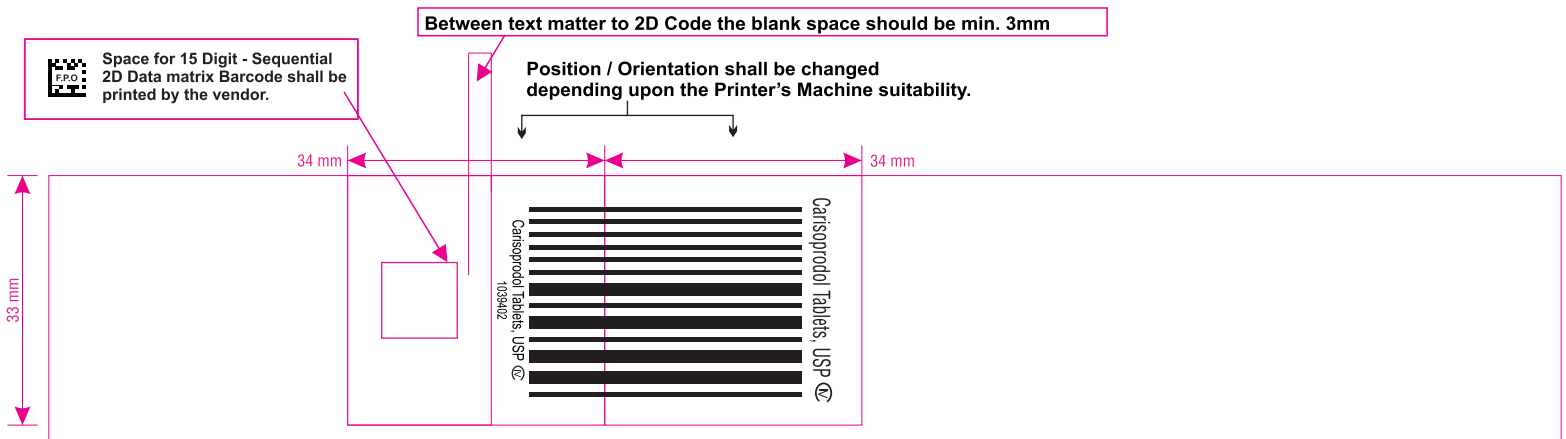

320 mm

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use carisoprodol tablets USP safely and effectively. See full prescribing information for carisoprodol tablets USP.

CARISOPRODOL tablets USP for oral Use, C-IV
Initial U.S. Approval: 1959

INDICATIONS AND USAGE

Carisoprodol tablets USP is a muscle relaxant indicated for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults (1)

Limitation of Use

- Should only be used for acute treatment periods up to two or three weeks (1)

DOSAGE AND ADMINISTRATION

- Recommended dose is 250 mg to 350 mg three times a day and at bedtime. (2)

DOSAGE FORMS AND STRENGTHS

- Tablets: 250 mg, 350 mg (3)

CONTRAINDICATIONS

- Acute intermittent porphyria (4)
- Hypersensitivity reactions to a carbamate such as meprobamate (4)

WARNINGS AND PRECAUTIONS

- Due to sedative properties, may impair ability to perform hazardous tasks such as driving or operating machinery (5.1)
- Additive sedative effects when used with other CNS depressants including alcohol (5.1)
- Cases of abuse, dependence, and withdrawal (5.2, 9.2, 9.3)
- Seizures (5.3)

ADVERSE REACTIONS

Most common adverse reactions (incidence > 2%) are drowsiness, dizziness, and headache (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Strides Pharma Inc. at 1-877-244-9825 or go to www.strides.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- CNS depressants (e.g., alcohol, benzodiazepines, opioids, tricyclic antidepressants) - additive sedative effects (5.1 and 7.1)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 08/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

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3 DOSAGE FORMS AND STRENGTHS
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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Carisoprodol tablets USP is indicated for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults.

Limitation of Use

Carisoprodol tablets USP should only be used for short periods (up to two or three weeks) because adequate evidence of effectiveness for more prolonged use has not been established and because acute, painful musculoskeletal conditions are generally of short duration *[see Dosage and Administration (2)]*.

