CLASSES
Muscle Relaxants, Centrally Acting, Plain

DEA CLASS
Rx

DESCRIPTION
Oral, centrally acting, skeletal muscle relaxant; use has fallen out of favor; drug has been associated with hepatotoxicity.

COMMON BRAND NAMES
Lorzone, Parafon Forte DSC, Relax-DS

HOW SUPPLIED
Chlorzoxazone/Lorzone/Parafon Forte DSC/Relax-DS Oral Tab: 375mg, 500mg, 750mg

DOSAGE & INDICATIONS
For adjunctive therapy to rest, physical therapy, and other measures for the relief of musculoskeletal pain associated with acute, painful musculoskeletal conditions.

Oral dosage

Adults, Adolescents, and the Geriatric
Initially, 250 to 500 mg PO given 3 to 4 times per day. Doses up to 750 mg PO given 3 to 4 times per day may be given for severe muscle spasm, but reduce when possible to lowest effective dose. Use with extreme caution in geriatric patients, as unpredictable, fatal hepatotoxicity has been reported.

Children†
Initially, 20 mg/kg/day PO given in 3 to 4 divided doses; or 600 mg/m2/day PO given in 3 to 4 divided doses.

MAXIMUM DOSAGE

Adults
3000 mg/day PO.

Elderly
3000 mg/day PO.

Adolescents
3000 mg/day PO.

Children
Maximum dosage limits are not available.

DOSING CONSIDERATIONS

Hepatic Impairment
Avoid use in patients with hepatic impairment. Although causal factors are not known, chlorzoxazone has been associated with severe (and fatal) hepatotoxicity, even in patients without concurrent hepatic impairment.

Renal Impairment
No dosage adjustment is recommended; however, use with caution as metabolites are excreted via the kidneys.

ADMINISTRATION

Oral Administration

Oral Solid Formulations
If stomach upset occurs, chlorzoxazone may be taken with food or milk. The tablets may be crushed and mixed with food, milk, or fruit juice. Parafon Forte DSC (500 mg) is a scored caplet and may be cut in half if a 250 mg dosage form is needed.
Lorzone (chlorzoxazone) dose, indications, adverse effects, interactions... from PDR.net

ADVERSE REACTIONS

Chlorzoxazone is ineffective in the treatment of skeletal muscle hyperactivity or spasticity secondary to chronic neurological disease. Unlike neuromuscular blocking agents, chlorzoxazone does not depress neuronal conduction, neuromuscular transmission, or muscle excitability.

Neurological disease

Chlorzoxazone has not been evaluated for safe use during pregnancy; therefore, its effects on the fetus are unknown (most closely corresponds to FDA pregnancy risk category C). The molecular weight of the drug suggests that placental transfer is likely. In one surveillance study, 42 newborns had been exposed to chlorzoxazone during the first trimester. One major birth defect was observed and two were expected. Earlier data from the same study reported on 264 first trimester exposures with 17 defects observed and 17 expected. The reproductive effects of chlorzoxazone in animals have not been studied. Until further information becomes available, chlorzoxazone should be used during pregnancy only when the benefits to the mother strongly outweigh any potential risks to the fetus. The effects of chlorzoxazone during labor and delivery are unknown.

Breast-feeding

There are no breast-feeding recommendations available from the manufacturer. It is not known if chlorzoxazone is distributed into breast milk; however, the molecular weight of the drug is low enough that excretion into breast milk is likely. The effects of chlorzoxazone on a nursing infant are unknown. Because no information is available on the use of chlorzoxazone during breast-feeding, an alternate muscle relaxant may be preferred (or an alternate form of feeding), especially while nursing a newborn or premature infant. If chlorzoxazone administration cannot be avoided during breast-feeding, the nursing infant should be monitored for commonly encountered adverse effects of chlorzoxazone, such as sedation. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect may impair driving or operating machinery or the ability to perform other hazardous activities.

