# Concert Genetic Testing: ~~Dermatologic Conditions~~Dermatology

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Revision Log

Coding implications

**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.~~

This policy addresses the use of tests for fungal infection of the nails (onychomycosis), which can sometimes affect surrounding skin. These criteria are intended for use in the outpatient setting.

For additional information see the Rationale section.

# 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~~2024, 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, ~~associated laboratories,~~ CPT codes, and ICD codes ~~contained within~~referenced in this ~~document serve only as examples to help users navigate claims and corresponding criteria; as such, they~~policy are not comprehensive, and ~~are~~their inclusion does not represent a guarantee of coverage or non-coverage. ~~Please see the Concert 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~~ CRITERIA SECTIONS | ~~Example Tests (Labs)~~EXAMPLE TESTS (LABS) | ~~Common CPT Codes~~COMMON BILLING CODES | ~~Common ICD Codes~~REF | ~~Ref~~ |
|---|---|---|---|---|
| **~~Capillary Malformation-Arteriovenous Malformation Syndrome (CM-AVM)~~Onychomycosis (Nail Fungus) Tests** | | | | |
| ~~*RASA1* and *EPHB4* Sequencing and/or Deletion/Duplication Analysis or Multigene Panel~~Microscopy/Peroxidase Tests for Onychomycosis | ~~Capillary Malformation-Arteriovenous Malformation Syndrome (CM-AVM) Panel, Sequencing and Deletion/Duplication (ARUP Laboratories)~~Fungus Stain (LabCorp) | ~~8147987~~206, 87220 | ~~Q27.3, Q27.9~~ | 1, 2 |
| | KOH Prep (Pacific Medical) | | | |
| Fungal Culture for Onychomycosis | ~~Vascular Malformation NGS Panel (Greenwood Genetic Center)~~Culture, Fungus, Miscellaneous (Quest Diagnostics) | 87101, 87102, 87106, 87107, 87143, 87149 | | |
| | ~~RASA1 Full Gene Sequencing and Deletion/Duplication (Invitae)~~Fungus (Mycology) | | | |

| | | | | |
|---|---|---|---|---|
| | ~~EPHB4 Full Gene Sequencing and Deletion/Duplication (Invitae)~~Culture/Dermatophyte Culture (LabCorp) | | | |
| ~~**Congenital Ichthyosis**~~ | Fungal Isolate Identification (Quest Diagnostics) | | | |
| ~~Congenital Ichthyosis Multigene Panels~~Culture-Independent Molecular Tests (NAAT/PCR) for Onychomycosis | ~~Ichthyosis Panel (Blueprint Genetics)~~Nail-ID (Vikor Scientific) | ~~81405*, 81479~~87481, 87500, 87641, 87652, 87653, 87798 | ~~Q80~~ | ~~2~~ |
| | ~~Ichthyosis NGS Panel (HNL Lab Medicine)~~ | | | |
| | ~~Invitae Congenital Ichthyosis Panel (Invitae)~~ | | | |
| ~~**Covered Dermatologic Conditions**~~ | | | | |
| ~~Other Covered Dermatologic Conditions~~ | ~~See Below~~ | ~~81401*, 81402*, 81403*, 81404*, 81405*, 81406*, 81407*, 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~~infectious 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.~~. Please refer to:

- ~~***Genetic Testing:*** ***General Approach to Genetic and Molecular***~~***Laboratory Testing*** for criteria related to ~~genetic testing for a~~ dermatologic ~~condition~~conditions, including known familial variant testing, that is not specifically discussed in this or another ~~more specific~~non-general policy~~, including known familial variant testing~~

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# 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~~

### ~~*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~~ ONYCHOMYCOSIS (NAIL FUNGUS) TESTS

### Microscopy/Peroxidase Tests for Onychomycosis

I. Microscopy/peroxidase tests for onychomycosis are considered **medically necessary** when:

~~A.~~ The member/enrollee ~~displays one~~shows signs or ~~more~~symptoms of onychomycosis (e.g., nails that are discolored, deformed, brittle, and/or foul-smelling; subungual debris; separation of the ~~following:~~

~~1. Capillary malformations, **OR**~~

~~2. Arteriovenous malformations/arteriovenous fistulas, **OR**~~

A. ~~Parkes Weber syndrome phenotype, a cutaneous capillary malformation associated with underlying multiple micro-AVFs and soft tissue and skeletal hypertrophy of~~nail from the ~~affected limb.~~nail bed), **AND**

~~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~~

B. ~~Multigene panel analysis to establish or confirm a diagnosis of congenital ichthyosis (81405, 81479~~Results of testing would influence the member/enrollee's clinical management.

II. Current evidence does not support microscopy/peroxidase tests for for all other indications.

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## Fungal Culture for Onychomycosis

I. Fungal culture for onychomycosis (presumptive and/or definitive) is considered **medically necessary** when:

~~A.~~ The member/enrollee ~~has scaly skin with~~shows signs or ~~without a history~~symptoms of ~~harlequin ichthyosis, collodion membrane, or thick, hyperkeratotic skin, **AND**~~

A. ~~One or more~~onychomycosis (e.g., nails that are discolored, deformed, brittle, and/or foul-smelling; subungual debris; separation of the ~~following:~~nail from the nail bed), **AND**

~~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).~~

B. ~~Multigene panel analysis to establish or confirm a diagnosis of congenital ichthyosis (81405, 81479) is considered **investigational**~~Results of testing would influence the member/enrollee's clinical management.

