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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.

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

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.

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 health care 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, alkaline phosphatase and bilirubin) 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.

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 related to a maternally ingested drug, healthcare providers are encouraged to report the adverse effect to the FDA.

Neurological disease

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

ADVERSE REACTIONS

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

amnesia / 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
cholestasis / 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
paresthesias / Delayed / 0-1.0
drowsiness / Early / 10.0
dizziness / Early / 10.0
urine discoloration / Early / 10.0
malaise / Early / Incidence not known
agitation / Early / Incidence not known
ecchymosis / Delayed / Incidence not known
petechiae / Delayed / Incidence not known
diarrhea / 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. 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. 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; Dihydrocodeine: 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; Dichloralphenazone; Isometheptene: Additive CNS depression is possible if skeletal muscle relaxants are used concomitantly with other CNS depressants. Dosage adjustments of one or both medications may be necessary.
Acetaminophen; 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 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.
Acetaminophen; Oxycodone: 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 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; naltrexone, aspirin, 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.
Acetaminophen; Pentazocine: Use pentazocine with caution in any patient receiving medication with CNS depressant and/or anticholinergic activity. Coadministration of pentazocine with skeletal muscle relaxants may result in additive respiratory and CNS depression and anticholinergic effects, such as urinary retention and constipation.
Alfentanil: 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.
Alprazolam: 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.
Amitriptyline; Chlordiazepoxide: 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.
Amobarbital: 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.
Aspirin, ASA; 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.
Aspirin, ASA; 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. 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. 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.
Aspirin, ASA; Caffeine; Dihydrocodeine: 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.
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 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.
Aspirin, ASA; Oxycodone: 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 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; naltrexone, aspirin, 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.
Atracurium: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.
Atropine; Hyoscyamine; Phenobarbital; Scopolamine: 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.
Azelastine: 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 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.
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 walking), or if any existing symptom worsens during use of a botulinum toxin.
Brompheniramine; 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.
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 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.
Brompheniramine; 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.
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.
Butabarbital: 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.
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; Chlorpheniramine; 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; Diphenhydramine; 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; 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: 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; Pseudoephedrine: 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; 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.
Carbidopa; Levodopa; Entacapone: COMT inhibitors should be given cautiously with other agents that cause CNS depression, including skeletal muscle relaxants, due to the possibility of additive sedation.
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.
Carbinoxamine; 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.
Chlordiazepoxide: 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.
Chlordiazepoxide; Clidinium: 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.
Chlorpheniramine; 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.
Chlorpheniramine; Dihydrocodeine; Phenylephrine: 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.
Chlorpheniramine; Dihydrocodeine; Pseudoephedrine: 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.
Chlorpheniramine; Guaifenesin; 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.
Chlorpheniramine; 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 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.

Chlorpheniramine; 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.

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.

Cisatracurium: 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.

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 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.

Codeine; Guaifenesin: 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.

Codeine; Phenylephrine; Promethazine: 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.

Codeine; Promethazine: 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.

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.

Diazepam: 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 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.

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.

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

Dronabinol, THC: Concomitant use of skeletal muscle relaxants with dronabinol can result in additive CNS depression and dizziness, which can impair the ability to undertake tasks requiring mental alertness. Utilize appropriate caution if these drugs are given together.

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

Estazolam: 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.

