

Measure XXXX: Inflammatory Bowel Disease: Thiopurine methyltransferase (TPMT) testing (enzymatic activity or genotype) in all patients that was performed and results interpreted prior to starting thiopurines - National Quality Strategy Domain: Patient Safety

DESCRIPTION:

Percentage of patients that had TPMT testing that was performed and results interpreted prior to starting thiopurines.

INSTRUCTIONS: This measure is to be reported **once per reporting period** for **all** patients with TPMT testing performed and results interpreted prior to starting thiopurines. TPMT testing may have occurred at any time prior to the reporting period. This measure is intended to reflect the quality of services provided for patients with Inflammatory Bowel Disease (IBD). This measure may be reported by physicians or other qualified healthcare professionals who perform the quality actions described in the measure based on the services provided and the measure-specific denominator coding. Reporting period is defined from January 1 to December 31 of the reporting year.

Measure Reporting via Registry:

ICD-10-CM diagnosis codes, CPT codes, and patient demographics are used to identify patients who are included in the measure's denominator. The listed numerator options are used to report the numerator of the measure.

The quality-data codes listed do not need to be submitted for registry-based submissions; however, these codes may be submitted for those registries that utilize claims data.

DENOMINATOR

All patients with a diagnosis of Inflammatory Bowel Disease that newly initiated thiopurines during the reporting period.

Denominator Criteria (Eligible Cases):

All patients with a diagnosis of Inflammatory Bowel Disease that newly initiated thiopurines during the reporting period.

AND

Diagnosis for Inflammatory Bowel Disease (ICD-10-CM): K50.00, K50.011, K50.012, K50.013, K50.014, K50.018, K50.019, K50.10, K50.111, K50.112, K50.113, K50.114, K50.118, K50.119, K50.80, K50.811, K50.812, K50.813, K50.814, K50.818, K50.819, K50.90, K50.911, K50.912, K50.913, K50.914, K50.918, K50.919, K51.00, K51.011, K51.012, K51.013, K51.014, K51.018, K51.019, K51.20, K51.211, K51.212, K51.213, K51.214, K51.218, K51.219, K51.30, K51.311, K51.312, K51.313, K51.314, K51.318, K51.319, K51.40, K51.411, K51.412, K51.413, K51.414, K51.418, K51.419, K51.50, K51.511, K51.512, K51.513, K51.514, K51.518, K51.519, K51.80, K51.811, K51.812, K51.813, K51.814, K51.818, K51.819, K51.90, K51.911, K51.912, K51.913, K51.914, K51.918, K51.919

AND

Patient encounter during the reporting period (CPT): 99201, 99202, 99203, 99204, 99205, 99212, 99213, 99214, 99215, 99341, 99342, 99343, 99344, 99345, 99347, 99348, 99349, 99406, 99407

NUMERATOR:

Patients with a diagnosis of Inflammatory Bowel Disease who had TPMT testing performed and documentation in the medical record that results were interpreted prior to starting thiopurines.

NUMERATOR INSTRUCTIONS:

This measure is to be reported **once per reporting period** for **all** patients who had TPMT testing performed

and documentation in the medical record that results were interpreted prior to starting thiopurines. This measure is intended to reflect the quality of services provided for patients with Inflammatory Bowel Disease. This measure may be reported by physicians or other qualified healthcare professionals who perform the quality actions described in the measure based on the services provided and the measure-specific numerator coding.

Numerator Options:

Performance Met: Patients with a diagnosis of Inflammatory Bowel Disease who had TPMT testing performed and documentation in the medical record that results were interpreted prior to starting thiopurines. (GXXXX)

OR

Medical Performance Exclusion: Documentation in the medical record that patient had previously tolerated thiopurines without leukopenia (GXXXX)

OR

Patient Performance Exclusion: Documentation of patient reasons patient did not receive TPMT testing prior to starting thiopurines. (e.g. patient refused TPMT testing, cost of tests, time related to accessing testing equipment or other patient reasons). (GXXXX)

OR

Performance Not Met: Patient did NOT receive TPMT testing prior to starting thiopurines for reasons not otherwise specified. (GXXXX)

Rationale:

There are three RCT studies comparing TPMT testing to no testing with empiric weight based thiopurine dosing. Genotype was utilized in 2 studies and enzymatic activity in one study. In these studies, patients with a normal enzyme/genotype started full dose thiopurine while those with intermediate enzymatic activity/heterozygous genotype had a 50% dose reduction. Those with low/absent enzyme activity or homozygous genotype were not given the drug or given a reduced dose at 0-10% of the initiation dose. In the 1145 patients included in the studies, only 0.17% (n=2) were homozygous. Hematologic adverse events and treatment discontinuation were used as surrogate outcomes for benefits of TPMT testing. There was no significant difference in either outcome based on TPMT testing, with the relative risk of hematologic events of 0.94 (95% CI, 0.59-1.50) and treatment discontinuation of 1.09 (95% CI, 0.94-1.27). Additionally, there was also no significant difference in clinical remission in these groups based on TPMT checking (RR 1.03; 95% CI, 0.84-1.27). However, if an individual is intermediate enzymatic activity/heterozygous genotype or homozygous genotype/low enzymatic activity, then TPMT testing to guide dosing was associated with an 89% risk reduction of hematologic adverse events. Hence, while the risk of harm from not testing a TPMT level prior to initiating therapy is minimal in most cases, there is considerable risk of harm in the 0.3% patients who are homozygous genotype or have low/absent TPMT enzymatic activity. While this risk may be mitigated by routine laboratory CBC checking, adherence to regular monitoring in clinical practice is suboptimal. It is therefore important to continue to perform routine lab monitoring with CBC and liver enzyme monitoring after starting a thiopurine regardless of the TPMT testing results. (Feuerstein J, Nguyen G, Kupfer S, Falck-Ytter Y, Singh S. American Gastroenterological Association Institute Guideline on Therapeutic Drug Monitoring in Inflammatory Bowel Disease. Gastroenterology 2017;153:827–834).

CLINICAL RECOMMENDATION STATEMENTS:

Prior to commencing treatment with thiopurines, all patients should have TPMT testing performed and results interpreted in accordance with American Gastroenterological Association Institute Guideline on Therapeutic Drug Monitoring in Inflammatory Bowel Disease (Gastroenterology 2017;153:827–834).

Approximately 89% of the population has normal wild type TPMT, 11% is heterozygous and 0.3% is homozygous for TPMT mutation with little to absent TPMT enzyme activity. Although frequent CBC monitoring can reduce the risk of leukopenia, it has been shown that compliance with regular laboratory monitoring in reality is not optimal (Lewis JD, Abramson O, Pascua M, et al. Timing of Myelosuppression During Thiopurine Therapy for Inflammatory Bowel Disease: Implications for Monitoring Recommendations. *Clinical Gastroenterology and Hepatology* 2009; 7:1195-1201). TPMT testing prior to initiation of thiopurines thus identifies IBD patients at risks for leukopenia and provides an opportunity to mitigate this risk.

TPMT activity can be assessed with either genotyping or direct enzyme activity measurement. Since there is no consensus on how best TPMT activity should be assessed, either genotype or enzyme activity can be accepted as TPMT testing.

While the majority of IBD population have normal TPMT activity, the risk is significant for those who do not have normal TPMT activity. As there is little risk in performing TPMT testing, overall it is beneficial to routinely perform TPMT testing prior to initiating thiopurines.