2 DOSAGE AND ADMINISTRATION

The recommended dose of carisoprodol tablets USP is 250 mg to 350 mg three times a day and at bedtime. The recommended maximum duration of carisoprodol tablets USP use is up to two or three weeks.

3 DOSAGE FORMS AND STRENGTHS

250 mg Tablets: circular shaped, biconvex, white to off white colored, uncoated tablets, debossed " S " on one side and plain on the other side 434

350 mg Tablets: circular shaped, biconvex, white to off white colored, uncoated tablets, debossed " S " on one side and plain on the other side 435

4 CONTRAINDICATIONS

Carisoprodol tablets USP is contraindicated in patients with a history of acute intermittent porphyria or a hypersensitivity reaction to a carbamate such as meprobamate.

5 WARNINGS AND PRECAUTIONS

5.1 Sedation

Carisoprodol tablets USP has sedative properties (in the low back pain trials, 13% to 17% of patients who received carisoprodol tablets USP experienced sedation compared to 6% of patients who received placebo) *[see ADVERSE REACTIONS (6.1)]* and may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a motor vehicle or operating machinery. There have been post-marketing reports of motor vehicle accidents associated with the use of carisoprodol tablets USP.

Since the sedative effects of carisoprodol tablets USP and other CNS depressants (e.g., alcohol, benzodiazepines, opioids, tricyclic antidepressants) may be additive, appropriate caution should be exercised with patients who take more than one of these CNS depressants simultaneously.

5.2 Abuse, Dependence, and Withdrawal

Carisoprodol, the active ingredient in carisoprodol tablets USP, has been subject to abuse, dependence, and withdrawal, misuse, and criminal diversion. *[see Drug Abuse and Dependence (9.1, 9.2, 9.3)]*. Abuse of carisoprodol tablets USP poses a risk of overdosage which may lead to death, CNS and respiratory depression, hypotension, seizures, and other disorders *[see Overdosage (10)]*.

Post-marketing experience cases of carisoprodol abuse and dependence have been reported in patients with prolonged use and a history of drug abuse. Although most of these patients took other drugs of abuse, some patients solely abused carisoprodol. Withdrawal symptoms have been reported following abrupt cessation of carisoprodol tablets USP after prolonged use. Reported withdrawal symptoms included insomnia, vomiting, abdominal cramps, headache, tremors, muscle twitching, ataxia, hallucinations, and psychosis. One of carisoprodol's metabolites, meprobamate (a controlled substance), may also cause dependence *[see Clinical Pharmacology (12.3)]*.

To reduce the risk of carisoprodol tablets USP abuse assess the risk of abuse prior to prescribing. After prescribing, limit the length of treatment to three weeks for the relief of acute musculoskeletal discomfort, keep careful prescription records, monitor for signs of abuse and overdose, and educate patients and their families about abuse and on proper storage and disposal.

5.3 Seizures

There have been post-marketing reports of seizures in patients who received carisoprodol tablets USP. Most of these cases have occurred in the setting of multiple drug overdoses (including drugs of abuse, illegal drugs, and alcohol) *[see Overdosage (10)]*.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect rates observed in practice.

The data described below are based on 1387 patients pooled from two double blind, randomized, multicenter, placebo controlled, one-week trials in adult patients with acute, mechanical, lower back pain *[see Clinical Studies (14)]*. In these studies, patients were treated with 250 mg of carisoprodol tablets USP, 350 mg of carisoprodol tablets USP, or placebo three times a day and at bedtime for seven days. The mean age was about 41 years old with 54% females and 46% males and 74 % Caucasian, 16 % Black, 9% Asian, and 2% other.

There were no deaths and there were no serious adverse reactions in these two trials. In these two studies, 2.7%, 2%, and 5.4%, of patients treated with placebo, 250 mg of carisoprodol tablets USP, and 350 mg of carisoprodol tablets USP, respectively, discontinued due to adverse events; and 0.5%, 0.5%, and 1.8% of patients treated with placebo, 250 mg of carisoprodol tablets USP, and 350 mg of carisoprodol tablets USP, respectively, discontinued due to central nervous system adverse reactions.

