Gastrointestinal Pathogen Nucleic Acid Detection Panel Testing for Infectious Diarrhea (for Tennessee Only)

Policy Number: CS169TN.K
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➲ Instructions for Use

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Related Policies
None

Application

This Medical Policy applies to Medicaid and CoverKids in the state of Tennessee.

Coverage Rationale

The following are proven and medically necessary:

- Multiplex polymerase chain reaction (PCR) panel testing for gastrointestinal pathogens, including up to 5 targets, when performed as part of an evaluation that includes blood cultures for an individual with any one of the following:
  - Diarrhea for more than 7 days
  - Diarrhea with at least one of the following:
    - Fever
    - Bloody or mucoid stools
    - Severe abdominal cramping or tenderness
    - Signs of sepsis
  - Suspected enteric fever (i.e., typhoid, paratyphoid) in an individual with a history of recent travel to an endemic region (e.g., South Central Asia, Southeast Asia, Southern Africa) or who has consumed foods prepared by people with recent endemic exposure
- Multiplex PCR panel testing for gastrointestinal pathogens, including up to 11 targets, for the evaluation of persistent diarrhea in an individual with any one of the following:
  - At risk for Clostridium difficile colitis and one of the following:
    - Diarrhea for more than 7 days
    - Diarrhea with at least one of the following:
      - Fever
      - Bloody or mucoid stools
      - Severe abdominal cramping or tenderness
      - Signs of sepsis
  - AIDS
  - On immunosuppressive medications, either following an organ transplant or when used for treatment of an autoimmune disease

- Other condition causing immunosuppression and other stool diagnostic studies have failed to yield a pathogenic organism

The following are unproven and not medically necessary due to insufficient evidence of efficacy:
- Multiplex PCR panel testing for gastrointestinal pathogens for all other indications
- Multiplex PCR panel testing for gastrointestinal pathogens > 11 targets

Medical Records Documentation Used for Reviews

Benefit coverage for health services is determined by the federal, state, or contractual requirements, and applicable laws that may require coverage for a specific service. Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the services requested.

The patient's medical record must contain documentation that fully supports the medical necessity for the requested services. This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures. Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available upon request.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
87505	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (e.g., Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 3-5 targets
87506	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (e.g., Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 6-11 targets
87507	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (e.g., Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 12-25 targets

Description of Services

Clinical presentations of infections of the gastrointestinal tract can vary widely, and such infections can be caused by a wide spectrum of infectious agents. Most of these infections, especially noninflammatory diarrhea and acute gastroenteritis of brief duration, are self-limited and do not require laboratory testing. However, fecal testing for causes of infectious gastroenteritis using either culture or culture-independent methodologies is recommended for individuals who present with moderate to severe bloody, febrile, dysenteric, nosocomial, or persistent diarrhea or for individuals who are immunocompromised. The appropriate approach for diagnosis of diarrheal illness can be impacted by many factors, including age, disease severity, duration/type of illness, time of year, and geographic location (Miller et al., 2024).

Diarrhea and other intestinal infections are caused by various bacteria, viruses, protozoa, and parasites. Traditional diagnostic methods like culture, microscopy, and antigen detection are slow, have limited sensitivity, and require specialized laboratories and trained personnel. Advances in molecular diagnostics have led to the development of rapid antigen detection and molecular-based methods, which are increasingly replacing traditional techniques. Over the past decade, commercially available nucleic acid-based methods have targeted the detection of single or multiple pathogens using multiplex assays. Modern molecular techniques incorporate real-time polymerase chain reaction; end point polymerase chain reaction, with microfluidics and array technologies; and integrated platforms that combine nucleic acid

extraction, amplification, and analysis in one step (Amjad, 2020). When available, culture-independent testing methods are recommended for identifying bacterial pathogens in individuals for whom pathogen testing is indicated. Since viral gastroenteritis often resolves without treatment, multiplex panels that target viruses often have limited clinical usefulness but are recommended for individuals who are immunocompromised or for purposes of infection control. For individuals in whom diarrhea persists for longer than 7 days, testing for parasites should be considered, but multiplex panels are limited in terms of detectable parasitic agents (Miller et al., 2024).

Clinical Evidence

The Patel et al. (2024) systematic review synthesized 39 primary studies published between 2013 and 2023 that evaluated non-invasive diagnostics for diarrhea, with a prespecified focus on point-of-care molecular assays. Of these studies, 25 assessed polymerase chain reaction (PCR)-based testing as the index modality against conventional comparators such as stool culture, microscopy, or toxin assays. Populations spanned children under age 5, adults, and immunocompromised individuals in outpatient, emergency, inpatient, and refugee-camp settings worldwide, with individual study sample sizes ranging from ~40 to > 4000 specimens. Across these heterogeneous settings, PCR served as the exposure of interest, conventional methods were the comparator, and the primary outcomes were diagnostic accuracy metrics and operational features such as time-to-result and feasibility. Pooled ranges favored PCR, with sensitivity from 87.5% to 100% and specificity from 93.4% to 100%, indicating consistently high performance for detecting common bacterial and toxigenic targets directly from stool. Non-molecular comparators were overall less sensitive despite excellent specificity. The authors concluded that multiplex stool PCR may function as a reliable first line test when an infectious cause of diarrhea is suspected, particularly in settings where rapid, organism-level results can change immediate management, such as initiating or withholding antibiotics and implementing isolation precautions. Limitations of the systematic review include the variable quality of the included studies, small or non-generalizable samples in several reports, and inconsistent reference standards. (Montasser et al., 2022, Leli et al., 2020, and Tilmanne, et al., 2019, discussed below, are included in this systematic review.)

