# ESOTERIX *UPDATE*

*A NEWSLETTER FOR CLIENTS*

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## New Procedures

### 24-Hydroxylase Deficiency Screen, LC/MS-MS . . . . . 804105

**CPT** 82652
**Specimen** Serum (preferred) or plasma
**Volume** 1 mL
**Minimum Volume** 0.3 mL (**Note:** This volume does **not** allow for repeat testing.)
**Container** Red-top tube, gel-barrier tube, lavender-top (EDTA) tube, or green-top (heparin) tube
**Collection** Separate serum or plasma within one hour; transfer to a plastic transport tube.
**Storage Instructions** **Freeze**
**Use** Measurement of 24,25-dihydroxy vitamin D is useful in diagnosing idiopathic hypercalcemia, understanding blockages of the CYP24 enzyme, and studying clearance of vitamin D metabolites. This test may be useful for characterizing discrepant results from ligand-binding assay systems.[1] Some immunoassay systems designed to measure 25-hydroxy vitamin D cross-react with 24,25-dihydroxy vitamin D, leading to increased observed levels in some samples.
**Methodology** High-pressure liquid chromatography/tandem mass spectrometry (HPLC/MS-MS)
**Reference Interval** ***Target levels (all ages):*** 1.6–9.1 ng/mL
**Additional Information** 24,25-dihydroxy vitamin D is the most abundant product of vitamin D catabolism. 24,25-Dihydroxy vitamin D is produced by CYP24A1 the 24a-hydroxylase, a cytochrome P450 enzyme. CYP24A1 also converts 1,25-dihydroxy vitamin D to 1,24,25-trihydroxy vitamin D. Patients without adequate 24-hydroxylase activity can develop hypercalcemia, which may appear in infancy or remain asymptomatic for years. Decreased activity of CYP24A1 (24a-hydroxylase) leading to inappropriately high levels of 1,25-dihydroxy vitamin D may be caused by an inactivating mutation in the CYP24A1 gene. This gene defect has been described as idiopathic infantile hypercalcemia due to an "epidemic" of hypercalcemia caused by widespread dosing of vitamin D in the 1950s in England. Measurements of 24,25-dihydroxy vitamin D and 25-hydroxy vitamin D are helpful as biochemical screens for a genetic defect. 24,25-Dihydroxy vitamin D may be low also in patients with reduced glomerular filtration and reduced 25-dihydroxy vitamin D. Low or undetectable levels of 24,25-dihydroxy vitamin D in the presence of normal levels of 25-hydroxy vitamin D and normal eGFR strongly suggest the defect.

**Footnotes**

1. Cashman KD, Hayes A, Galvin K, et al. Significance of serum 24,25-dihydroxyvitamin D in the assessment of vitamin D status: A double-edged sword? *Clin Chem*. 2015 Apr; 61(4):636-645. PubMed 25710460

**References**

Berg AH, Powe CE, Evans MK, et al. 24,25-Dihydroxyvitamin D3 and vitamin D status of community-dwelling black and white Americans. *Clin Chem*. 2015 Jun; 61(6):877-884. PubMed 25922442

de Boer IH, Sachs MC, Chonchol M, Estimated GFR and circulating 24,25-dihydroxyvitamin D3 concentration: A participant-level analysis of 5 cohort studies and clinical trials. *Am J Kidney Dis*. 2014 Aug; 64(2):187-197. PubMed 24703961

Jacobs TP, Kaufman M, Jones G, et al. A lifetime of hypercalcemia and hypercalciuria, finally explained. *J Clin Endocrinol Metab*. 2014 Mar; 99(3):708-712. PubMed 24423361

Jones G, Prosser DE, Kaufmann M. 25-Hydroxyvitamin D-24-hydroxylase (CYP24A1): Its important role in the degradation of vitamin D. *Arch Biochem Biophys*. 2012 Jul 1; 523(1):9-18. PubMed 22100522

Ketha H, Kumar R, Singh RJ. LC-MS/MS for identifying patients with CYP24A1 mutations. Clin Chem. 2016 Jan; 62(1):236-242. PubMed 26585929

### Known Familial Mutation Sequencing Analysis . . . . . 804193

**CPT** 81403
**Special Instructions** Call laboratory before ordering. Documentation of known familial mutation is required. DNA sample from index patient as a positive control is recommended.
**Specimen** Whole blood
**Volume** 3.0 mL
**Minimum Volume** 1.0 mL (**Note:** This volume does **not** allow for repeat testing.)
**Container** Lavender-top (EDTA) tube or yellow-top (ACD) tube
**Collection** Ship specimen same day as collected.
**Storage Instructions** Room temperature
**Use** Single-exon sequence is performed to help clarify the genetic status of appropriate, at-risk members of a family in which a gene mutation has been identified previously.
**Methodology** Polymerase chain reaction of a single targeted gene exon, followed by bidirectional Sanger sequencing of a single PCR product

### Thiopurine Methyltransferase (TPMT) Genotyping . . . . . 804142

**CPT** 81401
**Synonyms** TPMT Genetic Testing
**Special Instructions** A completed *Informed Consent for TPMT Genetic Testing* should accompany specimens.
**Specimen** Whole blood or LabCorp buccal swab (buccal swab collection kit)
**Volume** 3 mL
**Minimum Volume** 1 mL (Note: This volume does not allow for repeat testing).
**Container** Lavender-top (EDTA) tube, yellow-top (ACD) tube, green-top (heparin) tube, or LabCorp buccal swab (from kit)
**Collection** Ship specimen same day as collected.
**Storage Instructions** Room temperature
**Causes for Rejection** Frozen sample; hemolysis
**Use** Detects the most common genotypes in approximately 95% of patients. Use is recommended prior to initiating thiopurine therapy.[1]
**Limitations** This assay will not detect approximately 5% of known deficiency mutations, and only the exons containing mutations in question are tested; polymorphisms or some sequence variants might affect efficiency of the PCR or mini-sequencing assays; assay does not distinguish between *TPMT**1/3A heterozygote and the very rare compound heterozygote *TPMT**3B/3C.
This test was developed, and its performance characteristics determined, by LabCorp. It has not been cleared or approved by the US Food and Drug Administration (FDA).
**Methodology** Polymerase chain reaction (PCR) and multiplex mini-sequencing

**Footnotes**

1. Relling MV, Gardner EE, Sandborn WJ, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing. *Clin Pharmacol Ther*. 2011 Mar; 89(3):387-391. PubMed 21270794

**References**

Lennard L. Implementation of TPMT testing. *Br J Clin Pharmacol*. 2014 Apr; 77(4):704-714. PubMed 23962279

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