Fever, hepatic disease, hepatitis, jaundice, vomiting

Chlorzoxazone should be used cautiously, if at all, in patients with a previous history of liver disease. Chlorzoxazone should not be used in patients with active hepatic disease or hepatitis. Serious (including fatal) hepatocellular toxicity has been rarely reported in patients receiving chlorzoxazone. Factors predisposing patients to hepatotoxicity are unknown. The clinician should strongly consider monitoring liver function tests (LFTs) during chlorzoxazone treatment. Patients should promptly report any signs of hepatic disease to their prescriber, including fever, rash, anorexia, nausea/vomiting, fatigue, right upper quadrant pain, dark urine or jaundice. Note that rarely a patient may observe orange or purple-red discoloration of the urine due to excretion of the phenolic metabolite. It is important that the healthcare professional distinguish this benign discoloration from that of darkened urine which may indicate hepatotoxicity. If signs and symptoms of liver toxicity occur, chlorzoxazone should be discontinued immediately. Additionally, if elevated hepatic enzymes (LFTs) (e.g., AST, ALT) are reported, chlorzoxazone should be immediately discontinued.

Renal failure, renal impairment

The 6-hydroxychlorzoxazone metabolite of chlorzoxazone is rapidly excreted in the urine; therefore, chlorzoxazone should be used with caution in patients with renal impairment (including renal failure) because renal dysfunction may alter drug excretion, possibly causing toxicity. The manufacturer of chlorzoxazone states that there is no evidence that the drug will lead to renal impairment.

Geriatric

Use chlorzoxazone with extreme caution in geriatric patients due to CNS depression, potentially irreversible hepatotoxicity, or other side effects. Initially, it may be advisable to start with lower dosages in the older adult. According to the Beers Criteria, skeletal muscle relaxants including chlorzoxazone are considered potentially inappropriate medications (PIMs) for use in geriatric patients and should be avoided because most muscle relaxants are poorly tolerated by older adults. Some muscle relaxants can cause anticholinergic effects, sedation, and are associated with an increased risk of fractures. In addition, there is questionable effectiveness of the dosages tolerated by older adults. The federal Omnibus Budget Reconciliation Act (OBRA) regulates the use of medications in residents of long-term care facilities. According to the OBRA guidelines, most muscle relaxants are poorly tolerated by older adults due to anticholinergic side effects, sedation, and/or weakness. However, periodic use (e.g., once every 3 months) for no more than 7 days may be appropriate when other interventions or alternative medications are not effective or indicated. Chronic use in individuals with complications due to multiple sclerosis, spinal cord injuries, cerebral palsy, and other select conditions may be indicated, although close monitoring is warranted. Abrupt discontinuation of some muscle relaxants may cause or predispose individuals to seizures or hallucinations.

Pregnancy

Chlorzoxazone has not been evaluated for safe use during pregnancy; therefore, its effects on the fetus are unknown (most closely corresponds to FDA pregnancy risk category C). The molecular weight of the drug suggests that placental transfer is likely. In one surveillance study, 42 newborns had been exposed to chlorzoxazone during the first trimester. One major birth defect was observed and two were expected. Earlier data from the same study reported on 264 first trimester exposures with 17 defects observed and 17 expected. The reproductive effects of chlorzoxazone in animals have not been studied. Until further information becomes available, chlorzoxazone should be used during pregnancy only when the benefits to the mother strongly outweigh any potential risks to the fetus. The effects of chlorzoxazone during labor and delivery are unknown.

ADVERSE REACTIONS

General information

Chlorzoxazone is contraindicated in any patient with a known or suspected hypersensitivity to the drug or any of the product ingredients. Use cautiously in any patient with a history of allergies to drugs. If a sensitivity reaction such as urticaria, pruritus, or skin erythema occurs, discontinue chlorzoxazone.

