PMP Test

Specimen No: SA0000001.1-P01
Physician: Ima Test

DOB: 01/01/2000
Sex: MALE

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

MEDICATION	DOSAGE FREQUENCY	REFERENCE RANGE LOWER LIMIT	REFERENCE RANGE UPPER LIMIT	CRITICAL VALUE	DDI*
IN THE MEDICAL RECORD:					
ACETAMINOPHEN Tylenol	325 mg PRN	Not Detected/PRN			▲
GABAPENTIN Neurontin	300 mg DAILY	2000 ng/mL	20000 ng/mL		⬢ ▲
OXYMORPHONE Opana	8 mg PRN	Detected			▲
NOT IN THE MEDICAL RECORD:					
ARIPIPRAZOLE Abilify	Not in medical record	150 ng/mL	500 ng/mL		▲
TRAMADOL Ultram	Not in medical record	615 ng/mL	1222 ng/mL		▲

Reference Range:

10.1 Within Range

999 Out of Range

***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.

MEDICATIONS NOT IN ASSAY:

LITHIUM (300 MG) ▲

Medical record transcription accuracy is the responsibility of the ordering physician

This PrecisMed™ test was developed and its performance characteristics determined by Phenomics Health™ Inc. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes, though results should not be intended for use as a sole means for a clinical diagnosis or patient management decisions. It should not be regarded as investigational or for research. Phenomics Health™ Inc. tests are not chiral specific and will not distinguish between enantiomeric forms of certain drugs. Use professional judgement when interpreting the results of the detected medications with consideration for the patient's known medications.

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Report Released: Feb. 04, 2022 12:50 EST
Analysis: Phenomics Health™ Inc.
Certified: N/A
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Interaction Details

GABAPENTIN / ACETAMINOPHEN: **MAJOR**

Evidence Level Likely Established

Description

The risk or severity of methemoglobinemia can be increased when Lidocaine is combined with Acetaminophen. Methemoglobinemia, condition characterized by increased quantities of hemoglobin in which the iron of heme is oxidized to the ferric (Fe3+) form [A37584], can occur either in congenital or acquired forms and is often manifested with grey cyanosis. It is also caused from exposure to drugs that directly oxidize hemoglobin to methemoglobin [A37584] or those that require metabolic activation to an oxidising species [A1745]. The risk for developing drug-induced methemoglobinemia may be elevated with the concomitant use of other agents known to cause the same adverse event due to an additive effect, and the duration or intensity of methemoglobinemia may be worsened. This interaction may be more profound in patients with glucose-6-phosphate dehydrogenase deficiency or congenital or idiopathic methemoglobinemia. Young infants under the age of 12 months may be particularly susceptible to this complication because of their low stomach acid production, large number of nitrite-reducing bacteria, and the relatively easy oxidation of fetal hemoglobin [A37584]. Small infants have lower erythrocyte levels of cytochrome b reductase [A37584].

Management

Caution should be exercised when methemoglobinemia-associated agent is used in conjunction with other agents with potential to cause methemoglobinemia. If methemoglobinemia develops, the use of these agents should be discontinued and appropriate medical intervention should be initiated. Such combination use should be avoided in patients with glucose-6-phosphate dehydrogenase deficiency or congenital or idiopathic methemoglobinemia, or in infants under the age of 12 months.

References

Rehman HU: Methemoglobinemia. West J Med. 2001 Sep;175(3):193-6. :: Coleman MD, Coleman NA: Drug-induced methaemoglobinaemia. Treatment issues. Drug Saf. 1996 Jun;14(6):394-405. :: Chalfa R, Elliott CG, Mathewson HS: Drug-induced methemoglobinemia in a healthy 20-year-old soldier undergoing shoulder surgery. Nurse Anesth. 1993 Dec;4(4):202-4. :: Turner MD, Karlis V, Glickman RS: The recognition, physiology, and treatment of medication-induced methemoglobinemia: a case report. Anesth Prog. 2007 Fall;54(3):115-7. doi: 10.2344/0003-3006(2007)54[115:TRPATO]2.0.CO;2.

