TPMT, NUDT15 and Medications

What are TPMT, NUDT15 and Thiopurine Medications?

When you take medications, your body needs a way to manage them. Our bodies have proteins called “enzymes” to metabolize (break down) or activate (turn on) medications. There are two enzymes called Thiopurine Methyltransferase (TPMT) and Nudix-Type Motif 15 (NUDT15). These enzymes break down a group of medications called thiopurines. Thiopurines include medications called mercaptopurine, thioguanine, and azathioprine.

Mercaptopurine and thioguanine are chemotherapy medications used to treat leukemia. Azathioprine is used to treat some autoimmune diseases or patients receiving transplant. Mercaptopurine and azathioprine are also used for inflammatory bowel disease conditions. How well these medications work can be very different from person to person.

Most people have no problem breaking down thiopurine medications. However, a small number of people have almost no ability to break down these medications. For these people, the medication can build up in the body and cause serious side effects, such as low blood counts.

What is Pharmacogenomic testing?

The study of genes and how your body interacts with medications is called pharmacogenomics. Each person has unique DNA, which means our bodies all work a little bit different. Genes are the instructions for how our body grow, develop, and function. Genes are made up of DNA.

The *TPMT* and *NUDT15* genes tell the TPMT and NUDT15 enzymes how to work in each person. Differences in your DNA that make up the *TPMT* or *NUDT15* gene can change how you break down thiopurine medications. There is a test that looks for differences in DNA. This can help your medical team know how well your TPMT and NUDT15 enzymes will work. Your doctor and pharmacist can then decide the best medication and right dose to give you.

What do my child’s test results mean?

The results of your *TPMT* and *NUDT15* pharmacogenomic test will place you into one of five groups:

Normal metabolizer – People in this group have normal TPMT or NUDT15 enzyme function (TPMT normal metabolizer or NUDT15 normal metabolizer). No medication changes might be needed.

Intermediate metabolizer or **possible intermediate metabolizer** **–** People in this group have slightly less TPMT or NUDT15 enzyme function (e.g., TPMT intermediate metabolizer or NUDT15 intermediate metabolizer). Lower doses of thiopurine medications might be needed to avoid side effects.

Poor metabolizer – People in this group have no or low TPMT or NUDT15 enzyme function. These people are at high risk for side effects such as low blood counts that could be life-threatening. Much lower doses of thiopurine medications might be needed to avoid side effects. In certain scenarios, a different medication might be better.

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Approved by PFE 10/11/23

Indeterminate – This result means we don't have a full understanding of the changes in your DNA and how that affects thiopurine medications.

After the first few weeks, the dose of thiopurine may change based on blood counts. Your clinical team will follow this closely to improve your treatment and lower side effects.

What do I do if I want more information?

Scientists continue to find new information about which medicines are affected by gene test results. Talk to your doctor or pharmacist if you have questions about your medication, side effects, or pharmacogenomic testing.
If you have questions about your pharmacogenomic testing done at Children's Hospital Los Angeles, you can e-mail the Clinical Pharmacogenomics team at pharmacogenomics@chla.usc.edu

KEY POINTS ABOUT TPMT AND NUDT15
• TPMT and NUDT15 are enzymes that help the body break down medications called thiopurines (mercaptopurine, thioguanine, azathioprine) • People who are TPMT or NUDT15 poor metabolizers are at risk for serious side effects if they take normal doses of thiopurines. • Pharmacogenomic testing can help identify people who are intermediate or poor metabolizers. This helps doctors and pharmacists know to order lower doses of medicine.