

# Multiple Endocrine Neoplasia Type 1

## Indications for Ordering

Confirm diagnosis of suspected multiple endocrine neoplasia type 1 (MEN1) syndrome

## Test Description

- Polymerase chain reaction followed by sequencing of entire coding region and intron/exon boundaries of *MEN1* gene
- Multiplex ligation-dependent probe amplification to identify large exonic deletions/duplications in *MEN1* gene

## Tests to Consider

### Primary tests

[Multiple Endocrine Neoplasia Type 1 \(MEN1\) Sequencing and Deletion/Duplication 2005360](#)

- Preferred initial test to confirm diagnosis of MEN1

[Multiple Endocrine Neoplasia Type 1 \(MEN1\) Sequencing 2005359](#)

- Acceptable initial test to confirm diagnosis of MEN1

[Cancer Panel, Hereditary, Sequencing and Deletion/Duplication, 47 Genes 2012032](#)

- Confirm diagnosis of a hereditary cancer syndrome with personal or family history consistent with features of more than one cancer syndrome

[Familial Mutation, Targeted Sequencing 2001961](#)

- Useful when a pathogenic familial variant identifiable by sequencing is known

### Related tests

Anterior pituitary tumor testing

- [Adrenocorticotrophic Hormone 0070010](#)
- [IGF-1 \(Insulin-Like Growth Factor 1\) 0070125](#)
- [Prolactin 0070115](#)

Carcinoid tumor testing

- [5-Hydroxyindoleacetic Acid \(HIAA\), Urine 0080420](#)
- [Gastrin 0070075](#)
- [Serotonin, Whole Blood 0080395](#)

Gastrinoma testing

- [Gastrin 0070075](#)

Medullary thyroid carcinoma testing

- [Calcitonin 0070006](#)
- [Thyroid Stimulating Hormone with Reflex to Free Thyroxine 2006108](#)

Pancreatic neuroendocrine tumor testing

- [Chromogranin A 0080469](#)
- [C-Peptide, Serum or Plasma 0070103](#)
- [Glucagon 0099165](#)
- [Pancreatic Polypeptide 0099436](#)
- [Proinsulin/Insulin Ratio 0070256](#)
- [Somatostatin Quantitative, Plasma 2010001](#)
- [Vasoactive Intestinal Peptide 0099435](#)

Parathyroid tumor testing

- [Parathyroid Hormone, Intact with Calcium 0070172](#)

Pheochromocytoma testing

- [Metanephrines Fractionated by HPLC-MS/MS, Urine 2007996](#)
- [Metanephrines, Plasma \(Free\) 0050184](#)

## Disease Overview

**Incidence** – 1/30,000

### Symptoms

- MEN1 can include development of multiple endocrine and nonendocrine tumors
- Common endocrine tumors
  - Parathyroid
  - Pancreatic islet cell
  - Pituitary
  - Gastrinoma
  - Medullary carcinoma of the thyroid
  - Carcinoid
- Nonendocrine tumors
  - Facial angiofibromas
  - Collagenomas
  - Meningiomas
  - Ependymomas
  - Leiomyomas

### Genetics

**Gene** – *MEN1*

**Inheritance** – autosomal dominant

**Penetrance** – variable

- ~50% by 20 years
- >95% by 40 years

**De novo variants** – ~10%

**Variants** – inactivating variants of *MEN1* tumor suppressor gene

## Test Interpretation

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### Clinical sensitivity – combined testing ~94%

- Sequencing – 90%
- Deletion/duplication – 4%

### Results

- Positive
  - One pathogenic variant detected in *MEN1*
    - Confirms diagnosis and etiology of MEN1
- Negative
  - No detectable pathogenic variant detected in *MEN1*
    - Reduces, but does not exclude, a diagnosis of MEN1
- Unknown – variants of unknown clinical significance may be detected

### Limitations

- Not evaluated
  - Regulatory region or deep intronic variants
  - Breakpoints of large deletions/duplications
  - Variants in genes other than *MEN1*
- Diagnostic errors can occur due to rare sequence variations