PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION
NAME:	**Ben Greenfield**	**SPECIMEN TYPE:**	Buccal Swab	CYNTHIA TAYLOR
ACC #:	21102071694	**COLLECTION DATE:**	10/15/2021	905000
DOB:	12/20/1981	**RECEIVED DATE:**	10/15/2021	
SEX:	Male	**REPORT DATE:**	10/22/2021	

Pharmacogenetic Report

Risk Management

Thrombophilia

Normal Risk of Thrombosis

The patient does not carry the F5 c.1601G>A variant (also known as Factor V Leiden) or the F2 c.*97G>A variant (also known as Factor II 20210G>A).

The patient's risk of thrombosis is not increased (average risk of clotting is about 1 in 1000 for anyone in a year). However, because this test cannot find all of the inherited reasons for abnormal clotting, other factors may affect this risk assessment.

Assess thrombotic risk based on other genetic and/or circumstantial risk factors such as smoking, obesity, malignancy, prolonged immobilization or surgery.

Estrogen-containing contraceptive and hormone replacement therapy: unless other genetic and/or circumstantial risk factors are present, consider standard prescribing and monitoring practices.

A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	**ACTIONABLE** — Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA, EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.
Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.	
The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.	**INFORMATIVE** — There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

GetMyDNA™

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Cardiovascular	Angiotensin II Receptor Antagonists	Azilsartan (Edarbi®, Edarbyclor®) *Candesartan (Atacand®)* *Eprosartan (Teveten®)* Irbesartan (Avapro®) Losartan (Cozaar®, Hyzaar®) *Olmesartan (Benicar®)* *Telmisartan (Micardis®)* *Valsartan (Diovan®, Entresto®)*		
	Antianginal Agents	Ranolazine (Ranexa®)		
	Antiarrhythmics	*Amiodarone (Nexterone®, Pacerone®)* *Disopyramide (Norpace®)* *Quinidine (Quinidine®)* *Sotalol (Betapace®, Sorine®, Sotylize®)*	Flecainide (Tambocor®) Mexiletine (Mexitil®) Propafenone (Rythmol®)	
	Anticoagulants	*Apixaban (Eliquis®)* *Betrixaban (Bevyxxa®)* *Dabigatran Etexilate (Pradaxa®)* *Edoxaban (Savaysa®)* *Fondaparinux (Arixtra®)* *Rivaroxaban (Xarelto®)* Warfarin (Coumadin®)		
	Antiplatelets	*Prasugrel (Effient®)* *Ticagrelor (Brilinta®)* *Vorapaxar (Zontivity®)*		Clopidogrel (Plavix®)
	Beta Blockers	*Atenolol (Tenormin®)* *Bisoprolol (Zebeta®)* Carvedilol (Coreg®) *Labetalol (Normodyne®, Trandate®)* Nebivolol (Bystolic®) Propranolol (Inderal®)	Metoprolol (Lopressor®) Timolol (Blocadren®)	
	Diuretics	Torsemide (Demadex®)		

GetMyDNA™

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Diabetes	Statins	Fluvastatin (Lescol®) Pitavastatin (Livalo®) Pravastatin (Pravachol®) Rosuvastatin (Crestor®)	Atorvastatin (Lipitor®) Lovastatin (Mevacor®, Altoprev®, Advicor®) Simvastatin (Zocor®)	
	Meglitinides	Nateglinide (Starlix®) Repaglinide (Prandin®, Prandimet®)		
	Sulfonylureas	*Chlorpropamide (Diabinese®)* *Glimepiride (Amaryl®)* *Glipizide (Glucotrol®)* *Glyburide (Micronase®)* *Tolbutamide (Orinase®)*		
Gastrointestinal	Antiemetics	*Aprepitant (Emend-oral®)* Dolasetron (Anzemet®) Dronabinol (Marinol®) *Fosaprepitant (Emend-IV®)* Fosnetupitant / Palonosetron (Akynzeo-IV®) *Granisetron (Sancuso®, Sustol®)* Netupitant / Palonosetron (Akynzeo-oral®) Palonosetron (Aloxi®) *Rolapitant (Varubi®)*	Metoclopramide (Reglan®) Ondansetron (Zofran®, Zuplenz®)	
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant®, Kapidex®) Esomeprazole (Nexium®) Lansoprazole (Prevacid®) Omeprazole (Prilosec®) Pantoprazole (Protonix®) Rabeprazole (Aciphex®)		

