

EMR Tutorial for Drug Interactions

The complexity of drug/drug interactions is growing so rapidly that it is virtually impossible for anyone to know all of the contraindications for the use of even the most common medications without considering those medications which are uncommonly used. This is such the case that the first “common clinical pitfall of monitoring drug interactions” listed below is, “Relying on memory as to which drugs interact.”

While NextGen EMR has a very complete drug/drug interaction check built into the medication module, the implications of the Cytochrome P450 system is such that special attention needs to be drawn to those drugs which are detoxified by this system.

SETMA’s **Drug Interactions Suite of Templates** has been built for the purpose of informing providers about this very important field which affects their daily prescriptive habits.

How to find the Drug Interactions Template

AAA Home

The screenshot displays the SETMA EMR interface. At the top left is the logo for Southeast Texas Medical Associates, LLC. The patient information section includes fields for Patient (Jonny1), ZTest, Sex (M), Age (69), DOB (08/17/1940), Home Phone ((409)833-9797), Work Phone ((409)504-5566), and Patient's Code Status (Full Code). A red alert banner states "Patient has one or more alerts!" with a link to "Click Here to View Alerts". Below this is a navigation menu with various links. The "Drug Interactions" link is highlighted with a red box. Other links include SETMA's LESS Initiative, Preventing Diabetes, Preventing Hypertension, Medical Home Coordination, Charge Posting Tutorial, ICD-9 Code Tutorial, E&M Coding Recommendations, Master GP, Nursing Home, Ophthalmology, Pediatrics, Physical Therapy, Podiatry, Rheumatology, Daily Progress, Admission Orders, Discharge, Insulin Infusion, Colorectal Surgery, Pain Management, Exercise, CHF Exercise, Diabetic Exercise, Smoking Cessation, Hydration, Nutrition, Guidelines, Lab Future, Lab Results, Disease Management, Acute Coronary Syn, Angina, Asthma, CHF, Diabetes, Headaches, Hypertension, Lipids, Cardiometabolic Risk Syndrome, Weight Management, Renal Failure, Diabetes Edu, Patient's Pharmacy, Pending Referrals, Archived Referrals, Referral History, and Chart Note. The Pending Referrals table shows a list of referrals with status, priority, referral, and referring provider. The Archived Referrals table is empty. The Chart Note section includes buttons for Return Info, Return Doc, Email, Telephone, Records Request, and Transfer of Care Doc.

Patient: Jonny1 ZTest Sex: M Age: 69 DOB: 08/17/1940
Home Phone: (409)833-9797 Work Phone: (409)504-5566
Patient's Code Status: Full Code

Patient has one or more alerts! [Click Here to View Alerts](#)

[SETMA's LESS Initiative](#) | [Preventing Diabetes](#) | [Preventing Hypertension](#) | [Medical Home Coordination](#)
[Charge Posting Tutorial](#) | [ICD-9 Code Tutorial](#) | [E&M Coding Recommendations](#) | **Needs Attention!!**

[Master GP](#) | [Nursing Home](#) | [Ophthalmology](#) | [Pediatrics](#) | [Physical Therapy](#) | [Podiatry](#) | [Rheumatology](#)
[Daily Progress](#) | [Admission Orders](#) | [Discharge](#) | [Insulin Infusion](#) | [Colorectal Surgery](#) | [Pain Management](#) |
[Exercise](#) | [CHF Exercise](#) | [Diabetic Exercise](#) | **Drug Interactions** | [Smoking Cessation](#) |
[Hydration](#) | [Nutrition](#) | [Guidelines](#) | [Lab Future](#) | [Lab Results](#) |

Disease Management
[Acute Coronary Syn](#) | [Angina](#) | [Asthma](#) | [CHF](#) | [Diabetes](#) | [Headaches](#) | [Hypertension](#) | [Lipids](#) | [Cardiometabolic Risk Syndrome](#) |
[Weight Management](#) | [Renal Failure](#) | [Diabetes Edu](#)

Patient's Pharmacy: Bruce's Pharmacy
Phone: (409)962-4431
Fax: (409)962-0723
[Rx Sheet - Active](#)
[Rx Sheet - New](#)
[Rx Sheet - Complete](#)
[Home Health](#)