GABAPENTIN / LITHIUM (not in assay): **MODERATE**

Evidence Level Likely Established

Description

Gabapentin enacarbil may decrease the excretion rate of Lithium carbonate which could result in a higher serum level. This interaction is related to the fact that both drugs are mainly excreted renally. Theoretically, this drug interaction will produce a decrease in the elimination of either drug via competition for renal excretion, producing an increase in serum concentration of either the drug or its metabolites. The increased serum concentration of either drug or its metabolites may lead to increased adverse effects. It is important to consider this interaction when drugs with a narrow therapeutic index are administered, as a change in the serum concentration of these agents may lead to serious effects. Narrow therapeutic index drugs must be maintained within a certain range to ensure safety and efficacy.[A37372,A37373,A173998,A174001,A174004]

Management

Monitor the patient closely when these drugs are given concomitantly. Change or adjust the dose of either drug as required. Refer to individual product monographs for specific guidance on dosing or monitoring. Guidance will vary according to the drugs being used.

References

Tamargo J, Le Heuzey JY, Mabo P: Narrow therapeutic index drugs: a clinical pharmacological consideration to flecainide. Eur J Clin Pharmacol. 2015 May;71(5):549-67. doi: 10.1007/s00228-015-1832-0. Epub 2015 Apr 15. :: Greenberg RG, Melloni C, Wu H, Gonzalez D, Ku L, Hill KD, Hornik CP, Cohen-Wolkowiez M, Guptill JT: Therapeutic Index Estimation of Antiepileptic Drugs: A Systematic Literature Review Approach. Clin Neuropharmacol. 2016 Sep-Oct;39(5):232-40. doi: 10.1097/WNF.0000000000000172. :: Doogue MP, Polasek TM: Drug dosing in renal disease. Clin Biochem Rev. 2011 May;32(2):69-73. :: Lepist EI, Ray AS: Renal Transporter-Mediated Drug-Drug Interactions: Are They Clinically Relevant? J Clin Pharmacol. 2016 Jul;56 Suppl 7:S73-81. doi: 10.1002/jcph.735. :: Lea-Henry TN, Carland JE, Stocker SL, Sevastos J, Roberts DM: Clinical Pharmacokinetics in Kidney Disease: Fundamental Principles. Clin J Am Soc Nephrol. 2018 Jul 6;13(7):1085-1095. doi: 10.2215/CJN.00340118. Epub 2018 Jun 22.

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TRAMADOL / GABAPENTIN: **MODERATE**

Evidence Level Established

Description

The risk or severity of CNS depression can be increased when Gabapentin enacarbil is combined with Tramadol. Due to additive pharmacodynamic effects, the concomitant use of tramadol with other CNS depressants, such as the subject drug, may result in profound CNS depression.[L9257] This combination of agents may increase the risk of sedation, respiratory depression, coma, and death.[L9257]

Management

Reserve the combined use of tramadol with other CNS depressants for use in patients for whom alternatives are inappropriate. Limit the dosages and duration of treatment with concomitant CNS depressants to the minimum required. Patients should be monitored closely for signs and symptoms of excessive CNS depression.

References

TRAMADOL / OXYMORPHONE: **MODERATE**

Evidence Level Established

Description

The risk or severity of serotonin syndrome can be increased when Oxymorphone is combined with Tramadol. Tramadol has been implicated in the development of serotonin syndrome, [A173980,L9257] particularly in combination with other medications that can precipitate or contribute to serotonin syndrome, such as the subject drug. Symptoms of serotonin syndrome include altered mental status, neuromuscular abnormalities, and autonomic hypersensitivity.[A173980]

Management

If concomitant therapy with multiple serotonergic agents is necessary, the patient should be monitored carefully for the above signs and symptoms of serotonin syndrome, particularly during initiation of therapy and with any increases in dose. If serotonin syndrome is suspected, tramadol should be discontinued immediately.[L9257]

References

Beakley BD, Kaye AM, Kaye AD: Tramadol, Pharmacology, Side Effects, and Serotonin Syndrome: A Review. Pain Physician. 2015 Jul-Aug;18(4):395-400.

