Medica Central Coverage Policy

Policy Name:	**Genetic Testing – Specialty Testing: Orthopedics MP9603**
Effective Date:	**July 01, 2025**

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica Central plans. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage.

Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions may call the Provider Service Center. Please use the Quick Reference Guide on the Provider Communications page for the appropriate phone number. https://mo-central.medica.com/Providers/SSM-employee-health-plan-for-IL-MO-OK-providers

Medica Central coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment.

OVERVIEW

This policy addresses the use of tests for rare skeletal dysplasias and other bone disorders. Pre-test and post-test genetic counseling that facilitates informed decision-making, addresses the possibility of secondary or incidental findings, and a plan for returning results before testing occurs is strongly advised.

For additional information see the Rationale section.

The tests, CPT codes, and ICD codes referenced in this policy are not comprehensive, and their inclusion does not represent a guarantee of coverage or non-coverage.

POLICY REFERENCE TABLE

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	REF
Osteogenesis Imperfecta (OI)			
Osteogenesis Imperfecta	Osteogenesis imperfecta COL1A1 & COL1A2 NGS Panel (HNL Genomics)	81406, 81408, 81479, Q78.0, Z82.79	3

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	REF
	Osteogenesis Imperfecta Panel (PreventionGenetics, part of Exact Sciences)		
	Osteogenesis Imperfecta NGS Panel - Dominant & Recessive (HNL Genomics)		
Skeletal Dysplasias and Rare Bone Disorders			
Multigene Panel Analysis for Skeletal Dysplasia or Rare Bone Disorder	Skeletal Disorders Panel (Invitae)	81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 81479, M85, Q77, Q78	1, 7, 8
	Skeletal Dysplasia Core & Extended NGS Panel (HNL Genomics)		
	Comprehensive Skeletal Dysplasias and Disorders Panel (Blueprint Genetics)		
Other Covered Skeletal Dysplasias and Rare Bone Disorders			
Other Covered Skeletal Dysplasias and Rare Bone Disorders	See list below	81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 81479, M85, Q77, Q78	2, 4, 5, 6

RELATED POLICIES

This policy document provides coverage criteria for testing related to skeletal dysplasia and rare bone disorders. Please refer to:

- ***Specialty Testing: Cardiovascular*** for coverage criteria related to diagnostic tests for inherited and sporadic cardiovascular conditions.
- ***Specialty Testing: Multisystem Genetic Conditions*** for coverage criteria related to diagnostic tests for genetic disorders that affect multiple organ systems (e.g. whole exome and genome sequencing, chromosomal microarray, and multigene panels for broad phenotypes).
- ***General Approach to Laboratory Testing*** for coverage criteria related to skeletal dysplasias and rare bone disorders, including known familial variant testing, that is not specifically discussed in this or another non-general policy.

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COVERAGE CRITERIA

OSTEOGENESIS IMPERFECTA (OI)

Osteogenesis Imperfecta

I. *COL1A1* and *COL1A2* variant analysis or multigene panel analysis that includes *COL1A1* and *COL1A2* to establish or confirm a diagnosis of osteogenesis imperfecta (OI) is considered **medically necessary** when:

   A. The member has any of the following:

      1. Fractures with minimal or no trauma in the absence of other factors, such as non-accidental trauma (NAT) or other known disorders of bone, **OR**
      2. Short stature, often with bone deformity, **OR**
      3. Blue/gray scleral hue, **OR**
      4. Dentinogenesis imperfecta (DI), **OR**
      5. Progressive, postpubertal hearing loss, **OR**
      6. Ligamentous laxity or other signs of connective tissue abnormality, **OR**
      7. Family history of OI, **OR**
      8. Fractures of varying ages and stages of healing (often of the long bones), **OR**
      9. “Codfish” vertebrae, **OR**
      10. Wormian bones, **OR**
      11. Protrusio acetabuli, **OR**
      12. Low bone mass or osteoporosis.

II. *COL1A1* and *COL1A2* variant analysis or multigene panel analysis that includes *COL1A1* and *COL1A2* to establish or confirm a diagnosis of osteogenesis imperfecta is considered **investigational** for all other indications.