Pending Referrals

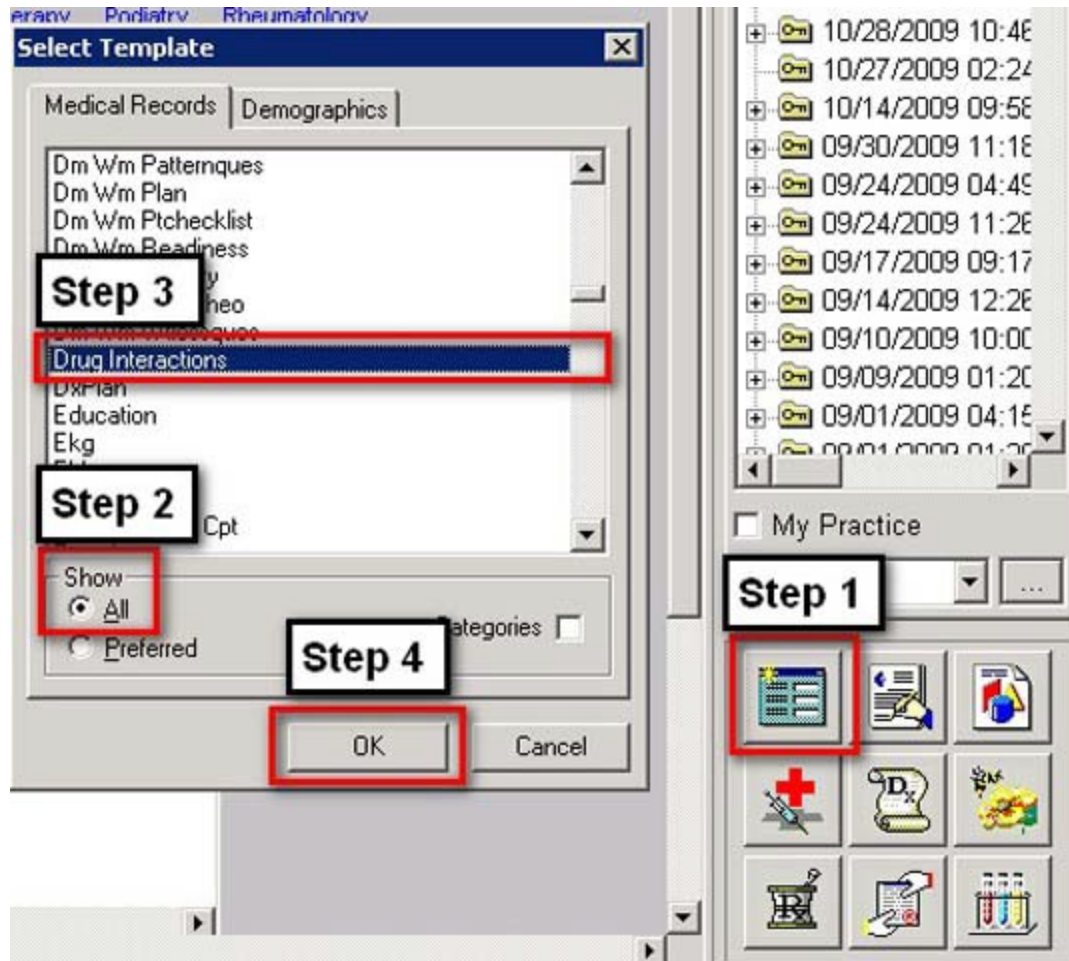
Status	Priority	Referral	Referring Provider
Completed	Immediate	SETMA Infectious Disease	Ahmed
Completed	Routine	PFT	Holly
Completed	Routine	CPET	Abbas
Completed	Stat	Adenosine Cardiolite	Ahmed
Completed	Routine	Thyroid Scan	Holly

Archived Referrals - Do not use for new referrals [Referral History](#)

Status	Priority	Referral	Referring Provider
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Chart Note
[Return Info](#)
[Return Doc](#)
[Email](#)
[Telephone](#)
[Records Request](#)
[Transfer of Care Doc](#)

Master Tool Bar Icon



- When the Template button is clicked you will be presented with the preference list.
- If the **Drug Interactions** Template is listed as one of your preferences, select it.
- If it is not one of your preferences, select the All radio button and scroll down until you find it in the list. Then you may select the template by either double-clicking on the name or single click on the name (so that it is highlighted in blue) and then click the OK button.

NOTE: For more on how to set up your preferences, [Click Here](#)

Drug Interactions Master Template

This template presents a brief introduction to the subject of the Cytochrome P-450 system.