TRAMADOL / ARIPIPRAZOLE: **MODERATE**

Evidence Level Established

Description

The risk or severity of serotonin syndrome can be increased when Aripiprazole lauroxil is combined with Tramadol. Tramadol has been implicated in the development of serotonin syndrome, [A173980,L9257] particularly in combination with other medications that can precipitate or contribute to serotonin syndrome, such as the subject drug. Symptoms of serotonin syndrome include altered mental status, neuromuscular abnormalities, and autonomic hypersensitivity.[A173980]

Management

If concomitant therapy with multiple serotonergic agents is necessary, the patient should be monitored carefully for the above signs and symptoms of serotonin syndrome, particularly during initiation of therapy and with any increases in dose. If serotonin syndrome is suspected, tramadol should be discontinued immediately.[L9257]

References

Beakley BD, Kaye AM, Kaye AD: Tramadol, Pharmacology, Side Effects, and Serotonin Syndrome: A Review. Pain Physician. 2015 Jul-Aug;18(4):395-400.

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TRAMADOL / LITHIUM (not in assay): **MODERATE**

Evidence Level Established

Description

The risk or severity of CNS depression can be increased when Lithium carbonate is combined with Tramadol. Due to additive pharmacodynamic effects, the concomitant use of tramadol with other CNS depressants, such as the subject drug, may result in profound CNS depression.[L9257] This combination of agents may increase the risk of sedation, respiratory depression, coma, and death.[L9257]

Management

Reserve the combined use of tramadol with other CNS depressants for use in patients for whom alternatives are inappropriate. Limit the dosages and duration of treatment with concomitant CNS depressants to the minimum required. Patients should be monitored closely for signs and symptoms of excessive CNS depression.

References

OXYMORPHONE / GABAPENTIN: **MODERATE**

Evidence Level Likely Established

Description

The risk or severity of adverse effects can be increased when Oxymorphone is combined with Gabapentin enacarbil. The use of central nervous system depressants may potentiate the effects of another drug in the same class. The concomitant use of opioids, including certain cough medications, with benzodiazepines, or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of similar pharmacologic properties, it is reasonable to expect similar risk with concomitant use of opioid cough medications and benzodiazepines, other CNS depressants, or alcohol. The risk of CNS depression resulting from the combination of central nervous system depressant drugs varies according to the degree of sedation from each agent. Effects may range from mild sedation to severe and lethal respiratory/cardiovascular depression.

Management

Avoid concomitant use of CNS depressants. If it is deemed necessary to combine CNS depressants, consider lowering the doses of CNS depressants when used concomitantly. Monitor closely for signs of CNS depression. Each interaction between CNS depressants should be considered individually. The degree/severity of interaction largely depends on the CNS depressant agents being administered concomitantly. Refer to individual product monographs for guidance on dosing and monitoring.

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OXYMORPHONE / ARIPIPRAZOLE: **MODERATE**

Evidence Level Likely Established

Description

The risk or severity of adverse effects can be increased when Oxymorphone is combined with Aripiprazole lauroxil. The use of central nervous system depressants may potentiate the effects of another drug in the same class. The concomitant use of opioids, including certain cough medications, with benzodiazepines, or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of similar pharmacologic properties, it is reasonable to expect similar risk with concomitant use of opioid cough medications and benzodiazepines, other CNS depressants, or alcohol. The risk of CNS depression resulting from the combination of central nervous system depressant drugs varies according to the degree of sedation from each agent. Effects may range from mild sedation to severe and lethal respiratory/cardiovascular depression.

