

## Rx Test

Specimen No: SAMPLE000.0-A08  
Physician: Ima Test

DOB: 01/01/2000  
Sex: FEMALE

Sample Collection: Jan. 01, 2021 08:00 EST  
Sample Analysis: Jan. 04, 2021 08:00 EST

MEDICATION	DOSAGE FREQUENCY	RESULT	DDI*	INDICATION
<b>IN THE MEDICAL RECORD:</b>				
AMLODIPINE Norvasc	10 mg DAILY			Cardiovascular agents / Calcium channel blocking agents
BREXPIPIRAZOLE REXULTI	3 mg DAILY			Psychotherapeutic agents / Antipsychotics
<b>NOT IN THE MEDICAL RECORD:</b>				
BUPRENORPHINE Subutex	Not in medical record			Central nervous system agents / Analgesics
DICLOFENAC Voltaren	Not in medical record			Central nervous system agents / Analgesics
LORAZEPAM Ativan	Not in medical record			Central nervous system agents / Anxiolytics, sedatives, and hypnotics
NALOXONE Narcan	Not in medical record			Central nervous system agents / Other CNS drugs

### Result:

-  Above minimum reference value
-  Below minimum reference value\*

\*Drug-Drug Interaction (DDI): See details on the following pages.

-  Major - The use of these medications together is contraindicated. Rare exceptions may exist.
-  Moderate - The use of these medications together may be contraindicated in a select group of patients. The patient should be monitored for possible manifestations of the interaction.

A medication may be below our reference value in the sample due to various reasons including time between last dose and sample collection, non-adherence, taking only as needed, and/or rapid metabolism.

### MEDICATIONS NOT IN ASSAY:

LEVOTHYROXINE (75 MCG)

**Medical record transcription accuracy is the responsibility of the ordering physician**

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## Interaction Details

### NALOXONE / DICLOFENAC: **MAJOR**

#### Evidence Level Established

##### Description

The metabolism of Diclofenac can be decreased when combined with Naloxone. The subject drug is a strong CYP3A4 inhibitor and the affected drug is metabolized by CYP3A4. Concomitant administration will decrease the metabolism of the affected drug, increasing serum concentrations, as well as the risk and severity of adverse effects.

##### Management

The combination is contraindicated. If no alternatives can be found, adjust doses according to instructions on the label and monitor the patient carefully.

##### References

Lynch T, Price A: The effect of cytochrome P450 metabolism on drug response, interactions, and adverse effects. Am Fam Physician. 2007 Aug 1;76(3):391-6. :: Zhou SF: Drugs behave as substrates, inhibitors and inducers of human cytochrome P450 3A4. Curr Drug Metab. 2008 May;9(4):310-22. :: Klein K, Zanger UM: Pharmacogenomics of Cytochrome P450 3A4: Recent Progress Toward the "Missing Heritability" Problem. Front Genet. 2013 Feb 25;4:12. doi: 10.3389/fgene.2013.00012. eCollection 2013.

### NALOXONE / LORAZEPAM: **MAJOR**

#### Evidence Level Established

##### Description

The metabolism of Lorazepam can be decreased when combined with Naloxone. The subject drug is a strong CYP3A4 inhibitor and the affected drug is metabolized by CYP3A4. Concomitant administration will decrease the metabolism of the affected drug, increasing serum concentrations, as well as the risk and severity of adverse effects.

##### Management

The combination is contraindicated. If no alternatives can be found, adjust doses according to instructions on the label and monitor the patient carefully.

##### References

Lynch T, Price A: The effect of cytochrome P450 metabolism on drug response, interactions, and adverse effects. Am Fam Physician. 2007 Aug 1;76(3):391-6. :: Zhou SF: Drugs behave as substrates, inhibitors and inducers of human cytochrome P450 3A4. Curr Drug Metab. 2008 May;9(4):310-22. :: Klein K, Zanger UM: Pharmacogenomics of Cytochrome P450 3A4: Recent Progress Toward the "Missing Heritability" Problem. Front Genet. 2013 Feb 25;4:12. doi: 10.3389/fgene.2013.00012. eCollection 2013.

