

Subject:	Respiratory Viral Panel Testing in the Outpatient Setting	Publish Date:	04/01/2021
Guideline #:	CG-LAB-14	Last Review Date:	11/05/2020
Status:	Revised		

Description

This document addresses the use of respiratory viral panel (RVP) testing in the outpatient setting. RVPs are multiplexed nucleic acid tests used to detect respiratory viruses including, but not limited to: adenovirus, coronavirus (229E, HKU1, NL63, OC43, severe acute respiratory syndrome coronavirus 2), human bocavirus, human metapneumovirus, human rhinovirus/enterovirus, influenza A (A, H1, H1-2009, H3), influenza B, parainfluenza (1, 2, 3, 4), respiratory syncytial virus (A, B). This document does not address RVP testing in the inpatient setting.

Note: This document does *not* address tests that detect *only* severe acute respiratory syndrome coronavirus 2 and influenza virus types A and B, with or without respiratory syncytial virus.

Note: Please see the following related document for additional information:

- ADMIN.00007 Immunizations

Clinical Indications

Medically Necessary:

Respiratory viral panel testing in the outpatient setting is considered **medically necessary** when all of the following criteria have been met:

1. Use of limited panels involving 5 targets or less; **and**
2. Testing is for individuals who are at high risk for complications of respiratory viral infection including, but not limited to, individuals who are immunocompromised (for example, lung transplant recipients); **and**
3. The results of testing will be used to guide or alter management.

Not Medically Necessary:

Respiratory viral panel testing in the outpatient setting is considered **not medically necessary** when the criteria above have not been met and for all other indications, including but not limited to:

1. Testing average risk individuals;
2. Use of large panels involving 6 or more targets.

Coding

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue's standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

The following codes for treatments and procedures applicable to this guideline are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT

87631 Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types of subtypes, 3-5 targets

ICD-10 Diagnosis

All diagnoses including, but not limited to, the following:

B20	Human immunodeficiency virus [HIV] disease
D80.0-D80.9	Immunodeficiency with predominantly antibody defects
D81.0-D81.9	Combined immunodeficiencies
D82.0-D82.9	Immunodeficiencies associated with other major defects
D83.0-D83.9	Common variable immunodeficiency
D84.0-D84.9	Other immunodeficiencies
D86.0-D86.9	Sarcoidosis
D89.81-D89.89	Other specified disorders involving the immune mechanism not elsewhere classified
D89.9	Disorder involving the immune mechanism, unspecified
Z94.0-Z94.9	Transplanted organ and tissue status

When services are Not Medically Necessary:

For the procedure codes listed above when criteria are not met or for situations designated in the Clinical Indications section as not medically necessary.

When services are also Not Medically Necessary:

For the following procedure codes; or when the code describes a procedure designated in the Clinical Indications section as not medically necessary.

CPT

87632 Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types of subtypes, 6-11 targets

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue's standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

87633	Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types of subtypes, 12-25 targets
0115U	Respiratory infectious agent detection by nucleic acid (DNA and RNA), 18 viral types and subtypes and 2 bacterial targets, amplified probe technique, including multiplex reverse transcription for RNA targets, each analyte reported as detected or not detected ePlex Respiratory Pathogen (RP) Panel, GenMark Diagnostics, Inc, GenMark Diagnostics, Inc
0151U	Infectious disease (bacterial or viral respiratory tract infection), pathogen specific nucleic acid (DNA or RNA), 33 targets, real-time semi-quantitative PCR, bronchoalveolar lavage, sputum, or endotracheal aspirate, detection of 33 organismal and antibiotic resistance genes with limited semi-quantitative results BioFire® FilmArray® Pneumonia Panel, BioFire® Diagnostics
0202U	Infectious disease (bacterial or viral respiratory tract infection), pathogen-specific nucleic acid (DNA or RNA), 22 targets including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), qualitative RT-PCR, nasopharyngeal swab, each pathogen reported as detected or not detected BioFire® Respiratory Panel 2.1 (RP2.1), BioFire® Diagnostics, BioFire® Diagnostics, LLC
0223U	Infectious disease (bacterial or viral respiratory tract infection), pathogen-specific nucleic acid (DNA or RNA), 22 targets including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), qualitative RT-PCR, nasopharyngeal swab, each pathogen reported as detected or not detected QIAstat-Dx Respiratory SARS CoV-2 Panel, QIAGEN Sciences, QIAGEN GmbH
0225U	Infectious disease (bacterial or viral respiratory tract infection) pathogen-specific DNA and RNA, 21 targets, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), amplified probe technique, including multiplex reverse transcription for RNA targets, each analyte reported as detected or not detected ePlex® Respiratory Pathogen Panel 2, GenMark Dx, GenMark Diagnostics, Inc