Table 1 displays adverse reactions reported with frequencies greater than 2% and more frequently than placebo in patients treated with carisoprodol tablets USP in the two trials described above.

Table 1. Patients with Adverse Reactions in Controlled Studies

Adverse Reaction	Placebo (n=560) n (%)	Carisoprodol Tablets USP 250 mg (n=548) n (%)	Carisoprodol Tablets USP 350 mg (n=279) n (%)
Drowsiness	31 (6)	73 (13)	47 (17)
Dizziness	11 (2)	43 (8)	19 (7)
Headache	11 (2)	26 (5)	9 (3)

6.2 Post-marketing Experience

The following events have been reported during postapproval use of carisoprodol tablets USP. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Cardiovascular: Tachycardia, postural hypotension, and facial flushing *[see Overdosage (10)]*.

Central Nervous System: Drowsiness, dizziness, vertigo, ataxia, tremor, agitation, irritability, headache, depressive reactions, syncope, insomnia, and seizures *[see Overdosage (10)]*.

Gastrointestinal: Nausea, vomiting, and epigastric discomfort.
Hematologic: Leukopenia, pancytopenia

7 DRUG INTERACTIONS

7.1 CNS Depressants

The sedative effects of carisoprodol tablets USP and other CNS depressants (e.g., alcohol, benzodiazepines, opioids, tricyclic antidepressants) may be additive. Therefore, caution should be exercised with patients who take more than one of these CNS depressants simultaneously. Concomitant use of carisoprodol tablets USP and meprobamate, a metabolite of carisoprodol tablets USP, is not recommended *[see Warnings and Precautions (5.1)]*.

7.2 CYP2C19 Inhibitors and Inducers

Carisoprodol USP is metabolized in the liver by CYP2C19 to form meprobamate *[see Clinical Pharmacology (12.3)]*. Co-administration of CYP2C19 inhibitors, such as omeprazole or fluvoxamine, with carisoprodol tablets USP could result in increased exposure of carisoprodol USP and decreased exposure of meprobamate. Co-administration of CYP2C19 inducers, such as rifampin or St. John's Wort, with carisoprodol tablets USP could result in decreased exposure of carisoprodol USP and increased exposure of meprobamate. Low dose aspirin also showed an induction effect on CYP2C19. The full pharmacological impact of these potential alterations of exposures in terms of either efficacy or safety of carisoprodol tablets USP is unknown.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Data over many decades of carisoprodol use in pregnancy have not identified a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Data on meprobamate, the primary metabolite of carisoprodol, also do not show a consistent association between maternal use of meprobamate and an increased risk of major birth defects (*see Data*).

In a published animal reproduction study, pregnant mice administered carisoprodol orally at 2.6-and 4.1-times the maximum recommended human dose ([MRHD] of 1400 mg per day [350 mg QID] based on body surface area [BSA] comparison) from gestation through weaning resulted in reduced fetal weights, postnatal weight gain, and postnatal survival (*see Data*).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Human Data

Retrospective case-control and cohort studies of meprobamate use during the first trimester of pregnancy have not consistently identified an increased risk or pattern of major birth defects. For children exposed to meprobamate in-utero, one study found no adverse effect on mental or motor development or IQ scores.

Animal Data

Embryofetal development studies in animals have not been completed. In a published pre-and post-natal development animal study, pregnant mice administered carisoprodol orally at 300, 750, or 1200 mg/kg/day (approximately 1-, 2.6-, and 4.1-times the MRHD based on BSA comparison) from 7-days prior to gestation through birth and from lactation through weaning resulted in reduced fetal weights, postnatal weight gain, and postnatal survival at 2.6-and 4.1-times the MRHD.

8.2 Lactation

Risk Summary

Data from published literature report that carisoprodol and its metabolite, meprobamate, are present in breastmilk. There are no data on the effect of carisoprodol on milk production. There is one report of sedation in an infant who was breastfed by a mother taking carisoprodol (*see Clinical Considerations*). Because there have been no consistent reports of adverse events in breastfed infants over decades of use, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for carisoprodol tablets USP and any potential adverse effects on the breastfed infant from carisoprodol tablets USP or from the underlying maternal condition.

