I. POLICY

Genetic testing for hereditary pancreatitis may be considered medically necessary for patients aged 18 years and under with unexplained recurrent (>1 episode) acute or chronic pancreatitis with documented elevated amylase or lipase.

Genetic testing for hereditary pancreatitis is considered investigational in all other situations. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

II. PRODUCT VARIATIONS

This policy is applicable to all programs and products administered by Capital BlueCross unless otherwise indicated below.

FEP PPO*

* Refer to FEP Medical Policy Manual MP-2.04.99 Genetic Testing for Hereditary Pancreatitis
The FEP Medical Policy Manual can be found at: www.fepblue.org

III. DESCRIPTION/BACKGROUND

Acute and chronic pancreatitis (CP) is caused by trypsin activation within the pancreas, resulting in autodigestion, inflammation, elevation of pancreatic enzymes in serum, and abdominal pain. CP is defined as an ongoing inflammatory state associated with chronic/recurrent symptoms and progression to exocrine and endocrine pancreatic insufficiency.
Alcohol is the major etiologic factor in 80% of CP, which has a peak incidence in the 4th and 5th decades of life. Gall stones, hypercalcemia, inflammatory bowel disease, autoimmune pancreatitis, and peptic ulcer disease can also cause CP. About 20% of CP is idiopathic. A small percentage of CP is categorized as HP, which usually begins with recurrent episodes of acute pancreatitis in childhood and evolves into CP by age 20 years. Multiple family members may be affected over several generations, and pedigree analysis often reveals an autosomal dominant pattern of inheritance. Clinical presentation and family history alone are sometimes insufficient to distinguish between idiopathic CP and hereditary pancreatitis, especially early in the course of the disease. HP is a rare disorder, in 1997 there were about 1000 people with HP in the United States.1

**Genetic Determinants of HP**

**PRSS1 Mutations**
In 1996, Whitcomb et al discovered that mutations of protease, serine, 1 (trypsin 1) (PRSS1) on chromosome 7q35 cause HP. PRSS1 encodes cationic trypsinogen. Gain of function mutations of the PRSS1 gene cause HP by prematurely and excessively converting trypsinogen to trypsin, which then results in pancreatic autodigestion. Between 60% and 80% of people who have a PRSS1 mutation will experience pancreatitis in their lifetimes; 30% to 40% will develop CP. Most, but not all, people with a mutation of PRSS1 will have inherited it from one of their parents. The proportion of HP caused by a spontaneous mutation of PRSS1 is unknown. In families with 2 or more affected individuals in 2 or more generations, genetic testing shows that most have a demonstrable PRSS1 mutation. In 60% to 100%, the mutation is detected by sequencing technology (Sanger or next generation), and duplications of exons or the whole PRSS1 gene are seen in about 6%. Two PRSS1 point mutations (p.Arg122His, p.Asn29Ile) are most common, accounting for 90% of mutations in affected individuals. Over 40 other PRSS1 sequence variants have been found, but their clinical significance is uncertain. Pathogenic PRSS1 mutations are present in 10% or less of individuals with CP.2

Targeted analysis of exons 2 and 3, where the common mutations are found, or PRSS1 sequencing, are first-line tests, followed by duplication analysis. The general indications for PRSS1 testing and emphasis on pre- and posttest genetic counseling have remained central features of reviews and guidelines.1,3 However, several other genes have emerged as significant contributors to both HP and CP. These include cystic fibrosis (CF) transmembrane conductance regulator (CFTR) gene, serine peptidase inhibitor, Kazal type 1 (SPINK1) gene, chymotrypsin C (CTRC) gene, and claudin-2 (CLDN-2) gene.

**CFTR Mutations**
Autosomal recessive mutations of CFTR cause CF, a chronic disease with onset in childhood that causes severe sinopulmonary disease and numerous gastrointestinal abnormalities. The signs and symptoms of CF can vary widely. On rare occasions, an affected individual may have mild pulmonary disease, pancreatic exocrine sufficiency, and may present with acute, recurrent acute, or CP.1 Individuals with heterozygous mutations of the CFTR gene (CF carriers) have a 3- to 4-
fold increased risk for CP. Individuals with 2 CFTR mutations (homozygotes or compound heterozygotes) will benefit from CF-specific evaluations, therapies, and genetic counseling.