ICD-10 Diagnosis

All diagnoses

Discussion/General Information

RVPs are multiplexed nucleic acid tests used for the simultaneous detection of respiratory pathogens. Examples of these respiratory pathogens include adenovirus, coronavirus (229E, HKU1, NL63, OC43, severe acute respiratory syndrome coronavirus 2), human bocavirus, human metapneumovirus, human rhinovirus/enterovirus, influenza A (A, H1, H1-2009, H3), influenza B, parainfluenza (1, 2, 3, 4), and respiratory syncytial virus (A, B). The panels vary based on the extent of multiplexing (4 to 22 targets), level of the method (moderate to high), throughput (low

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue's standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

to high), and time to results (less than 1 hour to 8 hours). Effective antiviral agents are available for certain respiratory viruses (for example, influenza) but not for others. Results of these panels may be used in the inpatient setting to aid in decisions regarding discontinuation of RSV prevention [Synagis® (palivizumab) prophylaxis; AstraZeneca, Cambridge, United Kingdom], initiation or continuation/discontinuation of antibiotic therapy, anti-influenza therapy, or isolation or cohorting of hospitalized individuals.

High Risk Individuals

Studies evaluating the use of RVP testing in the outpatient setting have generally been limited to high risk populations, for example, immunocompromised individuals, including lung transplant recipients. Respiratory viral infections (RVI) can cause significant morbidity and mortality in high risk populations (Bridevaux, 2014; Fisher, 2016; Gottlieb, 2009; Kumar, 2012; Magnusson, 2013; Soccal, 2010). In conditions such as lung transplantation, infections with respiratory viruses are a common and potentially serious complication, and often present with nonspecific clinical findings; furthermore, management strategies vary depending on the specific virus causing the infection. As reported in a surveillance study conducted by Kumar and colleagues (2010), respiratory viral infections are commonly detected in bronchoalveolar lavages (BAL) obtained from lung transplant individuals. After BAL samples collected from 93 lung transplant individuals underwent RVP testing using the xTAG® Respiratory Viral Panel (Luminex Corporation, Austin, TX), the authors found that “biopsy-proven acute rejection (\geq grade 2) or decline in forced expiratory volume in 1 sec \geq 20% occurred in 16 of 48 (33.3%) patients within 3 months of RVI when compared with 3 of 45 (6.7%) RVI-negative patients within a comparable time frame ($p=0.001$)” (Kumar, 2010). While acknowledging that further studies are needed, the authors postulated that since asymptomatic or symptomatic respiratory viral infections can trigger acute rejection, RVP testing may help with clinical disease management in lung transplant individuals.

As noted in a retrospective study (Hammond 2012), timely diagnosis is recommended for rapid care in high risk populations to help with clinical disease management. In an effort to identify a diagnostic test with a faster turnaround time than conventional methods, Hammond and colleagues evaluated the performance of the FilmArray® Respiratory Panel EZ (RP EZ) (bioMérieux, Inc., Marcy-l'Étoile, France) as compared to standard clinical testing in immunocompromised individuals ($n=87$). Through verification with real-time PCR, the evaluators found that the FilmArray assay identified significantly more respiratory viral pathogens than standard clinical testing ($p=0.001$), and concluded that it can provide rapid and accurate diagnosis in immunocompromised individuals, which is critical for clinical disease management.