Clinical Considerations

Infants exposed to carisoprodol through breast milk should be monitored for sedation.

8.4 Pediatric Use

The efficacy, safety, and pharmacokinetics of carisoprodol tablets USP in pediatric patients less than 16 years of age have not been established.

8.5 Geriatric Use

The efficacy, safety, and pharmacokinetics of carisoprodol tablets USP in patients over 65 years old have not been established.

8.6 Renal Impairment

The safety and pharmacokinetics of carisoprodol tablets USP in patients with renal impairment have not been evaluated. Since carisoprodol tablets USP are excreted by the kidney, caution should be exercised if carisoprodol tablets USP are administered to patients with impaired renal function. Carisoprodol USP is dialyzable by hemodialysis and peritoneal dialysis.

8.7 Hepatic Impairment

The safety and pharmacokinetics of carisoprodol tablets USP in patients with hepatic impairment have not been evaluated. Since carisoprodol tablets USP is metabolized in the liver, caution should be exercised if carisoprodol tablets USP is administered to patients with impaired hepatic function.

8.8 Patients with Reduced CYP2C19 Activity

Patients with reduced CYP2C19 activity have higher exposure to carisoprodol. Therefore, caution should be exercised in administration of carisoprodol tablets USP to these patients *[see Clinical Pharmacology (12.3)]*.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Carisoprodol tablets USP contains carisoprodol USP, a Schedule IV controlled substance. Carisoprodol USP has been subject to abuse, misuse, and criminal diversion for nontherapeutic use *[see Warnings and Precautions (5.2)]*.

9.2 Abuse

Abuse of carisoprodol USP poses a risk of overdosage which may lead to death, CNS and respiratory depression, hypotension, seizures and other disorders *[see Warnings and Precautions (5.2) and Overdosage (10)]*. Patients at high risk of carisoprodol tablets USP abuse may include those with prolonged use of Carisoprodol USP, with a history of drug abuse, or those who use carisoprodol tablets USP in combination with other abused drugs.

Prescription drug abuse is the intentional non-therapeutic use of a drug, even once, for its rewarding psychological effects. Drug addiction, which develops after repeated drug abuse, is characterized by a strong desire to take a drug despite harmful consequences, difficulty in controlling its use, giving a higher priority to drug use than to obligations, increased tolerance, and sometimes physical withdrawal. Drug abuse and drug addiction are separate and distinct from physical dependence and tolerance (for example, abuse or addiction may not be accompanied by tolerance or physical dependence) *[see Drug Abuse and Dependence (9.3)]*.

200 mm

Front Side

ARTWORK DETAIL LABEL

Product	**Carisoprodol Tablets USP, 250 mg / 350 mg**				
Buyer/Country	STRIDES PHARMA INC - US	Component	Outsert		
Dimension	**Open Size : 200 x 320 mm ; Folded Size 34 x 33mm**			Pack	---
New Item Code	**1039402**	Old Item Code	1035837		
Colour Shades	**BLACK**			No. of Colours	1

Change Control No.	Record Number: 223693	Artwork Version	2.0
Design/Style	Front & Back side printing. To be supplied in the Booklet form with pasting and folding size of 34 x 33mm		
Substrate	40 / 45 GSM paper		
Special Instructions	Printing clarity should be clear and sharp.		
Autocartonator Requirements	NA		

Caution to the printer: Before processing, please ensure that the ARTWORK received for printing is exactly in line with APPROVED ARTWORK provided to you. In case of any FONTS/DESIGN are Mis-matching with the APPROVED ARTWORK, please inform PDC for further action. **DO NOT MAKE ANY CHANGE TO THE ARTWORK WITHOUT WRITTEN INSTRUCTIONS FROM PDC.**

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9.3 Dependence

Tolerance is when a patient's reaction to a specific dosage and concentration is progressively reduced in the absence of disease progression, requiring an increase in the dosage to maintain the same. Physical dependence is characterized by withdrawal symptoms after abrupt discontinuation or a significant dose reduction of a drug. Both tolerance and physical dependence have been reported with the prolonged use of carisoprodol tablets USP. Reported withdrawal symptoms with carisoprodol tablets USP include insomnia, vomiting, abdominal cramps, headache, tremors, muscle twitching, anxiety, ataxia, hallucinations, and psychosis. Instruct patients taking large doses of carisoprodol tablets USP or those taking the drug for a prolonged time to not abruptly stop carisoprodol tablets USP *[see Warnings and Precautions (5.2)]*.