The López Muñoz (2024) PRISMA-guided systematic review synthesized primary observational research published from 2014 to 2024 across six databases to evaluate PCR–based diagnostics for infectious diarrhea. Eighteen original studies met eligibility after screening 2760 records, comprising 12 cross-sectional and six cohort designs drawn largely from routine care and outbreak investigations in high-income settings. Studies generally enrolled individuals with acute gastroenteritis (AGE) across the lifespan, with a notable predominance of participants under five years old. The review excluded non-human studies and papers restricted to special populations such as pregnant individuals or those defined by chronic comorbidities, as well as articles not using molecular methods. The diagnostic intervention was PCR, typically compared with standard stool culture and routine non-molecular testing. Prespecified outcomes centered on diagnostic performance (sensitivity, specificity, detection yield, and time-to-result) and breadth of pathogen detection, with organism-level focus most often on *Shigella*, followed by *Escherichia coli*, *Campylobacter*, *Giardia*, and *Salmonella*. Across studies, PCR methods consistently outperformed culture by increasing the overall detection of bacteria-positive stools and identifying more distinct bacterial pathogens, with the review citing gains of 60% in culture-positive yield and 39.4% more bacterial pathogens detected when PCR was used. Multiplex platforms also compressed time-to-result from days to hours and broadened simultaneous bacterial, viral, and protozoal detection. Representative panels reported sensitivity greater than 94% and specificity greater than 98% vs conventional testing. However, the review did not meta-analyze accuracy and rarely provided effect sizes with confidence intervals or p values, so specific statistically significant estimates could not be confirmed at the review level. Important limitations include heterogeneity in assays and reference standards, under-representation of low- and middle-income settings, selective reflex culture (risking bias), lack of a universally accepted reference standard for some panels, and the fact that multiplex PCR alone does not provide antibiotic susceptibility or reliably distinguish closely related organisms such as *Shigella* vs enteroinvasive *E. coli*. These findings support early multiplex PCR for individuals with acute infectious diarrhea when rapid organism-level clarification will change management or infection control, but formal evidence on individual outcomes remains limited. (Mohtar et al., 2024, Leli et al., 2020, Tilmanne et al., 2019, and Kellner, et al., 2019, discussed below, are included in this systematic review.)

Mohtar et al. (2024) conducted a multicenter, cross-sectional study that focused on the implementation and impact of multiplex PCR for diagnosing and surveilling enteric pathogens. This study was conducted over a period of 1 year and analyzed 271 samples from participants with AGE using the Seegene Allplex Gastrointestinal Assay. The Allplex Gastrointestinal Assay is a multiplex, one-step, real-time PCR assay that detects and identifies 25 gastrointestinal pathogens, including six viruses, 13 bacteria, and six parasites simultaneously. Enteropathogens were detected in 71% of cases, with 46% being single infections and 54% mixed infections. Bacterial infections were the most prevalent (48%), followed by parasites (12%) and viruses (11%). The most frequently identified pathogens were enteroaggregative *Escherichia coli* (EAEC), enterotoxigenic *E coli* (ETEC), and enteropathogenic *E coli* (EPEC). These enteric pathogens

were prevalent during summer, fall, and winter. This study has several limitations, including the absence of a control group, a small sample size, and limited facilities, along with other limitations related to an observational study; additionally, the geographic location was limited to Lebanon, the seasonal variation did not account for factors such as changes in health care–seeking behavior or environmental conditions, and possible selection bias was present. These limitations suggest that while the findings are promising, further research with larger, more diverse populations and control groups is needed to validate the utility of this 25-pathogen test. Study materials were supplied in part by Seegene. (This study is included in the systematic review by López Muñoz et al., 2024.)

In an unblinded, randomized controlled trial, Xie et al. (2023) investigated whether the use of a large, multiplex stool diagnostic panel test (FilmArray® 22-pathogen gastrointestinal panel) impacted the practice of pediatric emergency medicine physicians when they treated children with hematochezia in a pediatric emergency department. The study included 60 children with acute hematochezia, who were aged 6 months to 18 years and randomized into two cohorts: one that included those whose stool was tested with standard microbiological methods and another that included those whose stool was tested using the FilmArray panel. The primary outcome was the performance of any blood tests (e.g., complete blood cell count) within a 72-hour time frame. The study results showed that the time to results was reduced in participants in the FilmArray group (median, 3 hours, IQR, 3-4 hours vs median, 42 hours, IQR, 23.5-47.3 hours; a difference of -38 hours; 95% CI, -41 to -22 hours). A total of 65% of participants in the FilmArray group were found to have a detectable pathogen per the FilmArray test. In the same group, 37% of the children had a detectable pathogen by standard testing. Although a greater number of bacteria were found in paired samples from children in the FilmArray group when using the FilmArray vs standard-of-care (SOC) testing, the added knowledge of these pathogens was not found to have a significant clinical impact. In the SOC group, 35% of children had an identified pathogen. In the FilmArray arm, the most frequent pathogen that was found was EPEC (19%), followed by *Campylobacter* (16%) and *Salmonella* (13%). The SOC group findings included *Campylobacter spp* (20%) and *Salmonella spp* (9%); additionally, two participants had *E coli* O157:H7, and one child had a non-O157 Shiga toxin–producing *E coli* (STEC). Overall, the two groups had no difference in the primary outcome; in the FilmArray group, 52% of participants had blood testing within 72 hours, and in the SOC group, 62% had blood tests within 72 hours (difference of -10.5%; 95% CI, -35.4% to 14.5%). In addition, no differences were found between the groups related to administration of intravenous fluid, antibiotic treatment, hospitalization, or diagnostic imaging. The FilmArray test was not associated with a clinically significant reduction in the utilization of health care resources or improved clinical outcomes in the participants of this study. This study was limited by the small sample size and lack of blinding as well as a focus on only children with bloody diarrhea, which impacts overall generalizability. The authors advised that education regarding the implementation of gastrointestinal panel testing is needed to improve integration of this technology into clinical care, and further large, multicenter studies are recommended.

In another study focused on the use of the FilmArray Gastrointestinal Panel, Carmon et al. (2023) used FilmArray to evaluate gastrointestinal infection and the distribution of pathogens in the stool samples of 91 hospitalized patients in a medical center in Israel. The clinical and demographic information for those with negative and positive samples was also compared. Overall, 61 total samples were considered positive. The most commonly identified pathogen was *Campylobacter* (34.4%), followed by *Salmonella* (24.6%), EAEC (19.7%), and EPEC (16.4%). Of note, 37.7% of the patients who tested positive had multiple pathogens detected; these were most commonly EAEC and EPEC (a total of 17.4% of those with multiple pathogens detected). Significantly higher use of antibiotics post diagnosis (63.9% vs 36.7%; p = 0.014), a shorter length of stay and time to discharge (p = 0.035, p = 0.003, respectively), and a slightly younger age (p = 0.012) were associated with positive test results in this study. The authors concluded that the use of FilmArray led to earlier identification of causal infectious drivers and improved clinical outcomes. The study was limited due to the retrospective nature of the analysis as well as the small sample size. Further high-quality studies, with larger sample numbers, are recommended to determine the overall benefit with gastrointestinal panel testing.