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Infections	Antifungals	*Amphotericin B (AmBisome®, Abelcet®)* *Anidulafungin (Eraxis®)* *Caspofungin (Cancidas®)* *Fluconazole (Diflucan®)* *Isavuconazonium (Cresemba®)* *Itraconazole (Sporanox®)* *Micafungin (Mycamine®)* *Posaconazole (Noxafil®)* Voriconazole (Vfend®)		
	Anti-HIV Agents	*Dolutegravir (Tivicay®, Triumeq®)* *Doravirine (Pifeltro®)* Efavirenz (Sustiva®) *Etravirine (Edurant®)* *Raltegravir (Isentress®, Dutrebis®)* *Rilpivirine (Intelence®)*		
	Antimalarials	*Proguanil (Malarone®)*		
	Fibromyalgia Agents	*Milnacipran (Savella®)*		
	Muscle Relaxants	Carisoprodol (Soma®) *Cyclobenzaprine (Flexeril®, Amrix®)* *Metaxalone (Skelaxin®)* *Methocarbamol (Robaxin®)*		
Pain	NSAIDs	Celecoxib (Celebrex®) *Diclofenac (Voltaren®)* Flurbiprofen (Ansaid®) Ibuprofen (Advil®, Motrin®) *Indomethacin (Indocin®)* *Ketoprofen (Orudis®)* *Ketorolac (Toradol®)* Meloxicam (Mobic®) *Nabumetone (Relafen®)* *Naproxen (Aleve®)* Piroxicam (Feldene®) *Sulindac (Clinoril®)*		

GetMyDNA™

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Opioids	*Alfentanil (Alfenta®)* *Buprenorphine (Butrans®, Buprenex®)* Dihydrocodeine (Synalgos-DC®) *Hydromorphone (Dilaudid®, Exalgo®)* *Levorphanol (Levo Dromoran®)* *Meperidine (Demerol®)* Methadone (Dolophine®) Oxycodone (Percocet®, Oxycontin®) *Oxymorphone (Opana®, Numorphan®)* *Sufentanil (Sufenta®)* *Tapentadol (Nucynta®)*	Benzhydrocodone (Apadaz®) Codeine (Codeine; Fioricet® with Codeine) Fentanyl (Actiq®) Hydrocodone (Vicodin®) Morphine (MS Contin®) Tramadol (Ultram®)	
	Antiaddictives	Bupropion (Wellbutrin®, Zyban®, Aplenzin®, Contrave®) Lofexidine (Lucemyra®) Naltrexone (Vivitrol®, Contrave®)		
	Anti-ADHD Agents	Amphetamine (Adderall®, Evekeo®) *Clonidine (Kapvay®)* Dextroamphetamine (Dexedrine®) *Guanfacine (Intuniv®)* Lisdexamfetamine (Vyvanse®)	Atomoxetine (Strattera®) Dexmethylphenidate (Focalin®) Methylphenidate (Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®)	

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Psychotropic	Anticonvulsants	Brivaracetam (Briviact®) *Carbamazepine (Tegretol®, Carbatrol®, Epitol®)* *Eslicarbazepine (Aptiom®)* *Ethosuximide (Zarontin®)* *Ezogabine (Potiga®)* *Felbamate (Felbatol®)* Fosphenytoin (Cerebyx®) *Gabapentin (Neurontin®)* *Lacosamide (Vimpat®)* *Lamotrigine (Lamictal®)* *Levetiracetam (Keppra®)* *Oxcarbazepine (Trileptal®, Oxtellar XR®)* *Perampanel (Fycompa®)* Phenytoin (Dilantin®) *Pregabalin (Lyrica®)* *Rufinamide (Banzel®)* *Tiagabine (Gabitril®)* *Topiramate (Topamax®)* *Valproic Acid (Depakene®)* *Vigabatrin (Sabril®)*	Phenobarbital (Luminal®) Primidone (Mysoline®) Zonisamide (Zonegran®)	
	Antidementia Agents	Donepezil (Aricept®) Galantamine (Razadyne®) *Memantine (Namenda®)*		
	Antidepressants	Desvenlafaxine (Pristiq®) *Duloxetine (Cymbalta®)* Fluoxetine (Prozac®, Sarafem®) *Levomilnacipran (Fetzima®)* *Mirtazapine (Remeron®)* Nefazodone (Serzone®) Paroxetine (Paxil®, Brisdelle®) Sertraline (Zoloft®) *Trazodone (Oleptro®)* *Vilazodone (Viibryd®)* Vortioxetine (Trintellix®)	Amitriptyline (Elavil®) Amoxapine (Amoxapine®) Citalopram (Celexa®) Clomipramine (Anafranil®) Desipramine (Norpramin®) Doxepin (Silenor®) Escitalopram (Lexapro®) Fluvoxamine (Luvox®) Imipramine (Tofranil®) Maprotiline (Ludiomil®) Nortriptyline (Pamelor®) Protriptyline (Vivactil®) Trimipramine (Surmontil®)	Venlafaxine (Effexor®)

