hcp/clinical-guidance/strep-throat.html.

Centers for Medicare & Medicaid Services. Clinical Laboratory Fee Schedule Files. Updated 2026. https://www.cms.gov/medicare/payment/fee-schedules/clinical-laboratory-fee-schedule-clfs/files.

Ferrieri P, Thonen-Kerr E, Nelson K, Arbefeville S. Prospective Evaluation of Xpert® Xpress Strep A Automated PCR Assay vs. Solana® Group A Streptococcal Nucleic Acid Amplification Testing vs. Conventional Throat Culture. Curr Microbiol. 2021;78(8):2956-2960. Doi:10.1007/s00284-021-02547-0.

Mägdefrau A-S, Kathner-Schaffert C, Matthes A, Bleidorn J, Markwart R. The Impact of Point-of-Care Testing for Group A Streptococcal Pharyngitis on Antibiotic Prescribing and Patient Health Outcomes in Outpatient Care: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Open Forum Infect Dis. 2025;12(7):ofaf407. Doi:10.1093/ofid/ofaf407

Thompson TZ, McMullen AR. Group A Streptococcus Testing in Pediatrics: the Move to Point-of-Care Molecular Testing. J Clin Microbiol. 2020;58(6):e01494-19. Doi:10.1128/JCM.01494-19.
U.S. Food and Drug Administration. Product Classification: Groups A, C and G Beta-Hemolytic Streptococcus Nucleic Acid Amplification System. Product code PGX. Updated May 18, 2026. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/classification.cfm?start_search=1&productcode=PGX

U.S. Food and Drug Administration. 510(k) Substantial Equivalence Determination Decision Summary: Alere i Strep A 2, K173653. 2018. https://www.accessdata.fda.gov/cdrh_docs/reviews/K173653.pdf

U.S. Food and Drug Administration. 510(k) Substantial Equivalence Determination Decision Summary: Xpert Xpress Strep A, K173398. 2018. https://www.accessdata.fda.gov/cdrh_docs/reviews/K173398.pdf

Policy updates

Initial review date: 5/2026 and clinical policy effective date: 7/2026

6/2026: Policy created.

Related codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy CCP.1563. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

Code	Code description
87650	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, direct probe technique.
87651	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, amplified probe technique.
87652	Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, quantification.
87880	Infectious agent antigen detection by immunoassay with direct optical observation; Streptococcus, group A. Included as an alternative standard testing code when rapid antigen detection testing is performed, subject to applicable coding manuals and plan requirements.
87081	Culture, presumptive, pathogenic organisms, screening only. Included as an alternative standard testing code when throat culture is performed, subject to applicable coding manuals and plan requirements.