Alcoholism, CNS depression, driving or operating machinery, ethanol intoxication

Use chlorzoxazone cautiously in patients with CNS depression and in patients using concomitant drugs that may cause CNS depression because of possible CNS depression exacerbation. Patients suffering from alcoholism or currently under ethanol intoxication should not use chlorzoxazone. Concomitant use of alcohol with chlorzoxazone will exacerbate the CNS depression and should be avoided. Additionally, alcohol use with chlorzoxazone may increase the possibility of hepatotoxicity, although specific data are not available. Warn patients that the CNS depressant effects of chlorzoxazone may impair driving or operating machinery or the ability to perform other hazardous activities.

Storage

Lorzone:
- Store at controlled room temperature (between 68 and 77 degrees F)
Parafon Forte DSC:
- Store at controlled room temperature (between 68 and 77 degrees F)
Relax-DS:
- Store at controlled room temperature (between 68 and 77 degrees F)
Remular S:
- Avoid exposure to heat
- Protect from light
- Store at controlled room temperature (between 68 and 77 degrees F)

CONTRAINDICATIONS / PRECAUTIONS

- Store at controlled room temperature (between 68 and 77 degrees F)
- Avoid exposure to light
- Protect from light
- Store at controlled room temperature (between 68 and 77 degrees F)

http://www.pdr.net/drug-summary/Lorzone-chlorzoxazone-3750
Severe
anaphylactoid reactions / Rapid / 0-1.0
torticollis / Delayed / Incidence not known
angioedema / Rapid / Incidence not known
hepatic failure / Delayed / Incidence not known
GI bleeding / Delayed / Incidence not known
hepatic necrosis / Delayed / Incidence not known

Moderate
anemia / Delayed / 0-1.0
dysarthria / Delayed / Incidence not known
erythema / Early / Incidence not known
hyperbilirubinemia / Delayed / Incidence not known
elevated hepatic enzymes / Delayed / Incidence not known
jaundice / Delayed / Incidence not known
cholestatics / Delayed / Incidence not known
constipation / Delayed / Incidence not known
hepatitis / Delayed / Incidence not known
anemia / Delayed / Incidence not known
neutropenia / Delayed / Incidence not known

Mild
rash (unspecified) / Early / 1.0-10.0
pruritus / Rapid / 1.0-10.0
urticaria / Rapid / 1.0-10.0
paresthesia / Delayed / 0-1.0
drowsiness / Early / 10.0
dizziness / Early / 10.0
uncontrollable ejaculation / Early / 10.0
malaise / Early / Incidence not known
agitation / Early / Incidence not known
eccymosis / Delayed / Incidence not known
petechiae / Delayed / Incidence not known
diabetes / Early / Incidence not known
nausea / Early / Incidence not known
anorexia / Delayed / Incidence not known
dyspepsia / Early / Incidence not known
fever / Early / Incidence not known
vomiting / Early / Incidence not known

DRUG INTERACTIONS
Acetaminophen; Butalbital: Additive CNS depression may occur if barbiturates are used concomitantly with skeletal muscle relaxants. Caution should be exercised during concomitant use of skeletal muscle relaxants and barbiturates; dosage reduction of one or both agents may be necessary.
Acetaminophen; Butalbital; Caffeine: Additive CNS depression may occur if barbiturates are used concomitantly with skeletal muscle relaxants. Caution should be exercised during concomitant use of skeletal muscle relaxants and barbiturates; dosage reduction of one or both agents may be necessary.
Acetaminophen; Butalbital; Caffeine; Codeine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opiate cough medications in patients taking skeletal muscle relaxants. Additive CNS depression may occur if barbiturates are used concomitantly with skeletal muscle relaxants. Caution should be exercised during concomitant use of skeletal muscle relaxants and barbiturates; dosage reduction of one or both agents may be necessary.
Acetaminophen; Caffeine; Dihydromorphone: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opiate cough medications in patients taking skeletal muscle relaxants.
Acetaminophen; Codeine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opiate cough medications in patients taking skeletal muscle relaxants.
Acetaminophen; Hydrocode: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioide pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, reduced initial doses are recommended. If a decision is made to start treatment with hydrocode extended-release tablets or capsules, initiate hydrocode at 20% to 30% of the usual dosage. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioide cough medications in patients taking skeletal muscle relaxants.
Acetaminophen; Oxycodone: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioide pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If oxycodone or oxycodone; naloxone is initiated in a patient taking a skeletal muscle relaxant, use an initial dose
of oxycodone at one-half to one-half the usual dosage and titrate to clinical response; reduced initial doses of oxycodone; naltr佐xone, aspirin, Aspirin, ASA; Carisoprodol; Codeine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If an opiate agonist is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Aspirin, ASA; Butalbital; Caffeine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If an opiate agonist is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opiate cough medications in patients taking skeletal muscle relaxants. Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