GetMyDNA™

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Antipsychotics	Aripiprazole (Abilify®, Aristada®) *Asenapine (Saphris®)* Brexpiprazole (Rexulti®) *Cariprazine (Vraylar®)* Chlorpromazine (Thorazine®) *Fluphenazine (Prolixin®)* Haloperidol (Haldol®) *Loxapine (Loxitane®, Adasuve®)* *Lurasidone (Latuda®)* *Olanzapine (Zyprexa®)* Paliperidone (Invega®) *Pimavanserin (Nuplazid®)* Pimozide (Orap®) *Quetiapine (Seroquel®)* Risperidone (Risperdal®) *Thiothixene (Navane®)* *Trifluoperazine (Stelazine®)* *Ziprasidone (Geodon®)*	Clozapine (Clozaril®) Iloperidone (Fanapt®) Perphenazine (Trilafon®)	Thioridazine (Mellaril®)
	Benzodiazepines	*Alprazolam (Xanax®)* *Clonazepam (Klonopin®)* Diazepam (Valium®)	Clobazam (Onfi®)	
	Other Neurological Agents	Deutetrabenazine (Austedo®) Dextromethorphan / Quinidine (Nuedexta®) Flibanserin (Addyi®) Valbenazine (Ingrezza®)	Tetrabenazine (Xenazine®)	
Rheumatology	Anti-Hyperuricemics and Anti-Gout Agents	*Colchicine (Mitigare®)* *Febuxostat (Uloric®)*		
	Immunomodulators	*Apremilast (Otezla®)* *Tofacitinib (Xeljanz®)*	Leflunomide (Arava®)	
Transplantation	Immunosuppressants	Tacrolimus (Prograf®)		
	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	*Dutasteride (Avodart®)* *Finasteride (Proscar®)*		

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Urologicals	Alpha-Blockers for Benign Prostatic Hyperplasia	*Alfuzosin (UroXatral®)* *Doxazosin (Cardura®)* *Silodosin (Rapaflo®)* Tamsulosin (Flomax®) *Terazosin (Hytrin®)*		
	Antispasmodics for Overactive Bladder	Darifenacin (Enablex®) Fesoterodine (Toviaz®) Mirabegron (Myrbetriq®) *Oxybutynin (Ditropan®)* *Solifenacin (Vesicare®)* Tolterodine (Detrol®) *Trospium (Sanctura®)*		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	*Avanafil (Stendra®)* *Sildenafil (Viagra®)* *Tadalafil (Cialis®)* *Vardenafil (Levitra®)*		

NON-PHARMACOGENETIC DRUGS

The drugs that appear in grey italics are not based on the patient's genetic results. At this time, these drugs do not have pharmacogenetic associations of clinical significance. They are included in order to provide a more complete list of alternative medications.

PATIENT INFORMATION

NAME: Ben Greenfield
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

Dosing Guidance

Amitriptyline
Elavil®

Increased Amitriptyline Exposure (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of amitriptyline to less active compounds and a subsequent increase in amitriptyline exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Neuropathic Pain: Amitriptyline therapy can be prescribed according to standard recommended dosage and administration when lower doses are considered. If higher doses are warranted, consider a 25% reduction of the recommended dose and monitor patient for side effects.

Amoxapine
Amoxapine®

Possible Increased Amoxapine Exposure (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

Like other tricyclic and tetracyclic antidepressants, amoxapine is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Decreased CYP2D6 activity may result in higher amoxapine concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function; therapy must be initiated cautiously and adjusted according to the patient's response.