Aiming to investigate the infectious agents that are responsible for chronic diarrhea in individuals who are newly diagnosed with HIV, Montalvo-Otivo et al. (2023) conducted an observational, cross-sectional study. The study included 24 participants with newly–diagnosed HIV who met the inclusion criteria, including age > 18 years, watery diarrhea for > 4 weeks, and recorded values for CD4 T-lymphocyte count and HIV viral load. The FilmArray 22-pathogen gastrointestinal panel was used to test samples from the participants. Of the 24 samples collected, 92% were considered positive, with bacteria found in 69%, parasites found in 18%, and viruses found in 13%. EPEC and EAEC were the most frequently identified bacteria. The parasite *Giardia lamblia* was found in 25% of the samples, and norovirus was the most frequent viral agent, which was present in 33% of the samples. The median number of infectious agents found in individual participants was three. Pathogens that were not identified with FilmArray included *Mycobacterium tuberculosis* and fungi. The researchers indicated that their results support the use of FilmArray to identify multiple pathogens that are related to diarrhea via a single test in individuals affected with HIV, as it allows earlier diagnosis and treatment. They also recommended continued use of conventional studies (e.g., parasite examinations with special dyes, the modified Ziehl-Neelsen staining) since FilmArray is not able to identify some specific opportunistic agents that may be present in

individuals with HIV. The authors stressed the importance of investigation of nonidentified agents through methods such as colonoscopy. The study is limited due to its observational approach and small sample size.

In a 2023 joint report, the Association for Molecular Pathology , American Society for Microbiology (ASM), Infectious Diseases Society of America (IDSA), and Pan American Society for Clinical Virology addressed the utility of multiplex panel molecular testing for the diagnosis of infection in various body sites (Lewinski et al.). Regarding gastrointestinal pathogen testing, the authors noted that while molecular testing methods have been shown to improve detection compared with culture, the value of multiplex testing for gastroenteritis and foodborne disease has been questioned due to the cost, and it continues to be studied. The benefits of syndromic multiplex panels compared with culture-based diagnostic methods include more rapid detection (resulting in more rapid treatment) and the ability to detect pathogens that may require specialized techniques for culture. However, limitations are noted as well. These include the restriction of panels to specific organisms and ability of multiplex panel testing to detect nucleic acid from both living and dead organisms. Overall, the authors stated that multiplex approaches to the diagnosis of infection are generally well established with benefit, but questions remain regarding the size of testing panels and potential for algorithmic approaches to maximize benefits for affected individuals and their providers. Further study is recommended.

In 2022, Truong et al. (included in the Hayes report below) performed a comparative study that assessed the impact of multiplex gastrointestinal PCR testing on the management of infectious diarrhea in children. A PCR panel test (FilmArray) was performed on each stool sample from 172 children. Data were collected on the children's clinical management prior to and after PCR results. The primary criteria for performing stool analysis were mucous/bloody diarrhea and/or traveler's diarrhea (TD; n = 130). PCR results were positive for 120 total participants (70%). The most common pathogens that were identified were EAEC (n = 39; 23%), EPEC (n = 34; 20%), *Shigella*/ enteroinvasive *E coli* (EIEC; n = 27; 16%), and *Campylobacter* (n = 21; 12%). When compared with stool cultures, PCR detected 21 vs 19 *Campylobacter*, 12 vs 10 *Salmonella*, 27 *Shigella*/EIEC vs 13 *Shigella*, two vs two *Yersinia enterocolitica*, and one vs one *Plesiomonas shigelloides*, respectively. Medical management was revised for 40 children (23%) based on PCR results, prior to results from stool cultures being available. The authors concluded that PCR results (1) impacted the medical management of gastroenteritis for almost a quarter of the children and (2) particularly impacted the use of the appropriate antibiotic treatment prior to stool culture results.

A prospective, randomized cohort study was performed in 2022 by Montasser et al. and evaluated the use of multiplex PCR for rapid detection of four major intestinal pathogens that cause gastroenteritis. The study included 200 stool samples from participants; pathogens were identified using both molecular diagnostics and stool cultures. The organisms, that were identified using conventional cultures were *Shigella* (27%), *Aeromonas* species (10%), and enterohemorrhagic *E coli* (EHEC) O157 (8%). When multiplex PCR was used, *Shigella* was again the most common pathogen (detected in 40.5% of positive samples), followed by *Aeromonas* (30%), EHEC (20%), and *Campylobacter* species (1%). Diagnostically, multiplex PCR showed a sensitivity of 100% for *Shigella*, EHEC, and *Aeromonas*, with a specificity of 88.5%, 92.4%, and 77.8%, respectively, related to conventional methods. The diagnosis of *Campylobacter* showed a specificity of 99% and negative predictive value (NPV) of 100%. In conclusion, the researchers asserted that multiplex PCR is a quick and accurate method of detection for common intestinal pathogens that cause severe gastroenteritis. (This study is included in the systematic review by Patel et al., 2024.)