II. Current evidence does not support fungal culture for onychomycosis (presumptive and/or definitive) 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~~
~~E. Epidermolysis Bullosa.~~

~~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).~~

~~***NOTE:*** 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~~ view rationale

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## Culture-Independent Molecular Tests (NAAT/PCR) for Onychomycosis

I. Current evidence does not support culture-independent molecular tests (NAAT/PCR) for onychomycosis for all indications.

# RATIONALE

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

~~*GeneReviews: Capillary Malformation-Arteriovenous Malformation Syndrome*~~

~~GeneReviews is an expert-authored review of current literature on 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~~Microscopy/Peroxidase Tests for Onychomycosis

*British Association of Dermatologists*

In their 2014 onychomycosis guidelines, the British Association of Dermatologists state 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~~ "Laboratory confirmation of a clinical diagnosis of tinea unguium should be obtained before starting treatment. This is important for several reasons: to eliminate nonfungal dermatological conditions from the diagnosis; to detect mixed infections; and to diagnose patients with less responsive forms of onychomycosis, such as toenail infections due to *T. rubrum*" (p. 942).

"Traditionally, laboratory detection and identification of dermatophytes consists of culture and microscopy" (p. 942).

*American Academy of Family Physicians*

In their 2021 rapid evidence review of onychomycosis, the AAFP listed the common signs and symptoms of onychomycosis, including: nails that are discolored, deformed, hypertrophic, or

hyperkeratotic; subungual debris; separation from the nail bed; brittle nails that break easily or crumble; and nails that are foul smelling (p. 360).

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## Fungal Culture for Onychomycosis

*British Association of Dermatologists*

In their 2014 onychomycosis guidelines, the British Association of Dermatologists state the following:

"Laboratory confirmation of a clinical diagnosis of tinea unguium should be obtained before starting treatment. This is important for several reasons: to eliminate nonfungal dermatological conditions from the diagnosis; to detect mixed infections; and to diagnose patients with less responsive forms of onychomycosis, such as toenail infections due to *T. rubrum*" (p. 942).

"Traditionally, laboratory detection and identification of ~~biallelic pathogenic variants in one of the genes listed below.~~dermatophytes consists of culture and microscopy" (p. 942).

~~"The twelve genes known to be associated with ARCI are *ABCA12, ALOX12B, ALOXE3, CASP14, CERS3, CYP4F22, LIPN, NIPAL4, PNPLA1, SDR9C7, SLC27A4, SULT2B1,* 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."~~

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## Culture-Independent Molecular Tests (NAAT/PCR) for Onychomycosis

*British Association of Dermatologists*

In their 2014 onychomycosis guidelines, the British Association of Dermatologists state the following:

"It appears that real-time PCR significantly increased the detection rate of dermatophytes compared with culture. However, PCR may detect nonpathogenic or dead fungus, which could

limit its use in identifying the true pathogen. Restriction fragment length polymorphism analysis, which identifies fungal ribosomal DNA, is very helpful for defining whether the disease is caused by repeat infection or another fungal strain when there is a lack of response to treatment. However, this technique has not been implemented into routine clinical practice" (p. 942).

*American Academy of Family Physicians*

In their 2021 rapid evidence review of onychomycosis, the AAFP states the following:

"A potassium hydroxide (KOH) preparation with direct microscopy is the preferred diagnostic method [for onychomycosis] because it is highly specific, has rapid results, and is cost-effective. Diagnosis by KOH preparation alone is sufficient for treatment initiation. However, if KOH results are negative and there is high clinical suspicion for onychomycosis, other testing may be performed to confirm the diagnosis" (p. 361).

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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 |
| RASA1 and EPHB4 Sequencing and/or Deletion/Duplication Analysis or Multigene Panel: Updated title in Background and Rationale from 'Capillary Malformation-Arteriovenous Malformation Syndrome (CM-AVM)' to 'RASA1 and EPHB4 Sequencing and/or Deletion/Duplication Analysis or Multigene Panel' to align with criteria set name; Updated dates in References. Congenital Ichthyosis Multigene Panel: Updated GeneReviews copyright dates in Reference list. Other Covered | 1/25 | 3/31/25 | 5/1/25 |

| Reviews, Revisions, and Approvals | Revision Date | Approval Date | Effective Date |
|---|---|---|---|
| Dermatologic Conditions: Added one disorder to list (Epidermolysis Bullosa). | | | |
| Annual review. Policy title changed from Concert Genetic Testing: Dermatologic Conditions to Concert Genetic Testing: Dermatology. Minor wording changes throughout without clinical significance. Other Covered Dermatologic Conditions: Added gene names for each condition listed in the criteria. "Investigational" policy statements changed to note that "current evidence does not support…" Coding table, rationale and references updated. | 03/26 | | |

# 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; 1993-2024. 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; 1993-2024. 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; 1993-2024. 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/~~
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1. ~~back to top~~Ameen M, Lear JT, Madan V, Mohd Mustapa MF, Richardson M. British Association of Dermatologists' guidelines for the management of onychomycosis 2014. Br J Dermatol. 2014;171(5):937-958.
2. Frazier WT, Santiago-Delgado ZM, Stupka KC. Onychomycosis: rapid evidence review. Am Fam Physician. 2021;104(4):359-367.


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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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