| Gene    | Genotype                  | Phenotype    | Cautionary Medications*  |
|---------|---------------------------|--------------|--|
| CYP2C9  | *1/*1                     | normal       | Warfarin   |
| SLCO1B1 | *1/*1                     | normal       |  |
| CYP2C19 | *1/*17                    | rapid        | Amitriptyline, Citalopram, Clomipramine, Doxepin,<br>Escitalopram, Imipramine, Trimipramine,<br>Voriconazole   |
| CYP2B6  | *1/*6                     | intermediate | . Efavirenz  |
| CYP3A5  | *3/*3                     | роог         |  |
| CYP3A4  | *1/*22                    | intermediate | I  |
| CYP2D6  | *4/*10                    | intermediate | Amitriptyline, Amoxapine, Atomoxetine, Clomipramine, Codeine, Desipramine, Doxepin, Eliglustat, Flecainide, Imipramine, Meclizine, Metoprolol, Nortriptyline, Paroxetine, Pimozide, Propafenone, Tamoxifen, Tramadol, Trimipramine, Zuclopenthixol |
| F2      | wt/wt                     | negative     |  |
| F5      | wt/wt                     | negative     | İ  |
| VKORC1  | *1/*2                     | intermediate | Warfarin   |
| NUDT15  | *1/*1                     | normal       | Azathioprine, Mercaptopurine, Thioguanine  |
| G6PD    | b(reference)/b(reference) | normal       |  |
| ABCG2   | 9/9                       | normal       |  |
| CYP4F2  | *1/*1                     | normal       | . Warfarin   |
| CYP2C   | a/a                       | normal       | !  |

#### What is this card?

This card contains information that can help inform your healthcare providers about how your body processes or reacts to specific medications. Please keep this with you at all times.

DO NOT stop or change how you take your medications without speaking with a healthcare professional.

# For use by healthcare professionals only

The Clinical Pharmacology physician can be reached by calling the Foothills Medical Centre switchboard at 403-944-1110 and asking to speak with the Clinical Pharmacology physician on call. THIS PHONE NUMBER IS FOR USE BY HEALTHCARE PROVIDERS ONLY.

For more information, visit sequence2script.com

# Personal Pharmacogenetics Information card

For more information, visit: sequence2script.com

Patient Name: John Doe Date of Issue: 05/08/2025

#### Wallet Card Instructions

To the Provider: To assist in sharing these test results with your patient, please give this page of the report to you patient. This page includes a wallet card, which the patient can share with their other healthcare providers (e.g., pharmacists).

To the Patient: Your doctor recently ordered a pharmacogenetic test for you. Pharmacogenetic testing is a special type of genetic test that can help your doctor and pharmacist:

- (1) Select medications that are the best match for you.(2) Identify the dose of
- (2) Identify the dose of medication right for you.
- (3) Estimate your risk for potentially serious side effects.

Pharmacogenetic testing has limitations worth noting:
(a) Testing only looks at common gene differences.
Rare gene differences that may account for the way you react to medications are not tested:

- (b) Many factors may influence the way you react to medications. Things like your age, weight, other medications and other medical conditions. Your doctor will need to consider these factors along with your test results to advise on the best course of action;
- (c) Your results cannot be used to guide medication selection or dosing of your family members.

Your test results are listed in the wallet card on this page. You may want to cut the card out and share it with your doctors and pharmacists.

#### Patient Genetic Results

| Gene    | Genotype                  | Activity Score | Phenotype    | Phenotype<br>adjusted for<br>concomitant<br>medications* | Additional<br>Comments |
|---------|---------------------------|----------------|--------------|--|------------------------|
| CYP2C9  | *1/*1                     | 2.00           | normal       | normal   | None                   |
| SLCO1B1 | *1/*1                     |                | normal       | normal   | None                   |
| CYP2C19 | *1/*17                    |                | rapid        | гаріd  | None                   |
| CYP2B6  | *1/*6                     |                | intermediate | intermediate   | None                   |
| CYP3A5  | *3/*3                     |                | роог         | роог   | None                   |
| CYP3A4  | *1/*22                    |                | intermediate | intermediate   | None                   |
| CYP2D6  | *4/*10                    | 0.25           | intermediate | intermediate   | None                   |
| F2      | wt/wt                     |                | negative     | negative   | None                   |
| F5      | wt/wt                     |                | negative     | negative   | None                   |
| VKORC1  | *1/*2                     |                | intermediate | intermediate   | None                   |
| NUDT15  | *1/*1                     |                | normal       | normal   | None                   |
| G6PD    | b(reference)/b(reference) |                | normal       | normal   | None                   |
| ABCG2   | g/g                       |                | normal       | normal   | None                   |
| CYP4F2  | *1/*1                     |                | normal       | normal   | None                   |
| CYP2C   | g/g                       |                | normal       | normal   | None                   |

<sup>\*</sup>Phenotype adjusted for concomitant medications is based on the presence of inhibitors and inducers. See the "Regarding Phenotype Adjustment" section at the end of the report for full details.