**SPINK Mutations**
The SPINK gene encodes a protein that binds to trypsin and thereby inhibits its activity. Mutations in SPINK are not associated with acute pancreatitis but are found, primarily as modifiers, in recurrent acute pancreatitis and seem to promote the development of CP, including for individuals with compound heterozygous mutations of the CFTR gene. Autosomal recessive familial pancreatitis may be caused by homozygous or compound heterozygous SPINK mutations.4

**CTRC Mutations**
CTRC is important for the degradation of trypsin and trypsinogen, and 2 mutations (p.R254W and p.K247R254del) are associated with increased risk for idiopathic CP (odds ratio [OR], 4.6), alcoholic pancreatitis (OR=4.2), and tropical pancreatitis (OR=13.6).5

**CLDN2 Mutations**
CLDN2 encodes a member of the claudin protein family, which acts as an integral membrane protein at tight junctions and has tissue-specific expression. Several single nucleotide polymorphisms in CLDN2 have been associated with CP.

**Genetic Testing for Mutations Associated With HP**
Testing for mutations associated with HP are typically done by direct sequence analysis or next-generation sequencing (NGS). A number of laboratories offer testing for the relevant genes, either individually or as genetic panels. For example, Arup Laboratories (Salt Lake City, UT) offers a Pancreatitis Panel, which includes direct (Sanger) sequencing of CFTR, CTRC, PRSS1, and SPINK.6 Prevention Genetics (Marshfield, WI) offers a Chronic Pancreatitis NextGen Sequencing Panel, which includes NGS of CASR, CFTR, CTRC, PRSS1, and SPINK1.7

**Regulatory Status**
Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Improvement Act (CLIA). Genetic testing for hereditary pancreatitis is available under the auspices of CLIA. Laboratories that offer LDTs must be licensed by CIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of these tests.

**IV. RATIONALE**
This evidence review was created in August 2013 and updated periodically with literature reviews, most recently through July 8, 2015 (see Appendix Table 1 for genetic testing categories).
Analytic Validity
Testing for mutations in the protease, serine, 1 (trypsin 1) (PRSS1), serine peptidase inhibitor (SPINK), and cystic fibrosis (CF) transmembrane conductance regulator (CFTR) genes is usually done by direct sequence analysis, which is the criterion standard for detecting a mutation that is present and/or excluding a mutation that is absent. Testing can also be done by next-generation sequencing, which has an accuracy that approaches that of direct sequencing. In patients who test negative by either of these methods, duplication/deletion analysis may be performed to detect copy number variations. These genetic testing methods are considered to have high analytic validity.

Clinical Validity
The clinical validity of genetic testing for hereditary pancreatitis (HP) refers to the mutation detection rate in patients who have known HP.

There is a lack of published evidence on the percent of patients who are first identified as having clinically defined HP and then tested for genetic mutations. Most studies that examine the mutation detection rate use a population of patients with idiopathic chronic pancreatitis (CP) and do not necessarily require that patients have a family history of CP. In other studies, cohorts of patients with HP were defined by the presence of genetic mutations or family history, which therefore may include patients with genetic mutations who do not have a family history of CP.

A summary of representative studies reporting the sensitivity and specificity of genetic testing in patients with HP is included in Table 1.

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Genes Tested</th>
<th>Clinical Sensitivity</th>
<th>Clinical Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schwarzenberg (2015)</td>
<td>170 children, 76 with CP and 94 with acute recurrent pancreatitis</td>
<td>PRSS1 SPINK CFTR CTRC</td>
<td>67% (51/76 with CP)</td>
<td>NR</td>
</tr>
<tr>
<td>Poddar (2015)</td>
<td>68 children with pancreatitis (35.3% acute, 32.3% acute recurrent, 32.3% chronic); 25 healthy controls</td>
<td>PRSS1 SPINK CFTR CTRC</td>
<td>44% (38/88) 96% (24/25)</td>
<td>NR</td>
</tr>
<tr>
<td>Masson (2014)</td>
<td>253 patients with idiopathic CP</td>
<td>PRSS1 SPINK CFTR CTRC</td>
<td>23.7% &quot;causal&quot; mutation (60/253) 24.5% &quot;contributory&quot; mutation (62/253)</td>
<td>NR</td>
</tr>
<tr>
<td>Wang (2014)</td>
<td>75 children with idiopathic CP</td>
<td>PRSS1 SPINK CFTR CTRC CLDN2</td>
<td>66.7% (50/75) (with PRSS1 or SPINK mutations)</td>
<td>NR</td>
</tr>
<tr>
<td>Ceppa (2013)</td>
<td>87 patients with HP, defined by known genetic mutation or family history</td>
<td>PRSS1 SPINK CFTR CTRC</td>
<td>62% (54/87)</td>
<td>NR</td>
</tr>
<tr>
<td>Sultan (2012)</td>
<td>29 children with recurrent acute or CP</td>
<td>PRSS1 SPINK CFTR CTRC</td>
<td>79% (23/29)</td>
<td>NR</td>
</tr>
</tbody>
</table>
These data on clinical validity demonstrate that genetic mutations are common in patients with CP. A very limited amount of evidence reports that genetic mutations are found in a small percentage of patients without pancreatitis. However, the true clinical sensitivity and specificity for genetic testing in cases of HP are uncertain for a number of reasons. First, the populations in these studies are defined differently, with most not consisting of patients with clinically defined HP. The populations are from different geographic regions, in which the prevalence of genetic mutations may vary. Some of the studies mix adult and pediatric populations, while others report on either adults or children. In the 2 studies that exclusively enrolled children, the rate of mutation detection was generally higher than other studies (67% and 79%). Finally, mutations tested for in these studies differ, with many studies not including all of the known genes that are associated with HP.