Atomoxetine
Strattera®

Possible Atomoxetine Underexposure Leading to Decreased Response (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

The genotype result indicates that the patient is likely to have an insufficient response due to inadequate drug exposure following standard dosing. Consider the following dosing strategy:

- Initiate treatment at 40 mg/day, increase to 80 mg/day after 3 days and maintain dose.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider a dose increase to 100 mg/day.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider therapeutic drug monitoring 1-2 hours post dose. If the plasma concentration is less than 200 ng/ml consider a dose increase to a target of 400 ng/ml. Doses greater than 100 mg/day may be needed to achieve a targeted therapeutic concentration. (Therapeutic range: 200-1000 ng/ml).

Atorvastatin
Lipitor®

Altered Response to Atorvastatin (CYP3A4: Intermediate Metabolizer) — **INFORMATIVE**

The genotype result indicates that the patient carries the CYP3A4*22 allele (this allele is associated with lower CYP3A4 enzyme activity). Preliminary studies have shown that patients carrying the CYP3A4*22 allele may achieve an optimal lipid control goal with lower atorvastatin dose requirements.

Benzhydrocodone
Apadaz®

Possible Altered Response to Benzhydrocodone (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

Benzhydrocodone is a prodrug of hydrocodone and is converted to active hydrocodone by intestinal enzymes. Decreased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 intermediate metabolizers. However, there is insufficient evidence whether these patients have decreased analgesia when taking benzhydrocodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Citalopram
Celexa®

Delayed Response to Citalopram (SLC6A4: Low Serotonin Transporter Expression) — **INFORMATIVE**

The genotype predicts significantly decreased serotonin transporter levels resulting in less efficient transporter function. A longer titration period may be required to achieve maximal antidepressant response. The patient may respond to citalopram more slowly (up to 12 weeks) and may experience more side effects. The patient may benefit from non-selective antidepressants.

Clobazam
Onfi®

Possible Sensitivity to Clobazam (CYP2C19: Intermediate Metabolizer) — **ACTIONABLE**

In CYP2C19 intermediate metabolizers, plasma levels of the active metabolite N-desmethylclobazam were 2-fold higher than those found in CYP2C19 normal metabolizers. The dose adjustment for intermediate metabolizers is not well established, and therefore the recommendation for poor metabolizers is proposed. The starting dose should be 5 mg/day, and dose titration should proceed slowly according to weight. Patients should be titrated initially to 10 mg /day (≤30 kg body weight) or 20 mg/day (>30 kg body weight). If necessary and based upon clinical response, an additional titration to the maximum doses 20 mg/day (≤30 kg body weight) or 40 mg/day (>30 kg body weight) may be started on day 21.

Clomipramine
Anafranil®

Increased Clomipramine Exposure (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of clomipramine to less active compounds and a subsequent increase in clomipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Clopidogrel
Plavix®

Reduced Response to Clopidogrel (CYP2C19: Intermediate Metabolizer) — **ACTIONABLE**

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Clozapine
Clozaril®

Unfavorable Response to Clozapine (HTR2A: Homozygous for the C allele (rs6311)) — **INFORMATIVE**

The patient does not carry the HTR2A variant rs6311. Preliminary studies suggest that this genotype may be associated with an unfavorable response to clozapine in patients with European ancestry.

Codeine
Codeine; Fioricet® with Codeine

Decreased Exposure to Codeine Active Metabolite (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

The patient genotype is associated with decreased conversion of codeine to its active metabolite (morphine), which may result in decreased effectiveness.

Codeine can be prescribed at standard label-recommended age- or weight-based dosing. If no response and opioid use is warranted, consider a non-tramadol opioid. Alternative opioids may include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Desipramine
Norpramin®

Increased Desipramine Exposure (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of desipramine to less active compounds and a subsequent increase in desipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Dexmethylphenidate

Decreased Response to Dexmethylphenidate (COMT: Intermediate COMT Activity) — **INFORMATIVE**

Focalin®

The patient's genotype result predicts a less optimal response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Doxepin
Silenor®

Increased Doxepin Exposure (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of doxepin to less active compounds and a subsequent increase in doxepin exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Insomnia: Doxepin can be prescribed according to the standard recommended dosage and administration.