## Pharmacogenomics Report

Name: Doe, John

DOB: 01/01/1950

Gender: M

Report ID: PGX000001

Sample Type: Buccal Swab

Report Date: 05/08/2025

Received: 05/05/2025

## **Medications Summary**

| Therapeutic Area | Standard Precautions Typical risk for indicated use. Follow standard dosing guidelines   | Action May Be Required Adjustment to standard dose or alternative medicine may be required  |
|------------------|--|---|
| Psychiatry       | Amphetamine Aripiprazole Brexpiprazole Clobazam Clonidine Clozapine Dextromethorphan-Bupropion Diazepam Duloxetine Fluoxetine Fluoxetine Fluoxamine Haloperidol Iloperidone Lofexidine Methylphenidate Mirtazapine Moclobemide | Amitriptyline Amoxapine Atomoxetine Citalopram Clomipramine Desipramine Doxepin Escitalopram Imipramine Nortriptyline Paroxetine Pimozide Trimipramine Zuclopenthixol |

| Therapeutic Area | Standard Precautions Typical risk for indicated use. Follow standard dosing guidelines  | Action May Be Required Adjustment to standard dose or alternative medicine may be required |
|------------------|---|--|
|                  | Olanzapine Perphenazine Quetiapine Risperidone Sertraline Thioridazine Venlafaxine Viloxazine Vortioxetine  |  |
| Cardiology       | Acenocoumarol Amiodarone Atenolol Atorvastatin Bisoprolol Carvedilol Clopidogrel Fluvastatin Lovastatin Mavacamten Nebivolol Pitavastatin Prasugrel Pravastatin Propranolol Rosuvastatin Simvastatin Ticagrelor | Flecainide<br>Metoprolol<br>Propafenone<br>Warfarin  |
| Dermatology      | Abrocitinib   |  |
| Endocrinology    | Chlorpropamide<br>Glibenclamide<br>Glimepiride<br>Glipizide<br>Nateglinide<br>Tolazamide<br>Tolbutamide   | Eliglustat   |
| Gastroenterology | Dexlansoprazole Dronabinol Esomeprazole Lansoprazole Metoclopramide Omeprazole Ondansetron Pantoprazole Rabeprazole   |  |

| Therapeutic Area   | Standard Precautions Typical risk for indicated use. Follow standard dosing guidelines   | Action May Be Required Adjustment to standard dose or alternative medicine may be required |
|--------------------|--|--|
|                    | Tropisetron  | dicernative incurring may be required  |
| Hematology         | Avatrombopag<br>Eltrombopag<br>Lusutrombopag<br>Methylene Blue   |  |
| Immunology         | Cevimeline<br>Tacrolimus   |  |
| Infectious Disease | Ceftriaxone Dapsone Hydroxychloroquine Nalidixic Acid Nitrofurantoin Primaquine Tafenoquine  | Efavirenz<br>Voriconazole  |
| Neurology          | Brivaracetam Deutetrabenazine Donepezil Galantamine Pitolisant Tetrabenazine Valbenazine   |  |
| Oncology           | Erdafitinib<br>Gefitinib<br>Rasburicase  | Tamoxifen  |
| Other              | Siponimod<br>Toluidine Blue  | Meclizine  |
| Pain               | Aspirin Carisoprodol Celecoxib Elagolix Flurbiprofen Hydrocodone Ibuprofen Lornoxicam Meloxicam Naproxen Oliceridine Oxycodone Piroxicam Tenoxicam | Codeine<br>Tramadol  |
| Rheumatology       | Pegloticase  |  |
| Urology            | Darifenacin<br>Fesoterodine<br>Mirabegron  |  |

| Therapeutic Area | Standard Precautions Typical risk for indicated use. Follow standard dosing guidelines | Action May Be Required Adjustment to standard dose or alternative medicine may be required |
|------------------|--|--|
|                  | Tamsulosin<br>Tolterodine  |  |

#### **Current Medications**

Medication NameDescriptionGenesRecommendationStrength of RecommendationSourcePathwayNo current medications

\*Note: Inhibitor and inducer information was based on the Drug Interactions Flockhart Table

## **Medications Being Considered**

| Medication<br>Name   | Therapeutic<br>Area | Genes | Recommendation | Strength of<br>Recommendation | Source | Pathway |  |
|--|---------------------|-------|----------------|-------------------------------|--------|---------|--|
| No consist of displacements of the constant of |                     |       |                |                               |        |         |  |

No current medications

The strength of a recommendation is based exclusively on pharmacogenetic information published in guidelines. They do not reflect the strength of a recommendation based on phenotypes that have been adjusted due to the presence of concomitant inhibitors or inducers.

#### **Medication Recommendations**

| Therapeutic<br>Area | Medication Name | Genes             | Recommendation   | Strength of Recommendation | Source      | Pathway        |
|---------------------|-----------------|-------------------|--|----------------------------|-------------|----------------|
| Psychiatry          | Amitriptyline   | CYP2C19<br>CYP2D6 | Consider alternative drug not metabolized by CYP2C19.  | OPTIONAL                   | <u>CPIC</u> | pathway        |
| Psychiatry          | Amoxapine       | CYP2D6            | May alter systemic concentrations.   | OPTIONAL                   | <u>FDA</u>  | <u>pathway</u> |
| Psychiatry          | Amphetamine     | CYP2D6            | No action required. Initiate therapy with recommended starting dose.                                   | N/A                        | FDA         | pathway        |
| Psychiatry          | Aripiprazole    | CYP2D6            | No action required. Initiate therapy with recommended starting dose.                                   | N/A                        | <u>DPWG</u> | pathway        |
| Psychiatry          | Atomoxetine     | CYP2D6            | CHILD: Initiate with a dose of 0.5 mg/kg/day and if no clinical response and in the absence of adverse | MODERATE                   | CPIC        | pathway        |

