



# PharmGKB Training Exercise – General Medicine

## 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](http://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](mailto:feedback@pharmgkb.org)

## Part 1

An adult patient who has recently had back surgery and was prescribed codeine to control the pain has presented with symptoms of a fungal infection in the surgical wound. They also say that they are not getting adequate pain relief with tramadol.

You want to prescribe the antifungal drug voriconazole as well as switching to tramadol to manage the patient's pain.

The patient has had genotyping carried out by a direct-to-consumer genetics testing company and is concerned that they may carry a variant which is causing their lack of pain relief when using codeine and that there might be other variants which could affect their response to tramadol or voriconazole.

1) Are there any Clinical Guideline annotations, FDA Drug Label annotations or Level 1 Clinical Annotations for codeine?

2) Are there any Clinical Guideline annotations, FDA Drug Label annotations or Level 1 Clinical Annotations for tramadol?

3) Are there any Clinical Guideline annotations, FDA Drug Label annotations or Level 1 Clinical Annotations for voriconazole?

4) Which genes do you need to check for variants which might affect the patient's response to codeine, tramadol or voriconazole?

## Part 2

These are the patient's genotypes at the relevant genes:

Gene	Genotype/Diplotype
CYP2C19	*2/*2
CYP2D6	*4/*6

- 5) What is the patient's CYP2C19 metabolizer status?
- 6) What is the patient's CYP2D6 metabolizer status?
- 7) Do the patient's genotypes explain their poor response to codeine?
- 8) Would you prescribe tramadol to this patient? Why? Would you make any changes to the standard dosage?

Further testing of the fungus infecting the wound strongly suggests that voriconazole is the best treatment for this patient.

- 9) Would you prescribe voriconazole to this patient? Why? Would you make any changes to the standard dosage?

An adult patient who has recently had back surgery and was prescribed codeine to control the pain has presented with symptoms of a fungal infection in the surgical wound. They also say that they are not getting adequate pain relief with tramadol.

You want to prescribe the antifungal drug voriconazole as well as switching to tramadol to manage the patient's pain.

The patient has had genotyping carried out by a direct-to-consumer genetics testing company and is concerned that they may carry a variant which is causing their lack of pain relief when using codeine and that there might be other variants which could affect their response to tramadol or voriconazole.

1) Are there any Clinical Guideline annotations, FDA Drug Label annotations or Level 1 Clinical Annotations for codeine?

Yes, three Level 1A clinical annotations, an FDA label with Actionable PGx and three clinical guidelines for codeine and CYP2D6. A 'no recommendation' from CPIC for codeine and COMT and OPRM1.

2) Are there any Clinical Guideline annotations, FDA Drug Label annotations or Level 1 Clinical Annotations for tramadol?

Yes, three Level 1A clinical annotations, an FDA label with Actionable PGx and three clinical guidelines for tramadol and CYP2D6. A 'no recommendation' from CPIC for tramadol and COMT and OPRM1.

3) Are there any Clinical Guideline annotations, FDA Drug Label annotations or Level 1 Clinical Annotations for voriconazole?

Yes, a Level 1A clinical annotation, an FDA label with Actionable PGx, a CPIC guideline and a DWPG guideline for voriconazole and CYP2C19.

4) Which genes do you need to check for variants which might affect the patient's response to tramadol, codeine or voriconazole?

CYP2D6 (tramadol, codeine) and CYP2C19 (voriconazole)

These are the patient's genotypes at the relevant genes:

Gene	Genotype/Diplotype
CYP2C19	*2/*2
CYP2D6	*4/*6

5) What is the patient's CYP2C19 metabolizer status? **Poor metabolizer**

6) What is the patient's CYP2D6 metabolizer status? **Poor metabolizer**

7) Do the patient's genotypes explain their poor response to codeine?

Yes, CYP2D6 poor metabolizers are thought to be at risk of diminished analgesia.

8) Would you prescribe tramadol to this patient? Why? Would you make any changes to the standard dosage?

No, an alternative analgesic which is not metabolized by CYP2D6 should be prescribed, e.g. NSAID or other non-opioid analgesic.

Further testing of the fungus infecting the wound strongly suggests that voriconazole is the best treatment for this patient.

9) Would you prescribe voriconazole to this patient? Why? Would you make any changes to the standard dosage?

Yes, you can prescribe voriconazole to this patient. Although they are a CYP2C19 poor metabolizer, the CPIC recommendation states that voriconazole can be administered, but at a low dosage and with careful therapeutic drug monitoring. The DPWG recommends a 50% dose reduction in these patients.