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SKELETAL DYSPLASIAS AND RARE BONE DISORDERS

Multigene Panel Analysis For Skeletal Dysplasia Or Rare Bone Disorder

I. Multigene panel analysis to confirm or establish a post-natal diagnosis of a skeletal dysplasia or a rare bone disorder may be considered **medically necessary** when:

A. The differential diagnosis includes more than one type of skeletal dysplasia or bone disorder, **AND**

B. The member displays one or more of the following clinical features of a skeletal dysplasia:

1. Prenatal ultrasound that showed shortening of the bones of the arms and legs more than 3 standard deviations below the mean, **OR**

2. Prenatal ultrasound that showed head circumference greater than 75th percentile, **OR**

3. Prenatal ultrasound that showed bone irregularities (e.g., bowed, fractured, thickened, thin, undermineralized, etc.), **OR**

4. Prenatal ultrasound that showed abnormal ribs or a small chest circumference, **OR**

5. Postnatal short stature with height or length less than 3rd percentile.

II. Multigene panel analysis to confirm or establish a diagnosis of a skeletal dysplasia or a rare bone disorder is considered **investigational** for all other indications.

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OTHER COVERED SKELETAL DYSPLASIAS AND RARE BONE DISORDERS

Other Covered Skeletal Dysplasias and Rare Bone Disorders

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 skeletal dysplasias or rare bone disorders to guide management is considered **medically necessary** when the member demonstrates clinical features[1] consistent with the disorder (the list is not meant to be comprehensive, see II below):

A. Achondroplasia Group

1. Achondroplasia

2. Hypochondroplasia

3. Thanatophoric Dysplasia

B. Type II Collagenopathies

1. Hypochondrogenesis

2. Spondyloepiphyseal Dysplasia

C. Type XI Collagen Disorders

1. Fibrochondrogenesis

2. Otospondylomegaepiphyseal Dysplasia (OSMED)

D. Sulfation Disorders

1. Achondrogenesis IB
2. Atelosteogenesis II
3. Diastrophic Dysplasia
4. Chondrodysplasia with Congenital Joint Dislocations

E. Filamin Disorders and Similar Disorders

1. Atelosteogenesis Type I
2. Atelosteogenesis Type III
3. Larsen Syndrome
4. Spondylo-Carpal-Tarsal Dysplasia

F. Short-Rib Dysplasias (with and without Polydactyly)

1. Chondroectodermal Dysplasia (Ellis-van Creveld (EVC))
2. Short-Rib Polydactyly Syndrome I, II, III, IV including Asphyxiating Thoracic Dystrophy

G. Metaphyseal Dysplasias

1. Cartilage-Hair Hypoplasia

H. Spondylo-Epi-(Meta)-Physeal Dysplasia

1. SEMD, Short Limb Abnormal Calcification Type

I. Acromesomelic Disorders

1. Acromesomelic Dysplasia, Type Maroteaux

J. Mesomelic and Rhizo-Mesomelic Dysplasias

1. Langer Type (Homozygous Dyschondrosteosis)

K. Bent Bone Dysplasias

1. Campomelic Dysplasia
2. Stuve-Wiedemann Dysplasia
3. Bent Bone Dysplasia FGFR2 Type

L. Slender Bone Dysplasia

1. Microcephalic Osteodysplastic Primordial Dwarfism

2. Osteocraniostenosis

M. Neonatal Osteosclerotic Dysplasias

1. Bloomstrand Dysplasia
2. Caffey Disease (Infantile)
3. Raine Dysplasia

N. Increased Bone Density Group

1. Osteopetrosis

O. Abnormal Mineralization Group

1. Hypophosphatasia

P. Multiple Epiphyseal Dysplasia and Pseudoachondroplasia Group

1. Multiple Epiphyseal Dysplasia (MED) - Autosomal Dominant
2. Multiple Epiphyseal Dysplasia (MED) - Autosomal Recessive
3. Stickler Syndrome

Q. Hereditary Multiple Osteochondromas

II. Genetic testing to establish or confirm the diagnosis of all other skeletal dysplasias or rare bone disorders not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Laboratory Testing* (see policy for coverage criteria).

[1]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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PRIOR AUTHORIZATION

Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

RATIONALE

Osteogenesis Imperfecta

GeneReviews: COL1A1/2 Osteogenesis Imperfecta

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 osteogenesis imperfecta is as follows:

COL1A1/2 osteogenesis imperfecta (OI) should be suspected in individuals with the following clinical, radiographic, and laboratory features.

- Fractures with minimal or no trauma in the absence of other factors, such as non-accidental trauma (NAT) or other known disorders of bone
- Short stature or stature shorter than predicted based on stature of unaffected family members, often with bone deformity
- Blue/gray scleral hue
- Dentinogenesis imperfecta (DI)
- Progressive, postpubertal hearing loss
- Ligamentous laxity and other signs of connective tissue abnormality
- Family history of OI, usually consistent with autosomal dominant inheritance

Radiographic features of OI change with age. The major findings include the following:

- Fractures of varying ages and stages of healing, often of the long bones but may also rarely involve ribs and skull. Metaphyseal fractures can be seen in a very small number of children with OI. Rib fractures are much more common in NAT than in OI.
- "Codfish" vertebrae, which are the consequence of spinal compression fractures, seen more commonly in adults.
- Wormian bones, defined as "sutural bones which are 6 mm by 4 mm (in diameter) or larger, in excess of ten in number, with a tendency to arrange in a mosaic pattern." Wormian bones are suggestive of but not pathognomonic for OI.
- Protrusio acetabuli, in which the socket of the hip joint is too deep and the acetabulum bulges into the cavity of the pelvis causing intrapelvic protrusion of the acetabulum.
- Low bone mass or osteoporosis detected by dual energy x-ray absorptiometry (DEXA). Bone density can be normal, especially in individuals with OI type I, as DEXA measures mineral content rather than collagen.