| Therapeutic<br>Area | Medication Name | Genes             | Recommendation  | Strength of Recommendation | Source      | Pathway        |
|---------------------|-----------------|-------------------|---|----------------------------|-------------|----------------|
|                     |                 |                   | events after 2 weeks, consider a proportional dose increase. If unacceptable side effects are present at any time, consider a reduction in dose. ADULT: Initiate with a dose of 40 mg/day and if no clinical response and in the absence of adverse events after 2 weeks increase dose to 80 mg/day. If response is inadequate after 2 weeks consider a proportional dose increase. If unacceptable side effects are present at any time, consider a reduction in dose. |                            |             |                |
| Psychiatry          | Brexpiprazole   | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>DPWG</u> | <u>pathway</u> |
| Psychiatry          | Citalopram      | CYP2C19           | Initiate therapy with recommended starting dose. If patient does not adequately respond to recommended maintenance dosing, consider titrating to a higher maintenance dose or switching to a clinically appropriate alternative antidepressant not predominantly metabolized by CYP2C19.  | OPTIONAL                   | <u>CPIC</u> | pathway        |
| Psychiatry          | Clobazam        | CYP2C19           | No action required. Initiate therapy with recommended starting dose.  | N/A                        | FDA         | pathway        |
| Psychiatry          | Clomipramine    | CYP2C19<br>CYP2D6 | Consider alternative drug not metabolized by CYP2C19.   | OPTIONAL                   | CPIC        | <u>pathway</u> |
| Psychiatry          | Clonidine       | CYP2D6            | No action required. Initiate  | N/A                        | DPWG        | pathway        |

| Therapeutic<br>Area | Medication Name                | Genes             | Recommendation   | Strength of<br>Recommendation | Source      | Pathway        |
|---------------------|--------------------------------|-------------------|--|-------------------------------|-------------|----------------|
|                     |                                |                   | therapy with recommended starting dose.  |                               |             |                |
| Psychiatry          | Clozapine                      | CYP2D6            | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>DPWG</u> | <u>pathway</u> |
| Psychiatry          | Desipramine                    | CYP2D6            | Consider a 25% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.  | OPTIONAL                      | <u>CPIC</u> | <u>pathway</u> |
| Psychiatry          | Dextromethorphan-<br>Bupropion | CYP2D6            | Use according to the product label   | N/A                           | <u>FDA</u>  | pathway        |
| Psychiatry          | Diazepam                       | CYP2C19           | No action required. Initiate therapy with recommended starting dose.   | N/A                           | FDA         | <u>pathway</u> |
| Psychiatry          | Doxepin                        | CYP2C19<br>CYP2D6 | Consider alternative drug not metabolized by CYP2C19.  | OPTIONAL                      | <u>CPIC</u> | pathway        |
| Psychiatry          | Duloxetine                     | CYP2D6            | No recommendation due to minimal evidence regarding tolerability or efficacy.  | N/A                           | <u>CPIC</u> | <u>pathway</u> |
| Psychiatry          | Escitalopram                   | CYP2C19           | Initiate therapy with recommended starting dose. If patient does not adequately respond to recommended maintenance dosing, consider titrating to a higher maintenance dose or switching to a clinically appropriate alternative antidepressant not predominantly metabolized by CYP2C19. | OPTIONAL                      | CPIC        | pathway        |
| Psychiatry          | Fluoxetine                     | CYP2D6            | No action recommended based on genotype for fluoxetine because of minimal evidence regarding the impact on efficacy or side effects.   | N/A                           | <u>CPIC</u> | pathway        |
| Psychiatry          | Fluphenazine                   | CYP2D6            | No action required. Initiate   | N/A                           | <u>DPWG</u> | <u>pathway</u> |

| Therapeutic<br>Area | Medication Name | Genes             | Recommendation  | Strength of<br>Recommendation | Source      | Pathway        |
|---------------------|-----------------|-------------------|---|-------------------------------|-------------|----------------|
|                     |                 |                   | therapy with recommended starting dose.   |                               |             |                |
| Psychiatry          | Fluvoxamine     | CYP2D6            | Initiate therapy with recommended starting dose.  | MODERATE                      | <u>CPIC</u> | <u>pathway</u> |
| Psychiatry          | Haloperidol     | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                           | <u>DPWG</u> | pathway        |
| Psychiatry          | Iloperidone     | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                           | <u>FDA</u>  | pathway        |
| Psychiatry          | Imipramine      | CYP2C19<br>CYP2D6 | Consider alternative drug not metabolized by CYP2C19.   | OPTIONAL                      | <u>CPIC</u> | <u>pathway</u> |
| Psychiatry          | Lofexidine      | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                           | FDA         | <u>pathway</u> |
| Psychiatry          | Methylphenidate | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                           | <u>DPWG</u> | <u>pathway</u> |
| Psychiatry          | Mirtazapine     | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                           | <u>DPWG</u> | pathway        |
| Psychiatry          | Moclobemide     | CYP2C19           | No recommendation due to minimal evidence regarding tolerability or efficacy.   | N/A                           | <u>DPWG</u> | pathway        |
| Psychiatry          | Nortriptyline   | CYP2D6            | Consider a 25% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. | MODERATE                      | <u>CPIC</u> | pathway        |
| Psychiatry          | Olanzapine      | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                           | <u>DPWG</u> | <u>pathway</u> |
| Psychiatry          | Paroxetine      | CYP2D6            | Consider a lower starting dose and slower titration   | OPTIONAL                      | <u>CPIC</u> | pathway        |