Escitalopram
Lexapro®

Delayed Response to Escitalopram (SLC6A4: Low Serotonin Transporter Expression) — **INFORMATIVE**

The genotype predicts significantly decreased serotonin transporter levels resulting in less efficient transporter function. A longer titration period may be required to achieve maximal antidepressant response. The patient may respond to escitalopram more slowly (up to 12 weeks) and may experience more side effects. The patient may benefit from non-selective antidepressants.

Fentanyl
Actiq®

Altered Response to Fentanyl (OPRM1: Altered OPRM1 Function) — **INFORMATIVE**

The patient carries one copy of the OPRM1 118A>G variant. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia at standard fentanyl doses. Therefore, the patient may require higher doses of this drug. Because fentanyl has a narrow therapeutic window, it is advised to carefully titrate this drug to a tolerable dose that provides adequate analgesia with minimal side effects.

Flecainide
Tambocor®

Increased Exposure to Flecainide (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

The patient's genotype may be associated with an increased flecainide exposure following standard dosing. Consider prescribing a lower flecainide dose for therapeutic indications. When compared to a CYP2D6 normal metabolizer, an intermediate metabolizer may require a 25% dose reduction. Careful titration with ECG recording and monitoring of flecainide plasma concentrations are recommended until a favorable clinical response is achieved.

Dose adjustments are not required when flecainide is utilized for diagnostic uses.

Fluvoxamine
Luvox®

Delayed Response to Fluvoxamine (SLC6A4: Low Serotonin Transporter Expression) — **INFORMATIVE**

The genotype predicts significantly decreased serotonin transporter levels resulting in less efficient transporter function. A longer titration period may be required to achieve maximal antidepressant response. The patient may respond to fluvoxamine more slowly (up to 12 weeks) and may experience more side effects. The patient may benefit from non-selective antidepressants.

Hydrocodone
Vicodin®

Altered Response to Hydrocodone (OPRM1: Altered OPRM1 Function) — **INFORMATIVE**

The patient carries one copy of the OPRM1 118A>G variant. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia and increased opioid side effects at standard or high hydrocodone doses. If the patient fails to respond to increased hydrocodone doses, an alternative opioid may be considered.

Hydrocodone
Vicodin®

Possible Decreased Exposure to Hydrocodone Active Metabolite (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

The patient genotype may be associated with a reduced conversion of hydrocodone to an active metabolite (hydromorphone), which may result in decreased effectiveness.

Hydrocodone can be prescribed at standard label-recommended age- or weight-based dosing. If no response and opioid use is warranted, consider a non-codeine or non-tramadol opioid. Alternative opioids may include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Iloperidone
Fanapt®

Moderate Sensitivity to Iloperidone (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

Because iloperidone is associated with QTc prolongation, caution is warranted when prescribing the drug in patients with reduced CYP2D6 activity. Iloperidone must be titrated slowly from a low starting dose to avoid orthostatic hypotension. If patients taking iloperidone experience symptoms that could indicate the occurrence of cardiac arrhythmias (e.g., dizziness, palpitations, or syncope), the prescriber should initiate further evaluation, including cardiac monitoring.

Imipramine
Tofranil®

Increased Imipramine Exposure (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of imipramine to less active compounds and a subsequent increase in imipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Leflunomide
Arava®

Increased Exposure to Leflunomide (CYP2C19: Intermediate Metabolizer) — **INFORMATIVE**

Leflunomide is metabolized by CYP2C19 and CYP1A2 to its active metabolite teriflunomide. Preliminary studies indicate that patients with decreased CYP2C19 activity have a higher risk of developing gastrointestinal side effects and hepatotoxicity. There is insufficient data to calculate dose adjustment. If leflunomide is prescribed at standard dosing, monitor closely the patient's response and be alert to increased side effects.

Full blood cell count (CBC) and liver function parameters should be checked no more than 6 months before beginning treatment, and every month for the initial 6 months of therapy. Blood pressure should be checked before beginning treatment and periodically thereafter.

Lovastatin
Mevacor®, Altoprev®, Advicor®

Altered Response to Lovastatin (CYP3A4: Intermediate Metabolizer) — **INFORMATIVE**

The genotype result indicates that the patient carries the CYP3A4*22 allele (this allele is associated with lower CYP3A4 enzyme activity). Preliminary studies have shown that patients carrying the CYP3A4*22 allele may achieve an optimal lipid control goal with lower lovastatin dose requirements.