“A multigene panel that includes *COL1A1*, *COL1A2*, 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 variants in genes that do not explain the underlying phenotype.”

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Multigene Panel Analysis For Skeletal Dysplasia Or Rare Bone Disorder

Krakow et al 2009

A guideline for prenatal diagnosis of fetal skeletal dysplasias (Krakow, Lachman, Rimoin, 2009) recommends the following criteria:

- Fetuses with long bone measurements at or less than the 5th centile or greater than 3 SD below the mean should be evaluated in a center with expertise in the recognition of skeletal dysplasias. If the patient cannot travel, arrangements may be able to be made for evaluation of ultrasound videotapes or hard copy images.
- The following fetal ultrasound measurements should be visualized and plotted against normative values: fetal cranium (biparietal diameter and head circumference), facial profile, mandible, clavicle, scapula, chest circumference, vertebral bodies, all fetal long bones, and the hands and feet. Fetuses with long bone parameters more than 3 SD below the mean should be strongly suspected of having a skeletal dysplasia, especially if the head circumference is greater than the 75th centile
- Lethality should be determined by chest circumference to abdominal circumference ratio and/or femur length to abdominal circumference measurement ratio. A chest-to abdominal circumference ratio of less than 0.6 or femur length to abdominal circumference ratio of 0.16 strongly suggests a perinatal lethal disorder, although there are exceptions. The findings should be conveyed to the physicians caring for the patient and to the patient (p. 5).

In addition, close attention should be paid to the shape and mineralization pattern of the fetal calvarium and fetal skeleton (poor or ectopic mineralization). Determining the elements of the skeleton that are abnormal, coupled with the findings of mineralization and shape of the bones can aid in diagnosis (p. 3).

American College of Medical Genetics and Genomics (ACMG)

For diagnosis of genetic causes of short stature, the American College of Medical Genetics clinical practice resource for evaluation of short stature (Seaver et al, 2009) is as follows:

> "The definition most commonly used for short stature is height-for-age less than two standard deviations below average for gender, which is demonstrated on the standard growth curves as a length or height less than the 3rd centile" (p. 466).

Scocchia, et al.

A 2021 study of the clinical utility of multigene panel testing for an unselected population of individuals with suspected skeletal dysplasia demonstrated a high diagnostic yield in individuals with a suspected skeletal dysplasia or growth disorder (p. 1).

A molecular diagnosis was established in 42% of patients (228/543). Diagnostic variants were identified in 71 genes, with variation in nearly half of these genes contributing to a molecular diagnosis for a single patient in this cohort. Overall, the most common genes in which molecular diagnoses were identified included: *COL2A1* associated with type II collagenopathies; *FGFR3* associated with achondroplasia, thanatophoric dysplasia, hypochondroplasia, and other conditions such as FGFR-related craniosynostoses; and *COL1A1* or *COL1A2*, associated with osteogenesis imperfecta. Together, these four genes accounted for over one third of all molecular diagnoses across the cohort (p. 2-3).

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Other Covered Skeletal Dysplasias and Rare Bone Disorders

International Skeletal Dysplasia Society

The International Skeletal Dysplasia Society published an updated categorization of skeletal dysplasias (Unger, 2023):

> "The 'Nosology of genetic skeletal disorders' has undergone its 11th revision and now contains 771 entries associated with 552 genes reflecting advances in molecular delineation of new disorders thanks to advances in DNA sequencing technology….As with the previous versions, the list of disorders and genes in the Nosology may be useful in considering the differential diagnosis in the clinic, directing bioinformatic analysis of next-generation sequencing results, and provide a basis for novel advances in biology and medicine" (p. 1165).

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DEFINITIONS

1. **Non-accidental Trauma (NAT)** - This refers to injury that is purposely inflicted upon a child (e.g., child abuse). NAT often occurs as injury to the skin and soft tissue, but approximately a third of NATs are fractures.

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Note: The Health Plan uses the genetic testing clinical criteria developed by Concert Genetics, an industry-leader in genetic testing technology assessment and policy development.

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