Aspirin, ASA; Butalbital; Caffeine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If an opiate agonist is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Aspirin, ASA; Caffeine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If an opiate agonist is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opiate cough medications in patients taking skeletal muscle relaxants. Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

Aspirin, ASA; Caffeine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If an opiate agonist is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opiate cough medications in patients taking skeletal muscle relaxants. Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

Atropine; Hyoscyamine; Phenobarbital; Scopolamine: Additive CNS depression may occur if barbiturates are used concomitantly with skeletal muscle relaxants. Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If an opiate agonist is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opiate cough medications in patients taking skeletal muscle relaxants. Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

Azathioprine: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block. Azelastine; Fluticasone: An enhanced CNS depressant effect may occur when azelastine is combined with other CNS depressants including skeletal muscle relaxants. Azelastine; Fluticasone: An enhanced CNS depressant effect may occur when azelastine is combined with other CNS depressants including skeletal muscle relaxants. Bacitracin: Use skeletal muscle relaxants cautiously in patients receiving systemic bacitracin. If bacitracin is administered parenterally during surgery, there may be increased skeletal muscle relaxation, and postoperative use may reinstate neuromuscular blockade. Barbiturates: Additive CNS depression may occur if barbiturates are used concomitantly with skeletal muscle relaxants. Caution should be exercised during concomitant use of skeletal muscle relaxants and barbiturates; dosage reduction of one or both agents may be necessary. Belladonna Alkaloids; Ergotamine; Phenobarbital: Additive CNS depression may occur if barbiturates are used concomitantly with skeletal muscle relaxants. Caution should be exercised during concomitant use of skeletal muscle relaxants and barbiturates; dosage reduction of one or both agents may be necessary. Belladonna; Opium: Concomitant use of skeletal muscle relaxants with benzodiazepines may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If an opiate agonist is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Benzodiazepines: Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given. Botulinum Toxins: Excessive neuromuscular weakness may be exacerbated by coadministration of a botulinum toxin with skeletal muscle relaxants. Advise patients to seek medical assistance if they develop any unusual symptoms (including difficulty with swallowing, speaking, or breathing), or if any existing symptom worsens during use of a botulinum toxin. Brompheniramine; Carbetapentane; Phenytophen: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants. Brompheniramine; Guaifenesin; Hydrocodone: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If an opiate agonist is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

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durations needed to achieve the desired clinical effect. If acetaminophen; hydrocodone or hydrocodone; ibuprofen is initiated in a patient taking a skeletal muscle relaxant, reduced initial doses are recommended. If a decision is made to start treatment with hydrocodone extended-release tablets or capsules, initiate hydrocodone at 20% to 30% of the usual dosage. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

Buspirone: Concomitant use of skeletal muscle relaxants with buspirone can result in additive CNS depression. Dosage adjustments of either or both medications may be necessary.

Butalbital: Additive CNS depression may occur if butalbital is used concomitantly with skeletal muscle relaxants. Caution should be exercised when butalbital is used concomitantly with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Chlorpheniramine: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Phenylephrine: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Phenylephrine: Pyrilamine: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Guaifenesin: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Guaifenesin: Phenylephrine: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Phenylephrine: Pyrilamine: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Phenylephrine: Pyrilamine: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Paracetamol: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Paracetamol: Phenylephrine: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Carbetapentane: Phenylephrine: Pyrilamine: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

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Carbetapentane: Phenylephrine: Pyrilamine: Drowsiness has been reported during administration of carbetapentane. An enhanced CNS depressant effect may occur when carbetapentane is combined with other CNS depressants including skeletal muscle relaxants.