10 OVERDOSAGE

Clinical Presentation

Overdosage of carisoprodol tablets USP commonly produces CNS depression. Death, coma, respiratory depression, hypotension, seizures, delirium, hallucinations, dystonic reactions, nystagmus, blurred vision, mydriasis, euphoria, muscular incoordination, rigidity, and/or headache have been reported with carisoprodol tablets USP overdosage. Serotonin syndrome has been reported with carisoprodol USP intoxication. Many of the carisoprodol USP overdoses have occurred in the setting of multiple drug overdoses (including drugs of abuse, illegal drugs, and alcohol). The effects of an overdose of carisoprodol tablets USP and other CNS depressants (e.g., alcohol, benzodiazepines, opioids, tricyclic antidepressants) can be additive even when one of the drugs has been taken in the recommended dosage. Fatal accidental and non-accidental overdoses of carisoprodol tablets USP have been reported alone or in combination with CNS depressants.

Treatment of Overdosage

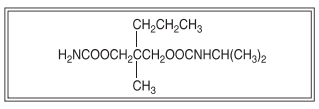
Basic life support measures should be instituted as dictated by the clinical presentation of the carisoprodol tablets USP overdose. Vomiting should not be induced because of the risk of CNS and respiratory depression, and subsequent aspiration. Circulatory support should be administered with volume infusion and vasopressor agents if needed. Seizures should be treated with intravenous benzodiazepines and the reoccurrence of seizures may be treated with phenobarbital. In cases of severe CNS depression, airway protective reflexes may be compromised and tracheal intubation should be considered for airway protection and respiratory support.

For decontamination in cases of severe toxicity, activated charcoal should be considered in a hospital setting in patients with large overdoses who present early and are not demonstrating CNS depression and can protect their airway.

For more information on the management of an overdose of carisoprodol tablets USP, **contact a Poison Control Center.**

11 DESCRIPTION

Carisoprodol tablets USP are available as 250 mg and 350 mg circular shaped, white to off white, biconvex tablets. Carisoprodol USP is a white, crystalline powder, having a mild, characteristic odor and a bitter taste. It is slightly soluble in water; freely soluble in alcohol, in chloroform, and in acetone; and its solubility is practically independent of pH. Carisoprodol USP is present as a racemic mixture. Chemically, carisoprodol USP is (±)-2-Methyl-2-propyl-1,3-propanediol carbamate isopropylcarbamate and the molecular formula is $C_{12}H_{24}N_2O_4$, with a molecular weight of 260.33. The structural formula is:



Other ingredients in the carisoprodol tablets USP drug product include microcrystalline cellulose, croscarmellose sodium, povidone, magnesium stearate and maize starch.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of carisoprodol USP in relieving discomfort associated with acute painful musculoskeletal conditions has not been clearly identified.

In animal studies, muscle relaxation induced by carisoprodol USP is associated with altered interneuronal activity in the spinal cord and in the descending reticular formation of the brain.

12.2 Pharmacodynamics

Carisoprodol USP is a centrally acting skeletal muscle relaxant that does not directly relax skeletal muscles.

A metabolite of carisoprodol, meprobamate, has anxiolytic and sedative properties. The degree to which these properties of meprobamate contribute to the safety and efficacy of carisoprodol tablets USP is unknown.

12.3 Pharmacokinetics

Absorption

The pharmacokinetics of carisoprodol USP and its metabolite meprobamate were studied in a crossover study of 24 healthy subjects (12 male and 12 female) who received single doses of 250 mg and 350 mg carisoprodol tablets USP (see Table 2). The exposure of carisoprodol USP and meprobamate was dose proportional between the 250 mg and 350 mg doses. The Cmax of meprobamate was 2.5 ± 0.5 mcg/mL (mean ± SD) after administration of a single 350 mg dose of carisoprodol tablets USP, which is approximately 30% of the Cmax of meprobamate (approximately 8 mcg/mL) after administration of a single 400 mg dose of meprobamate.