At the bottom of the template, the following appears:

Cytochrome P450 Tutorial with the following parts:

- Definitions
- Highlights of Cytochrome P450
- Humans and Cytochrome P450
- Aging and Cytochrome P450
- Phase 1 Metabolism
- Factors Affecting P450 Metabolism
- CYP3A4

Drug Interactions

More than 90% of human drug oxidation is due to six CYP isoenzymes

- 1A2
- 2C9 *
- 2C19 *
- 2D6
- 2E1
- 3A4 **

* Many antidepressants and antipsychotic medications are metabolized by either CYP2C19 or CYP2D6. This often results in clinically significant drug-drug interactions when treating an individual (e.g. psychotic depression) with both an antidepressant and an antipsychotic. Likewise, concerns about toxicity arise when co-prescribing both a TCA and an SSRI (an accepted practice for treatment resistant depression).

** CYP3A4 is involved in the metabolism of more than fifty (50) percent of ALL drugs. Furthermore, it often serves as the second isoenzyme system or "safety net" involved in drug metabolism.

Cytochrome P450 Tutorial

- [Definitions](#)
- [Highlights of Cytochrome P450](#)
- [Humans and Cytochrome P450](#)
- [Aging and Cytochrome P450](#)
- [Phase 1 Metabolism](#)
- [Factors Affecting P450 Metabolism](#)
- [CYP3A4](#)

Return

- [Drug-Drug Interactions](#)
- [Supp-Drug Interactions](#)
- [Common Pitfalls](#)
- [P450 Interactions](#)
- [P450 and the Statins](#)
- [Managing Hepatic Enzyme](#)
- [Grapefruit Juice](#)

Information

- [Cytochrome P450 Overview](#)
- [Medications and Grapefruit Juice](#)

To the right are seven navigation buttons to additional information about the system; they are:

- Drug-Drug Interactions
- Supplement-Drug Interactions
- Common Clinical Pitfalls
- Cytochrome P450 Interactions
- P450 and the Statins
- Managing Hepatic Enzyme
- Grapefruit Juice

Drug Interactions

More than 90% of human drug oxidation is due to six CYP isoenzymes

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Cytochrome P450 Tutorial

[Definitions](#)
[Phase 1 Metabolism](#)

[Highlights of Cytochrome P450](#)
[Factors Affecting P450 Metabolism](#)

[Humans and Cytochrome P450](#)
[CYP3A4](#)

[Aging and Cytochrome P450](#)

Return

[Drug-Drug Interactions](#)
[Supp-Drug Interactions](#)
[Common Pitfalls](#)
[P450 Interactions](#)
[P450 and the Statins](#)
[Managing Hepatic Enzyme](#)
[Grapefruit Juice](#)

Information

[Cytochrome P450 Overview](#)
[Medications and Grapefruit Juice](#)

Below the navigation buttons are two documents entitled:

- Cytochrome P450 Overview
- Medications and Grapefruit Juice

Drug Interactions

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Cytochrome P450 Tutorial

[Definitions](#)
[Phase 1 Metabolism](#)

[Highlights of Cytochrome P450](#)
[Factors Affecting P450 Metabolism](#)

[Humans and Cytochrome P450](#)
[CYP3A4](#)

[Aging and Cytochrome P450](#)

Return

[Drug-Drug Interactions](#)
[Supp-Drug Interactions](#)
[Common Pitfalls](#)
[P450 Interactions](#)
[P450 and the Statins](#)
[Managing Hepatic Enzyme](#)
[Grapefruit Juice](#)

Information

[Cytochrome P450 Overview](#)
[Medications and Grapefruit Juice](#)

Drug-Drug Interactions Template

Drug Interactions

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Cytocrome P450 Tutorial

- [Definitions](#)
- [Highlights of Cytochrome P450](#)
- [Humans and Cytochrome P450](#)
- [Aging and Cytochrome P450](#)
- [Phase 1 Metabolism](#)
- [Factors Affecting P450 Metabolism](#)
- [CYP3A4](#)

Information

- [Cytochrome P450 Overview](#)
- [Medications and Grapefruit Juice](#)

Return

- Drug-Drug Interactions**
- Supp-Drug Interactions
- Common Pitfalls
- P450 Interactions
- P450 and the Statins
- Managing Hepatic Enzyme
- Grapefruit Juice

This template displays information on “**Some Classic Deadly Combinations**” of medications.

