

CONCERT GENETIC TESTING: DERMATOLOGIC CONDITIONS

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See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

OVERVIEW

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.

POLICY REFERENCE TABLE

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2023, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only and may not support medical necessity. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

The tests and associated laboratories and CPT codes contained within this document serve only as examples to help users navigate claims and corresponding 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.

NOTE: Coverage is subject to each requested code's inclusion on the corresponding LDH fee schedule. Non-covered codes are denoted (*) and are reviewed for Medical Necessity for members under 21 years of age on a per case basis. The non-covered codes will only be denoted in the table below and not throughout the policy. Please only reference the policy reference table for covered and non-covered codes.

Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	Ref
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	Q27.3, Q27.9	1
	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	Q80	2
	Ichthyosis NGS Panel (Connective Tissue Gene Tests)			
	Invitae Congenital Ichthyosis Panel (Invitae)			
Covered Dermatologic Conditions				
Other Covered Dermatologic Conditions	See Below	81401*-81408*, 81479	Varies	3, 4, 5

OTHER RELATED POLICIES

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

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

CRITERIA

It is the policy of Louisiana Healthcare Connections that the specific genetic testing noted below is **medically necessary** when meeting the related criteria:

CAPILLARY MALFORMATION-ARTERIOVENOUS MALFORMATION (CM-AVM) SYNDROME

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

- I. *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 **medically necessary** when:
 - A. The member/enrollee displays one or more of the following:
 1. Capillary malformations, **OR**
 2. Arteriovenous malformations/arteriovenous fistulas, **OR**
 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.
- II. *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.

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CONGENITAL ICHTHYOSIS

Congenital Ichthyosis Multigene Panels

- I. Multigene panel analysis to establish or confirm a diagnosis of congenital ichthyosis (81405, 81479) is considered **medically necessary** when:
 - A. The member/enrollee has scaly skin with or without a history of harlequin ichthyosis, collodion membrane, or thick, hyperkeratotic skin, **AND**
 - B. One or more of the following:
 1. Ectropion (eversion of eyelids), **OR**

2. Eclabium (eversion of lips), **OR**
 3. Scarring alopecia, **OR**
 4. Palmar and/or plantar hyperkeratosis, **OR**
 5. Erythroderma (red skin)
- II. Multigene panel analysis to establish or confirm a diagnosis of congenital ichthyosis (81405, 81479) is considered **investigational** for all other indications.

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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.

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

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BACKGROUND AND RATIONALE

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 *RASAI* 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*, *RASAI*, 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*, *CASPI4*, *CERS3*, *CYP4F22*, *LIPN*, *NIPAL4*, *PNPLA1*, *SDR9C7*, *SLC27A4*, *SULT2B1*, and *TGMI*. 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, *TGMI* in individuals with ARCI without harlequin presentation at birth and *SLC27A4* in those presenting with ichthyosis-prematurity syndrome."

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Reviews, Revisions, and Approvals	Revision Date	Approval Date	Effective Date
Converted to local policy	09/23	11/27/23	
Semi-annual review. Overview, coding, reference-table, background and references updated. Throughout policy: replaced "coverage criteria" with "criteria. For Other Related Policies: added "Molecular". For Congenital Ichthyosis Multigene Panels: removed "81252" throughout. For Epidermolysis Bullosa Multigene Panels: in I.A. replaced "AND" with "OR"; in I.B.1 replaced with "May be" with "Is"; in I.B.4. replaced "Can lead" with "Leads"; in I.B.5. replaced "AND" with "OR"; in I.C. added "4. Natal teeth, OR". For Other Covered Dermatologic Conditions: added "and Molecular". For Background and Rationale: replaced "inheritance patterns" with "genetic testing".	12/23	2/27/24	
Semi-annual review. In Known Familial Variant Analysis for Dermatologic Conditions criteria, moved criteria to policy "Genetic Testing: General Approach to Genetic and Molecular Testing" to consolidate criteria for known familial variant tests. In Epidermolysis Bullosa Multigene Panels criteria, retired criteria set based on rarity of testing (low order volume and low claim volume). In Congenital Ichthyosis Multigene Panels criteria, removed minimum gene list; at present there is limited rationale for inclusion. Minor rewording for clarity throughout. Coding, reference-table, background and references updated.	6/24	9/17/24	10/17/24

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/>
2. Richard G. Autosomal Recessive Congenital Ichthyosis. 2001 Jan 10 [Updated 2023 April 20]. 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/NBK1420/>
 3. 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/>
 4. Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD). World Wide Web URL: <https://omim.org/>
 5. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US). Available from: <https://medlineplus.gov/genetics/>

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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