To further investigate potential quality improvements in clinical management, use of antibiotics, and in-hospital infection transmission in children with acute diarrhea, Yoo et al. (2021) analyzed the use of the FilmArray Gastrointestinal Panel in a prospective study that included a matched historical cohort. Participants in the prospective study included children younger than 19 years of age with new–onset diarrhea. A 1:1 matched historical cohort of children who were diagnosed with AGE during the 4 years prior to this investigation was analyzed as well. Children in the prospective cohort received stool testing with FilmArray, in addition to conventional methods. A total of 182 participants with suspected infectious diarrhea were included in the prospective cohort. The median age was 3.8 years, and 64.3% were male. Participants in this cohort were divided into two subgroups: community–onset diarrhea (85.7%) and hospital–onset diarrhea (14.3%). FilmArray had a higher pathogen-positivity rate for community–onset diarrhea (58.3%) than with both conventional studies (42.3%) and in the historical cohort (31.4%). Reporting time after admission averaged 25 hours in the FilmArray cohort and 72 hours in the historical cohort. In addition, there was a reduction in antibiotic use in the prospective cohort compared with the historical cohort (35.3% vs 71.8%). In the prospective cohort, 126 different pathogens from 91 stool samples were identified by FilmArray, and in the historical cohort, 51 pathogens were identified from 49 stool samples. Of the 26 participants with hospital–onset diarrhea, a single pathogen was detected in 64.3% of the children, and two or more pathogens were detected in 35.7%. Test results were used to make clinical decisions regarding isolation/precaution measures in the hospital. However, there were discrepancies between the results of FilmArray and traditional, routine testing in the prospective cohort; although FilmArray showed high detection rates of the pathogens that were included in the panel, 50% of the pathogens that were positive in the standard conventional studies and negative in FilmArray were bacteria that are not included in FilmArray but rather are cultured from stool, highlighting the importance of stool cultures

in the pathogenic diagnosis of AGE. The authors concluded that the rapid turnaround time of FilmArray and high positivity rate of the panel demonstrate the clinical benefit in children with acute diarrhea, including potentially reducing the use of antibiotics and enabling early use of infection precautions and/or isolation. This research was funded by BioFire Diagnostics.

Chang et al. (2021) performed a systematic review and meta-analysis that compared and evaluated the accuracy of the FilmArray and xTAG multiplex PCR gastrointestinal panels. Eleven studies, including a total of 7,085 stool samples, met the eligibility criteria. The FilmArray panel demonstrated higher sensitivity (> 0.90) than the xTAG Gastrointestinal Pathogen Panel (GPP; 0.81-0.95) for the majority of pathogens, except for *Rotavirus A* (equal sensitivity). Overall, multiplex PCR testing was highly accurate, with a specificity ≥ 0.98 for all pathogens, except *Yersinia enterocolitica*. According to the study results, the xTAG GPP and FilmArray Gastrointestinal Panel accurately detected more than 90% of common enteropathogens, with high sensitivity, specificity, and a shorter turnaround time. As such, the researchers stated that multiplex platforms can have a significant impact on clinical management by reducing the time to identify a pathogen, influencing outcomes by initiating treatment earlier, altering antimicrobial stewardship, and optimizing infection control. Although this systematic review included a large volume of samples and a robust analysis that followed the Cochrane guideline, limitations are present in the review. Relatively few data on FilmArray were available and did not allow subgroup analyses for some rare pathogens. In addition, the individuals' characteristics such as age, symptoms, and travel history varied among the studies that were included, and the number of studies included may be insufficient for some of the sensitivity analyses. There were also five studies that included discordant analysis, which could increase the sensitivity and specificity due to potentially elevating the true positive and negative cases. [Studies by Huang et al. (2016) and Khare et al. (2014), previously discussed in this policy, and Buss et al. (2015), discussed below, were included in this systematic review and meta-analysis.]

Machiels et al. (2020) published the results of a cross-sectional study that evaluated the clinical impact of using FilmArray, a broad, multiplex gastrointestinal panel, in individuals with gastroenteritis in a Dutch tertiary care center. FilmArray was tested in parallel with either one or a combination of standardly performed PCR panel tests based on clinical symptoms and history of illness. Testing was performed in 182 individuals. FilmArray detected one or more pathogens in 39.6% of the individuals, and routine testing detected one or more pathogens in 28.6% of the individuals. The time to receive results, including transport time, decreased from a median of 53 hours for the standard testing to 16 hours for FilmArray. The authors stated that this decrease in time to receive results could have resulted in 3.6 saved antibiotic days, earlier (29 hours) removal from isolation for 26 individuals, and prevention of additional imaging in five individuals. Limitations of this study include the small sample size, retrospective design, and single site of testing. BioFire Diagnostics supplied the FilmArray system and cartridges used in this study.

A 2020 systematic review and meta-analysis by Meyer et al. sought to analyze and report the pathogens that were identified through the use of a multiplex molecular array (FilmArray) in individuals with gastroenteritis. Publications reporting pathogens that had been identified via FilmArray were searched, and the proportions of pathogens that were identified were then pooled. A total of 14 studies, including 17,815 individuals, were included in the analysis. Of them, 39% (7,071) had positive FilmArray results. In addition, 18.1% of individuals had coinfections with more than one pathogen. The pathogens that were identified were as follows, in order of frequency: EPEC (27.5%), *Clostridium difficile* (*C. difficile*; 19.3%), norovirus (15.1%), EAEC (15%), *Campylobacter spp* (11.8%), *Salmonella spp* (8.1%), ETEC (7.3%), rotavirus (7.3%), sapovirus (7.1%), STEC (5.2%), *Shigella*/EIEC (4.9%), *Giardia lamblia* (4%), adenovirus (3.8%), *Cryptosporidium spp* (3.8%), astrovirus (2.8%), *Yersinia enterocolitica* (1.7%), *E coli* O157 (1.1%), *Plesiomonas shigelloides* (1.1%), *Cyclospora cayetanensis* (0.7%), *Vibrio spp* (0.5%), *Vibrio cholerae* (0.3%), and *Entamoeba histolytica* (0.3%). FilmArray was able to identify one or more pathogens in 48.2% of individuals who were tested vs 16.7% identified using standard conventional diagnostics when used. The authors indicated that although the FilmArray panel was positive in 39.7% of individuals with gastroenteritis, the carriage rates of identified organisms must be considered. They further proposed that restricted ordering of molecular panels specific to those individuals who might benefit from targeted treatment, could provide clinical value by quickly identifying the pathogen; as a result, individuals could receive the appropriate treatment. Additionally, future studies should focus on determining which of the identified pathogens in a test result are responsible for symptoms present and whether coinfections are associated with a more severe disease presentation. [Studies by Beal et al. (2017), Axelrad et al. (2019), and Khare et al. (2019), previously discussed in this policy, and Buss et al. (2015), Pouletty et al. (2019), and Leli et al. (2020), discussed below, were included in this systematic review and meta-analysis.]