Table 2. Pharmacokinetic Parameters of Carisoprodol USP and Meprobamate (Mean ± SD, n=24)

	250 mg Carisoprodol Tablets USP	350 mg Carisoprodol Tablets USP
Carisoprodol		
Cmax (mcg/mL)	1.2 ± 0.5	1.8 ± 1.0
AUC_{inf} (mcg*hr/mL)	4.5 ± 3.1	7.0 ± 5.0
Tmax (hr)	1.5 ± 0.8	1.7 ± 0.8
$T_{1/2}$ (hr)	1.7 ± 0.5	2.0 ± 0.5
Meprobamate		
Cmax (mcg/mL)	1.8 ± 0.3	2.5 ± 0.5
AUC_{inf} (mcg*hr/mL)	32 ± 6.2	46 ± 9.0
Tmax (hr)	3.6 ± 1.7	4.5 ± 1.9
$T_{1/2}$ (hr)	9.7 ± 1.7	9.6 ± 1.5

Absolute bioavailability of carisoprodol USP has not been determined. The mean time to peak plasma concentrations (Tmax) of carisoprodol USP was approximately 1.5 to 2 hours.

Food Effect: Co-administration of a high-fat meal with carisoprodol USP (350 mg tablet) had no effect on the pharmacokinetics of carisoprodol. Therefore, carisoprodol tablets USP may be administered with or without food.

Elimination

Metabolism: The major pathway of carisoprodol USP metabolism is via the liver by cytochrome enzyme CYP2C19 to form meprobamate. This enzyme exhibits genetic polymorphism (see Patients with Reduced CYP2C19 Activity below).

Excretion: Carisoprodol USP is eliminated by both renal and non-renal routes with a terminal elimination half-life of approximately 2 hours. The half-life of meprobamate is approximately 10 hours.

Specific Populations

Sex: Exposure of carisoprodol USP is higher in female than in male subjects (approximately 30-50% on a weight adjusted basis). Overall exposure of meprobamate is comparable between female and male subjects.

Patients with Reduced CYP2C19 Activity: Carisoprodol tablets USP should be used with caution in patients with reduced CYP2C19 activity. Published studies indicate that patients who are poor CYP2C19 metabolizers have a 4-fold increase in exposure to carisoprodol, and concomitant 50% reduced exposure to meprobamate compared to normal CYP2C19 metabolizers. The prevalence of poor metabolizers in Caucasians and African Americans is approximately 3-5% and in Asians is approximately 15-20%.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long term studies in animals have not been performed to evaluate the carcinogenic potential of carisoprodol.

Mutagenesis

Carisoprodol tablets USP was not formally evaluated for genotoxicity. In published studies, carisoprodol USP was mutagenic in the *in vitro* mouse lymphoma cell assay in the absence of metabolizing enzymes, but was not mutagenic in the presence of metabolizing enzymes. Carisoprodol USP was clastogenic in the *in vitro* chromosomal aberration assay using Chinese hamster ovary cells with or without the presence of metabolizing enzymes. Other types of genotoxic tests resulted in negative findings. Carisoprodol USP was not mutagenic in the Ames reverse mutation assay using *S. typhimurium* strains with or without metabolizing enzymes, and was not clastogenic in an *in vivo* mouse micronucleus assay of circulating blood cells.

Impairment of Fertility

Carisoprodol tablets USP was not formally evaluated for effects on fertility. A published reproductive study in which female mice received carisoprodol orally at doses of 300, 750, or 1200 mg/kg/day (approximately 1, 2.6, and 4.1 times the MRHD of 1400 mg per day [350 mg QID] based on body surface area [BSA] comparison) from 1-week prior to mating, to 27-weeks post-mating found no alteration in fertility although an alteration in reproductive cycles characterized by a greater time spent in estrus was observed at a carisoprodol dose of 1200 mg/kg/day. In a 13week toxicology study that did not determine fertility, mouse testes weight and sperm motility were reduced at a dose of 1200 mg/kg/day (maternal doses equivalent to 4.2-times the MRHD based on BSA comparison). In both studies, the no effect level was 750 mg/kg/day, corresponding to approximately 2.6-times the MRHD based on a BSA comparison. The significance of these findings for human fertility is not known.