Given the emerging nature of the coronavirus disease 2020 (COVID-19) pandemic, coupled with limited information available to characterize the spectrum of clinical illness associated with COVID-19, the Centers for Disease Control and Prevention (CDC) recommends that clinicians test for other causes of respiratory illness (CDC, 2020). As noted by the National Institutes of Health (NIH): “the vast majority of patients who are critically ill with COVID-19 have attributes and co-morbidities that place them at higher risk for serious disease, such as older age, hypertension, cardiovascular disease, diabetes, chronic respiratory disease, cancer, renal disease, and obesity”; (NIH, 2020) however, the possible risk of progression from mild or moderate clinical presentation to severe illness remains under continued evaluation.

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue’s standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue’s Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

In 2018, the Infectious Diseases Society of America published guidelines entitled, Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. In it, the following graded recommendations were made with “Good” (A), “Moderate” (B) and “Poor evidence to support a recommendation” (C) graded evidence to support, and quality II (based on “Evidence from 1 or more well-designed clinical trials, without randomization; from cohort or case-controlled analytic studies [preferably from >1 center]; from multiple time-series; or from dramatic results from uncontrolled experiments”) and III recommendations (based on “Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees”).

Outpatients (including emergency department patients).

- Clinicians should test for influenza in high-risk patients, including immunocompromised persons who present with influenza-like illness, pneumonia, or nonspecific respiratory illness (eg, cough without fever) if the testing result will influence clinical management (A–III).
- Clinicians should test for influenza in patients who present with acute onset of respiratory symptoms with or without fever, and either exacerbation of chronic medical conditions (eg, asthma, chronic obstructive pulmonary disease [COPD], heart failure) or known complications of influenza (eg, pneumonia) if the testing result will influence clinical management (A–III).
- Clinicians can consider influenza testing for patients not at high risk for influenza complications who present with influenza-like illness, pneumonia, or nonspecific respiratory illness (eg, cough without fever) and who are likely to be discharged home if the results might influence antiviral treatment decisions or reduce use of unnecessary antibiotics, further diagnostic testing, and time in the emergency department, or if the results might influence antiviral treatment or chemoprophylaxis decisions for high-risk household contacts (C–III).
- Clinicians should use rapid molecular assays (ie, nucleic acid amplification tests) over rapid influenza diagnostic tests (RIDTs) in outpatients to improve detection of influenza virus infection (A–II) [targeted panel tests].

Hospitalized Patients

- Clinicians should use multiplex RT-PCR assays targeting a panel of respiratory pathogens, including influenza viruses, in hospitalized immunocompromised patients (A–III).
- Clinicians can consider using multiplex RT-PCR assays targeting a panel of respiratory pathogens, including influenza viruses, in hospitalized patients who are not immunocompromised if it might influence care (eg, aid in isolation decisions, reduce other testing or antibiotic use) (B–III) (Uyeki, 2019).

Antibiotic Stewardship in Average Risk Individuals in the Outpatient Setting

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue’s standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue’s Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

While RVP testing for antibiotic stewardship has been evaluated in average risk individuals in the outpatient setting, as described below, the evidence lacks clinical utility.

Doan and colleagues (2009) published a randomized controlled trial with the aim to evaluate the rate of ancillary testing and antibiotic prescription rate in pediatric cases in the emergency department (ED). Using a computer randomization program, individuals were randomly assigned to received RVP testing (n=90) or nasopharyngeal washing for rapid viral diagnostic test (n=110). The authors did not find a statistically significant difference in rate of ancillary testing [(chest X-ray: RR 0.86; 95% confidence interval [CI], 0.44, 1.11), (blood work: RR 0.59; 95% CI, 0.28, 1.23), (urine analysis: RR 1.12; 95% CI, 0.73, 1.71)] or antibiotic prescription rate (RR 0.86; 95% CI, 0.48, 1.53) in the ED.