Drug - Drug Interactions

Some Classic Deadly Combinations

Aspirin or NSAIDs	+	Warfarin	=	Hemorrhage
Erythromycin	+	Seldane	=	Fatal Arrhythmia (TdP)
Nizolol	+	Propulsid	=	Fatal Arrhythmia (TdP)
Baycol	+	Lopid	=	Rhabdomyolysis
MAOI's	+	Tyramine	=	Hypertensive Crisis
CNS Depressants	+	CNS Depressants	=	Respiratory Depression
Viagra	+	Nitroglycerin	=	Fatal Hypotension
ACE Inhibitors	+	Potassium-Sparing Diuretics	=	Hyperkalemia

[Combining Serotonin Enhancing Drugs](#)

[Combinations That Can Decrease Glycemic Control](#)

[Combining Insulin-Enhancing Drugs](#)

[Combining Drugs That Affect Dopamine](#)

[Combining Vasodilators](#)

[Combinations That Interact With Glucophage](#)

[Drug Combinations that Increase QT Interval](#)

[Drug Combinations That Cause CNS Depression](#)

Return

At the bottom of the template are 8 documents on the following subjects:

- Combining Serotonin Enhancing Drugs
- Combinations that can Decrease Glycemic control
- Combining Insulin-Enhancing Drugs
- Combining Drugs that Affect Dopamine
- Combining Vasodilators
- Combinations That Interact with Glucophage
- Drug Combinations that increase QT Interval
- Drug Combinations that Cause CNS Depression

Drug - Drug Interactions

Some Classic Deadly Combinations

Aspirin or NSAIDs	+	Warfarin	=	Hemorrhage
Erythromycin	+	Seldane	=	Fatal Arrhythmia (TdP)
Nizoral	+	Propulsid	=	Fatal Arrhythmia (TdP)
Baycol	+	Lopid	=	Rhabdomyolysis
MAO's	+	Tyramine	=	Hypertensive Crisis
CNS Depressants	+	CNS Depressants	=	Respiratory Depression
Viagra	+	Nitroglycerin	=	Fatal Hypotension
ACE Inhibitors	+	Potassium-Sparing Diuretics	=	Hyperkalemia

Combining Serotonin Enhancing Drugs	Combining Vasodilators
Combinations That Can Decrease Glycemic Control	Combinations That Interact With Glucophage
Combining Insulin-Enhancing Drugs	Drug Combinations that Increase QT Interval
Combining Drugs That Affect Dopamine	Drug Combinations That Cause CNS Depression

Dietary Supplements & Drug Interactions

Drug Interactions

More than 90% of human drug oxidation is due to six CYP isoenzymes

- 1A2
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Cytochrome P450 Tutorial

Definitions	Phase 1 Metabolism
Highlights of Cytochrome P450	Factors Affecting P450 Metabolism
Humans and Cytochrome P450	CYP3A4
Aging and Cytochrome P450	

Information

[Cytochrome P450 Overview](#)

[Medications and Grapefruit Juice](#)

This template identifies the drug/drug interactions of 28 commonly used supplements which are not FDA regulated. By clicking in the box, and selecting the supplement, a pop-up will appear which will give you information about potential problems with the selected supplement.

Dietary Supplements & Drug Interactions

Some of the more common supplement-drug interactions effect...

- Blood Caogulation/Clotting
- Central Nervous System
- Blood Pressure
- Drug Metabolism

Select a supplement from the list below to view interaction information.

Di Supplement

5 HTP
ALA/GLA
Black Cohosh
CoQ10
Dong Quai (Angelica)
Echinacea
Ephedra (Ma Huang)
Feverfew
Fish Oils (EPA, DHA)
Garlic
German Chamomile
Ginger
Ginkgo
Ginseng
Glucosamine/Chondroitin
Goldenseal
Green Tea
Kava
L-Arginine
Licorice
L-Tryptophan
Melatonin
SAMA
St. John's Wort
Stinging Nettle
Valerian
Vitamin E
Yohimbe

Information

[What Herbs Should I Avoid?](#)

[Warfarin and Supplements](#)

[Tricyclic Antidepressants and S](#)

[SSRIs and Supplements](#)

[Statins and Supplements](#)

Dietary Supplements & Drug Interactions

Some of the more common supplement-drug interactions effect...

- Blood Caogulation/Clotting
- Central Nervous System
- Blood Pressure
- Drug Metabolism

Select a supplement from the list below to view interaction information.

Di Supp Fishoil

Fish Oils

Fish Oils may increase the risk of HYPotension in patients taking anihypertensive drugs.

Fish Oils (EPA, DHA) decrease platelet aggregation and may affect antithrombotic therapies such as Aspirin and Clopidogrel (Plavix) or anticoagulant therapies such as Enoxaparin (Lovenox), Heparin, and Warfarin (Coumadin).

Information

[What Herbs Should I Avoid?](#)

[Warfarin and Supplements](#)

[Tricyclic Antidepressants and S](#)

[SSRIs and Supplements](#)

[Statins and Supplements](#)

At the bottom of the template there are the following information pieces:

- What Herbs Should I Avoid?
- Warfarin and Supplements
- Tricyclic Antidepressants and Supplements
- SSRIs and Supplements
- Statins and Supplements

Dietary Supplements & Drug Interactions

Some of the more common supplement-drug interactions effect...

