

# Medical Policy

<b>Subject:</b>	<b>Machine Learning Derived Probability Score for Rapid Kidney Function Decline</b>		
<b>Document#:</b>	<b>LAB.00041</b>	<b>Publish Date:</b>	<b>07/07/2021</b>
<b>Status:</b>	<b>New</b>	<b>Last Review Date:</b>	<b>05/13/2021</b>

## Description/Scope

**This document addresses the use of a machine learning derived probability score (i.e., artificial intelligence) which may combine a variety a clinical characteristics such as, biomarkers, genetics, gender or race, to generate prognostic information with the end-goal of facilitating a more personalized approach to the management of chronic kidney disease (e.g., KidneyIntelX™). This document does not address the standard use of blood-based biomarkers, estimated glomerular filtration rate (eGFR) or urinary albumin and creatinine levels in the prognostic evaluation of newly diagnosed kidney disease.**

## Position Statement

### **Investigational and Not Medically Necessary:**

**Use of a machine learning derived probability score (e.g., KidneyIntelX) to predict rapid kidney function decline in chronic kidney disease is considered investigational and not medically necessary for all indications.**

## Rationale

**Chronic kidney disease (CKD) is defined by the Kidney Disease Improving Global Outcomes (KDIGO) organization as abnormalities of kidney structure or function, present for > 3 months. In the KDIGO Clinical Practice Guidelines for the Evaluation and Management of Chronic Kidney Disease, factors associated with CKD progression to inform prognosis include the etiology of CKD (e.g., diabetes, hypertension, etc.), level of GFR, level of albuminuria, age, sex, race/ethnicity, elevated blood pressure, hyperglycemia, dyslipidemia, smoking, obesity, history of cardiovascular disease and ongoing exposure to nephrotoxic agents (ungraded recommendation; Stevens, 2012). A standardized system for integrating sociodemographic risk factors with clinically relevant biomarkers to accurately identify those most at risk for progression is not yet available in most practice settings, potentially hampering clinicians' timely**

**This Medical Policy provides assistance in understanding Healthy Blue's standard Medicaid benefit plan. When evaluating coverage for a specific member benefit, reference to federal and state law, as well as contractual requirements may be necessary, since these may differ from our standard benefit plan. In the event of a conflict with standard plan benefits, federal, state and/or contractual requirements will govern. Before using this policy, please check all federal, state and/or contractual requirements applicable to the specific benefit plan coverage. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Medical Policy 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.**

**Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.**

**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.**

## Medical Policy

### Machine Learning Derived Probability Score for Rapid Kidney Function Decline

**intervention in CKD management. Recently, the use of machine learning approaches that can combine biomarkers and electronic health record data to produce prognostic risk scores have been explored. One such approach is the KidneyIntelX, a proprietary artificial intelligence-enabled algorithm which combines blood-based biomarkers, genetics and personalized data from electronic health records to generate a unique risk score which is then used to develop a prediction of progressive kidney function decline in diabetes-related CKD.**

**To date, the only published peer-reviewed study evaluating the clinical utility of KidneyIntelX is a large retrospective cohort by Chan and colleagues (2020), which enrolled 1146 individuals with diabetes-related CKD age 21-81. During the follow-up period (median of 4.3 years) 241 study enrollees (21%) experienced progressive decline in kidney function. KidneyIntelX stratified 46%, 37% and 16.5% of validation cohort (n=460) into low-, intermediate- and high-risk groups, respectively, with a positive predictive value (PPV) of 62% (PPV of 37% for the clinical model and 40% for KDIGO; p<0.001) in the high-risk group and a negative predictive value (NPV) of 91% in the low-risk group. The net reclassification index for events into the high-risk group was 41% (p<0.05). In this retrospective, exploratory validation study, KidneyIntelX scores accurately classified more cases into the KidneyIntelX-defined low, intermediate and high-risk strata (p-value<0.05) relative to KDIGO risk strata. The study authors conclude, “A machine learned model combining plasma biomarkers and EHR [electronic health record] data improved prediction of progressive decline in kidney function within 5 years over KDIGO and standard clinical models in patients with early DKD [diabetes-related CKD].” Given the retrospective study design and marginal statistical significance, further investigation in the setting of a large, ideally randomized, trial is warranted to establish whether use of KidneyIntelX materially improves net health outcomes compared to established alternatives, such as the KDIGO guideline’s specified sociodemographic risk factors, pertinent health history and clinically relevant biomarkers.**

#### Summary

**Currently, there is no guidance from specialty medical societies addressing the use of machine learning to generate prognostic information in the treatment of CKD. The published peer-reviewed medical literature has not established KidneyIntelX, or any technology like it, as a proven method that materially improves net health outcomes nor has any benefit been established beyond currently available alternatives (e.g. KDIGO guidelines).**

#### **Background/Overview**

**This Medical Policy provides assistance in understanding Healthy Blue’s standard Medicaid benefit plan. When evaluating coverage for a specific member benefit, reference to federal and state law, as well as contractual requirements may be necessary, since these may differ from our standard benefit plan. In the event of a conflict with standard plan benefits, federal, state and/or contractual requirements will govern. Before using this policy, please check all federal, state and/or contractual requirements applicable to the specific benefit plan coverage. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Medical Policy 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.**

**Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.**

**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.**

## Medical Policy

### Machine Learning Derived Probability Score for Rapid Kidney Function Decline

In 2019, approximately 37 million Americans reportedly had chronic kidney disease (CKD), with nearly 118,000 requiring initiation of treatment for kidney failure, also known as end stage renal disease (ESRD). There was a steady rise in the rate of ESRD from 1980 to 2011, since then, the incidence rate of ESRD has started to decline. The most prevalent cause of kidney disease is diabetes, which accounts for approximately 38% of ESRD cases (CDC, 2019). On average, 50,000 individuals with diabetic kidney disease progress to kidney failure annually in the United States (Chan, 2020).