In 2011, Brittain-Long and colleagues performed a multicenter, open-label, randomized control trial to assess the impact of RVP testing on antibiotic prescription rates in adult individuals. RVP testing was performed on all individuals who were then randomized into the rapid results cohort (n=202) or the delayed result cohort (n=204). Based on randomization, the treating physician received the results from the RVP testing either on the day following inclusion (the rapid result cohort) or 8 to 12 days later (the delayed result cohort). The results showed 4.5% of individuals in the rapid results cohort received antibiotics at the initial visit compared to 12.3% of individuals in the delayed result cohort (p=0.005); however, there was no significant difference between the two groups at the follow-up visit (10 days post-initial visit) [13.9% in the rapid result group and 17.2% in the delayed result group (p=0.359)]. Further research is needed to identify how to sustain the initial results.

In 2016, Green and colleagues also evaluated the impact of RVP testing on antibiotic prescription rates in adult individuals (n=295) through a retrospective chart review. Individuals' charts were evaluated based on three test groups: tested positive for influenza virus (n=105), tested positive for a non-influenza virus pathogen (n=109), and no respiratory pathogen detected (n=81). The authors found a significant difference in rates of oseltamivir (p<0.0001) and antibiotic prescriptions (p=0.005) among the three groups; however, there was no significant difference in antibiotic prescription rates between the non-influenza virus pathogen group and the no respiratory pathogen detected group (p=1.0). The authors concluded that "testing positive for influenza virus was associated with receiving fewer antibiotic prescriptions, but no such effect was seen for those who tested positive for a non-influenza virus. These data suggest that testing for influenza viruses alone may be sufficient" (Green, 2016).

Echavarría and colleagues (2018) published the results of a prospective, randomized, non-blinded study that assessed the impact of RVP testing on antibiotic and antiviral prescription, and use of complementary studies (chest x-ray, computerized tomography scan, complete blood count, urinary antigen for *Streptococcus pneumoniae* or *Legionella pneumoniae*, and bacterial cultures of blood, urine or sputum). During the 2016 and 2017 respiratory seasons (April-November 2016 and April-October 2017), 432 individuals (156 children and 276 adults) who presented to a single center emergency department with signs and symptoms of an acute lower respiratory infection had testing performed via the FilmArray assay (n=289) or immunofluorescence assay (IFA) (n=143). High risk individuals, such as those with cancer, HIV, immunosuppression, or organ transplants, were excluded from the study. The results showed a change in medical management was significantly more likely in the FilmArray assay group than the IFA group in both children (odds ratio [OR]=8.07; CI 95% 3.03–21.47; p<0.001) and adults (OR=2.67; CI 95% 1.32–5.40; p=0.006). For antibiotics, a significant change in treatment plan was observed in

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue's standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

both children (OR=12.23; CI 95% 1.56–96.09; $p=0.017$) and adults (OR=15.52; CI 95% 1.99–120.83; $p=0.009$) in the FilmArray assay group versus the IFA group. While there were significant changes noted in antiviral prescription for both FluA/B positive adults ($p=0.091$) and FluA/B negative adults ($p=0.042$), there was no significant change in antiviral prescription noted in children between the two study groups. As for complementary studies, there was a significant decrease of usage noted in children between the two groups ($p=0.001$); however, a significant change was not noted in adults. While this study has some positive findings, more studies are needed to validate these results in the average risk population.

Sensitivity, Specificity, and Predictive Value

RVP can replace conventional methods such as viral culture and direct fluorescent antibody testing. Multiple studies have demonstrated that multiplex PCR provides greater yield and sensitivity than conventional methods in immunocompromised individuals, including lung transplant recipients (Gottlieb, 2009; Hopkins, 2003; Kumar, 2005; Weinberg, 2002).