- Blood Coagulation/Clotting
- Central Nervous System
- Blood Pressure
- Drug Metabolism

Select a supplement from the list below to view interaction information.

Information

- [What Herbs Should I Avoid?](#)
- [Warfarin and Supplements](#)
- [Tricyclic Antidepressants and Supplements](#)
- [SSRIs and Supplements](#)
- [Statins and Supplements](#)

Common Pitfalls Template

This template lists 12 common pitfalls which increase the probability of experiencing drug/drug interactions.

Drug Interactions

More than 90% of human drug oxidation is due to six CYP isoenzymes

- 1A2
- 2C9 *
- 2C19 *
- 2D6
- 2E1

Return

Drug-Drug Interactions

Supp-Drug Interactions

Common Pitfalls

P450 Interactions

P450 and the Statins

Inhibiting Hepatic Enzyme

Grapefruit Juice

Information

[chrome P450 Overview](#)

[Interactions and Grapefruit Juice](#)

Common Clinical Pitfalls of Monitoring Drug Interactions

1. Relying on memory as to which drugs interact
2. Relying heavily on personal clinical experience
3. Failure to understand the statistics of rare events
4. Failure to consider the effects of dose on the outcome of the interaction
5. Assuming that all members of a drug class will interact homogenously
6. Failure to appreciate the time-course of drug interactions
7. Failure to consider the effects of sequence of administration
8. Assuming that separating doses will circumvent absorption interactions
9. Assuming a similar magnitude of drug interactions among patients
10. Assuming that all routes of administration interact in the same way
11. Failure to consider the pharmacogenetics of the patient
12. Failure to consider herbal or dietary habits of patient or drug abuse potential

Ways to minimize the impact or frequency of interactions...

- Knowledge of mechanisms and time course
- Increased monitoring
- Use the lowest effective dose
- Discontinue ineffective therapies (clean out useless meds)
- Continually update drug history

OK Cancel

Then the template displays 5 ways to minimize the impact or frequency of interactions.

Drug Interactions

More than 90% of human drug oxidation is due to six CYP isoenzymes

- 1A2
- 2C9 *
- 2C19 *
- 2D6
- 2E1
- 3A4 **

Return

Drug-Drug Interactions

Supp-Drug Interactions

Common Pitfalls

P450 Interactions

P450 and the Statins

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Grapefruit Juice

Information
[chrome P450 Overview](#)
[Interactions and Grapefruit Juice](#)

DI Drugpitfalls

Common Clinical Pitfalls of Monitoring Drug Interactions

1. Relying on memory as to which drugs interact
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Ways to minimize the impact or frequency of interactions...

- Knowledge of mechanisms and time course
- Increased monitoring
- Use the lowest effective dose
- Discontinue ineffective therapies (clean out useless meds)
- Continually update drug history

OK

Cancel

P450 Interactions Template

This template presents a list of 32 classes of drugs. When a class is marked, the box below will present a pick list of all of the drugs in that class which interact with the P450 system.

Drug Interactions

More than 90% of human drug oxidation is due to six CYP isoenzymes

- 1A2
- 2C9 *
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- 2E1
- 3A4 **

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Cytochrome P450 Tutorial

[Definitions](#) [Phase 1 Metabolism](#)
[Highlights of Cytochrome P450](#) [Factors Affecting P450 Metabolism](#)
[Humans and Cytochrome P450](#) [CYP3A4](#)
[Aging and Cytochrome P450](#)

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[Cytochrome P450 Overview](#)
[Medications and Grapefruit Juice](#)

Return

Drug-Drug Interactions

Supp-Drug Interactions

Common Pitfalls

P450 Interactions

P450 and the Statins

Managing Hepatic Enzyme

Grapefruit Juice

DI Pop

1. First select a category of medication.

☐ Acid Reflux

☐ Antipsychotics

☐ Cough Suppressant

☐ Nausea/Vomiting

☐ Alzheimer's

☐ Arrhythmia

☐ Depression

☐ Nerves

☐ Antacid

☐ Asthma

☐ Diabetic

☐ NSAIDs

☐ Antibiotics

☐ Benzodiazepines

☐ Diuretics

☐ Pain Relievers

☐ Anticoagulants

☐ Beta Blockers

☐ Fungal

☐ Steroids

☐ Angiotensin Receptor Blockers

☐ Calcium Blockers

☐ Hormones

☐ Unique

☐ Antiepileptics

☐ Cancer

☐ Muscle Relaxer

☐ Viral

☐ Antihistamines

☒ Cholesterol

☐ Narcotics

☐ Unusual Interactions

2. Then select a drug from the box below to view the information.

Din Cholesterol

Atorvastatin

Cerivastatin

Fluvastatin

Lovastatin

Simvastatin

Close

the cytochrome(s)