14 CLINICAL STUDIES

The safety and efficacy of carisoprodol tablets USP for the relief of acute, idiopathic mechanical low back pain was evaluated in two, 7-day, double blind, randomized, multicenter, placebo controlled, U.S. trials (Studies 1 and 2). Patients had to be 18 to 65 years old and had to have acute back pain (£ 3 days of duration) to be included in the trials. Patients with chronic back pain; at increased risk for vertebral fracture (e.g., history of osteoporosis); with a history of spinal pathology (e.g., herniated nucleus pulposus, spondylolisthesis or spinal stenosis); with inflammatory back pain, or with evidence of a neurologic deficit were excluded from participation. Concomitant use of analgesics (e.g., acetaminophen, NSAIDs, tramadol, opioid agonists), other muscle relaxants, botulinum toxin, sedatives (e.g., barbiturates, benzodiazepines, promethazine hydrochloride), and anti-epileptic drugs was prohibited.

In Study 1, patients were randomized to one of three treatment groups (i.e., carisoprodol tablets USP 250 mg, carisoprodol tablets USP 350 mg, or placebo) and in Study 2 patients were randomized to two treatment groups (i.e., carisoprodol tablets USP 250 mg or placebo). In both studies, patients received study medication three times a day and at bedtime for seven days.

The primary endpoints were the relief from starting backache and the global impression of change, as reported by patients, on Study Day 3. Both endpoints were scored on a 5-point rating scale from 0 (worst outcome) to 4 (best outcome) in both studies. The primary statistical comparison was between the carisoprodol tablets USP 250 mg and placebo groups in both studies.

The proportion of patients who used concomitant acetaminophen, NSAIDs, tramadol, opioid agonists, other muscle relaxants, and benzodiazepines was similar in the treatment groups.

The results for the primary efficacy evaluations in the acute, low back pain studies are presented in Table 3.

Table 3. Results of the Primary Efficacy Endpoints[a] in Studies 1 and 2

Study	Parameter	Placebo	Carisoprodol Tablets USP 250 mg	Carisoprodol Tablets USP 350 mg
1	**Number of Patients**	n=269	n=264	n=273
	Relief from Starting Backache, Mean (SE)[b]	1.4 (0.1)	1.8 (0.1)	1.8 (0.1)
	Difference between carisoprodol tablets USP and Placebo, Mean (SE)[b] (95% CI)		0.4 (0.2, 0.5)	0.4 (0.2, 0.6)
	Global Impression of Change, Mean (SE)[b]	1.9 (0.1)	2.2 (0.1)	2.2 (0.1)
	Difference between carisoprodol tablets USP and Placebo, Mean (SE)[b] (95% CI)		0.2 (0.1, 0.4)	0.3 (0.1, 0.4)
2	**Number of Patients**	n=278	n=269	
	Relief from Starting Backache, Mean (SE)[b]	1.1 (0.1)	1.8 (0.1)	
	Difference between carisoprodol tablets USP and Placebo, Mean (SE)[b] (95% CI)		0.7 (0.5, 0.9)	
	Global Impression of Change, Mean (SE)[b]	1.7 (0.1)	2.2 (0.1)	
	Difference between carisoprodol tablets USP and Placebo, Mean (SE)[b] (95% CI)		0.5 (0.4, 0.7)	

[a] The primary efficacy endpoints (Relief from Starting Backache and Global Impression of Change) were assessed by the patients on Study Day 3. These endpoints were scored on a 5-point rating scale from 0 (worst outcome) to 4 (best outcome).

[b] Mean is the least squared mean and SE is the standard error of the mean. The ANOVA model was used for the primary statistical comparison between the carisoprodol tablets USP 250 mg and placebo groups.