Other studies have reported on the rates of genetic mutations among populations of patients who were identified using less selective criteria, such as patients with isolated unexplained or recurrent acute pancreatitis or unexplained CP. Ballard et al reported results of a retrospective cohort study of 370 adults with unexplained pancreatitis, including recurrent acute pancreatitis, CP, or symptoms consistent with CP, who underwent pancreas-specific genetic testing at a single center. Although 67 patients (18.1%) had any mutation detected, only 24 of these (6.4%) were found to have high-risk mutations, defined as (1) a single copy mutation of PRSS1, (2) homozygous mutations of CFTR, SPINK1, or CTRC, or (3) compound heterozygous mutations of CFTR, SPINK, and/or CTRC. High-risk mutations were more likely to be detected in patients who underwent complete gene sequencing methods compared with those who had targeted mutation testing methods. In a case-control study, Rai et al reported that SPINK1 mutations were found in 12.0% of 183 patients with acute pancreatitis, compared with 2.4% of 168 controls (p=0.006). In a cohort study of 67 patients with acute recurrent pancreatitis of unknown etiology, Werlin et al reported that 34% of patients had a mutation in at least one gene associated with HP.

The mutation detection rate for children with CP appears to be higher than for adults. Similarly, the proportion of patients with acute pancreatitis attributable to genetic causes is higher among
younger patients. In a group of 309 subjects with acute pancreatitis, patients aged 35 and younger (n=66) were more likely to have a genetic cause of pancreatitis identified (10% vs 1.5%, p=0.003).23

Section Summary: Clinical Validity for Testing for Mutations Associated With HP
A number of studies report the mutation detection rate in various populations of patients with CP, but few studies enroll a population of patients with clinically defined HP. Therefore, the true clinical sensitivity and specificity cannot be determined. In studies that report on children, the detection rates are generally higher than other studies, suggesting that the mutation detection rate may be higher in children than in adults.

Clinical Utility
Potential types of clinical utility for testing of genes associated with HP include confirmation of the diagnosis of HP, predictive testing in asymptomatic relatives, and prognostic testing to determine the course of the disease. In each case, demonstration of clinical utility depends on whether identification of a genetic defect leads to changes in medical and/or surgical management options, and whether these changes lead to improved health outcomes. Preconception (carrier) testing and prenatal (in utero) testing can also be performed, but are not addressed in this literature review.

Diagnostic Testing
There are no direct outcome data regarding the clinical utility of testing for confirmation of HP (i.e., there are no studies that report outcome data in patients who have been tested for HP compared with patients who have not been tested).

Confirmatory testing can be performed in patients who experience acute pancreatitis that is otherwise unexplained, for recurrent acute pancreatitis of unclear cause, and/or for idiopathic CP. In all of these scenarios, a substantial percentage of patients will be found to have a genetic defect, thereby confirming the diagnosis of HP. Most treatments for the pain, maldigestion, and diabetes caused by HP are fundamentally the same as for other types of CP. Therefore, if a deleterious mutation associated with HP is found, treatment for CP is unlikely to change. Interventions for CP include a low-fat diet with multiple small meals, maintenance of good hydration, use of antioxidants, and avoidance of smoking and alcohol use. While all of these interventions may alter the natural history of the disease, there is no evidence that the impact differs for HP compared with other etiologies of CP.

