blue of california

Medical Policy

Pharmacogenomic and Metabolite Markers in Inflammatory Bowel Disease	
Type: Medical Necessity and Investigational / Experimental	**Policy Specific Section:** Laboratory/Pathology
Original Policy Date: December 7, 2006	**Effective Date:** February 22, 2013

Definitions of Decision Determinations

Medically Necessary: A treatment, procedure or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

Investigational/Experimental: A treatment, procedure or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California / Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a Split Evaluation, where a treatment, procedure or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Description

Thiopurines are immunomodulators used to treat malignancies, rheumatic diseases, dermatologic conditions, inflammatory bowel disease and solid organ transplantation. These drugs include azathioprine (Imuran®), mercaptopurine (6-MP) (Purinethol®), and thioguanine (6-TG)

(Tabloid®). Thiopurines are converted by the enzyme thiopurine methyltransferase (TPMT) into metabolites. Measurement of TPMT activity may help to identify patients at risk for excessive toxicity, most often myelosuppression, after receiving standard doses of thiopurine medications. Measurement of metabolites (metabolite markers) may help to tailor individualized drug therapy.

Azathioprine is considered an effective immunosuppressive treatment of inflammatory bowel disease, particularly in patients with corticosteroid-resistant disease. In the course of one year, 50% of patients with Crohn's disease will require treatment with corticosteroids; of these, 50% will either be corticosteroid resistant or corticosteroid dependent, and thus candidates for immunosuppressive therapy. Azathioprine therapy eliminates the need for corticosteroids in about 75% of patients; azathioprine is also considered an effective therapy for fistulizing disease.

Policy

One-time genotypic or phenotypic analysis of the enzyme thiopurine methyltransferase (TPMT) is considered **medically necessary** in **either** of the following situations:

- Patients beginning therapy with azathioprine, mercaptopurine (6-MP) or thioguanine (6-TG)
- Patients on thiopurine therapy with abnormal complete blood count results that do not respond to dose reduction

Analysis of the metabolite markers of azathioprine and mercaptopurine (6-MP), including 6-methyl-mercaptopurine ribonucleotides (6-MMRP) and 6-thioguanine nucleotides (6-TGN), is considered **investigational**.

Policy Guideline

TPMT testing cannot substitute for complete blood count (CBC) monitoring in patients receiving thiopurines. Early drug discontinuation may be considered in patients with abnormal CBC results. Dosage reduction is recommended in patients with reduced TPMT activity. Alternate therapies may need to be considered for patients who have low or absent TPMT activity (homozygous for nonfunctional alleles). Accurate phenotyping results are not possible in patients who received recent blood transfusions. Genotyping and phenotyping of TPMT would only need to be performed once.

The analysis of common variants of the TPMT gene would be reported with CPT code 81401 - Molecular pathology procedure, Level 2 (e.g., 2-10 single nucleotide polymorphisms [SNPs], 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat).

There are no specific CPT codes for metabolite markers of azathioprine, mercaptopurine (6-MP) or thioguanine.

Several commerical laboratories offer pharmacogenomic and metabolite testing, including Prometheus, Quest and Specialty Laboratories.

An Independent Member of the Blue Shield Association

Internal Information

There is an MD Determination Form for this Medical Policy. It can be found on the following Web page:
http://myworkpath.com/healthcareservices/MedicalOperations/PSR_Determination_Pages.htm

Documentation Required for Clinical Review
• History and physical • Laboratory report(s)

The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available.

Click here to view the appendix for this policy

An Independent Member of the Blue Shield Association