Gadsby and colleagues (2010) reported on a retrospective study that compared the xTAG® Respiratory Viral Panel FAST (Luminex Corporation, Austin, TX), commonly known as the RVP Fast assay, with viral culture, a direct fluorescent assay (DFA), and a panel of single and multiplex real-time PCRs in the testing of 286 respiratory specimens. The sensitivity and specificity of the RVP Fast assay compared to the multiplex real-time PCR were 78.8% and 99.6%, respectively; however the sample set used had a low number of specimens that were not positive for several of viruses, such as influenza and parainfluenza. More studies are needed with larger numbers of positive specimens to properly assess the RVP Fast assay.

In 2017, Chiu and colleagues published a prospective study with the aim to compare FilmArray assay to cell culture and PCR. A total of 60 samples were collected from November 2016 to January 2017. Of the 60 samples, 52 tested positive for respiratory pathogens. While the FilmArray assay showed higher sensitivity than PCR and a positive predictive value of 100%, the results of the FilmArray assay and cell culture were identical. In addition, the study did not evaluate clinical utility of the FilmArray assay.

Large Respiratory Viral Panels

Large viral panels, those containing 6 or more pathogen targets, often include uncommon clinical viral targets such as pathogens unlikely to be found in the specific populations being tested, or pathogens that, if identified, do not change management. Evidence is lacking to support the use of large viral panels versus limited viral panels containing 5 or less pathogen targets in the outpatient setting. Comparative data does not demonstrate added clinical utility over panels that consist of combinations of influenza A and B with or without RSV.

Large respiratory panel testing conducted on a series of 1206 patients with suspected COVID-19 during the 2020 pandemic found modest rates of co-infection between severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and other respiratory pathogens (20%). However, the authors found that testing for non-SARS-CoV-2 respiratory pathogens (influenza A/B, respiratory syncytial virus, non-SARS-CoV-2 Coronaviridae, adenovirus, parainfluenza 1-4, human metapneumovirus, rhinovirus/ enterovirus, Chlamydia pneumoniae, Mycoplasma

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue's standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

pneumonia) did not change disease management unless co-infection indicated the presence of virus amenable to targeted therapy (for example, neuraminidase inhibitors for influenza in appropriate patients) (Kim, 2020).

Summary

At this time, the evidence supporting RVP testing in the outpatient setting is limited to individuals who are at high risk for complications of respiratory viral infection, including immunocompromised individuals as well as including lung transplant recipients, when the result of testing is used to guide or alter management. Evidence does not demonstrate clinical utility in average risk individuals; use of these tests have not been shown to change treatment decisions and improve subsequent clinical outcomes. Large viral panels containing 6 or more pathogen targets have not demonstrated clinical utility as compared to targeted viral panels containing 5 or less pathogen targets in the outpatient setting.

Definitions

Antibiotic stewardship: Coordinated efforts designed to optimize treatment of infections and reduce adverse events associated with antibiotic use.

Multiplexed nucleic acid test: Simultaneous detection of DNA or RNA to determine the presence of one or more viruses in a specimen.

References**Peer Reviewed Publications:**

1. Babady NE, England MR, Jurcic Smith KL, et al. Multicenter evaluation of the ePlex respiratory pathogen panel for the detection of viral and bacterial respiratory tract pathogens in nasopharyngeal swabs. *J Clin Microbiol.* 2018; 56(2). pii: e01658-17.
2. Bridevaux PO, Aubert JD, Soccal PM, et al. Incidence and outcomes of respiratory viral infections in lung transplant recipients: a prospective study. *Thorax.* 2014; 69(1):32-8.
3. Brittain-Long R, Westin J, Olofsson S, et al. Access to a polymerase chain reaction assay method targeting 13 respiratory viruses can reduce antibiotics: a randomised, controlled trial. *BMC Med.* 2011; 9:44.
4. Chiu SC, Lin YC, Wang HC, et al. Surveillance of upper respiratory infections using a new multiplex PCR assay compared to conventional methods during the influenza season in Taiwan. *Int J Infect Dis.* 2017; 61:97-102.
5. Doan QH, Kisson N, Dobson S, et al. A randomized, controlled trial of the impact of early and rapid diagnosis of viral infections in children brought to an emergency department with febrile respiratory tract illnesses. *J Pediatr.* 2009; 154(1):91-95.
6. Echavarría M, Marcone DN, Querci M, et al. Clinical impact of rapid molecular detection of respiratory pathogens in patients with acute respiratory infection. *J Clin Virol.* 2018; 108:90-95.
7. Fisher CE, Preiksaitis CM, Lease ED, et al. Symptomatic respiratory virus infection and chronic lung allograft dysfunction. *Clin Infect Dis.* 2016; 62(3):313-319.