Leli et al. (2020) evaluated and compared the diagnostic yield of the FilmArray Gastrointestinal Panel with that of routine stool culture for an etiologic diagnosis of infectious diarrhea. Stool samples (n = 183) that were collected as part of routine care from March 2016 to March 2019 were included in this retrospective analysis. Samples were then cultured and tested by FilmArray, and the following results from the comparison of diagnostic accuracy between culture and FilmArray, with respect to *Campylobacter*, *Salmonella*, *Shigella*, *Yersinia enterocolitica*, and STEC 0157, were reported: 100% (95% CI,

85%-100%) sensitivity; 93.4% (95% CI, 87.9%-96.6%) specificity; 74.3% (95% CI, 57.5%-86.4%) positive predictive value; 100% (95% CI, 96.7%-100%) NPV; 2.9% (95% CI, 1.6%-5.1%) positive likelihood ratio; and zero negative likelihood ratio. The FilmArray Gastrointestinal Panel identified 34.5% more pathogens than traditional culture methods (p = 0.001). The authors concluded that FilmArray identified a spectrum of pathogens and had good diagnostic performance compared with standard culture for the diagnosis of infectious diarrhea. However, the study lacks clinical data and was performed in a single site in a community hospital setting, thus the pathogen detection rate cannot be completely generalized, and positive results for *C. difficile* and viruses were not confirmed with alternative or reference methods. [This study is included in the systematic reviews by López Muñoz et al. (2024) and Patel et al. (2024).]

Pouletty et al. (2019) used multiplex PCR on stool samples to determine the pathogen distribution of TD in children who were traveling from tropical countries. From August 2014 to October 2015, children with TD who were admitted to two university hospitals were included in the prospective study. The FilmArray gastrointestinal PCR panel was used to identify 22 pathogens. Comparisons for the detection of *Salmonella*, *Shigella*, and *Campylobacter* by PCR and culture were made. The prevalence of extended-spectrum beta–lactamase–producing Enterobacteriaceae was also evaluated. In 58 of the 59 (98%) children, at least one pathogen was recognized. This included nine enteropathogenic bacteria, five viruses, and two parasites. The detection of enteropathogenic bacteria by multiplex PCR was enhanced by 25%. EAEC (n = 32), EPEC (n = 26), ETEC (n = 19), *Salmonella enterica* (n = 16), EIEC/*Shigella* (n = 16), *Cryptosporidium* (n = 11), sapovirus (n = 11), *Campylobacter jejuni* (n = 10), norovirus (n = 10), rotavirus (n = 9), *Giardia* (n = 8), and STEC (n = 4) were the most frequent pathogens identified. Coinfections (n = 52) were reported, including bacteria and viruses (n = 21), multiple bacteria (n = 14), or bacteria and parasites (n = 10). Extended-spectrum beta-lactamase was found in 28 cases. The authors concluded that PCR demonstrated a high prevalence of diverse enteric pathogens and coinfections in children with TD. Multiplex PCR optimized the number of treated participants by 27% compared with culture. The authors concluded that because major enteropathogenic bacteria were detected more often by PCR, the technique may allow earlier and more appropriate antibiotic treatment and increase the number of correctly diagnosed individuals. Noted limitations of this study include the lack of controls (traveling children without diarrhea and nontraveling children); lack of PCR testing for all the children admitted for TD; and participant recruitment being solely from the emergency department (these children likely had more severe symptoms). Lastly, comparison of this study's results with those of other existing studies should be considered cautiously, as the techniques and pathogens detected were not the same.

The Allplex Gastrointestinal Assay, xTAG GPP, and BD MAX™ Enteric Assays were compared by Yoo et al. (2019) to determine the efficiency of gastrointestinal pathogen detection from 858 clinical stool samples. Positive percentage agreements (PPAs) for Allplex Gastrointestinal Assay, xTAG GPP, and BD MAX Enteric Assays were 94% (258 of 275), 92% (254 of 275), and 78% (46 of 59), respectively. The xTAG GPP showed a low negative percentage agreement for Salmonella (n = 31). For viruses, positive/negative percentage agreements for Allplex Gastrointestinal Assay and xTAG GPP were 99%/96% and 93%/99%, respectively. The authors suggested that these assays are promising for the detection of gastrointestinal pathogens simultaneously.

A prospective study from the Alberta Provincial Pediatric Enteric Infection Team was conducted by Kellner et al. (2019) between December 2014 and March 2018 to determine agreement for the bacterial pathogens of interest between stool bacterial culture methods and the xTAG GPP. The primary outcome was bacterial pathogen detection agreement from a cohort of 3,089 children with gastroenteritis. This was measured as overall percentage agreements, PPA, and Cohen κ between stool bacterial culture and the GPP for bacterial pathogens sought by both detection methods: *Campylobacter spp*, *E coli* 0157, *Salmonella spp*, and *Shigella spp*. A secondary analysis targeted *Salmonella spp*, which included phenotype assessment, additional testing of GPP-negative/culture-positive isolate suspensions with the GPP, and in-house and commercial confirmatory nucleic acid testing of GPP-positive/culture-negative extracts. The overall percentage agreement between the two testing methods was > 99% for each individual pathogen and 98.9% (95% CI, 98.5%-99.3%) for all combined pathogens. Overall, the PPA was 83% (73/88; 95% CI, 73.1%-89.8%). Cohen κ was > 0.70 for *E coli* 0157, *Shigella spp*, and *Salmonella spp* and 0.89 for *Campylobacter spp*. *Salmonella spp*, the most frequently identified pathogen, was detected from the samples of 64 participants: 12 (19%) by culture only, 9 (14%) by GPP only, and 43 (67%) by both technologies. The PPA for *Salmonella spp* was 78.2% (95% CI, 64.6%-87.8%). Isolate suspensions from 12 participants with GPP negative/culture positive for Salmonella tested positive by GPP. GPP-positive/culture-negative samples tested positive using additional assays for zero of two *Campylobacter*-positive specimens, zero of four *E coli* 0157–positive samples, zero of nine *Salmonella*-positive samples, and two of three *Shigella*-positive samples. For rectal swab and stool samples, the median cycle threshold values, determined using quantitative PCR, were higher for GPP-negative/culture-positive samples than for GPP-positive/culture positive samples (for rectal swabs: 36.9, IQR, 33.7-37.1 vs 30, IQR, 26.2-33.2, respectively, p = 0.002; for stool samples: 36.9, IQR, 33.7-37.1 vs 29.0, IQR, 24.8-30.8, respectively, p = 0.001). The authors concluded that GPP overall had high concordance with culture methods; however, the PPA was suboptimal for shared bacterial targets. *Salmonella spp* identification by GPP had a propensity for false positives and negatives. Therefore, the accuracy of GPP and other nucleic acid amplification tests (NAATs) requires

further studies to determine the clinical validity and utility before culture replacement is considered. (This study is included in the systematic review by López Muñoz et al., 2024.)

