PharmGKB Training Exercise – Cardiology

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

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Part 1

A patient has a suspected thromboembolism, which you want to treat with warfarin. They also have epilepsy, which is well-controlled by phenytoin.

The patient's medical records state that their starting dose of phenytoin was reduced because they have previously had their genome sequenced and were found to have the CYP2C9 diplotype *2/*3.

1) Is CYP2C9 also associated with response to warfarin?

2) What is the patient's CYP2C9 metabolizer status?

3) Using the flow chart in Figure 2 of the CPIC guideline, which other genes should you check for variants?

4) Look at the annotated FDA label for warfarin on the PharmGKB website. Are there any other genes which could affect your decision to prescribe warfarin to this patient? Why?

5) What other information do you require to use the flow chart and dose calculator?

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Part 2

A different patient with CYP2C9*2/*3 is a 57-year-old Caucasian. They are 173cm tall and weigh 90kg. They tell you that they are not taking amiodarone or any CYP2C9 inducers.

These are the patient's genotypes at the relevant genes. They do not have protein C deficiency or protein S deficiency.

Gene	Genotype/Diplotype
CYP4F2	CC
VKORC1	GG

6) Do you prescribe warfarin to this patient?

7) Using the flow chart and, if applicable, the IWPC warfarin dose calculator (which can be downloaded from the annotated CPIC guideline for warfarin on PharmGKB), calculate the patient's weekly starting dose.

8) The day after beginning warfarin treatment, you notice that the patient's notes have been updated overnight to show that they were recently prescribed amiodarone by another doctor. How does this new information affect the starting dose?

PharmGKB Training Exercise – Cardiology Answers

A patient has a suspected thromboembolism, which you want to treat with warfarin. They also have epilepsy, which is well-controlled by phenytoin.

The patient's medical records state that their starting dose of phenytoin was reduced because they have previously had their genome sequenced and were found to have the CYP2C9 diplotype *2/*3.

1) Is CYP2C9 also associated with response to warfarin? Yes

2) What is the patient's CYP2C9 metabolizer status? Poor metabolizer

3) Using the flow chart in Figure 2 of the CPIC guideline, which other genes should you check for variants? VKORC1, CYP4F2

4) Look at the annotated FDA label for warfarin on the PharmGKB website. Are there any other genes which could affect your decision to prescribe warfarin to this patient? Why? PROC (encodes protein C) and PROS1 (encodes protein S). Deficiency in protein C or protein S has been associated with tissue necrosis following administration of warfarin.

5) What other information do you require to use the flow chart and dose calculator? Age, height, weight, race, taking amiodarone or other CYP2C9 inducers.

A different patient with CYP2C9*2/*3 is a 57-year-old Caucasian. They are 173cm tall and weigh 90kg. They tell you that they are not taking amiodarone or any CYP2C9 inducers.

These are the patient's genotypes at CYP4F2 and VKORC1. They do not have protein C deficiency or protein S deficiency.

Gene	Genotype/Diplotype
CYP4F2	CC
VKORC1	GG

6) Do you prescribe warfarin to this patient? Yes.

7) Using the flow chart and, if applicable, the IWPC warfarin dose calculator (which can be downloaded from the annotated CPIC guideline for warfarin on PharmGKB), calculate the patient's weekly starting dose. 25mg/week

8) The day after beginning warfarin treatment, you notice that the patient's notes have been updated overnight to show that they were recently prescribed amiodarone by another doctor. How does this new information affect the starting dose?
Reduce from 25mg/week to 20mg/week