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue's standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

8. Gadsby NJ, Hardie A, Claas EC, et al. Comparison of the luminex respiratory virus panel fast assay with in-house real-time PCR for respiratory viral infection diagnosis. *J Clin Microbiol.* 2010; 48(6):2213-2216.
9. Gottlieb J, Schulz TF, Welte T, et al. Community-acquired respiratory viral infections in lung transplant recipients: a single season cohort study. *Transplantation.* 2009; 87(10):1530-1537.
10. Green DA, Hitoalaj L, Kotansky B, et al. Clinical utility of on-demand multiplex respiratory pathogen testing among adult outpatients. *J Clin Microbiol.* 2016; 54(12):2950-2955.
11. Hammond SP, Gagne LS, Stock SR, et al. Respiratory virus detection in immunocompromised patients with FilmArray respiratory panel compared to conventional methods. *J Clin Microbiol.* 2012; 50(10):3216-3221.
12. Hopkins PM, Plit ML, Carter IW, et al. Indirect fluorescent antibody testing of nasopharyngeal swabs for influenza diagnosis in lung transplant recipients. *J Heart Lung Transplant.* 2003; 22(2):161-168.
13. Kim D, Quinn J, Pinsky B, et al. Rates of Co-infection between SARS-CoV-2 and other respiratory pathogens. *JAMA.* 2020; 323(20):2085-2086.
14. Kumar D, Erdman D, Keshavjee S, et al. Clinical impact of community-acquired respiratory viruses on bronchiolitis obliterans after lung transplant. *Am J Transplant.* 2005; 5(8):2031-2036.
15. Kumar D, Husain S, Chen MH, et al. A prospective molecular surveillance study evaluating the clinical impact of community-acquired respiratory viruses in lung transplant recipients. *Transplantation.* 2010; 89(8):1028-33.
16. Magnusson J, Westin J, Andersson LM, et al. The impact of viral respiratory tract infections on long-term morbidity and mortality following lung transplantation: a retrospective cohort study using a multiplex PCR panel. *Transplantation.* 2013; 95(2):383-388.
17. Soccal PM, Aubert JD, Bridevaux PO, et al. Upper and lower respiratory tract viral infections and acute graft rejection in lung transplant recipients. *Clin Infect Dis.* 2010; 51(2):163-170.
18. Weinberg A, Zamora MR, Li S, et al. The value of polymerase chain reaction for the diagnosis of viral respiratory tract infections in lung transplant recipients. *J Clin Virol.* 2002; 25(2):171-175.

Government Agency, Medical Society, and Other Authoritative Publications:

1. Centers for Disease Control and Prevention (CDC). Guide for considering influenza testing when influenza viruses are circulating in the community. Updated September 1, 2020. Available at: <https://www.cdc.gov/flu/professionals/diagnosis/consider-influenza-testing.htm>. Accessed on October 13, 2020.
2. Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical practice guidelines by the Infectious Diseases Society of America: 2018 update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. *Clin Infect Dis.* 2019; 68(6):895-902.