Maprotiline
Ludiomil®

Possible Increased Maprotiline Exposure (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Decreased CYP2D6 activity results in higher maprotiline concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function therefore, therapy must be initiated at a low dosage and gradually adjusted according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.

Methylphenidate
Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®

Decreased Response to Methylphenidate (COMT: Intermediate COMT Activity) — **INFORMATIVE**

The patient's genotype result predicts a less optimal response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Metoclopramide
Reglan®

Possible Sensitivity to Metoclopramide (CYP2D6: Intermediate Metabolizer) — INFORMATIVE

There is no data documenting the changes in plasma concentrations of metoclopramide in CYP2D6 intermediate metabolizers. Metoclopramide can be prescribed at standard label-recommended dosage and administration with careful monitoring for possible increase of side effects.

Metoprolol
Lopressor®

Increased Exposure to Metoprolol (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

The patient's genotype may be associated with an increased metoprolol exposure following standard dosing. When compared to a normal metabolizer, an intermediate metabolizer may require a 50% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).

Mexiletine
Mexitil®

Increased Sensitivity to Mexiletine (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

Consider prescribing a lower mexiletine dose. A slow titration with ECG recording and monitoring of mexiletine plasma concentrations are recommended until a favorable clinical response is achieved.

Morphine
MS Contin®

Altered Response to Morphine (OPRM1: Altered OPRM1 Function) — INFORMATIVE

The patient carries one copy of the OPRM1 118A>G variant. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with possible reduced analgesia at standard morphine doses and decreased risk for nausea and vomiting during the first 24-hour postoperative period. Therefore, the patient may require higher doses of this drug. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

Nortriptyline
Pamelor®

Increased Nortriptyline Exposure (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of nortriptyline to less active compounds and a subsequent increase in nortriptyline exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Ondansetron
Zofran®, Zuplenz®

Lack of Benefit from Ondansetron Treatment in Early Onset Alcoholism (SLC6A4: Low Serotonin Transporter Expression) — INFORMATIVE

Ondansetron has been shown to be effective in inhibiting heavy drinking behaviors in patients with early onset alcoholism. This patient carries two short or S alleles of SLC6A4 5-HTTLPR variant. Preliminary studies demonstrate that use of ondansetron may not benefit patients with this genotype. The abstinence rates from alcohol and the number of drinks per drinking day were not significantly different between patients treated with placebo or ondansetron.

Perphenazine
Trilafon®

Possible Sensitivity to Perphenazine (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

Patients with a decreased CYP2D6 function will eliminate perphenazine more slowly, which can result in higher drug concentrations and possibly more adverse events (extrapyramidal symptoms). Consider close monitoring and dose reduction to avoid toxicity.

Phenobarbital
Luminal®

Possible Sensitivity to Phenobarbital (CYP2C19: Intermediate Metabolizer) — INFORMATIVE

CYP2C19 is partly involved in the metabolism of phenobarbital, and although CYP2C19 intermediate metabolizers have a lower clearance of phenobarbital than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, phenobarbital can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Primidone
Mysoline®

Possible Sensitivity to Primidone (CYP2C19: Intermediate Metabolizer) — INFORMATIVE

CYP2C19 is partly involved in the metabolism of primidone, and although CYP2C19 intermediate metabolizers have a lower clearance of phenobarbital (active metabolite) than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, primidone can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Propafenone
Rythmol®

Increased Exposure to Propafenone (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

The patient's genotype may be associated with an increased propafenone exposure following standard dosing. There is insufficient data to allow calculation of dose adjustment. Titrate carefully and adjust the dose in response to plasma concentration and ECG monitoring. An alternative medication such as sotalol, disopyramide, quinidine or amiodarone may also be considered.

Dose adjustments with co-medications: concurrent use of propafenone along with CYP3A4 inhibitors and CYP2D6 inhibitors may significantly increase the plasma concentration of propafenone increasing the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with both a CYP2D6 inhibitor and a CYP3A4 inhibitor.

Protriptyline
Vivactil®

Possible Increased Protriptyline Exposure (CYP2D6: Intermediate Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, protriptyline is metabolized by CYP2D6. Decreased CYP2D6 activity results in higher protriptyline concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function. Therefore, therapy must be initiated at a low dosage and gradually adjusted according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.