### NALOXONE / AMLODIPINE: **MODERATE**

#### Evidence Level Established

##### Description

The metabolism of Amlodipine can be decreased when combined with Naloxone. The FDA label for amlodipine indicates that strong inhibitors of the CYP3A4 enzyme may lead to decreased metabolism and increased accumulation of amlodipine, which is a CYP3A4 substrate [A32032]. This may result in hypotension or an increase in the adverse effects of amlodipine.

##### Management

Amlodipine should be used with caution when administered concomitantly with CYP3A4 enzyme inhibitors [F3757], [FDA label]. Monitor for edema and regularly monitor blood pressure if this combination is coadministered. Some combinations may be contraindicated.

##### References

Zhu Y, Wang F, Li Q, Zhu M, Du A, Tang W, Chen W: Amlodipine metabolism in human liver microsomes and roles of CYP3A4/5 in the dihydropyridine dehydrogenation. Drug Metab Dispos. 2014 Feb;42(2):245-9. doi: 10.1124/dmd.113.055400. Epub 2013 Dec 3.

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### NALOXONE / BREXPIPIRAZOLE: **MODERATE**

#### Evidence Level Established

##### Description

The metabolism of Brexpiprazole can be decreased when combined with Naloxone. Brexpiprazole is partially metabolized by CYP3A4, and thus, concomitant administration of brexpiprazole with a strong CYP3A4 inhibitor will reduce the metabolism and increase the serum concentrations of brexpiprazole.[A38385, L717] Elevated serum levels of brexpiprazole may increase the risk of adverse effects associated with this medication.

##### Management

Reduce the dose of brexpiprazole by 50% when also using a strong CYP3A4 inhibitor.[L717] Consult the official product monograph for additional information if the patient is a CYP2D6 poor metabolizer or if they are also taking a CYP2D6 inhibitor.

##### References

Eaves S, Rey JA: Brexpiprazole (Rexulti): A New Monotherapy for Schizophrenia and Adjunctive Therapy for Major Depressive Disorder. P T. 2016 Jul;41(7):418-22.

### BREXPIPIRAZOLE / BUPRENORPHINE: **MODERATE**

#### Evidence Level Established

##### Description

Brexpiprazole may increase the central nervous system depressant (CNS depressant) activities of Buprenorphine. Buprenorphine is a central nervous system depressant. Administering other drugs within the central nervous system (CNS) depressant class of drugs may potentiate these effects. Significant respiratory depression and death have been reported in association with buprenorphine, especially when taken by the intravenous (IV) route in combination with other CNS depressants.

##### Management

According to the FDA label, consider reduced doses of other CNS depressants, and avoid such drugs in patients at high risk of buprenorphine overuse/self-injection. Initiate buprenorphine patches (Butrans brand) at 5 mcg/hr when used with other CNS depressants. Monitor closely for signs of CNS depression.

##### References

### LORAZEPAM / BUPRENORPHINE: **MODERATE**

#### Evidence Level Established

##### Description

Lorazepam may increase the central nervous system depressant (CNS depressant) activities of Buprenorphine. Buprenorphine is a central nervous system depressant. Administering other drugs within the central nervous system (CNS) depressant class of drugs may potentiate these effects. Significant respiratory depression and death have been reported in association with buprenorphine, especially when taken by the intravenous (IV) route in combination with other CNS depressants.

##### Management

According to the FDA label, consider reduced doses of other CNS depressants, and avoid such drugs in patients at high risk of buprenorphine overuse/self-injection. Initiate buprenorphine patches (Butrans brand) at 5 mcg/hr when used with other CNS depressants. Monitor closely for signs of CNS depression.

##### References

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