Chlorzoxazone: Carbetapentane: Carbinoxamine; Hydrocodone: Phenylephrine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If acetaminophen; hydrocodone or hydrocodone; ibuprofen is initiated in a patient taking a skeletal muscle relaxant, reduced initial doses are recommended. If a decision is made to start treatment with hydrocodone extended-release tablets or capsules, initiate hydrocodone at 20% to 30% of the usual dosage. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

Chlorzoxazone: Carbetapentane: Carbinoxamine; Hydrocodone; Phenylephrine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If acetaminophen; hydrocodone or hydrocodone; ibuprofen is initiated in a patient taking a skeletal muscle relaxant, reduced initial doses are recommended. If a decision is made to start treatment with hydrocodone extended-release tablets or capsules, initiate hydrocodone at 20% to 30% of the usual dosage. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

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Chlorzoxazone: Carbetapentane: Carbinoxamine; Hydrocodone; Phenylephrine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If acetaminophen; hydrocodone or hydrocodone; ibuprofen is initiated in a patient taking a skeletal muscle relaxant, reduced initial doses are recommended. If a decision is made to start treatment with hydrocodone extended-release tablets or capsules, initiate hydrocodone at 20% to 30% of the usual dosage. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

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**Chlorpheniramine; Hydrocodone; Pseudoephedrine:** Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If acetaminophen; hydrocodone or hydrocodone; ibuprofen is initiated in a patient taking a skeletal muscle relaxant, reduced initial doses are recommended. If a decision is made to start treatment with hydrocodone extended-release tablets or capsules, initiate hydrocodone at 20% to 30% of the usual dosage. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

**Clonazepam:** Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

**Clorazepate:** Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

**Codeine:** Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

**Codiene; Guaifenesin:** Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

**Codeine; Promethazine:** Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

**COMT inhibitors:** COMT inhibitors should be given cautiously with other agents that cause CNS depression, including skeletal muscle relaxants, due to the possibility of additive sedation.

**Dexmedetomidine:** Due to the anesthetic effects of dexmedetomidine, concurrent use with other CNS depressants, such as skeletal muscle relaxants, could result in additive sedative effects and possibly prolong recovery from anesthesia. Dosage adjustments of either or both medications may be necessary.

**Dexamfetamine:** Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

**Dihydrocodeine; Guaifenesin; Pseudoephedrine:** Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

**Diphenhydramine; Hydrocodone; Phenylephrine:** Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If acetaminophen; hydrocodone or hydrocodone; ibuprofen is initiated in a patient taking a skeletal muscle relaxant, reduced initial doses are recommended. If a decision is made to start treatment with hydrocodone extended-release tablets or capsules, initiate hydrocodone at 20% to 30% of the usual dosage. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

**Doxaxurum:** Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.

**Clonazepam:** Concomitant use of skeletal muscle relaxants with benzodiazepines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.
Hydromorphone: Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

Capsules, initiate hydrocodone at 20% to 30% of the usual dosage. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation. Avoid prescribing opioid cough medications in patients taking skeletal muscle relaxants.

Hydrocodone; Potassium Guaiacolsulfonate: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Guaifenesin; Hydrocodone: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

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Hydrocodone; Ibuofen: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Hydrocodone; Phenylephrine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

Hydrocodone; Potassium Guaiacolsulfonate; Pseudoeophrine: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opioid pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.
are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If oxycodone or oxycodone; naloxone is initiated in a patient taking a skeletal muscle relaxant, use an initial dose of oxycodone at one-third to one-half the usual dosage and titrate to clinical response; reduced initial doses of oxycodone; naloxone; ASA; oxycodone, and ibuprofen; oxycodone are also recommended. If a decision is made to start treatment with acetaminophen; oxycodone extended-release tablets, start with 1 tablet PO every 12 hours. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

**Levorphanol:** Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If levorphanol is initiated in a patient taking a skeletal muscle relaxant, reduce the initial dose of levorphanol by approximately 50% or more. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

**Lorzone (chlorzoxazone) dose, indications, adverse effects, interactions... from PDR.net**

Lorzone (chlorzoxazone) dose, indications, adverse effects, interactions... from PDR.net

Concomitant use of skeletal muscle relaxants with other CNS depressants, such as lorzone, can result in additive CNS depression. Persons taking other CNS-active medications such as, skeletal muscle relaxants, should discuss the use of herbal supplements with their health care professional prior to consuming lorzone kava. Patients should not abruptly stop taking their prescribed medications.