Calcium channel blockers are currently being investigated as a potential treatment for HP. One small uncontrolled trial of amlodipine in 9 patients was identified in the literature.24 This trial included patients 6 years or older who had CP and a known PRSS1 mutation. Treatment was continued for up to 11 weeks, and 4 patients successfully completed the full course of treatment. All 4 patients reported decreased symptoms, and 3 of the 4 patients had improved scores on the 36-Item Short-Form Health Survey outcome instrument. There were no differences before and after treatment in blood pressure, laboratory tests, or physical exam.

Total pancreatectomy with islet cell transplantation (or total pancreatectomy with islet autotransplantation [TP-IAT]) has been investigated in CP or recurrent acute pancreatitis,
particularly as a treatment for intractable pain in patients with impaired quality of life in whom medical, endoscopic, or prior surgical treatment have failed. However, questions remain about the best timing of surgery, selection of candidates, evaluation of outcomes, and follow-up.\textsuperscript{25} Chinnakotla et al conducted a retrospective study that compared outcomes after TP-IAT for patients with HP or familial pancreatitis compared with other causes of CP among 484 patients treated at a single institution from 1977 to 2012, 80 of whom had HP.\textsuperscript{26} Genetic testing was not available for all patients with suspected HP. Multiple causes of HP or familial pancreatitis were included: 38 with \textit{PRSS1} mutations; 9 with \textit{SPINK1} mutations; 14 with \textit{CFTR} mutations; and 19 with familial pancreatitis without a mutation specified. Patients with HP were younger at the time of TP-IAT (mean age, 21.9 years vs 37.9 years in nonhereditary CP, p<0.001), but had a longer history of pancreatitis (mean, 10.1 years vs 6.4 years in nonhereditary CP, p<0.001). Pain scores significantly improved after TP-IAT (p<0.001), with no significant differences between HP and nonhereditary CP.

\textbf{Predictive Testing}

Predictive testing can be performed in asymptomatic relatives of patients with known HP to determine the likelihood of CP. For this population, no direct evidence was identified that compared outcomes in patients tested for genetic mutations compared with patients not tested for genetic mutations. It is possible that at-risk relatives who are identified with genetic mutations may alter lifestyle factors such as diet, smoking and alcohol use, and this may delay the onset or prevent CP. However, evidence on this question is lacking, so that conclusions cannot be made on whether testing of asymptomatic family members of patients with HP improves outcomes.

\textbf{Prognostic Testing}

Several studies were identified that examined whether the severity and/or natural history of CP differs in patients with and without genetic mutations. A number of studies have reported that patients with HP have an earlier age of onset compared with patients with other etiologies of CP.\textsuperscript{27} Other studies have examined whether the severity and natural history differs for patients with HP, but these studies have not reported consistent findings. Some studies have reported that the progression of disease is slower in patients with HP\textsuperscript{27,29} and that surgical intervention is required less often for patients with HP.\textsuperscript{28} However, 1 study also reported that the cumulative risk for exocrine failure was more than twice as high for patients with genetic mutations compared with patients without mutations.\textsuperscript{29} In another small study that compared the clinical course of patients with HP to those with alcoholic CP, most clinical manifestations were similar, but patients with HP had a higher rate of pseudocysts.\textsuperscript{30}

Individuals with CP due to HP, like others with CP, are at increased risk for pancreatic cancer. In a survey of 246 patients with HP from 10 countries, the cumulative risk of pancreatic cancer by age 70 was estimated to be 40%.\textsuperscript{31} In a series of 200 patients with HP from France, the cumulative incidence of pancreatic cancer at 50 years was 11\% for men and 85\% for women. At 75 years of age, the cumulative risk was 49\% for men and 55\% for women. There was no evidence identified that the risk of pancreatic cancer differs for patients with HP compared with patients with other forms of CP.
Screening for pancreatic cancer with computed tomography scanning, endoscopic ultrasound, and/or endoscopic retrograde cholangiopancreatography has been recommended for patients with CP irrespective of etiology, but close surveillance has not yet been demonstrated to improve long-term survival for any of these methods in patients with CP.

