# PharmGKB Training Exercise – Pediatrics

## How to use this exercise

This exercise is intended to help new users familiarize themselves with the PharmGKB website and some of the different types of information available. **This exercise is not for use in a classroom setting for credit**, including professional development such as CME, as the answer sheet is freely available on the PharmGKB website.

We recommend that the trainer first provide an introduction to the PharmGKB website and its key features, including the genotype pickers available for the CPIC dosing guidelines. This exercise can then be used to reinforce areas covered in the introduction.

The 'What is PharmGKB?' page at www.pharmgkb.org/whatIsPharmgkb has helpful explanations of the different types of information that can be accessed on the PharmGKB website. This page will be useful for any trainers who are themselves unfamiliar with the PharmGKB website.

This exercise should take about 20-30 minutes to complete following an introduction to the website.

During the training session, each person will require access to an internet-connected computer where they can access the PharmGKB website.

This exercise is split into two parts; Part 1 and Part 2. Participants work through Part 1 to determine which genes they require genotype information for. Once they have completed Part 1, they should be given Part 2, which provides the genotype information. An answer sheet is provided at the end of this document.

PharmGKB is for research purposes only and does not provide medical advice or recommend when to order a pharmacogenetic test. All questions are written under the assumption that a patient's genetic information is already available.

If you have any questions or comments regarding this training exercise, please contact the PharmGKB team at feedback@pharmgkb.org

# PharmGKB Training Exercise – Pediatrics

## Part 1

A pediatric patient has been diagnosed with acute lymphoblastic leukemia and has had their genome sequenced through your department's clinical pharmacogenetic program.

You would normally prescribe mercaptopurine as a chemotherapy agent, however, the patient's sibling was treated for a similar cancer five years ago and had an adverse response to mercaptopurine treatment.

You decide to check the patient's sequencing data to see if they're carrying any variants which could affect their response to mercaptopurine.

1) Are there any Clinical Guideline Annotations or FDA Drug Label Annotations for mercaptopurine?

2) Which gene(s) should you check for variants?

# PharmGKB Training Exercise – Pediatrics

## Part 2

The patient has the *1/*3A diplotype at TPMT and the *1/*1 diplotype at NUDT15.

3) What is the patient's TPMT metabolizer status?

4) What is the patient's NUDT15 metabolizer status?

5) Based on this information, would you prescribe mercaptopurine to the patient? If so, would you make any changes to the normal dosage?

The patient begins mercaptopurine treatment. After three weeks, they develop seizures as a side effect of treatment.

You want to prescribe oxcarbazepine or diazepam and recheck the sequencing data to see if the patient has any variants which might affect treatment.

6) Look for clinical guideline annotations for oxcarbazepine and diazepam. Which gene(s) should you check for variants?

The sequencing results show that the patient has the diplotype *15:02:01/*40:02:01 in this gene.

7) Which antiepileptic drug should you prescribe to this patient? Why?

# PharmGKB Training Exercise – Pediatrics Answers

A pediatric patient has been diagnosed with acute lymphoblastic leukemia and has had their genome sequenced through your department's clinical pharmacogenetic program.

You would normally prescribe mercaptopurine as a chemotherapy agent, however, the patient's sibling was treated for a similar cancer five years ago and had an adverse response to mercaptopurine treatment.

You decide to check the patient's sequencing data to see if they're carrying any variants which could affect their response to mercaptopurine.

1) Are there any Clinical Guideline Annotations or FDA Drug Label Annotations for mercaptopurine?
Yes, a CPIC guideline for TPMT and NUDT15, DPWG guidelines for TPMT and NUDT15 and an FDA drug label.

2) Which gene(s) should you check for variants? TPMT and NUDT15

The patient has the *1/*3A diplotype at TPMT and the *1/*1 diplotype at NUDT15.

3) What is the patient's TPMT metabolizer status? Intermediate metabolizer

4) What is the patient's NUDT15 metabolizer status? Normal metabolizer

5) Based on this information, would you prescribe mercaptopurine to the patient? If so, would you make any changes to the normal dosage?
Mercaptopurine can still be prescribed but start with reduced doses and slowly titrate dose upwards.

The patient begins mercaptopurine treatment. After three weeks, they develop seizures as a side effect of treatment.

You want to prescribe oxcarbazepine or diazepam and recheck the sequencing data to see if the patient has any variants which might affect treatment.

6) Look for clinical guideline annotations for oxcarbazepine and diazepam. Which gene(s) should you check for variants? HLA-B

The sequencing results show that the patient has the diplotype *15:02:01/*40:02:01 in this gene.

7) Which antiepileptic drug should you prescribe to this patient? Why?
Diazepam should be prescribed. Carrying one or two copies of HLA-B*15:02 increases the risk of the patient experiencing cutaneous adverse reactions such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) when taking oxcarbazepine.