**Levodopa:** Concomitant use of skeletal muscle relaxants with other CNS depressants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If levodopa is initiated in a patient taking a skeletal muscle relaxant, reduce the initial dose of levodopa by approximately 50% or more. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

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depression and sedation.

**Pancuronium**: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.

**Pentazocine**: Use pentazocine with caution in any patient receiving medication with CNS depressant and/or anticholinergic activity. Co-administration of pentazocine with skeletal muscle relaxants may result in additive respiratory and CNS depression and anticholinergic effects, such as urinary retention and constipation.

**Pentazocine; Naloxone**: Use pentazocine with caution in any patient receiving medication with CNS depressant and/or anticholinergic activity. Co-administration of pentazocine with skeletal muscle relaxants may result in additive respiratory and CNS depression and anticholinergic effects, such as urinary retention and constipation.

**Phenobarbital**: Additive CNS depression may occur if barbiturates are used concomitantly with skeletal muscle relaxants. Caution should be exercised during concomitant use of skeletal muscle relaxants and barbiturates; dosage reduction of one or both agents may be necessary.

**Phenolamine**: Use phenolamine with caution in any patient receiving medication with CNS depressant activity. Co-administration of phenolamine with skeletal muscle relaxants may result in additive CNS depression and anticholinergic effects, such as urinary retention and constipation.

**Phenoxybenzamine**: Use phenoxybenzamine with caution in any patient receiving medication with CNS depressant activity. Co-administration of phenoxybenzamine with skeletal muscle relaxants may result in additive CNS depression and anticholinergic effects, such as urinary retention and constipation.

**Primidone**: Additive CNS depression may occur if barbiturates are used concomitantly with skeletal muscle relaxants. Caution should be exercised during concomitant use of skeletal muscle relaxants and barbiturates; dosage reduction of one or both agents may be necessary.

**Quazepam**: Concomitant use of skeletal muscle relaxants with benzodiazipines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

**Rapacuronium**: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.

**Remifentanil**: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

**Rocuronium**: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.

**Secobarbital**: Additive CNS depression may occur if barbiturates are used concomitantly with skeletal muscle relaxants. Caution should be exercised during concomitant use of skeletal muscle relaxants and barbiturates; dosage reduction of one or both agents may be necessary.

**Sodium Oxycodone**: Sodium oxycodone should not be used in combination with CNS depressant anxiolytics, sedatives, and hypnotics or other sedative CNS depressant drugs. Additive CNS depressant effects may be possible when sodium oxycodone is used concurrently with skeletal muscle relaxants.

**Succinylcholine**: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.

**Sufentanil**: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of the opiate and titrate to clinical response. If a skeletal muscle relaxant is prescribed for a patient taking an opiate agonist, use a lower initial dose of the skeletal muscle relaxant and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

**Tapentadol**: Concomitant use of opiate agonists with skeletal muscle relaxants may cause respiratory depression, hypotension, profound sedation, and death. Limit the use of opiate pain medications with skeletal muscle relaxants to only patients for whom alternative treatment options are inadequate. If concurrent use is necessary, use the lowest effective doses and minimum treatment durations needed to achieve the desired clinical effect. If an opiate agonist is initiated in a patient taking a skeletal muscle relaxant, use a lower initial dose of tapentadol and titrate to clinical response. Educate patients about the risks and symptoms of respiratory depression and sedation.