Websites for Additional Information

1. Centers for Disease Control and Prevention (CDC). Available at: <https://www.cdc.gov/>. Accessed on October 12, 2020.
 - About Adenoviruses. Last reviewed: August 28, 2019.
 - Common Colds: Protect Yourself and Others. Last reviewed: October 7, 2020.
 - Coronavirus (COVID-19). Last reviewed: October 9, 2020.
 - Human Metapneumovirus (HMPV) Clinical Features. Last reviewed: September 5, 2019.

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue's standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

- Multiplex Assays Authorized for Simultaneous Detection of Influenza Viruses and SARS-CoV-2 by FDA. Page last reviewed: October 5, 2020
 - About Human Parainfluenza Viruses (HPIVs). Last reviewed: October 31, 2019.
 - Influenza (Flu). Last reviewed: October 9, 2020.
 - About RSV. Last reviewed: June 26, 2018.
2. National Institutes of Health (NIH). Available at: <https://www.nih.gov/> . Accessed on October 12, 2020.
- Coronavirus (COVID-19). Last reviewed: June 12, 2020.
 - Influenza. Last reviewed: June 12, 2020.
 - Parainfluenza Virus Type 3. Last updated: August 30, 2016.
 - Respiratory Syncytial Virus (RSV). Last reviewed: December 12, 2008.

Index

BioFire® FilmArray® Pneumonia Panel
 ePlex® (GenMark Diagnostics, Inc., Carlsbad, CA)
 FilmArray Respiratory Panel EZ (RP EZ)
 NxTAG® Respiratory Pathogen Panel (Luminex Corporation, Austin, TX)
 VERIGENE® Respiratory Pathogens Flex Test (Luminex Corporation, Austin, TX)
 xTAG® Respiratory Viral Panel
 xTAG Respiratory Viral Panel FAST

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

History

Status	Date	Action
	04/01/2021	Updated Coding section with 04/01/2021 CPT changes; removed 0098U, 0099U, 0100U deleted 03/31/2021.
Revised	11/05/2020	Medical Policy & Technology Assessment Committee (MPTAC) review. Reformatted Clinical Indications. Updated Description, Discussion/General Information and References sections. Reformatted Coding section.
	10/09/2020	Clarified in the Description that this CUMG does <i>not</i> address tests that detect <i>only</i> severe acute respiratory syndrome coronavirus 2 and influenza virus types A and B, with or without respiratory syncytial virus.
	09/11/2020	Updated Coding section with CPT changes; added PLA code 0225U effective 08/10/2020.
	07/01/2020	Updated Coding section with CPT changes; added PLA code 0223U effective 06/25/2020.
	05/27/2020	Updated Coding section with CPT changes; added PLA code 0202U effective 05/20/2020.

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue's standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.

Respiratory Viral Panel Testing in the Outpatient Setting

	05/04/2020	Updated Discussion/General Information section.
	05/01/2020	Updated Discussion/General Information, References, and Websites for Additional Information sections.
Revised	11/07/2019	MPTAC review. Revised MN and NMN statements to address the number of targets used in testing panels. Updated Coding section including addition of 01/01/2020 CPT changes; added 0151U with note effective 01/01/20.
Reviewed	08/22/2019	MPTAC review. Updated Discussion/General Information, References, and Websites for Additional Information sections. Updated Coding section with 10/01/2019 CPT changes; added 0115U.
	06/27/2019	Updated Coding section with 07/01/2019 CPT changes; added 0098U-0100U.
New	11/08/2018	MPTAC review. Initial document development.

This Clinical UM Guideline is intended to provide assistance in interpreting Healthy Blue's standard Medicaid benefit plan. When evaluating insurance coverage for the provision of medical care, federal, state and/or contractual requirements must be referenced, since these may limit or differ from the standard benefit plan. In the event of a conflict, the federal, state and/or contractual requirements for the applicable benefit plan coverage will govern. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Clinical UM Guideline is provided for informational purposes. It does not constitute medical advice. Healthy Blue may also use tools and criteria developed by third parties, to assist us in administering health benefits. Healthy Blue's Policies and Guidelines are intended to be used in accordance with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from the health plan.