| Therapeutic<br>Area | Medication Name | Genes             | Recommendation  | Strength of Recommendation | Source      | Pathway        |
|---------------------|-----------------|-------------------|---|----------------------------|-------------|----------------|
|                     |                 |                   | schedule as compared to normal metabolizers.  |                            |             |                |
| Psychiatry          | Perphenazine    | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>FDA</u>  | pathway        |
| Psychiatry          | Pimozide        | CYP2D6            | Use no more than 80% of<br>the standard maximum<br>dose. For adults, 16 mg/<br>day. For children, 0.08 mg/<br>kg per day to a maximum<br>of 3 mg/day. | OPTIONAL                   | <u>DPWG</u> | pathway        |
| Psychiatry          | Quetiapine      | CYP3A4            | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>DPWG</u> | <u>pathway</u> |
| Psychiatry          | Risperidone     | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>DPWG</u> | pathway        |
| Psychiatry          | Sertraline      | CYP2C19<br>CYP2B6 | Initiate therapy with recommended starting dose.  | MODERATE                   | <u>CPIC</u> | <u>pathway</u> |
| Psychiatry          | Thioridazine    | CYP2D6            | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>FDA</u>  | pathway        |
| Psychiatry          | Trimipramine    | CYP2C19<br>CYP2D6 | Consider alternative drug not metabolized by CYP2C19 (e.g., nortriptyline).   | OPTIONAL                   | <u>CPIC</u> | pathway        |
| Psychiatry          | Venlafaxine     | CYP2D6            | No action recommended based on genotype for venlafaxine because of minimal evidence regarding the impact on efficacy or side effects.                 | N/A                        | <u>CPIC</u> | pathway        |
| Psychiatry          | Viloxazine      | CYP2D6            | Use according to the product label  | N/A                        | FDA         | pathway        |
| Psychiatry          | Vortioxetine    | CYP2D6            | Initiate therapy with recommended starting dose.  | MODERATE                   | <u>CPIC</u> | <u>pathway</u> |
| Psychiatry          | Zuclopenthixol  | CYP2D6            | Reduce dose by 25% or select alternative drug not   | OPTIONAL                   | <u>DPWG</u> | pathway        |

| Therapeutic<br>Area | Medication Name | Genes             | Recommendation   | Strength of Recommendation | Source      | Pathway        |
|---------------------|-----------------|-------------------|--|----------------------------|-------------|----------------|
|                     |                 |                   | metabolized by CYP2D6.   |                            |             |                |
| Cardiology          | Acenocoumarol   | VKORC1            | No action required. Initiate therapy with recommended starting dose.   | N/A                        | <u>DPWG</u> | pathway        |
| Cardiology          | Amiodarone      | CYP2D6            | No action required. Initiate therapy with recommended starting dose.   | N/A                        | <u>DPWG</u> | pathway        |
| Cardiology          | Atenolol        | CYP2D6            | No action required. Initiate therapy with recommended starting dose.   | N/A                        | <u>DPWG</u> | pathway        |
| Cardiology          | Atorvastatin    | SLCO1B1           | Prescribe desired starting dose and adjust doses based on disease-specific guidelines.                               | STRONG                     | <u>CPIC</u> | pathway        |
| Cardiology          | Bisoprolol      | CYP2D6            | No action required. Initiate therapy with recommended starting dose.   | N/A                        | <u>DPWG</u> | <u>pathway</u> |
| Cardiology          | Carvedilol      | CYP2D6            | No action required. Initiate therapy with recommended starting dose.   | N/A                        | <u>DPWG</u> | pathway        |
| Cardiology          | Clopidogrel     | CYP2C19           | If considering clopidogrel,<br>use at standard dose (75<br>mg/day)   | STRONG                     | <u>CPIC</u> | pathway        |
| Cardiology          | Flecainide      | CYP2D6            | Indications other than diagnosis of Brugada syndrome: reduce the dose to 75% of the standard dose and record an ECG. | OPTIONAL                   | DPWG        | pathway        |
| Cardiology          | Fluvastatin     | SLCO1B1<br>CYP2C9 | Prescribe desired starting dose and adjust doses based on disease-specific guidelines.                               | STRONG                     | <u>CPIC</u> | <u>pathway</u> |
| Cardiology          | Lovastatin      | SLCO1B1           | Prescribe desired starting dose and adjust doses based on disease-specific guidelines.                               | STRONG                     | <u>CPIC</u> | pathway        |
| Cardiology          | Mavacamten      | CYP2C19           | The recommended starting dose is 5 mg orally   | STRONG                     | <u>FDA</u>  | pathway        |