The clinical validity of molecular testing for adult outpatients with diarrhea and the validation of the IDSA 2017 testing recommendation was the primary objective of Clark et al. (2019). IDSA recommends US Food and Drug Administration–approved molecular testing panels for increased sensitivity and decreased turnaround times vs bacterial cultures for the detection of enteric pathogens, even though these molecular methods have not proven to be cost-effective and may not have a significant effect on clinical management. A retrospective chart review from the University of Virginia was performed for 629 samples using the FilmArray Gastrointestinal Panel for adults with diarrhea between March 2015 and July 2016. This review revealed that 127 of 629 specimens (20.2%) had a detected pathogen; the most common identified were EPEC [47 (7.5%)], norovirus [24 (3.8%)], EAEC [14 (2.2%)], *Campylobacter* [9 (1.4%)], and *Salmonella* [9 (1.4%)]. The clinical yield was low, resulting in antimicrobial treatment indicated for 18 individuals (2.9%) and a change in clinical management of any kind indicated for 33 individuals (5.2%). Following the 2017 IDSA guidelines, which recommend diagnostic testing for individuals with fever, abdominal pain, bloody stool, or an immunocompromising condition, would have reduced testing by 32.3%, without significantly reducing clinical yield (sensitivity, 97%; 95% CI, 84.2%-99.9%; NPV, 99.5%; 95% CI, 97.3%-100.0%). In conclusion, the authors claimed that the IDSA guidelines were validated for use as sensitive but not specific clinical criteria for diagnostic testing and demonstrated that following these guidelines could reduce testing by one-third, without reducing clinical yield.

Beckman and Ferrieri (2019) compared the integrity of Verigene Enteric Pathogens Test (PCR/microarray) with that of traditional enteric culture methods for identifying Salmonella and Shigella from stool samples from February 2016 to August 2016. Positive bacterial pathogen samples underwent confirmatory cultures. Valid results were in 3,767 of 3,795 samples (99.3%); 487 (13.2%) were positive for at least one bacterial and/or viral pathogen by the Verigene test, and 45.5% tested positive for one or more bacterial pathogens. The most frequently identified pathogens by the Verigene test were norovirus (50.3%), *Campylobacter* (18.3%), *Salmonella* (13.7%), and *Shigella* (5.8%). Agreement between positive culture-based testing and Verigene was 85.3%. Verigene testing revealed 95.2% and 87.5% sensitivity and 99.8% and 99.8% specificity for Salmonella and Shigella, respectively, compared with cultures. Based on their findings, the authors concluded that the Verigene PCR/microarray platform reliably produced valid stool test results for common bacterial/viral causes of acute diarrhea, in addition to detecting pathogens that were not identified using culture-based methods.

Performance characteristics of PCR for the detection of Salmonella compared with those of the gold standard of culture were evaluated by Hapuarachchi et al. (2019). The sensitivity and specificity of PCR using the BD MAX Enteric Bacterial Panel was compared with those of enrichment culture during a 9-month prospective, comparative study; all stool samples underwent both PCR and culture for Salmonella. Selenite enrichment culture for *Salmonella* was confirmed using the API 10S and serotyping. A sample size of 6,372 stool cultures and PCR pairs was studied. The Salmonella prevalence was reported as 1.2%. The sensitivity, specificity, positive predictive value, and NPV of PCR vs those of culture was 89% (67/75), 99.8% (6,286/6,297), 86% (67/78), and 99% (6,286/6,294), respectively. The authors concluded that the enrichment culture was substantially more sensitive than PCR using BD MAX for identifying *Salmonella* in stool samples and recommended that when PCR testing is used for detection of enteric pathogens, enrichment culture testing for salmonella should be performed in parallel.

Tilmanne et al. (2019) compared the results of molecular testing methods and routine diagnostic methods for the detection of causative pathogens for AGE in symptomatic children and asymptomatic controls. A total of 178 participants who were admitted to a pediatric emergency department from two hospitals in Brussels from May 2015 to October 2016 were included in the study; 165 asymptomatic controls originated from the same hospitals. Stool samples were taken from all participants and analyzed for common pathogenic bacteria (culture), viruses (immunochromatography), and parasites (microscopy). The Luminex xTAG GPP was used for the detection of common enteropathogens using multiplex PCR. An enteropathogen was detected in 62.4% (111/178) of cases when combining the two methods [56.2% (100/178) by xTAG; 42.7% (76/178) with routine methods] and 29.1% (48/165) of controls [24.2% (40/165) by xTAG and 10.3% (17/165) by routine methods]. *Campylobacter*, *Shigella*, and *Yersinia* were missed by xTAG but detected by the culture method. However, xTAG detected Salmonella more often than routine methods [29/178 (16.3%) vs 7/178 (3.9%); $p < 0.05$]. The authors raised concerns about the pathogens missed by xTAG vs those detected by culture. While the high positivity and rapid turnaround time for the diagnosis of AGE by xTAG are promising, the authors' concern was noted regarding difficulty of result interpretation due to high positivity rates in cases and controls. [This study is included in the systematic reviews by López Muñoz et al. (2024) and Patel et al. (2024).]