Simvastatin
Zocor®

Altered Response to Simvastatin (CYP3A4: Intermediate Metabolizer) — INFORMATIVE

The genotype result indicates that the patient carries the CYP3A4*22 allele (this allele is associated with lower CYP3A4 enzyme activity). Preliminary studies have shown that patients carrying the CYP3A4*22 allele may achieve an optimal lipid control goal with lower simvastatin dose requirements.

Tetrabenazine
Xenazine®

Normal Sensitivity to Tetrabenazine (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 intermediate metabolizers of CYP2D6 is 100 mg with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

Thioridazine
Mellaril®

Increased Sensitivity to Thioridazine (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

Reduced cytochrome CYP2D6 activity results in elevated plasma levels of thioridazine, would be expected to augment the prolongation of the QTc interval associated with thioridazine, and may increase the risk of serious, potentially fatal, cardiac arrhythmias, such as Torsades de pointes-type arrhythmias. Such an increased risk may result also from the additive effect of coadministering thioridazine with other agents that prolong the QTc interval. Therefore, thioridazine is contraindicated in patients with reduced levels of CYP2D6 activity.

Timolol
Blocadren®

Possible Sensitivity to Timolol (CYP2D6: Intermediate Metabolizer) — INFORMATIVE

Potentiated systemic beta-blockade (e.g., bradycardia) has been reported during timolol treatment by patients with decreased CYP2D6 activity. Monitor patient for treatment-related adverse effects.

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

Tramadol

Ultram®

Decreased Exposure to Tramadol Active Metabolite (CYP2D6: Intermediate Metabolizer) **INFORMATIVE**

The patient genotype is associated with decreased conversion of tramadol to its active metabolite (O-desmethyltramadol), which may result in decreased effectiveness.

Tramadol can be prescribed at standard label-recommended age- or weight-based dosing and monitoring. If no response and opioid use is warranted, consider a non-codeine opioid. Alternative opioids may include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Trimipramine

Surmontil®

Increased Trimipramine Exposure (CYP2D6: Intermediate Metabolizer) **INFORMATIVE**

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of trimipramine to less active compounds and a subsequent increase in trimipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Venlafaxine

Effexor®

Increased Exposure to Venlafaxine (CYP2D6: Intermediate Metabolizer) **ACTIONABLE**

The patient has a decreased CYP2D6 activity which may result in elevated plasma concentrations of venlafaxine at standard doses. Consider an alternative medication or consider prescribing venlafaxine at a reduced dose and be extra alert for adverse events; adjust the dose based on tolerability and therapeutic monitoring.

If therapeutic drug monitoring is utilized, the sum of venlafaxine and O-desmethylvenlafaxine (an active metabolite) plasma concentrations should be used for efficacy. While the sum of the parent and the active metabolite are informative for efficacy, a higher parent (venlafaxine) concentration may be associated with higher side effects, including QT prolongation.

Zonisamide

Zonegran®

Possible Sensitivity to Zonisamide (CYP2C19: Intermediate Metabolizer) **INFORMATIVE**

CYP2C19 is partly involved in the metabolism of zonisamide, and although preliminary studies show that CYP2C19 intermediate metabolizers have a slightly lower (15%) zonisamide clearance than normal metabolizers, no significant change in the clinical outcome has been reported with this antiepileptic drug. Therefore, zonisamide can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