**Section Summary: Clinical Utility for Testing for Mutations Associated With HP**

The evidence on clinical utility does not support an improvement in health outcomes associated with genetic testing. For diagnostic testing, there is a lack of evidence that genetic testing leads to management changes. Several treatments for CP, including calcium channel blockers and TPIAT, are under investigation; however, the evidence to date is insufficient to determine whether patients with HP respond differently to such treatments than other patients with CP. For prognostic testing, there have been some differences reported regarding the natural course of CP in patients with and without genetic mutations. The age of onset is consistently younger, and the progression of disease may be slower, but it is not possible to conclude whether the overall severity of disease or need for surgical intervention differs. The risk of pancreatic cancer is high for patients with HP, but no evidence was identified that establishes whether the risk of cancer is greater for patients with HP compared with other etiologies of CP. For testing asymptomatic, at-risk family members, there is a lack of evidence that genetic testing leads to interventions that delay or prevent the onset of pancreatitis.

**Summary of Evidence**

The evidence for the use of genetic testing for mutations associated with hereditary pancreatitis (HP) among patients with chronic pancreatitis (CP) or recurrent acute pancreatitis in adulthood or childhood includes cohort and case-control studies that evaluate the yield of genetic testing (clinical validity). Relevant outcomes are test accuracy, symptoms, change in disease status, morbid events, and hospitalizations. Numerous studies demonstrate that genetic mutations are found in a large percentage of patients with idiopathic CP. However, these studies are limited by wide variations in the patient populations and genes tested; as a result, it is not possible to determine the true prevalence of HP among patients with idiopathic CP, nor the sensitivity and specificity of genetic testing (clinical validity) in patients with a familial pattern of disease. The clinical utility of testing has not been demonstrated empirically. While testing can confirm the diagnosis of HP, there is no evidence that treatment is altered by testing or that health outcomes are improved. Similarly, predictive testing of at-risk relatives and prognostic testing have not been shown to improve outcomes. Predictive testing can better define the risk of developing CP, but there is no evidence that early interventions based on genetic testing alter the prevalence or course of disease. The prognosis of HP may differ from other etiologies of CP, but this evidence is mixed and there are no changes in management that result from refining the prognosis of CP. Overall, direct evidence of improved health outcomes following use of genetic testing for HP lacking. The changes in clinical management that would occur as a result of testing are not well-defined. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for the use of genetic testing for mutations associated with HP among asymptomatic individuals with family members with HP includes a very limited number of
studies. Relevant outcomes are test accuracy, symptoms, change in disease status, morbid events, and hospitalizations. No direct evidence was identified that compared outcomes in patients tested for genetic mutations compared with patients not tested for genetic mutations. It is possible that at-risk relatives who are identified with genetic mutations may alter lifestyle factors such as diet, smoking, and alcohol use, and this may delay the onset or prevent CP. Direct evidence of improved health outcomes following the use of genetic testing for HP in at-risk family members is lacking. The changes in clinical management that would occur as a result of testing are not well-defined. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 4 academic medical centers (one of which provided 2 responses) and 2 specialty medical societies (one of which provided 2 responses) when this policy was under review in 2014, with specific focus on testing in children. There was consensus among reviewers that genetic testing for HP is medically necessary in children.

Practice Guidelines and Position Statements

American College of Medical Genetics
The American College of Medical Genetics issued a policy statement on laboratory standards and guidelines for population-based cystic fibrosis (CF) carrier screening in 2001, which were updated in 2004 and reaffirmed in 2013. These guidelines provide recommendations about specific mutation testing in CF, but do not specifically address genetic testing for suspected HP.

European Consensus Conference
A 2001 European Consensus Conference developed guidelines for genetic testing of the PRSS1 gene, genetic counseling, and consent for genetic testing for HP. The recommended indications for symptomatic patients included:

- Recurrent (2 or more separate, documented episodes with hyperamylasemia) attacks of acute pancreatitis for which there is no explanation
- Unexplained chronic pancreatitis
- A family history of pancreatitis in a first- or second-degree relative
- Unexplained pancreatitis in a child – if recurrent or requiring hospitalization

Predictive genetic testing, defined as genetic testing in an asymptomatic “at-risk” relative of an individual proven to have HP, was considered more complex. Candidates for predictive testing should be a first-degree relative of an individual with a well-defined HP gene mutation, capable of informed consent, and able to demonstrate an understanding of autosomal dominant
inheritance, incomplete penetrance, variable expressivity, and the natural history of HP. Written informed consent must be documented before the genetic test is performed.

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

There is no national coverage determination (NCD).