| Therapeutic<br>Area | Medication Name | Genes            | Recommendation   | Strength of<br>Recommendation | Source      | Pathway        |
|---------------------|-----------------|------------------|--|-------------------------------|-------------|----------------|
|                     |                 |                  | once daily. The maximum dose is 15 mg once daily.  |                               |             |                |
| Cardiology          | Metoprolol      | CYP2D6           | If a gradual reduction in heart rate is desired, or in the event of symptomatic bradycardia, increase the dose in smaller steps and/ or prescribe no more than 50% of the standard dose. | OPTIONAL                      | DPWG        | pathway        |
| Cardiology          | Nebivolol       | CYP2D6           | No action required. Initiate therapy with recommended starting dose.   | N/A                           | FDA         | pathway        |
| Cardiology          | Pitavastatin    | SLCO1B1          | Prescribe desired starting dose and adjust doses based on disease-specific guidelines.   | STRONG                        | <u>CPIC</u> | <u>pathway</u> |
| Cardiology          | Prasugrel       | CYP2C19          | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>DPWG</u> | <u>pathway</u> |
| Cardiology          | Pravastatin     | SLCO1B1          | Prescribe desired starting dose and adjust doses based on disease-specific guidelines.   | STRONG                        | <u>CPIC</u> | pathway        |
| Cardiology          | Propafenone     | CYP2D6           | Perform an ECG and be alert to reduced efficacy of the therapy or choose an alternative (e.g., sotalol, disopyramide, quinidine and amiodarone).   | OPTIONAL                      | DPWG        | pathway        |
| Cardiology          | Propranolol     | CYP2D6           | No action required. Initiate therapy with recommended starting dose.   | N/A                           | FDA         | pathway        |
| Cardiology          | Rosuvastatin    | SLCO1B1<br>ABCG2 | Prescribe desired starting dose and adjust doses of rosuvastatin based on disease-specific and specific population guidelines.   | STRONG                        | <u>CPIC</u> | pathway        |
| Cardiology          | Simvastatin     | SLCO1B1          | Prescribe desired starting dose and adjust doses based on disease-specific   | STRONG                        | <u>CPIC</u> | <u>pathway</u> |

| Therapeutic<br>Area | Medication Name | Genes                      | Recommendation   | Strength of Recommendation | Source      | Pathway        |
|---------------------|-----------------|----------------------------|--|----------------------------|-------------|----------------|
|                     |                 |                            | guidelines.  |                            |             |                |
| Cardiology          | Ticagrelor      | CYP2C19                    | No action required. Initiate therapy with recommended starting dose.   | N/A                        | <u>DPWG</u> | pathway        |
| Cardiology          | Warfarin        | CYP2C9<br>VKORC1<br>CYP4F2 | Calculate warfarin dose using a validated pharmacogenetic algorithm (e.g., http://warfarindosing.org).   | STRONG                     | <u>N/A</u>  | N/A            |
| Dermatology         | Abrocitinib     | CYP2C19                    | No action required. Initiate therapy with recommended starting dose.   | N/A                        | <u>FDA</u>  | pathway        |
| Endocrinology       | Chlorpropamide  | G6PD                       | Use according to the product label   | N/A                        | <u>FDA</u>  | <u>pathway</u> |
| Endocrinology       | Eliglustat      | CYP2D6                     | Coadministration with strong CYP3A inhibitors is contraindicated. FDA recommends 84mg orally twice daily.  | STRONG                     | <u>DPWG</u> | pathway        |
| Endocrinology       | Glibenclamide   | G6PD                       | Use according to the product label   | STRONG                     | <u>FDA</u>  | <u>pathway</u> |
| Endocrinology       | Glimepiride     | G6PD                       | Use according to the product label   | N/A                        | <u>FDA</u>  | <u>pathway</u> |
| Endocrinology       | Glipizide       | G6PD                       | Use according to the product label   | N/A                        | <u>FDA</u>  | pathway        |
| Endocrinology       | Nateglinide     | CYP2C9                     | No action required. Initiate therapy with recommended starting dose.   | N/A                        | <u>FDA</u>  | pathway        |
| Endocrinology       | Tolazamide      | G6PD                       | Use according to the product label   | N/A                        | <u>FDA</u>  | <u>pathway</u> |
| Endocrinology       | Tolbutamide     | G6PD                       | Use according to the product label   | N/A                        | <u>FDA</u>  | <u>pathway</u> |
| Gastroenterology    | Dexlansoprazole | CYP2C19                    | Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for | OPTIONAL                   | <u>CPIC</u> | pathway        |

| Therapeutic<br>Area | Medication Name | Genes   | Recommendation   | Strength of<br>Recommendation | Source      | Pathway        |
|---------------------|-----------------|---------|--|-------------------------------|-------------|----------------|
|                     |                 |         | efficacy   |                               |             |                |
| Gastroenterology    | Dronabinol      | CYP2C9  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | <u>pathway</u> |
| Gastroenterology    | Esomeprazole    | CYP2C19 | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>CPIC</u> | <u>pathway</u> |
| Gastroenterology    | Lansoprazole    | CYP2C19 | Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy. | MODERATE                      | <u>CPIC</u> | pathway        |
| Gastroenterology    | Metoclopramide  | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | <u>pathway</u> |
| Gastroenterology    | Omeprazole      | CYP2C19 | Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy. | MODERATE                      | CPIC        | <u>pathway</u> |
| Gastroenterology    | Ondansetron     | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>CPIC</u> | pathway        |
| Gastroenterology    | Pantoprazole    | CYP2C19 | Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in                                      | MODERATE                      | <u>CPIC</u> | <u>pathway</u> |