Inhibitors

(inhibit P450 metabolism)

Inducers

(increase P450 metabolism therefore decreasing the level of the substrate)

OK

Cancel

11 of 17

When a drug is selected, the following will be displayed:

- **Substrate** – the selected drug. The Cytochrome P450 enzyme which affects the substrate, will be displayed.
- **Inhibitors** – those drugs which will increase the concentration in the blood of the target.
- **Inducers** -- those drugs which will decrease the concentration in the blood of the target drug.

The screenshot shows a software window titled "Di Pop" with a close button in the top right corner. The window is divided into two main sections. The first section, "1. First select a category of medication.", contains a grid of radio buttons for various medical categories: Acid Reflux, Antipsychotics, Cough Suppressant, Nausea/Vomiting, Alzheimers, Arrhythmia, Depression, Nerves, Antacid, Asthma, Diabetic, NSAIDs, Antibiotics, Benzodiazepines, Diuretics, Pain Relievers, Anticoagulants, Beta Blockers, Fungal, Steroids, Angiotensin Receptor Blockers, Calcium Blockers, Hormones, Unique, Antiepileptics, Cancer, Muscle Relaxer, Viral, Antihistamines, Cholesterol, Narcotics, and Unusual Interactions. The "Unusual Interactions" option is selected. The second section, "2. Then select a drug from the box below to view the information.", features a text box containing "erivastatin" and a dropdown menu showing "CYP3A4". Below these are two columns: "Inhibitors" (inhibit P450 metabolism therefore increasing the level of the substrate) and "Inducers" (increase P450 metabolism therefore decreasing the level of the substrate). The Inhibitors list includes Ketoconazole, Itraconazole, Fluconazole, Erythromycin, Clarithromycin, Tricyclic Antidepressants, Nefazodone, Venlafaxine, Fluvoxamine, Fluoxetine, Sertraline, Cyclosporine, Tacrolimus, Omeprazole, Lansoprazole, Calcium Channel Blockers, Midazolam, Corticosteroids, Grapefruit Juice, and Tamoxifen. The Inducers list includes Phenytoin, Phenobarbital, Barbiturates, Rifampin, Erythromycin, Omeprazole, Lansoprazole, Dexamethasone, Sex Steroids, Cyclophosphamide, and Carbamazepine. At the bottom are "OK" and "Cancel" buttons.

1. First select a category of medication.

☐ Acid Reflux ☐ Antipsychotics ☐ Cough Suppressant ☐ Nausea/Vomiting

☐ Alzheimers ☐ Arrhythmia ☐ Depression ☐ Nerves

☐ Antacid ☐ Asthma ☐ Diabetic ☐ NSAIDs

☐ Antibiotics ☐ Benzodiazepines ☐ Diuretics ☐ Pain Relievers

☐ Anticoagulants ☐ Beta Blockers ☐ Fungal ☐ Steroids

☐ Angiotensin Receptor Blockers ☐ Calcium Blockers ☐ Hormones ☐ Unique

☐ Antiepileptics ☐ Cancer ☐ Muscle Relaxer ☐ Viral

☐ Antihistamines ☒ Cholesterol ☐ Narcotics ☐ **Unusual Interactions**

2. Then select a drug from the box below to view the information.

erivastatin is a substrate of the cytochrome(s) CYP3A4

Inhibitors
(inhibit P450 metabolism therefore increasing the level of the substrate)

Ketoconazole; Itraconazole; Fluconazole; Erythromycin;
Clarithromycin; Tricyclic Antidepressants; Nefazodone; Venlafaxine;
Fluvoxamine; Fluoxetine; Sertraline; Cyclosporine; Tacrolimus;
Omeprazole; Lansoprazole; Calcium Channel Blockers; Midazolam;
Corticosteroids; Grapefruit Juice; Tamoxifen

Inducers
(increase P450 metabolism therefore decreasing the level of the substrate)

Phenytoin; Phenobarbital; Barbiturates; Rifampin; Erythromycin;
Omeprazole; Lansoprazole; Dexamethasone; Sex Steroids;
Cyclophosphamide; Carbamazepine