Predicting which newly diagnosed diabetic kidney disease cases may progress to ESRD has proved challenging for clinicians, potentially resulting in delayed diagnosis of individuals and the subsequent need for life-saving dialysis or kidney transplants. Typically, prognosis is achieved through integration of established sociodemographic risk factors (i.e., smoking, obesity, and race/ethnicity) along with clinically relevant biomarkers, such as glycemic levels, eGFR, and lipid levels. KidneyIntelX is described by the manufacturer (RenalytixAI) as a validated machine-learned, prognostic risk score which combines data from EHRs and circulating biomarkers to predict diabetic kidney disease progression. The risk score is purported to help clinicians manage individuals with diabetes-related CKD in a streamlined fashion with the end goal of slowing the progression of kidney disease and potentially preventing the occurrence of progressive kidney function decline such as kidney failure and the resultant need for long-term dialysis or kidney transplant (Chan, 2020).

#### Definitions

Artificial Intelligence (AI): A science of computer simulated thinking processes and human behaviors, which involves computer science, psychology, philosophy and linguistics.

Chronic renal disease: The permanent loss of kidney function.

End stage renal disease: Persistent decline in renal function as documented by falling creatinine clearance in an individual diagnosed with a renal disease whose natural history is progression to renal impairment requiring renal replacement (dialysis or transplant).

Glomerular filtration rate (GFR): A test used to check how well the kidneys are functioning by estimating how much blood passes through the glomeruli each minute.

This Medical Policy provides assistance in understanding Healthy Blue's standard Medicaid benefit plan. When evaluating coverage for a specific member benefit, reference to federal and state law, as well as contractual requirements may be necessary, since these may differ from our standard benefit plan. In the event of a conflict with standard plan benefits, federal, state and/or contractual requirements will govern. Before using this policy, please check all federal, state and/or contractual requirements applicable to the specific benefit plan coverage. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Medical Policy 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.

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

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.

## Machine Learning Derived Probability Score for Rapid Kidney Function Decline

**Glomeruli: A cluster of nerve endings, spores, or small blood vessels, in particular a cluster of capillaries around the end of a kidney tubule, where waste products are filtered from the blood.**

### **Coding**

*The following codes for treatments and procedures applicable to this document 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 are Investigational and Not Medically Necessary:**

**For the following procedure code, or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.**

#### **CPT**

**0105U**

**Nephrology (chronic kidney disease), multiplex electrochemiluminescent immunoassay (ECLIA) of tumor necrosis factor receptor 1A, receptor superfamily 2 (TNFR1, TNFR2), and kidney injury molecule-1 (KIM-1) combined with longitudinal clinical data, including APOL1 genotype if available, and plasma (isolated fresh or frozen), algorithm reported as probability score for rapid kidney function decline (RKFD) KidneyIntelX™, RenalytixAI, RenalytixAI**

#### **ICD-10 Diagnosis**

**All diagnoses**

### **References**

#### **Peer Reviewed Publications:**

- 1. Chan L, Nadkarni G, Fleming F, et al. Derivation and validation of a machine learning risk score using biomarker and electronic patient data to predict progression of diabetic kidney disease. Diabetologia. 2021 Apr 2. [Epub ahead of print].**

#### **Government Agency, Medical Society, and Other Authoritative Publications:**

**This Medical Policy provides assistance in understanding Healthy Blue's standard Medicaid benefit plan. When evaluating coverage for a specific member benefit, reference to federal and state law, as well as contractual requirements may be necessary, since these may differ from our standard benefit plan. In the event of a conflict with standard plan benefits, federal, state and/or contractual requirements will govern. Before using this policy, please check all federal, state and/or contractual requirements applicable to the specific benefit plan coverage. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Medical Policy 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.**

**Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.**

**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.**

Machine Learning Derived Probability Score for Rapid Kidney Function Decline

1. Centers for Disease Control and Prevention. National chronic kidney disease fact sheet. Available at: [https://www.cdc.gov/kidneydisease/pdf/2019\\_National-Chronic-Kidney-Disease-Fact-Sheet.pdf](https://www.cdc.gov/kidneydisease/pdf/2019_National-Chronic-Kidney-Disease-Fact-Sheet.pdf). Accessed on April 12, 2021.
2. Stevens PE, Levin A; Kidney Disease: Improving Global Outcomes Chronic Kidney Disease Guideline Development Work Group Members. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes (KDGO) 2012 clinical practice guideline. Ann Intern Med. 2013; 158(11):825-830.

**Websites for Additional Information**

1. American Society of Nephrology. Available at: <https://www.asn-online.org/>. Accessed on April 12, 2021.
2. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). What is Kidney Failure? Updated January 2018. Available at <https://www.niddk.nih.gov/health-information/kidney-disease/kidney-failure/what-is-kidney-failure>. Accessed on April 12, 2021.

**Index**

**KidneyIntelX**

**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.**

**Document History**

<u>Status</u>	<u>Date</u>	<u>Action</u>
New	05/13/2021	Medical Policy & Technology Assessment Committee (MPTAC) review. Initial document development.

This Medical Policy provides assistance in understanding Healthy Blue’s standard Medicaid benefit plan. When evaluating coverage for a specific member benefit, reference to federal and state law, as well as contractual requirements may be necessary, since these may differ from our standard benefit plan. In the event of a conflict with standard plan benefits, federal, state and/or contractual requirements will govern. Before using this policy, please check all federal, state and/or contractual requirements applicable to the specific benefit plan coverage. Healthy Blue reserves the right to modify its Policies and Guidelines as necessary and in accordance with legal and contractual requirements. This Medical Policy 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.

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

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.