Management

Avoid concomitant use of CNS depressants. If it is deemed necessary to combine CNS depressants, consider lowering the doses of CNS depressants when used concomitantly. Monitor closely for signs of CNS depression. Each interaction between CNS depressants should be considered individually. The degree/severity of interaction largely depends on the CNS depressant agents being administered concomitantly. Refer to individual product monographs for guidance on dosing and monitoring.

References

OXYMORPHONE / LITHIUM (not in assay): **MODERATE**

Evidence Level Likely Established

Description

The risk or severity of adverse effects can be increased when Oxymorphone is combined with Lithium carbonate. The use of central nervous system depressants may potentiate the effects of another drug in the same class. The concomitant use of opioids, including certain cough medications, with benzodiazepines, or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of similar pharmacologic properties, it is reasonable to expect similar risk with concomitant use of opioid cough medications and benzodiazepines, other CNS depressants, or alcohol. The risk of CNS depression resulting from the combination of central nervous system depressant drugs varies according to the degree of sedation from each agent. Effects may range from mild sedation to severe and lethal respiratory/cardiovascular depression.

Management

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ARIPIPRAZOLE / ACETAMINOPHEN: **MODERATE**

Evidence Level Established

Description

The metabolism of Aripiprazole lauroxil can be increased when combined with Acetaminophen. Aripiprazole is metabolized by CYP3A4 enzymes, therefore, concomitant administration of aripiprazole and its prodrugs with inducers of CYP3A4 of any strength is not recommended as the serum concentration of aripiprazole and prodrugs may be significantly decreased [F1189].

Management

Double the oral aripiprazole or aripiprazole prodrug dose and closely monitor the clinical response. Reduce the oral dose of aripiprazole to 10-15 mg/day if the inducer is discontinued. Avoid the use of CYP3A4 inducers for more than 14 days with extended-release injectable forms of aripiprazole or its prodrug.

References

Molden E, Lunde H, Lunder N, Refsum H: Pharmacokinetic variability of aripiprazole and the active metabolite dehydroaripiprazole in psychiatric patients. Ther Drug Monit. 2006 Dec;28(6):744-9. doi: 10.1097/01.ftd.0000249944.42859.bf. :: Azuma J, Hasunuma T, Kubo M, Miyatake M, Koue T, Higashi K, Fujiwara T, Kitahara S, Katano T, Hara S: The relationship between clinical pharmacokinetics of aripiprazole and CYP2D6 genetic polymorphism: effects of CYP enzyme inhibition by coadministration of paroxetine or fluvoxamine. Eur J Clin Pharmacol. 2012 Jan;68(1):29-37. doi: 10.1007/s00228-011-1094-4. Epub 2011 Jul 8.

ARIPIPRAZOLE / GABAPENTIN: **MODERATE**

Evidence Level Likely Established

Description

The risk or severity of adverse effects can be increased when Gabapentin enacarbil is combined with Aripiprazole lauroxil. The use of central nervous system depressants may potentiate the effects of another drug in the same class. The concomitant use of opioids, including certain cough medications, with benzodiazepines, or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. Because of similar pharmacologic properties, it is reasonable to expect similar risk with concomitant use of opioid cough medications and benzodiazepines, other CNS depressants, or alcohol. The risk of CNS depression resulting from the combination of central nervous system depressant drugs varies according to the degree of sedation from each agent. Effects may range from mild sedation to severe and lethal respiratory/cardiovascular depression.

Management

Avoid concomitant use of CNS depressants. If it is deemed necessary to combine CNS depressants, consider lowering the doses of CNS depressants when used concomitantly. Monitor closely for signs of CNS depression. Each interaction between CNS depressants should be considered individually. The degree/severity of interaction largely depends on the CNS depressant agents being administered concomitantly. Refer to individual product monographs for guidance on dosing and monitoring.

