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
- Adrenocorticotropic Hormone 0070010
- Insulin-Like Growth Factor 1 (IGF-1) with calculated Z-score 2007698
- 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, Other 3000529
- C-Peptide, Serum or Plasma 0070103
- Glucagon 0099165
- Pancreatic Polypeptide 0099436
- Proinsulin, Intact/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

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