OK Cancel

DI Pop

1. First select a category of medication.

<input type="radio"/> Acid Reflux	<input type="radio"/> Antipsychotics	<input type="radio"/> Cough Suppressant	<input type="radio"/> Nausea/Vomiting
<input type="radio"/> Alzheimers	<input type="radio"/> Arrhythmia	<input type="radio"/> Depression	<input type="radio"/> Nerves
<input type="radio"/> Antacid	<input type="radio"/> Asthma	<input type="radio"/> Diabetic	<input type="radio"/> NSAIDs
<input type="radio"/> Antibiotics	<input type="radio"/> Benzodiazepines	<input type="radio"/> Diuretics	<input type="radio"/> Pain Relievers
<input type="radio"/> Anticoagulants	<input type="radio"/> Beta Blockers	<input type="radio"/> Fungal	<input type="radio"/> Steroids
<input type="radio"/> Angiotensin Receptor Blockers	<input type="radio"/> Calcium Blockers	<input type="radio"/> Hormones	<input type="radio"/> Unique
<input type="radio"/> Antiepileptics	<input type="radio"/> Cancer	<input type="radio"/> Muscle Relaxer	<input type="radio"/> Viral
<input type="radio"/> Antihistamines	<input checked="" type="radio"/> Cholesterol	<input type="radio"/> Narcotics	<input type="radio"/> Unusual Interactions

2. Then select a drug from the box below to view the information.

Cerivastatin is a substrate of the cytochrome(s) CYP3A4

Inhibitors (inhibit P450 metabolism therefore increasing the level of the substrate)

Inducers (increase P450 metabolism therefore decreasing the level of the substrate)

DI Inducers

Cytochrome P450 Inducers

An inducer is a compound that "speeds up" the metabolism of a substrate by a given enzyme.

For example, carbamazepine speeds up the metabolism of clozapine (substrate) by both CYP1A2 and CYP3A4. In this case carbamazepine acts as an inducer. As a result, clozapine plasma levels will fall. Conversely, if carbamazepine is discontinued, clozapine levels will rise. This can result in adverse effects such as an unanticipated seizure.

Cytochrome P450 and the Statins

This template lists the common statins in order from those which are most sensitive to the Cytochrome P450 System down to those which are the least sensitive.

Drug Interactions

More than 90% of human drug oxidation is due to six CYP isoenzymes

- 1A2
- 2C9 *
- 2C19 *
- 2D6
- 2E1
- 3A4 **

* Many antidepressants and antipsychotic medications are metabolized by either CYP2C19 or CYP2D6. This often results in clinically significant drug-drug interactions when treating an individual (e.g. psychotic depression) with both an antidepressant and an antipsychotic. Likewise, concerns about toxicity arise when co-prescribing both a TCA and an SSRI (an accepted practice for treatment resistant depression).

** CYP3A4 is involved in the metabolism of more than fifty (50) percent of ALL drugs. Furthermore, it often serves as the second isoenzyme system or "safety net" involved in drug metabolism.

Return

Drug-Drug Interactions

Supp-Drug Interactions

Common Pitfalls

P450 Interactions

P450 and the Statins

Managing hepatic enzyme

Grapefruit Juice

Cytochrome P450 Tutorial

Definitions	Phase 1 Metabolism
Highlights of Cytochrome P450	Factors Affecting P450 Metabolism
Humans and Cytochrome P450	CYP3A4
Aging and Cytochrome P450	

Information

[Cytochrome P450 Overview](#)

[Medications and Grapefruit Juice](#)

When you check the radial box next to the name of the statin, the P450 enzyme which detoxifies it, the inhibitors and the inducers will appear below. There is also a comment box.

Di P450statins

Cytochrome P450 and the Statins

Select a statin from the list below...

*** Organized in descending order of sensitivity to P450 metabolism. Those at the bottom of the list are the LEAST sensitive to P450 metabolism.*

☒ Simvastatin (Zocor)
☐ Lovastatin (Mevacor)
☐ Atorvastatin (Lipitor)
☐ Fluvastatin (Lescol)
☐ Rosuvastatin (Crestor)
☐ Pravastatin (Pravachol)

Substrate

Simvastatin (Zocor) is metabolized by CYP3A4.

Some Common Inhibitors (raise serum concentration levels) *** Scroll in box for more...*

Clarithromycin, Erythromycin, Diltiazem, Verapamil (max Zocor 20 mg qd), Itraconazole, Ritonavir, Nelfinavir, Cyclosporine (initially Zocor 5 mg qd, max 10 mg qd), Grapefruit Juice, Amiodorone (max Zocor 20 mg qd). If fibrates such as lipid or niacin greater than 1 gram per day, then avoid Zocor. If

Some Common Inducers (lowers serum concentration levels)

Carbamazepine, Rifampin, St. John's Wort, Phenobarbital, Phenytoin

Comments

Simvastatin (Zocor) and Lovastatin (Mevacor) are the most dependent upon the CYP3A4 enzyme and are therefore the most sensitive to inhibitors of this enzyme with resultant increase of toxicity of these statins.