| Therapeutic<br>Area   | Medication Name    | Genes    | Recommendation  | Strength of Recommendation | Source      | Pathway        |
|-----------------------|--------------------|----------|---|----------------------------|-------------|----------------|
|                       |                    |          | divided doses. Monitor for efficacy.  |                            |             |                |
| Gastroenterology      | Rabeprazole        | CYP2C19  | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>CPIC</u> | pathway        |
| Gastroenterology      | Tropisetron        | CYP2D6   | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>CPIC</u> | pathway        |
| Hematology            | Avatrombopag       | F5<br>F2 | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>FDA</u>  | pathway        |
| Hematology            | Eltrombopag        | F5       | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>FDA</u>  | pathway        |
| Hematology            | Lusutrombopag      | F5<br>F2 | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>FDA</u>  | pathway        |
| Hematology            | Methylene Blue     | G6PD     | Use according to the product label  | STRONG                     | <u>CPIC</u> | pathway        |
| Immunology            | Cevimeline         | CYP2D6   | No action required. Initiate therapy with recommended starting dose.  | N/A                        | <u>FDA</u>  | pathway        |
| Immunology            | Tacrolimus         | CYP3A5   | Initiate therapy with standard recommended dose. Use therapeutic drug monitoring to guide dose adjustments. | STRONG                     | <u>CPIC</u> | pathway        |
| Infectious<br>Disease | Ceftriaxone        | G6PD     | Use according to the product label  | N/A                        | <u>FDA</u>  | pathway        |
| Infectious<br>Disease | Dapsone            | G6PD     | Use according to the product label  | STRONG                     | <u>CPIC</u> | <u>pathway</u> |
| Infectious<br>Disease | Efavirenz          | CYP2B6   | Consider initiating efavirenz with decreased dose of 400 mg/day.  | MODERATE                   | <u>CPIC</u> | pathway        |
| Infectious<br>Disease | Hydroxychloroquine | G6PD     | Use according to the product label  | N/A                        | <u>FDA</u>  | <u>pathway</u> |
| Infectious<br>Disease | Nalidixic Acid     | G6PD     | Use according to the product label  | N/A                        | <u>FDA</u>  | pathway        |

| Therapeutic<br>Area   | Medication Name  | Genes   | Recommendation   | Strength of<br>Recommendation | Source      | Pathway        |
|-----------------------|------------------|---------|--|-------------------------------|-------------|----------------|
| Infectious<br>Disease | Nitrofurantoin   | G6PD    | Use according to the product label   | STRONG                        | <u>CPIC</u> | pathway        |
| Infectious<br>Disease | Primaquine       | G6PD    | Use according to the product label   | STRONG                        | <u>CPIC</u> | pathway        |
| Infectious<br>Disease | Tafenoquine      | G6PD    | Use according to the product label   | STRONG                        | <u>CPIC</u> | <u>pathway</u> |
| Infectious<br>Disease | Voriconazole     | CYP2C19 | Choose an alternative agent that is not dependent on CYP2C19 metabolism (e.g., isavuconazole, liposomal amphotericin B, posaconazole). | MODERATE                      | <u>CPIC</u> | pathway        |
| Neurology             | Brivaracetam     | CYP2C19 | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | pathway        |
| Neurology             | Deutetrabenazine | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | pathway        |
| Neurology             | Donepezil        | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | pathway        |
| Neurology             | Galantamine      | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | pathway        |
| Neurology             | Pitolisant       | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | pathway        |
| Neurology             | Tetrabenazine    | CYP2D6  | The maximum recommended single dose is 37.5 mg and should not exceed 100 mg/day.   | STRONG                        | <u>FDA</u>  | pathway        |
| Neurology             | Valbenazine      | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | pathway        |
| Oncology              | Erdafitinib      | CYP2C9  | No action required. Initiate therapy with recommended starting   | N/A                           | <u>FDA</u>  | pathway        |

| Therapeutic<br>Area | Medication Name | Genes   | Recommendation   | Strength of<br>Recommendation | Source      | Pathway        |
|---------------------|-----------------|---------|--|-------------------------------|-------------|----------------|
|                     |                 |         | dose.  |                               |             |                |
| Oncology            | Gefitinib       | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>DPWG</u> | pathway        |
| Oncology            | Rasburicase     | G6PD    | Use according to the product label   | STRONG                        | <u>CPIC</u> | <u>pathway</u> |
| Oncology            | Tamoxifen       | CYP2D6  | Consider alternative hormonal therapy such as an aromatase inhibitor for postmenopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women. If aromatase inhibitor use is contraindicated, consider a higher but FDA approved tamoxifen dose (40 mg/day). Avoid use of CYP2D6 inhibitors. | MODERATE                      | <u>CPIC</u> | pathway        |
| Other               | Meclizine       | CYP2D6  | May affect systemic concentrations. Monitor for adverse reactions.   | MODERATE                      | <u>FDA</u>  | <u>pathway</u> |
| Other               | Siponimod       | CYP2C9  | The recommended maintenance dosage is 2 mg per day.  | MODERATE                      | <u>FDA</u>  | <u>pathway</u> |
| Other               | Toluidine Blue  | G6PD    | Use according to the product label   | STRONG                        | <u>CPIC</u> | pathway        |
| Pain                | Aspirin         | CYP2C9  | No recommendation due to minimal evidence regarding tolerability or efficacy.  | N/A                           | <u>CPIC</u> | <u>pathway</u> |
| Pain                | Carisoprodol    | CYP2C19 | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | <u>pathway</u> |
| Pain                | Celecoxib       | CYP2C9  | Initiate therapy with recommended starting dose.   | STRONG                        | <u>CPIC</u> | pathway        |
| Pain                | Codeine         | CYP2D6  | Use codeine label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider   | MODERATE                      | <u>CPIC</u> | pathway        |