In a 2018 Molecular Test Assessment (updated in 2022), Hayes conducted an evaluation of multiplex molecular panels for gastrointestinal infections. The report addressed multiple tests, including xTAG (15 targets), FilmArray (22 targets), Verigene (nine targets), and BioCode (17 targets), and found an overall low body of evidence related to study quality, a lack of a clear, ideal standard test, and a lack of evidence regarding clinical utility. However, the report notes that based

on the evidence reviewed, xTAG and FilmArray panels showed high clinical validity for most of the available pathogenic targets compared with conventional testing methods. Evidence for clinical utility was more limited. Additionally, although multiplex panels are likely to better detect coinfections, several of the targets in the test were rarely detected (e.g., *Vibrio spp*, *Yersinia entercolitica)*, making evaluation of clinical validity for those tests impossible.

In a prospective, observational study, Keske et al. (2018) aimed to detect the etiologic agents of acute diarrhea by PCR panel testing and assess its impact on antimicrobial stewardship programs (ASPs) for inpatients. Consecutive participants, who had acute watery diarrhea and fever for more than 72 hours or acute bloody diarrhea, were included in the study. An ASP was implemented in acute diarrhea cases, and the outcomes were compared in the pre-ASP and post-ASP periods. A US Food and Drug Administration–cleared, multiplexed gastrointestinal PCR panel system, FilmArray, was used, which detects 20 pathogens in stool. In total, 699 participants were included. In 499 participants (71%), at least one pathogen was detected; 176 of 499 participants (36%) were inpatients. The most commonly detected pathogens in acute diarrhea were EPEC, EAEC, ETEC, norovirus, STEC, and *Campylobacter* species. Notably, the authors found that PCR panel testing detected high rates of *C. difficile* in children as well as *Salmonella spp* and relatively high rates of *Campylobacter spp*; these are typically difficult to isolate by routine stool culture. According to the authors, using PCR panel testing in clinical practice significantly decreased the unnecessary use of antibiotics. Inappropriate antibiotic use decreased in the post-ASP period compared with the pre-ASP period among inpatients (43% and 26%, respectively). However, this was a single-center study. In addition, the authors stated that the detection of pathogens using PCR does not mean that the detected pathogen is the cause of diarrhea, so test results should be interpreted carefully.

Freeman et al. (2017) conducted a systematic review of the evidence for the clinical effectiveness for three multiplex GPP tests (xTAG, FilmArray, and Faecal Pathogens B). Overall, 23 studies, which included individuals with acute diarrhea who presented at a community or hospital setting, compared GPP tests with standard microbiology techniques. An evidential finding of the review was that GPP testing produces a greater number of pathogen-positive findings than conventional testing, but the clinical importance and consequence of these additional positive findings are uncertain. According to the authors, GPP testing can correctly identify the same positive cases as conventional methods, but GPP testing adds more false-positive results, which cause unnecessary treatment and potentially a delayed return to normal activities. The authors stated that an additional limitation of GPP tests is that although the presence of bacterial pathogens is identified, there is no bacterial culture to support either antimicrobial susceptibility testing or subtyping to support public health surveillance. Culturing from positive samples may be required to guide antimicrobial treatment or public health investigation when these are required. Studies by Khare et al. (2014), previously discussed in this policy, and Buss et al. (2015), discussed below, were included in this systematic review.

Buss et al. (2015) evaluated the clinical validity of the FilmArray GI Panel and standard bacterial culture testing. In this cross-sectional study, prospectively collected samples submitted for stool culture were used to evaluate the clinical validity (n = 1,556). The majority of the specimens (86.8%) were collected from outpatients, with hospitalized and emergency department individuals represented by 10.5% and 2.7% of the total study population, respectively. Cultures were set up within 4 days of specimen collection. FilmArray was performed by blinded BioFire personnel for comparator testing. With respect to standard methods of detection, results suggest that FilmArray is associated with sensitivities ranging from 94.5% to 100% and specificities ranging from 97.1% to 100% across pathogen types. [This study is included in the systematic reviews by Chang et al. (2021), Meyer et al. (2020), and Freeman et al. (2017).]

Clinical Practice Guidelines

American College of Gastroenterology (ACG)

In 2021, Kelly et al. published an ACG clinical guideline that addressed *C. difficile*. This guideline recommends that “C. difficile infection (CDI) testing algorithms should include both a highly sensitive and highly specific testing modality to help distinguish colonization from active infection.” The guideline also highlights that because NAAT cannot distinguish asymptomatic colonization from active infection, use of a two-step algorithm is preferred for optimal diagnostic accuracy.

The 2016 ACG Clinical Guidelines for Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults makes the following diagnosis recommendations (Riddle et al., 2016):

- Stool diagnostic studies may be used if available in cases of dysentery, moderate to severe disease, and symptoms that last > 7 days to clarify the etiology of the patient’s illness and enable specific directed therapy (strong recommendation, very low level of evidence).
- Traditional methods of diagnosis (e.g., bacterial culture, microscopy with or without special stains and immunofluorescence, antigen testing) fail to reveal the etiology of the majority of cases of acute diarrheal infection. If available, the use of US Food and Drug Administration–approved culture independent methods of diagnosis can be recommended, at least as an adjunct to traditional methods (strong recommendation, low level of evidence).

American Society for Microbiology (ASM)

In 2019, the ASM published a guideline that addressed the clinical utility of multiplex tests for respiratory and gastrointestinal pathogens. The guideline states that multiplex molecular panel tests provide the ability to test a single sample for multiple pathogens quickly and with high accuracy. Further noted is the lack of outcome-based evidence that supports the direct benefit to clinical care. Despite this evidence, the ASM guideline asserts that these tests improve patient care by providing accurate results in a timeline that allows actions that positively impact the care of affected patients, such as the timely initiation of appropriate therapies, which may lead to less transmission of disease, shortened duration of symptoms, and a decrease in the need for additional testing. Nonmedical interventions (e.g., isolation) can also be impacted by the detection of pathogens, and for those patients with infections that do not require an intervention, multiplex tests assist providers in determining when antibiotics should not be administered.