GetMyDNA™

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

Test Details

Gene	Genotype	Phenotype	Clinical Consequences
ADRA2A	C-1291G G/G	**Homozygous for G Allele**	Carriers of the G allele of ADRA2A C-1291G variant, show greater reduction of inattentive symptoms when administered Methylphenidate or Dexmethylphenidate.
COMT	Val158Met A/G	**Intermediate COMT Activity**	Consistent with a reduced catechol O-methyltransferase (COMT) function.
CYP1A2	Indeterminate	**Unknown Phenotype**	Test results were obtained for CYP1A2 but one or more analytes failed. The patient's CYP1A2 metabolism status cannot be determined based on the genotype results. Caution if CYP1A2 drug substrates are prescribed.
CYP2B6	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP2B6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2C19	*1/*2	**Intermediate Metabolizer**	Consistent with a moderate deficiency in CYP2C19 enzyme activity.
CYP2C9	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP2C9 enzyme activity.
CYP2D6	*2/*4	**Intermediate Metabolizer**	Consistent with a moderate deficiency in CYP2D6 enzyme activity.
CYP3A4	*1/*22	**Intermediate Metabolizer**	Consistent with a moderate deficiency in CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP3A5	*3/*3	**Poor Metabolizer**	Consistent with an absence of CYP3A5 enzyme expression (Non-Expresser). This phenotype is the most common in the general population.
F2 **F5**	rs1799963 GG rs6025 CC	**Normal Risk of Thrombosis**	Unless other genetic or circumstantial risk factors are present, the patient is not expected to have an increased risk for thrombosis.
HTR2A	-1438G>A C/C	**Homozygous for the C allele (rs6311)**	The patient does not carry the variant allele at rs6311 which may be associated with greater serotonin 2A receptor gene expression.
HTR2A	rs7997012 A/A	**Homozygous for the A allele (rs7997012)**	Possible increased response to citalopram and escitalopram
OPRM1	A118G A/G	**Altered OPRM1 Function**	Consistent with a reduced OPRM1 receptor signaling efficiency induced by exogenous opioids. This is associated with a possible reduced analgesia following standard opioid doses and a favorable response to naltrexone.
SLC6A4	S/S	**Low Serotonin Transporter Expression**	Consistent with decreased Serotonin Transporter levels.
SLCO1B1	521T>C T/T	**Normal Function**	Consistent with a typical SLCO1B1 transporter function.
VKORC1	-1639G>A G/G	**Low Warfarin Sensitivity**	Consistent with a typical VKORC1 expression.

Alleles Tested: **ADRA2A** C-1291G; **COMT** Val158Met; **CYP1A2** *1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W; **CYP2B6** *4, *5, *6, *7, *9, *16, *18; **CYP2C19** *2, *3, *4A, *4B, *6, *8, *9, *10, *17; **CYP2C9** *2, *3, *5, *6, *8, *11; **CYP2D6** *2, *3, *4, *4M, *6, *8, *9, *10, *17, *29, *35, *41, *5 (gene deletion), XN (gene duplication); **CYP3A4** *22; **CYP3A5** *3, *6, *7; **Factor II** rs1799963; **Factor V Leiden** rs6025; **HTR2A** -1438G>A, rs7997012; **OPRM1** A118G; **SLC6A4** La, S, Lg; **SLCO1B1** 521T>C; **VKORC1** -1639G>A

Limitation: This test does not detect all alleles known to result in altered or inactive function. This test does not account for all variations that may be present in the individual tested. Absence of a detectable variant does not rule out the possibility that a patient carries undetected polymorphisms that may confer a phenotype other than that reported. Phenotypes are also affected by factors such as drug-drug interactions, comorbidities, and lifestyle habits.

Methodology: Genomic DNA was extracted from buccal swabs or EDTA blood as indicated by the sample type listed on the first page of the report. Testing was performed using real-time PCR with TaqMan chemistry for all tests except SLC6A4, which was performed by PCR-RFLP analysis using MspI restriction endonuclease.

Lab Disclaimer: Gravity Diagnostics developed and determined the performance characteristics of this laboratory-developed genotype test. It has not been reviewed or approved by the U.S. Food and Drug Administration.

Translational Software Disclaimer: The information presented in this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist, or other healthcare professional should advise a patient on the use of the medications prescribed.

The genotype test results are interpreted by reporting software and genotype-phenotype associations developed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

Approved by Matt Vollmer

GetMyDNA™

PATIENT INFORMATION

NAME: **Ben Greenfield**
ACC #: 21102071694
DOB: 12/20/1981
SEX: Male

Patient Information Card

This is a summary genetic report for your patient to share with other healthcare providers. The card can be cut out along the dashed line and carried with the patient.

GRAVITYDIAGNOSTICS™

REPORT DETAILS

Patient: Ben Greenfield
DOB: 12/20/1981
ACC #: 21102071694

Pharmacogenetic Test Summary

CYP2C19	*1/*2	Intermediate Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*2/*4	Intermediate Metabolizer
CYP3A4	*1/*22	Intermediate Metabolizer
CYP3A5	*3/*3	Poor Metabolizer

VKORC1	-1639G>A G/G	Low Warfarin Sensitivity

For a complete report contact Gravity Diagnostics
www.gravitydiagnostics.com

Powered By Translational software