| Therapeutic<br>Area | Medication Name | Genes   | Recommendation   | Strength of<br>Recommendation | Source      | Pathway        |
|---------------------|-----------------|---------|--|-------------------------------|-------------|----------------|
|                     |                 |         | a non-tramadol opioid.   |                               |             |                |
| Pain                | Elagolix        | SLCO1B1 | No action required. Initiate therapy with recommended starting dose.   | N/A                           | FDA         | pathway        |
| Pain                | Flurbiprofen    | CYP2C9  | Initiate therapy with recommended starting dose.   | STRONG                        | <u>CPIC</u> | <u>pathway</u> |
| Pain                | Hydrocodone     | CYP2D6  | Use label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider non-codeine or non-tramadol opioid. | OPTIONAL                      | <u>CPIC</u> | <u>pathway</u> |
| Pain                | Ibuprofen       | CYP2C9  | Initiate therapy with recommended starting dose.   | STRONG                        | <u>CPIC</u> | pathway        |
| Pain                | Lornoxicam      | CYP2C9  | Initiate therapy with recommended starting dose.   | STRONG                        | <u>CPIC</u> | pathway        |
| Pain                | Meloxicam       | CYP2C9  | Initiate therapy with recommended starting dose.   | STRONG                        | <u>CPIC</u> | pathway        |
| Pain                | Naproxen        | CYP2C9  | No recommendation due to minimal evidence regarding tolerability or efficacy.  | N/A                           | <u>CPIC</u> | <u>pathway</u> |
| Pain                | Oliceridine     | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>FDA</u>  | <u>pathway</u> |
| Pain                | Oxycodone       | CYP2D6  | No action required. Initiate therapy with recommended starting dose.   | N/A                           | <u>DPWG</u> | <u>pathway</u> |
| Pain                | Piroxicam       | CYP2C9  | Initiate therapy with recommended starting dose.   | STRONG                        | <u>CPIC</u> | pathway        |
| Pain                | Tenoxicam       | CYP2C9  | Initiate therapy with recommended starting dose.   | STRONG                        | <u>CPIC</u> | pathway        |
| Pain                | Tramadol        | CYP2D6  | Use label recommended age- or weight-specific dosing. If no response and   | OPTIONAL                      | <u>CPIC</u> | pathway        |

| Therapeutic<br>Area | Medication Name | Genes  | Recommendation   | Strength of Recommendation | Source      | Pathway |
|---------------------|-----------------|--------|--|----------------------------|-------------|---------|
|                     |                 |        | opioid use is warranted,<br>consider a non-codeine<br>opioid         |                            |             |         |
| Rheumatology        | Pegloticase     | G6PD   | Use according to the product label                                   | STRONG                     | <u>CPIC</u> | pathway |
| Urology             | Darifenacin     | CYP2D6 | No action required. Initiate therapy with recommended starting dose. | N/A                        | <u>FDA</u>  | pathway |
| Urology             | Fesoterodine    | CYP2D6 | No action required. Initiate therapy with recommended starting dose. | N/A                        | <u>FDA</u>  | pathway |
| Urology             | Mirabegron      | CYP2D6 | No action required. Initiate therapy with recommended starting dose. | N/A                        | <u>FDA</u>  | pathway |
| Urology             | Tamsulosin      | CYP2D6 | No action required. Initiate therapy with recommended starting dose. | N/A                        | <u>FDA</u>  | pathway |
| Urology             | Tolterodine     | CYP2D6 | No action required. Initiate therapy with recommended starting dose. | N/A                        | <u>FDA</u>  | pathway |

### Regarding Phenotype Adjustment

There is currently no consensus on a method for adjusting inferred phenotypes when concomitant inhibitors or inducers are present.

Sequence2Script uses two strategies. The first strategy adjusts activity scores and only applies to CYP2C9 and CYP2D6. The activity score is multiplied by 0.50 if a moderate inhibitor is present, 0.00 if a strong inhibitor is present, and 1.50 if an inducer is present. The resulting activity score is than translated to the corresponding metabolizer phenotype using CPIC guidelines. The second strategy applies to CYP2B6, CYP2C19, CYP3A4, and CYP3A5. If a moderate inhibitor is present, the inferred phenotype is converted to the next lower activity phenotype (e.g., a normal metabolizer is converted to an intermediate metabolizer), whereas in the presence of a strong inhibitor the inferred phenotype is converted to a poor metabolizer, regardless of the inferred phenotype. In the presence of an inducer the inferred phenotype is converted to the next higher activity phenotype (e.g., an intermediate metabolizer is converted to a normal metabolizer). Sequence2Script does not perform adjustments for poor metabolizers in the presence of inhibitors or ultrarapid metabolizers in the presence of inducers because these phenotypes already represent the two extremes of the phenotype continuum. In cases where both a concomitant inhibitor and an inducer are present, the inferred phenotype in question is not adjusted as the evidence needed to guide the adjustment in these situations is limited. Finally, Sequence2Script does not perform adjustments for other factors such as age or inflammation that may alter inferred phenotypes. The aging process is accompanied by a decline in the function of numerous organs and systems that can affect pharmacokinetic processes to different extents, and this can make response to some drugs more variable. Inflammation (e.g., elevation in C reactive protein or proinflammatory cytokines) has been shown to have an inhibitory effect on several CYP450 enzymes (e.g., CYP3A4, CYP1A2, CYP2C9, CYP2C19, CYP2D6).