American Society of Transplantation Infectious Diseases Community of Practice

La Hoz and Morris (2019) recommended that "for the diagnosis of SOT (solid organ transplant) recipients with suspected gastrointestinal infections," gastrointestinal multiplex molecular assays are recommended to identify *Cryptosporidium, Cyclospora, and Giardia.*

Infectious Diseases Society of America (IDSA)

An IDSA Clinical Practice Guideline for Laboratory Diagnosis of Infectious Diseases (Miller et al., 2024) indicates that fecal testing to determine the cause of infectious gastroenteritis using either culture or culture-independent technologies is recommended for patients who present with moderate to severe, bloody, febrile, dysenteric, nosocomial, or persistent diarrhea or in patients who are immunocompromised. No laboratory testing is typically indicated for noninflammatory diarrhea and acute gastroenteritis of limited duration. Standard testing for pathogens other than *C. difficile* is often reserved for patients who have been in a hospital setting for more than 3 days. Culture-independent multiplex molecular tests have been reported to have greater sensitivity, faster turnaround time, and potentially higher rates of detection than culture; when available, these are recommended by the IDSA for the detection of bacterial pathogens. Since viral gastroenteritis often resolves independent of treatment, multiplex panels that target viruses typically have limited clinical impact but are indicated for patients who are immunocompromised. For parasites, the use of multiplex panels may be considered in patients who have diarrhea for greater than 7 days. Of note, highly multiplexed assays can also detect mixed infections, for which the importance of each individual pathogen is uncertain. These assays may also allow for the detection of pathogens such as EAEC or EPEC or viruses, for which the clinical importance and indication for appropriate therapy is indeterminate. It is noted that culture-independent methods should not be regarded as "tests of cure," because they detect both viable as well as nonviable organisms.

The 2017 IDSA Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea list the following recommendations (Shane et al., 2017):

- People with fever or bloody diarrhea should be evaluated for enteropathogens for which antimicrobial agents may confer clinical benefit, including *Salmonella enterica* subspecies, *Shigella*, and *Campylobacter* (strong recommendation, low level of evidence).
- Enteric fever should be considered when a febrile person (with or without diarrhea) has a history of travel to areas in which causative agents are endemic, has consumed foods prepared by people with recent endemic exposure, or has laboratory exposure to *Salmonella enterica* subspecies enterica serovar Typhi and *Salmonella enterica* subspecies enterica serovar Paratyphi (strong recommendation, moderate level of evidence).
- Stool testing should be performed for *Salmonella, Shigella, Campylobacter, Yersinia, C. difficile*, and STEC in people with diarrhea that is accompanied by fever, bloody or mucoid stools, severe abdominal cramping or tenderness, or signs of sepsis (strong recommendation, moderate level of evidence). Bloody stools are not an expected manifestation of infection with *C. difficile* (strong recommendation, moderate level of evidence).
- Stool testing should be performed under clearly identified circumstances for *Salmonella, Shigella, Campylobacter, Yersinia*, *C. difficile*, and STEC in symptomatic hosts (strong recommendation, low level of evidence). Specifically:
    - Test for *Yersinia enterocolitica* in people with persistent abdominal pain (especially school-aged children with right lower quadrant pain mimicking appendicitis who may have mesenteric adenitis) and in people with fever at epidemiologic risk for yersiniosis, including infants with direct or indirect exposures to raw or undercooked pork products.
    - In addition, test stool specimens for *Vibrio* species in people with large-volume, rice-water stools or either exposure to salty or brackish waters, consumption of raw or undercooked shellfish, or travel to cholera-endemic regions within 3 days prior to onset of diarrhea.
- A broad differential diagnosis is recommended in immunocompromised people with diarrhea, especially those with moderate and severe primary or secondary immune deficiencies, for evaluation of stool specimens by culture, viral studies, and examination for parasites (strong, moderate). People with AIDS with persistent diarrhea should undergo additional testing for other organisms, including but not limited to *Cryptosporidium, Cyclospora, Cystoisospora*,

microsporidia, Mycobacterium avium complex, and cytomegalovirus (strong recommendation, moderate level of evidence).

- Diagnostic testing is not recommended in most cases of uncomplicated TD, unless treatment is indicated. Travelers with diarrhea that lasts 14 days or longer should be evaluated for intestinal parasitic infections (strong, moderate). Testing for *C. difficile* should be performed in travelers treated with antimicrobial agent(s) within the preceding 8 to 12 weeks. In addition, gastrointestinal tract disease, including inflammatory bowel disease and postinfectious irritable bowel syndrome, should be considered for evaluation (strong recommendation, moderate level of evidence).
- Clinical consideration should be used for interpretation of results of multiple-pathogen NAATs because such assays detect DNA and not necessarily viable organisms (strong recommendation, low level of evidence).
- Blood cultures should be obtained from infants younger than 3 months of age, people of any age with signs of septicemia or when enteric fever is suspected, people with systemic manifestations of infection, people who are immunocompromised, people with certain high-risk conditions such as hemolytic anemia, and people who traveled to or have had contact with travelers from enteric fever–endemic areas with a febrile illness of unknown etiology (strong recommendation, moderate level of evidence).
- Culture-independent (including panel-based multiplex molecular diagnostics from stool and blood specimens) and, when indicated, culture-dependent diagnostic testing should be performed when there is a clinical suspicion of enteric fever (diarrhea uncommon) or diarrhea with bacteremia (strong recommendation, moderate level of evidence).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

There are several commercial multiplex polymerase chain reaction kits that have been cleared through the FDA 510(k) clearance process. These include but are not limited to xTAG Gastrointestinal Pathogen Panels; FilmArray Panels; Verigene panels; and BioCode Gastrointestinal Pathogen Panels.

To locate marketing clearance information for a specific panel, search the FDA 510(k) premarket notification database available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm (Use Product Codes PCH and PCI). (Accessed September 12, 2025)

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Policy History/Revision Information

Date	Summary of Changes

02/01/2026	**Medical Records Documentation Used for Reviews**
	• Added language to indicate:
	  ○ Benefit coverage for health services is determined by the federal, state, or contractual requirements, and applicable laws that may require coverage for a specific service
	  ○ Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the service requested
	  ○ The patient's medical record must contain documentation that fully supports the medical necessity for the requested services
	  ○ This documentation includes but is not limited to relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures
	  ○ Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available upon request
	Supporting Information
	• Updated *Clinical Evidence* and *References* sections to reflect the most current information
	• Archived previous policy version CS169TN.J

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state, or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state, or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state, or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state, or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.