BSC_CON_2.25	Genetic Testing: Dermatologic Conditions		
Original Policy Date:	February 1, 2024	**Effective Date:**	February 1, 2024
Section:	2.0 Medicine	**Page:**	Page 1 of 13

Example Test Table

The tests and associated laboratories and CPT codes contained within this document serve only as examples to help users navigate claims and corresponding coverage criteria; as such, they are not comprehensive and are not a guarantee of coverage or non-coverage. Please see the Concert Genetics Platform for a comprehensive list of registered tests.

Policy Statement Sections	Example Tests (Labs)	Common CPT Codes
Known Familial Variant Analysis for Dermatologic Conditions		
Known Familial Variant Analysis for Dermatologic Conditions	Targeted Mutation Analysis for a Known Familial Variant	81403
Capillary Malformation-Arteriovenous Malformation Syndrome (CM-AVM)		
Capillary Malformation-Arteriovenous Malformation Syndrome (CM-AVM)	Capillary Malformation- Arteriovenous Malformation Syndrome (CM-AVM) Panel, Sequencing and Deletion/Duplication (ARUP Laboratories)	81479
	Vascular Malformation Sequencing Panel (Greenwood Genetic Center)	
	RASA1 Full Gene Sequencing and Deletion/Duplication (Invitae)	
	EPHB4 Full Gene Sequencing and Deletion/Duplication (Invitae)	
Congenital Ichthyosis		
Congenital Ichthyosis Multigene Panels	Ichthyosis Panel (Blueprint Genetics)	81405, 81479
	Ichthyosis NGS Panel (Connective Tissue Gene Tests)	
	Invitae Congenital Ichthyosis Panel (Invitae)	
Epidermolysis Bullosa		
Epidermolysis Bullosa Multigene Panels	Epidermolysis Bullosa Panel (Blueprint Genetics)	81406, 81479
	Epidermolysis Bullosa NGS Panel (Connective Tissue Gene Tests)	
	Invitae Epidermolysis Bullosa and Palmoplantar Keratoderma Panel (Invitae)	
Covered Dermatologic Conditions		
Covered Dermatologic Conditions	See Below	81401-81408, 81479

Policy Statement

KNOWN FAMILIAL VARIANT ANALYSIS FOR DERMATOLOGIC CONDITIONS

I. Targeted mutation analysis for a known familial variant (81403) in a dermatologic condition may be considered **medically necessary** when:
   A. The member has a close relative with a known pathogenic or likely pathogenic variant causing the condition.

II. Targeted mutation analysis for a known familial variant (81403) in a dermatologic condition is considered **investigational** for all other indications.

CAPILLARY MALFORMATION-ARTERIOVENOUS MALFORMATION (CM-AVM) SYNDROME

RASA1 and *EPHB4* Sequencing and/or Deletion/Duplication Analysis or Multigene Panel

III. *RASA1* and *EPHB4* sequencing and/or deletion/duplication analysis or multi-gene panel analysis (81479) to establish a diagnosis of capillary malformation-arteriovenous malformation (CM-AVM) syndrome may be considered **medically necessary** when:
   A. The member displays **one or more** of the following:
      1. Capillary malformations
      2. Arteriovenous malformations/arteriovenous fistulas
      3. Parkes Weber syndrome phenotype, a cutaneous capillary malformation associated with underlying multiple micro-AVFs and soft-tissue and skeletal hypertrophy of the affected limb.

IV. *RASA1* and *EPHB4* sequencing and/or deletion/duplication analysis or multi-gene panel analysis (81479) to establish a diagnosis of capillary malformation-arteriovenous malformation (CM-AVM) syndrome is considered **investigational** for all other indications.

CONGENITAL ICHTHYOSIS

Congenital Ichthyosis Multigene Panel

V. Multigene panel analysis to establish or confirm a diagnosis of congenital ichthyosis (81405, 81479) may be considered **medically necessary** when **ALL** of the following criteria are met:
   A. The member has scaly skin with or without a history of harlequin ichthyosis, collodion membrane, or thick, hyperkeratotic skin
   B. **One or more** of the following:
      1. Ectropion (eversion of eyelids)
      2. Eclabium (eversion of lips)
      3. Scarring alopecia
      4. Palmar and/or plantar hyperkeratosis
      5. Erythroderma (red skin)
   C. The panel includes, at a minimum, the following genes: *ABCA12, SLC27A4*, and *TGM1*.