OK Cancel

Managing Hepatic Enzyme Induction Template

This template provides information on 4 principles of how to avoid problems with drug toxicity.

The screenshot shows a medical software interface. At the top, a window titled 'Drug Interactions' contains text about CYP isoenzymes and a list of them. Below this, a dialog box titled 'Managing Hepatic Enzyme Induction' is open. The dialog box has a title bar 'DI P450hepatic' and a close button. It contains two columns of lists: 'Prescription' and 'Nonprescription Agents'. Below these lists are four bullet points explaining the effects of hepatic enzyme induction. At the bottom of the dialog box are 'OK' and 'Cancel' buttons. To the right of the dialog box, a vertical menu is visible with options like 'Return', 'Drug-Drug Interactions', 'Supp-Drug Interactions', 'Common Pitfalls', 'P450 Interactions', 'P450 and the Statins', and 'Managing Hepatic Enzyme'. The 'Managing Hepatic Enzyme' option is highlighted with a red box. Below the menu, there are links for 'Overview' and 'Grapefruit Juice'.

Drug Interactions

More than 90% of human drug oxidation is due to six CYP isoenzymes:

- 1A2
- 2C9 *
- 2C19 *
- 2D6
- 2E1
- 3A4 **

* Many antidepressants and antipsychotic medications are metabolized by either CYP2C19 or CYP2D6. This often results in clinically significant drug-drug interactions when treating an individual (e.g. psychotic depression) with both an antidepressant and an antipsychotic. Likewise, concerns about toxicity arise when co-prescribing both a TCA and an SSRI (an accepted practice for treatment resistant depression).

Managing Hepatic Enzyme Induction

Prescription	Nonprescription Agents
1. Carbamazepine	1. Chronic cigarette smoking
2. Dexamethasone	2. Chronic ethanol use
3. Isoniazid	3. Chronic marijuana smoking
4. Modafinil	4. St. John's Wort
5. Omeprazole	
6. Oxcarbazepine	
7. Phenobarbital	
8. Phenytoin	
9. Prednisone	
10. Primidone	
11. Rifampin	

- Inducing agents can lower plasma levels of co-administered medications that are also metabolized by the liver.
- Most psychotropics are metabolized by the liver, and their therapeutic effect requires a minimum plasma concentration.
- Hepatic enzyme induction can result in subtherapeutic plasma levels and inadequate drug trials of prescribed psychotropics.
- Assume that any inducing agent may lower plasma levels and alter the efficacy of co-administered drugs that are also metabolized by the liver. Observe carefully, monitor plasma levels, use incremental dosing to assess and compensate for induction effects.

OK Cancel

[Overview](#)
[Grapefruit Juice](#)

Grapefruit Juice Template

This template displays 5 important facts about grapefruit juice and the Cytochrome P450 systems.

The screenshot shows a web application interface. At the top, there is a header 'Drug Interactions'. Below it, a modal window titled 'DI P450grapefruit' is open. The modal window has a title bar with a close button. The main content of the modal is titled 'Cytochrome P450 and Grapefruit Juice' and contains five bullet points:

- Grapefruit juice is a "suicide" inhibitor of CYP3A4.
- It destroys some of the CYP3A4 in the small intestine, and the body must make new CYP3A4 to reestablish normal activity.
- The effect of grapefruit juice on CYP3A4 can last long after it passes through the small intestine and is eliminated from the body.
- Therefore, one cannot avoid the grapefruit juice-drug interactions by staggering juice consumption and drug administration.
- Frequent consumption of grapefruit juice (several times a day for several days) can lead to inhibition of CYP3A4 even for 2 or 3 days after the grapefruit juice is stopped.

At the bottom of the modal window are 'OK' and 'Cancel' buttons. To the right of the modal window, there is a 'Return' button and a list of links: 'Drug-Drug Interactions', 'Supp-Drug Interactions', 'Common Pitfalls', 'P450 Interactions', 'P450 and the Statins', 'Managing Hepatic Enzyme', and 'Grapefruit Juice'. The 'Grapefruit Juice' link is highlighted with a red box. Below the links is an 'Information' section with two links: 'Cytochrome P450 Overview' and 'Medications and Grapefruit Juice'.