**V. DEFINITIONS**

N/A

**VI. BENEFIT VARIATIONS**

The existence of this medical policy does not mean that this service is a covered benefit under the member's contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member's individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member's benefit information or contact Capital for benefit information.

**VII. DISCLAIMER**

Capital's medical policies are developed to assist in administering a member’s benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member’s benefit information, the benefit information will govern. Capital considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

**VIII. CODING INFORMATION**

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.
Covered when medically necessary:

<table>
<thead>
<tr>
<th>CPT Codes®</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81401</td>
<td></td>
</tr>
<tr>
<td>81404</td>
<td></td>
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<tr>
<td>81222</td>
<td></td>
</tr>
<tr>
<td>81223</td>
<td></td>
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<tr>
<td>81479</td>
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</tbody>
</table>


<table>
<thead>
<tr>
<th>ICD-10-CM Diagnosis Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>K85.00</td>
<td>Idiopathic acute pancreatitis without necrosis or infection</td>
</tr>
<tr>
<td>K85.01</td>
<td>Idiopathic acute pancreatitis with uninfected necrosis</td>
</tr>
<tr>
<td>K85.02</td>
<td>Idiopathic acute pancreatitis with infected necrosis</td>
</tr>
<tr>
<td>K85.10</td>
<td>Biliary acute pancreatitis without necrosis or infection</td>
</tr>
<tr>
<td>K85.11</td>
<td>Biliary acute pancreatitis with uninfected necrosis</td>
</tr>
<tr>
<td>K85.12</td>
<td>Biliary acute pancreatitis with infected necrosis</td>
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<td>K85.20</td>
<td>Alcohol induced acute pancreatitis without necrosis or infection</td>
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<td>K85.80</td>
<td>Other acute pancreatitis without necrosis or infection</td>
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<td>K85.81</td>
<td>Other acute pancreatitis with uninfected necrosis</td>
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<td>K85.82</td>
<td>Other acute pancreatitis with infected necrosis</td>
</tr>
<tr>
<td>K86.1</td>
<td>Other chronic pancreatitis</td>
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</table>

*If applicable, please see Medicare LCD or NCD for additional covered diagnoses.

IX. REFERENCES


X. POLICY HISTORY

MP 2.318


7/24/14 Administrative change for the Medicare variation - For Novitas MAC jurisdictions, the LCD has been assigned a new number. Biomarkers for Oncology LCD changed from L33124 to L34796

11/18/14 Administrative change. Medicare variation removed.

CAC 1/27/15 Minor revision. Policy statements changed to indicate that genetic testing for hereditary pancreatitis may be considered medically necessary for children. FEP variation added to refer to the FEP medical policy manual. Policy coded for medically necessary indications.

CAC 1/26/16 Consensus review. No change to policy statements. References and rationale updated. Coding reviewed.

Administrative Update 11/10/16 Variation reformatting

Administrative Update 1/1/17 New diagnosis codes added effective 10/1/16

CAC 1/31/17 Consensus review. No changes to the policy statements. References and rationale updated. Appendix added. Coding reviewed.

References and rationale updated.

Appendix Table 1. Categories of Genetic Testing Addressed in this policy

<table>
<thead>
<tr>
<th>Category</th>
<th>Addressed</th>
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</thead>
<tbody>
<tr>
<td>1. Testing of an affected individual’s germline to benefit the individual</td>
<td></td>
</tr>
<tr>
<td>1a. Diagnostic</td>
<td>X</td>
</tr>
<tr>
<td>1b. Prognostic</td>
<td>X</td>
</tr>
<tr>
<td>1c. Therapeutic</td>
<td></td>
</tr>
<tr>
<td>2. Testing cancer cells from an affected individual to benefit the individual</td>
<td></td>
</tr>
<tr>
<td>2a. Diagnostic</td>
<td></td>
</tr>
<tr>
<td>2b. Prognostic</td>
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<tr>
<td>POLICY TITLE</td>
<td>GENETIC TESTING FOR HEREDITARY PANCREATITIS</td>
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</tbody>
</table>

2c. Therapeutic
3. Testing an asymptomatic individual to determine future risk of disease X
4. Testing of an affected individual’s germline to benefit family members
5. Reproductive testing
   5a. Carrier testing: preconception
   5b. Carrier testing: prenatal
   5c. In utero testing: aneuploidy
   5d. In utero testing: mutations
   5e. In utero testing: other