VI. Multigene panel analysis to establish or confirm a diagnosis of congenital ichthyosis (81405, 81479) is considered **investigational** for all other indications.

EPIDERMOLYSIS BULLOSA

Epidermolysis Bullosa Multigene Panel

VII. Multigene panel analysis to establish or confirm a diagnosis of epidermolysis bullosa (81406, 81479) may be considered **medically necessary** when:
   A. The panel includes, at a minimum, the following genes: *EXPH5, KRT5, KRT14, PLEC* **AND ANY** of the following criteria are met:
      1. The member has fragility of the skin manifested by blistering with little or no trauma
      2. The member has the presence of blistering that has **ANY** of the following characteristics:

a. Is present in the neonatal period
b. Primarily affects the hands and feet but can affect the whole body
c. Occurs in annular or curvilinear groups or clusters
d. Leads to progressive brown pigmentation interspersed with hypopigmented spots on the trunk and extremities (frequently disappears in adult life)
e. Is associated with palmar and plantar hyperkeratosis that may be severe

3. The member has **one or more** of the following:
   a. Nail dystrophy
   b. Milia
   c. Congenital pyloric atresia
   d. Natal teeth
   e. Ureteral and renal anomalies, including hydronephrosis, ureterocele, absent bladder, dysplastic kidneys, urinary collecting system/kidney duplication, obstructive uropathy, and glomerulosclerosis

VIII. Multigene panel analysis to establish or confirm a diagnosis of epidermolysis bullosa (81406, 81479) is considered **investigational** for all other indications.

OTHER COVERED DERMATOLOGIC CONDITIONS

The following is a list of conditions that have a known genetic association. Due to their relative rareness, it may be appropriate to cover these genetic tests to establish or confirm a diagnosis.

IX. Genetic testing to establish or confirm one of the following dermatologic conditions to guide management may be considered **medically necessary** when the member demonstrates clinical features* consistent with the condition (the list is not meant to be comprehensive, see X below):
   A. Hidrotic Ectodermal Dysplasia 2 (Clouston Syndrome)
   B. Hypohidrotic Ectodermal Dysplasia
   C. Ocular albinism, X-linked
   D. Oculocutaneous albinism

X. Genetic testing to establish or confirm the diagnosis of all other dermatologic conditions not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Genetic and Molecular Testing* (see policy coverage criteria).

*Clinical features for a specific disorder may be outlined in resources such as GeneReviews, OMIM, National Library of Medicine, Genetics Home Reference or other scholarly source.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

NOTES AND DEFINITIONS

1. **Close relatives** include first, second, and third degree blood relatives:
   a. **First-degree relatives** are parents, siblings, and children
   b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
   c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

Description

Genetic testing for dermatologic conditions and disorders that have many dermatologic findings may be used to confirm a diagnosis in a patient who has signs and/or symptoms of the disease. Confirming the diagnosis may alter some aspects of management and may eliminate the need for further diagnostic workup. This document addresses genetic testing for dermatologic conditions.

Related Policies

This policy document provides coverage criteria for Genetic Testing for Dermatologic Conditions. Please refer to:

- ***Genetic Testing: Hereditary Cancer Susceptibility*** for coverage criteria related to hereditary cancer syndromes that may have or present with dermatologic findings *(to be published)*
- ***Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay*** for coverage criteria related to tuberous sclerosis, neurofibromatosis, HHT, incontinentia pigmenti, proteus syndrome, pseudoxanthoma elasticum, and other disorders that affect the skin and other organ systems *(to be published)*
- ***Genetic Testing: General Approach to Genetic and Molecular Testing*** for coverage criteria related to genetic testing for a dermatologic condition that is not specifically discussed in this or another more specific policy.

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. 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.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

- N/A

Rationale

Known Familial Variant Analysis for Dermatologic Conditions

Genetic Support Foundation

The Genetic Support Foundation's Genetics 101 information on genetic testing says the following about testing for familial pathogenic variants:

Genetic testing for someone who may be at risk for an inherited disease is always easier if we know the specific genetic cause. Oftentimes, the best way to find the genetic cause is to start by testing someone in the family who is known or strongly suspected to have the disease. If their testing is positive, then we can say that we have found the familial pathogenic (harmful) variant. We can use this as a marker to test other members of the family to see who is also at risk.