#### Regarding Sources of Recommendations

The recommendations made in this report are based on the recommendations provided by the Clinical Pharmacogenetics Implementation Consortium (CPIC, https://cpicpgx.org), the Dutch Pharmacogenetics Working Group (DPWG, https://www.pharmgkb.org/page/dpwg), and the US Food and Drug Administration (FDA) product labels. Therapeutic recommendations are based on weighing the evidence from a combination of preclinical, functional, and clinical data.

#### Regarding Strengths of Recommendations

The strength of a recommendation is based exclusively on pharmacogenetic information published in guidelines. They do not reflect the strength of a recommendation based on phenotypes that have been adjusted due to the presence of concomitant inhibitors or inducers. Strong: The evidence supporting the recommendation is high quality. The desirable effects clearly outweigh the undesirable effects. Moderate: There is a close or uncertain balance as to whether the evidence for this recommendation is high quality. The desirable effects clearly outweigh the undesirable effects. Optional: The desirable effects are closely balanced with undesirable effects, or the evidence is weak or based on extrapolations. There is room for differences in opinion as to the need for the recommended course of action. No recommendation: There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice currently.

#### **Alleles Tested**

| Gene          | Alleles/Haplotypes  |
|---------------|---|
| CYP2B6        | *4, *5, *6, *7 ,*9 , *18, *22, *33, *34, *36  |
| CYP2C9        | *2, *3, *4, *5, *6, *8, *11, *14, *27, *35  |
| CYP2C19       | *2, *3, *4, *5, *6, *7, *8, *9, *10, *17  |
| CYP2D6        | *2, *3, *4, *5, *6, *7, *8,*9,*10, *11, *14, *17, *29, *34, *39, *41, *49, *64, *65, *69, *109, *114, copy<br>number variation (Exon 9) |
| CYP3A4        | *3, *22, *37  |
| CYP3A5        | *3, *6, *7  |
| SLCO1B1       | *5  |
| VKORC1        | *2  |
| F2            | rs1799963/20210G>A  |
| F5            | rs6025/1691G>A  |
| G6PD          | A, A- 202A_376G, Mediterranean, Dallas, Panama, Sassari, Cagliari, Birmingham, Chatham  |
| ABCG2         | rs2231142/421C>A  |
| CYP4F2        | *3, *4, *22   |
| NUDT15        | *2,*3   |
| CYP2C Cluster | rs12777823  |

Genotyping was performed using Assay Developed and Validated within the TruLab Dx Network. This report was generated using Sequence2Script technology. Limitations: This test will not detect all known variants/alleles that result in altered gene activity. \*1 or wild-type alleles are reported by default if those listed were not detected.

Only listed alleles are tested for and absence of a detected mutation does not rule out the possibility of sensitivity to a specific drug due to the presence of other mutations, clinical factors, drug-drug interactions, or environmental factors.

#### Report Inquiries

For additional clinical guidance guidance on interpreting this report, please contact TruLab Dx.

#### Disclaimer, Methods and Limitations

A multiplex Real-Time Polymerase Chain Reaction (RT-PCR) is carried out under optimized conditions to generate amplicons for the targeted alleles at analytical sensitivity and specificity >95%. This includes common variants with known clinical significance as well as copy number variation of CYP2D6 gene.

This assay was developed and characterized by a lab within TruLab Dx's Network. This assay has not been cleared or approved by the U.S. Food and Drug Administration (FDA). The FDA has determined that such approval is not necessary, provided that the laboratory maintains its good standing as a clinical testing laboratory with all mandatory accrediting agencies and continually demonstrates that its testing protocols and procedures achieve a high degree of analytical accuracy. Only a qualified healthcare professional should advise a person on the use of information in this report. All clinical decisions relative to the test results should be directed by your qualified healthcare provider. The laboratory makes no representations or recommendations regarding results.

This test does not detect all known variations that may result in altered or inactive gene function. The absence of a detectable gene variation or polymorphism does not rule out the possibility that a patient may exhibit intermediate or high-sensitivity phenotypes due to undetected polymorphisms or drug-drug interactions.

This report is intended for interpretation by licensed physicians, pharmacists, or other qualified healthcare professionals. It is designed as a clinical decision-support tool and is not a substitute for sound clinical judgment or appropriate medical oversight. Final therapeutic decisions must be made by the healthcare professional based on a comprehensive evaluation of the patient, prescribed medications, and all relevant clinical information.

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Do NOT stop or change your medications without consulting a qualified healthcare professional.