**Tapentadol**: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.

**Thiothixene**: Thiothixene can potentiate the CNS-depressant action of other drugs, such skeletal muscle relaxants. Caution should be exercised during concomitant use of skeletal muscle relaxants and barbiturates; dosage reduction of one or both agents may be necessary.

**Tolcapone**: COMT inhibitors should be given cautiously with other agents that cause CNS depression, including skeletal muscle relaxants, due to the possibility of additive sedation.

**Triazolam**: Concomitant use of skeletal muscle relaxants with benzodiazipines can result in additive CNS depression. The severity of this interaction may be increased when additional CNS depressants are given.

**Tubocurarine**: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.

**Vecuronium**: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.

**PREGNANCY AND LACTATION**

**Pregnancy**

Chlorzoxazone has not been evaluated for safe use during pregnancy; therefore, its effects on the fetus are unknown (most closely corresponds to Pregnancy category C). The molecular weight of the drug suggests that placental transfer is likely. In one surveillance study, 42 newboms had been exposed to chlorzoxazone during the first trimester. One major birth defect was observed and two were expected. Earlier data from the same study and from other data indicated that the reproductive effects of chlorzoxazone in animals have not been studied. Until further information becomes available, chlorzoxazone should be used during pregnancy only when the benefits to the mother strongly outweigh any potential risks to the fetus. The effects of chlorzoxazone during labor and delivery are unknown.

There are no breast-feeding recommendations available from the manufacturer. It is not known if chlorzoxazone is distributed into breast milk; however, the molecular weight of the drug is low enough that excretion into breast milk is likely. The effects of chlorzoxazone on a nursing infant are unknown. Because no information is available on the use of chlorzoxazone during breast-feeding, an alternate muscle relaxant may be preferred (see Diltiazem: Additive CNS depression, especially while nursing a newborn or premature infant). Chlorzoxazone administration cannot be avoided during breast-feeding, the nursing infant should be monitored for commonly encountered adverse effects of chlorzoxazone, such as sedation. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally ingested drug, healthcare providers are encouraged to report the adverse effect to the FDA.

**MECHANISM OF ACTION**

http://www.pdr.net/drug-summary/Lorzone-chlorzoxazone-3750
The exact mode of action of chlorzoxazone has not been identified, but appears to be related to its sedative properties. Animal and human studies show that chlorzoxazone acts primarily at the level of the spinal cord and subcortical areas of the brain. Inhibition of multisynaptic reflex arcs occur, resulting in inhibition of skeletal muscle spasms of varied etiology. Clinically, pain relief, a reduction in muscle spasm, and enhanced mobility of the affected muscle occurs. Pain relief is postulated to be due to alterations in the perception of pain. Unlike neuromuscular blockers, chlorzoxazone does not have an effect on neuronal conduction, neuromuscular transmission, or muscle excitability. Similar to carisoprodol and cyclobenzaprine, chlorzoxazone has no direct relaxant effect on skeletal muscle. Chlorzoxazone is not associated with significant anticholinergic effects.

The mechanism responsible for the rare hepatic toxicity seen with chlorzoxazone is unknown. The reaction is idiosyncratic and unpredictable. Factors that may predispose patients to hepatic toxicity with chlorzoxazone have not been identified.

PHARMACOKINETICS

Chlorzoxazone is administered orally. The drug is well distributed, with the highest concentrations found in plasma and fat, and lower concentrations found in the liver, muscle, brain and kidneys. The volume of distribution is roughly 14 L. It is not known if the drug is distributed into human milk or crosses the placenta. Metabolism occurs in the liver, producing an inactive metabolite, 6-hydroxychlorzoxazone, which is then rapidly excreted as the glucuronide in the urine. Less than 1% of a dose is excreted unchanged in urine within 24 hours; 74% of the metabolite is excreted within 10 hours. The half-life of chlorzoxazone is roughly 60 minutes in adults with normal hepatic function.

**Oral Route**

Absorption of chlorzoxazone from the GI tract is rapid and complete. Blood levels can be detected within the first 30 minutes after administration. Onset of action occurs in about 1 hour and lasts for 3—4 hours.