Capillary Malformation-Arteriovenous Malformation Syndrome (CM-AVM)

GeneReviews: Capillary Malformation-Arteriovenous Malformation Syndrome
GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online. The recommended diagnostic testing for CM-AVM is as follows:

"CM-AVM syndrome should be suspected in individuals who have any of the following:

- Capillary malformations (CMs), the hallmark of CM-AVM syndrome. CMs are generally:
  - Multifocal, atypical pink-to-reddish brown, multiple, small (1-2 cm in diameter), round-to-oval lesions sometimes with a white halo;
  - Composed of dilated capillaries in the papillary dermis
  - Mostly localized on the face and limbs;
  - Seen in combination with arteriovenous malformations (AVMs) or arteriovenous fistulas (AVF), but may be the only finding.
- AVMs/AVFs in soft tissue, bone, and brain that may be associated with overgrowth
- Parkes Weber syndrome phenotype, a cutaneous capillary malformation associated with underlying multiple micro-AVFs and soft-tissue and skeletal hypertrophy of the affected limb"

"The diagnosis of CM-AVM syndrome is established in a proband with suggestive clinical findings and a heterozygous pathogenic variant in *EPHB4* or *RASA1* identified by molecular genetic testing."

"When the phenotypic and laboratory findings suggest the diagnosis of CM-AVM syndrome, molecular genetic testing approaches can include use of a multigene panel. A multigene panel that includes *EPHB4*, *RASA1*, and other genes of interest is most likely to identify the genetic cause of the condition at the most reasonable cost while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype."

Congenital Ichthyosis Multigene Panels

GeneReviews: Autosomal Recessive Congenital Ichthyosis
GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online. The recommended diagnostic testing for nonsyndromic congenital ichthyosis is as follows:

"Autosomal recessive congenital ichthyosis (ARCI) encompasses several forms of nonsyndromic ichthyosis. Although most neonates with ARCI are collodion babies, the clinical presentation and severity of ARCI may vary significantly, ranging from harlequin ichthyosis, the most severe and often fatal form, to lamellar ichthyosis (LI) and (nonbullous) congenital ichthyosiform erythroderma (CIE). These phenotypes are now recognized to fall on a continuum; however, the phenotypic descriptions are clinically useful for clarification of prognosis and management."

- The diagnosis of ARCI is established in a proband (typically an infant):
  - With scaly skin with or without a history of harlequin ichthyosis, collodion membrane, or thick, hyperkeratotic skin AND the later development of ONE of the following:
    - Classic lamellar ichthyosis (LI). Brown, plate-like scale over the entire body, associated with ectropion (eversion of eyelids), eclabium (eversion of lips), scarring alopecia, and palmar and plantar hyperkeratosis
    - (Nonbullous) congenital ichthyosiform erythroderma (CIE). Erythroderma (red skin) with fine, white scale and often with palmoplantar hyperkeratosis
    - Intermediate forms with some features of both LI and CIE, or nonLI/nonCIE form with mild hyperkeratosis;

  AND/OR
- By identification of biallelic pathogenic variants in one of the genes listed below.

"The twelve genes known to be associated with ARCI are *ABCA12, ALOX12B, ALOXE3, CASP14, CERS3, CYP4F22, LIPN, NIPAL4, PNPLA1, SDR9C7, SLC27A4*, and *TGM1*. A multigene panel that includes these genes is the diagnostic test of choice. If such testing is not available, single-gene testing can be considered starting with *ABCA12* in individuals with harlequin ichthyosis, *TGM1* in individuals with ARCI without harlequin presentation at birth and *SLC27A4* in those presenting with ichthyosis-prematurity syndrome."

Epidermolysis Bullosa Multigene Panels

GeneReviews: Epidermolysis Bullosa Simplex
GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online. The recommended diagnostic testing for epidermolysis bullosa simplex and epidermolysis bullosa with pyloric atresia is as follows:

The diagnosis of epidermolysis bullosa simplex (EBS) is best established in a proband by the identification of biallelic pathogenic variants in *EXPH5* or *TGM5* or heterozygous (or rarely biallelic) pathogenic variants in *KRT5* or *KRT14* by molecular genetic testing

"The diagnosis of epidermolysis bullosa simplex (EBS) should be suspected in individuals with the following clinical findings:

- Fragility of the skin manifested by blistering with little or no trauma, which typically heals without scarring
- Blistering that:
  - May be present in the neonatal period
  - Primarily affects the hands and feet but can affect the whole body
  - Occurs in annular or curvilinear groups or clusters
  - Can lead to progressive brown pigmentation interspersed with hypopigmented spots on the trunk and extremities that frequently disappears in adult life
  - Is associated with palmar and plantar hyperkeratosis that may be severe
- Nail dystrophy
- Milia
- Family history that is consistent with either an autosomal recessive or autosomal dominant inheritance pattern

Note: Absence of a known family history of EBS does not preclude the diagnosis."