Ethanol: Alcohol is associated with CNS depression. The combined use of alcohol and CNS depressants can lead to additive CNS depression, which could be dangerous in tasks requiring mental alertness and fatal in overdose. Alcohol taken with other CNS depressants can lead to additive respiratory depression, hypotension, profound sedation, or coma. Consider the patient's use of alcohol or illicit drugs when prescribing CNS depressant medications. In many cases, the patient should receive a lower dose of the CNS depressant initially if the patient is not likely to be compliant with avoiding alcohol.
Fentanyl: 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.
Flurazepam: 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.
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 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.
Guaifenesin; 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.
Homatropine; 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 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.
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 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.
Hydrocodone; Ibuprofen: 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.
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.
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 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.
Hydrocodone; Potassium Guaiacolsulfonate; 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.
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.
Hydromorphone: 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 hydromorphone is initiated in a patient taking a skeletal muscle relaxant, use an initial dose of hydromorphone at 1/3 to 1/2 the usual dosage 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.
Ibuprofen; Oxycodone: 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 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; naltrexone, aspirin, 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.
Kava Kava, Piper methysticum: Concomitant use of skeletal muscle relaxants with other CNS depressants, such as kava kava 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 kava kava. Patients should not abruptly stop taking their prescribed medications.
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.
Lorazepam: 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.
Loxapine: Simultaneous use of skeletal muscle relaxants and other CNS depressants, such as antipsychotics, can increase CNS depression.
Mephobarbital: 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.
Methohexital: 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.
Midazolam: 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.
Mirtazapine: Skeletal muscle relaxants may cause additive CNS depression if used concomitantly with other drugs with CNS depressant properties such as mirtazapine. Combination therapy may amplify sedation and dizziness, which can impair the patient's ability to perform tasks requiring mental alertness. Dosage adjustments of either or both medications may be necessary in some instances. In addition, anecdotal evidence from case reports suggests that cyclobenzaprine may possess serotonin augmenting effects that may be clinically relevant during administration of the drug with serotonin-enhancing medications. In theory, there is a remote possibility that serotonin syndrome may occur from concurrent administration of cyclobenzaprine and mirtazapine since mirtazapine increases central serotonin activity. In addition, cyclobenzaprine is closely related to the tricyclic antidepressants, which are known to decrease serotonin reuptake. Caution is advisable during concurrent use with mirtazapine until more information about cyclobenzaprine's effects on serotonin becomes available.
Mivacurium: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.
Molindone: Simultaneous use of skeletal muscle relaxants and other CNS depressants, such as molindone, can increase CNS depression. In addition, antipsychotics are associated with anticholinergic effects; therefore, additive effects may be seen during concurrent use of molindone and other drugs having anticholinergic activity. Clinicians should note that antimuscarinic effects may be seen not only on GI smooth muscle, but also on bladder function, the eye, and temperature regulation.
Morphine: 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 morphine is initiated in a patient taking a skeletal muscle relaxant, reduced initial dosages are recommended. For extended-release products, start with the lowest possible dose of morphine (i.e., 15 mg PO every 12 hours, extended-release tablets; 30 mg or less PO every 24 hours, extended-release capsules). Use an initial morphine; naltrexone dose of 20 mg/0.8 mg PO every 24 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.
Morphine; Naltrexone: 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 morphine is initiated in a patient taking a skeletal muscle relaxant, reduced initial dosages are recommended. For extended-release products, start with the lowest possible dose of morphine (i.e., 15 mg PO every 12 hours, extended-release tablets; 30 mg or less PO every 24 hours, extended-release capsules). Use an initial morphine; naltrexone dose of 20 mg/0.8 mg PO every 24 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.
Nabilone: Concomitant use of nabilone with other CNS depressants like skeletal muscle relaxants can potentiate the effects of nabilone on respiratory depression, sedation and dizziness, which can impair the ability to undertake tasks requiring mental alertness.
Nalbuphine: Concomitant use of nalbuphine with other CNS depressants, such as skeletal muscle relaxants, can potentiate the effects of nalbuphine on respiratory depression, CNS depression, and sedation.
Neuromuscular blockers: Concomitant use of skeletal muscle relaxants with other CNS depressants can result in additive CNS depression. Also, dantrolene may potentiate neuromuscular block.
Oxazepam: 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.
Oxycodone: 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 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; naltrexone, aspirin, 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.
Oxymorphone: 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 oxymorphone is initiated in a patient taking a skeletal muscle relaxant, use an initial dose of oxymorphone at one-third to one-half the usual dosage and titrate to clinical response. If the extended-release oxymorphone tablets are used concurrently with a skeletal muscle relaxant, use an initial dosage of 5 mg 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.
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. Coadministration 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. Coadministration of pentazocine with skeletal muscle relaxants may result in additive respiratory and CNS depression and anticholinergic effects, such as urinary retention and constipation.
Pentobarbital: 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.
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.
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 benzodiazepines 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 Oxybate: Sodium oxybate 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 oxybate 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 tapentadol is initiated in a patient taking a skeletal muscle relaxant, a reduced initial dosage of tapentadol is recommended. If the extended-release tapentadol tablets are used concurrently with a skeletal muscle relaxant, use an initial tapentadol dose of 50 mg 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.
Temazepam: 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.
Thalidomide: Avoid the concomitant use of thalidomide with other central nervous system depressants such as skeletal muscle relaxants due to the potential for additive sedative effects.
Thiopental: 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.
Thiothixene: Thiothixene can potentiate the CNS-depressant action of other drugs, such skeletal muscle relaxants. Caution should be exercised during simultaneous use of these agents due to potential excessive CNS effects or additive hypotension.
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 benzodiazepines 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 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.

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 related to a maternally ingested drug, healthcare providers are encouraged to report the adverse effect to the FDA.

MECHANISM OF ACTION

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.