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ARIPIPRAZOLE / LITHIUM (not in assay): **MODERATE**

Evidence Level Likely Established

Description

Lithium carbonate may increase the neurotoxic activities of Aripiprazole lauroxil. The coadministration of lithium and antipsychotics may lead to mutually increased adverse effects, including extrapyramidal symptoms. When haloperidol and lithium are used concomitantly, case reports have been published regarding a neurotoxic syndrome characterized by weakness, lethargy, fever, tremulousness and confusion, extrapyramidal symptoms, leucocytosis, elevated serum enzymes, blood urea nitrogen and fasting blood glucose . Irreversible brain damage has occurred from this combination.

Management

The use of haloperidol and lithium in combination is not advised. Use caution when administering antipsychotics with lithium, and consider using less potent antipsychotics when possible.

References

Amdisen A: Lithium and drug interactions. Drugs. 1982 Aug;24(2):133-9. :: Tuglu C, Erdogan E, Abay E: Delirium and extrapyramidal symptoms due to a lithium-olanzapine combination therapy: a case report. J Korean Med Sci. 2005 Aug;20(4):691-4. doi: 10.3346/jkms.2005.20.4.691. :: Chen PS, Yang YK, Yeh TL, Lo YC, Wang YT: Nonketotic hyperosmolar syndrome from olanzapine, lithium, and valproic acid cotreatment. Ann Pharmacother. 2003 Jun;37(6):919-20. doi: 10.1345/aph.1D016. :: Colvard MD, Gentry JD, Mullis DM: Neurotoxicity with combined use of lithium and haloperidol decanoate. Prim Care Companion CNS Disord. 2013;15(6). pii: 13l01563. doi: 10.4088/PCC.13l01563.

ACETAMINOPHEN / LITHIUM (not in assay): **MODERATE**

Evidence Level Likely Established

Description

Acetaminophen may decrease the excretion rate of Lithium carbonate which could result in a higher serum level. This interaction is related to the fact that both drugs are mainly excreted renally. Theoretically, this drug interaction will produce a decrease in the elimination of either drug via competition for renal excretion, producing an increase in serum concentration of either the drug or its metabolites. The increased serum concentration of either drug or its metabolites may lead to increased adverse effects. It is important to consider this interaction when drugs with a narrow therapeutic index are administered, as a change in the serum concentration of these agents may lead to serious effects. Narrow therapeutic index drugs must be maintained within a certain range to ensure safety and efficacy.[A37372,A37373,A173998,A174001,A174004]

Management

Monitor the patient closely when these drugs are given concomitantly. Change or adjust the dose of either drug as required. Refer to individual product monographs for specific guidance on dosing or monitoring. Guidance will vary according to the drugs being used.

References

Tamargo J, Le Heuzey JY, Mabo P: Narrow therapeutic index drugs: a clinical pharmacological consideration to flecainide. Eur J Clin Pharmacol. 2015 May;71(5):549-67. doi: 10.1007/s00228-015-1832-0. Epub 2015 Apr 15. :: Greenberg RG, Melloni C, Wu H, Gonzalez D, Ku L, Hill KD, Hornik CP, Cohen-Wolkowiez M, Guptill JT: Therapeutic Index Estimation of Antiepileptic Drugs: A Systematic Literature Review Approach. Clin Neuropharmacol. 2016 Sep-Oct;39(5):232-40. doi: 10.1097/WNF.0000000000000172. :: Doogue MP, Polasek TM: Drug dosing in renal disease. Clin Biochem Rev. 2011 May;32(2):69-73. :: Lepist EI, Ray AS: Renal Transporter-Mediated Drug-Drug Interactions: Are They Clinically Relevant? J Clin Pharmacol. 2016 Jul;56 Suppl 7:S73-81. doi: 10.1002/jcph.735. :: Lea-Henry TN, Carland JE, Stocker SL, Sevastos J, Roberts DM: Clinical Pharmacokinetics in Kidney Disease: Fundamental Principles. Clin J Am Soc Nephrol. 2018 Jul 6;13(7):1085-1095. doi: 10.2215/CJN.00340118. Epub 2018 Jun 22.