GeneReviews: Epidermolysis Bullosa - Pyloric Atresia
"The diagnosis of epidermolysis bullosa simplex (EBS) is best established in a proband by the identification of biallelic pathogenic variants in *EXPH5* or *TGM5* or heterozygous (or rarely biallelic) pathogenic variants in *KRT5* or *KRT14* by molecular genetic testing. A multigene panel that includes *EXPH5, KRT5, KRT14, TGM5* and other genes of interest may also be considered."

"Epidermolysis bullosa with pyloric atresia (EB-PA) should be suspected in newborns with the following clinical features:

- Congenital pyloric atresia with vomiting and abdominal distension resulting from complete obstruction of the gastric outlet. Radiographs reveal that the stomach is distended and filled with air
- Fragility of the skin with:
  - Blistering with little or no trauma. Blistering may be mild or severe; however, blisters generally heal with no significant scarring
  - Significant oral and mucous membrane involvement
  - Large areas of absent skin (aplasia cutis congenita), often with a thin membranous covering, affecting the extremities or head

- Ureteral and renal anomalies, including hydronephrosis, ureterocele, absent bladder, dysplastic kidneys, urinary collecting system/kidney duplication, obstructive uropathy, and glomerulosclerosis."

References

1. Bayrak-Toydemir P, Stevenson DA. Capillary Malformation-Arteriovenous Malformation Syndrome. 2011 Feb 22 [Updated 2019 Sep 12]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK52764/
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3. So JY, Teng J. Epidermolysis Bullosa Simplex. 1998 Oct 7 [Updated 2022 Aug 4]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1369/
4. Pfendner EG, Lucky AW. Epidermolysis Bullosa with Pyloric Atresia. 2008 Feb 22 [Updated 2017 Sep 7]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1157/
5. Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1116/
6. Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD). World Wide Web URL: https://omim.org/
7. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US). Available from: https://medlineplus.gov/genetics/
8. Genetic Support Foundation. Genetics 101 Genetic Testing: Familial Pathogenic Variant. Accessed 10/4/2022. https://geneticsupportfoundation.org/genetics-101/#

Documentation for Clinical Review

Please provide the following documentation:

- Name of the test being requested or the Concert Genetics GTU identifier.
  The Concert Genetics GTU can be found at https://app.concertgenetics.com
- CPT codes to be billed for the particular genetic test (GTU required for unlisted codes)
- History and physical and/or consultation notes including:
  - Clinical findings:
    - Signs/symptoms leading to a suspicion of genetic condition
    - Family history if applicable
  - Prior evaluation/treatment:
    - Previous test results (i.e., imagining, lab work, etc.) related to reason for genetic testing
    - Family member's genetic test result, if applicable
  - Rationale
    - Reason for performing test
    - How test result will impact clinical decision making

Post Service (in addition to the above, please include the following):

- Results/reports of tests performed

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	81401	Molecular pathology procedure, Level 2 (e.g., 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
	81402	Molecular pathology procedure, Level 3 (e.g., >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD])
	81403	Molecular pathology procedure, Level 4 (e.g., analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
	81404	Molecular pathology procedure, Level 5 (e.g., analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
	81405	Molecular pathology procedure, Level 6 (e.g., analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)
	81406	Molecular pathology procedure, Level 7 (e.g., analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons)
	81407	Molecular pathology procedure, Level 8 (e.g., analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)
	81408	Molecular pathology procedure, Level 9 (e.g., analysis of >50 exons in a single gene by DNA sequence analysis)
	81479	Unlisted molecular pathology procedure
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
02/01/2024	New policy.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. 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 covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE	**AFTER** Blue font: Verbiage Changes/Additions
New Policy **Policy Statement:** N/A	**Genetic Testing: Dermatologic Conditions BSC_CON_2.25** **Policy Statement:** **KNOWN FAMILIAL VARIANT ANALYSIS FOR DERMATOLOGIC CONDITIONS** I. Targeted mutation analysis for a known familial variant (81403) in a dermatologic condition may be considered **medically necessary** when: A. The member has a close relative with a known pathogenic or likely pathogenic variant causing the condition. II. Targeted mutation analysis for a known familial variant (81403) in a dermatologic condition is considered **investigational** for all other indications. **CAPILLARY MALFORMATION-ARTERIOVENOUS MALFORMATION (CM-AVM) SYNDROME** ***RASA1* and *EPHB4* Sequencing and/or Deletion/Duplication Analysis or Multigene Panel** III. *RASA1* and *EPHB4* sequencing and/or deletion/duplication analysis or multi-gene panel analysis (81479) to establish a diagnosis of capillary malformation-arteriovenous malformation (CM-AVM) syndrome may be considered **medically necessary** when: A. The member displays **one or more** of the following: 1. Capillary malformations 2. Arteriovenous malformations/arteriovenous fistulas 3. Parkes Weber syndrome phenotype, a cutaneous capillary malformation associated with underlying multiple micro-AVFs and soft-tissue and skeletal hypertrophy of the affected limb. IV. *RASA1* and *EPHB4* sequencing and/or deletion/duplication analysis or multi-gene panel analysis (81479) to establish a diagnosis of

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BEFORE	AFTER Blue font: Verbiage Changes/Additions
	capillary malformation-arteriovenous malformation (CM-AVM) syndrome is considered **investigational** for all other indications. **CONGENITAL ICHTHYOSIS** **Congenital Ichthyosis Multigene Panel** V. Multigene panel analysis to establish or confirm a diagnosis of congenital ichthyosis (81405, 81479) may be considered **medically necessary** when **ALL** of the following criteria are met: A. The member has scaly skin with or without a history of harlequin ichthyosis, collodion membrane, or thick, hyperkeratotic skin B. **One or more** of the following: 1. Ectropion (eversion of eyelids) 2. Eclabium (eversion of lips) 3. Scarring alopecia 4. Palmar and/or plantar hyperkeratosis 5. Erythroderma (red skin) C. The panel includes, at a minimum, the following genes: *ABCA12, SLC27A4*, and *TGM1*. VI. Multigene panel analysis to establish or confirm a diagnosis of congenital ichthyosis (81405, 81479) is considered **investigational** for all other indications. **EPIDERMOLYSIS BULLOSA** **Epidermolysis Bullosa Multigene Panel** VII. Multigene panel analysis to establish or confirm a diagnosis of epidermolysis bullosa (81406, 81479) may be considered **medically necessary** when: A. The panel includes, at a minimum, the following genes: *EXPH5, KRT5, KRT14, PLEC* **AND ANY** of the following criteria are met: 1. The member has fragility of the skin manifested by blistering with little or no trauma 2. The member has the presence of blistering that has **ANY** of the following characteristics: a. Is present in the neonatal period

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BEFORE	AFTER Blue font: Verbiage Changes/Additions
	b. Primarily affects the hands and feet but can affect the whole body c. Occurs in annular or curvilinear groups or clusters d. Leads to progressive brown pigmentation interspersed with hypopigmented spots on the trunk and extremities (frequently disappears in adult life) e. Is associated with palmar and plantar hyperkeratosis that may be severe 3. The member has **one or more** of the following: a. Nail dystrophy b. Milia c. Congenital pyloric atresia d. Natal teeth e. Ureteral and renal anomalies, including hydronephrosis, ureterocele, absent bladder, dysplastic kidneys, urinary collecting system/kidney duplication, obstructive uropathy, and glomerulosclerosis VIII. Multigene panel analysis to establish or confirm a diagnosis of epidermolysis bullosa (81406, 81479) is considered **investigational** for all other indications. **OTHER COVERED DERMATOLOGIC CONDITIONS** The following is a list of conditions that have a known genetic association. Due to their relative rareness, it may be appropriate to cover these genetic tests to establish or confirm a diagnosis. IX. Genetic testing to establish or confirm one of the following dermatologic conditions to guide management may be considered **medically necessary** when the member demonstrates clinical features* consistent with the condition (the list is not meant to be comprehensive, see X below): A. Hidrotic Ectodermal Dysplasia 2 (Clouston Syndrome) B. Hypohidrotic Ectodermal Dysplasia C. Ocular albinism, X-linked D. Oculocutaneous albinism

POLICY STATEMENT	
BEFORE	**AFTER** **Blue font: Verbiage Changes/Additions**
	X. Genetic testing to establish or confirm the diagnosis of all other dermatologic conditions not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Genetic and Molecular Testing* (see policy coverage criteria). *Clinical features for a specific disorder may be outlined in resources such as GeneReviews, OMIM, National Library of Medicine, Genetics Home Reference or other scholarly source.