Patients treated with carisoprodol tablets USP experienced improvement in function as measured by the Roland-Morris Disability Questionnaire (RMDQ) score on Days 3 and 7.

16 HOW SUPPLIED/STORAGE AND HANDLING

Carisoprodol Tablets USP, 250 mg: circular shaped, biconvex, white to off white colored, uncoated tablets debossed " S " on one side and plain 434 on the other side, available as follows:

NDC 42543-434-01: Bottle of 100 tablets
NDC 42543-434-05: Bottle of 500 tablets
NDC 42543-434-10: Bottle of 1000 tablets

Carisoprodol Tablets USP, 350 mg: circular shaped, biconvex, white to off white colored, uncoated tablets debossed " S " on one side and plain 435 on the other side, available as follows:

NDC 42543-435-01: Bottle of 100 tablets
NDC 42543-435-05: Bottle of 500 tablets
NDC 42543-435-10: Bottle of 1000 tablets

Storage:

Store at 20° to 25°C (68° to 77°F).
[See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Patients should be advised to contact their physician if they experience any adverse reactions to carisoprodol tablets USP.

Sedation

Advise patients that carisoprodol tablets USP may cause drowsiness and/or dizziness, and has been associated with motor vehicle accidents. Patients should be advised to avoid taking carisoprodol tablets USP before engaging in potentially hazardous activities such as driving a motor vehicle or operating machinery *[see Warnings and Precautions (5.1)]*.

Avoidance of Alcohol and Other CNS Depressants

Advise patients to avoid alcoholic beverages while taking carisoprodol tablets USP and to check with their doctor before taking other CNS depressants such as benzodiazepines, opioids, tricyclic antidepressants, sedating antihistamines, or other sedatives *[see Warnings and Precautions (5.1)]*.

Carisoprodol tablets USP Should Only Be Used for Short-Term Treatment

Advise patients that treatment with carisoprodol tablets USP should be limited to acute use (up to two or three weeks) for the relief of acute, musculoskeletal discomfort. In the post-marketing experience with carisoprodol tablets USP, cases of dependence, withdrawal, and abuse have been reported with prolonged use. If the musculoskeletal symptoms still persist, patients should contact their healthcare provider for further evaluation.

Lactation

Advise nursing mothers using carisoprodol tablets USP to monitor neonates for signs of sedation *[see Use in Specific Populations (8.2)]*.

Manufactured by:
Strides Pharma Science Ltd.
Puducherry - 605014, India

Distributed by:
Strides Pharma Inc.
East Brunswick, NJ 08816

Revised: 08/2019

320 mm

8278

1039402

200 mm

8278

Back Side

ARTWORK DETAIL LABEL

Product	**Carisoprodol Tablets USP, 250 mg / 350 mg**				
Buyer/Country	STRIDES PHARMA INC - US	Component	Outsert		
Dimension	**Open Size : 200 x 320 mm ; Folded Size 34 x 33mm**			Pack	---
New Item Code	**1039402**	Old Item Code	1035837		
Colour Shades	**BLACK**			No. of Colours	1

Change Control No.	Record Number: 223693	Artwork Version	2.0
Design/Style	Front & Back side printing. To be supplied in the Booklet form with pasting and folding size of 34 x 33mm		
Substrate	40 / 45 GSM paper		
Special Instructions	Printing clarity should be clear and sharp.		
Autocartonator Requirements	NA		

Caution to the printer: Before processing, please ensure that the ARTWORK received for printing is exactly in line with APPROVED ARTWORK provided to you. In case of any FONTS/DESIGN are Mis-matching with the APPROVED ARTWORK, please inform PDC for further action. **DO NOT MAKE ANY CHANGE TO THE ARTWORK WITHOUT WRITTEN INSTRUCTIONS FROM PDC.**

RD/PD/003/F-08/R0

Technical & Non Printing Colours
Keyline

PRODUCT INFORMATION	
PRODUCT/BRAND NAME	Carisoprodol Tablets, USP
COMPONENT	Pack insert
FG CODE	3007835
MARKET TYPE	Export
MARKET(S)	USA
MFG LOCATION	Formulation-Pondy
NEW MATERIAL CODE	1039402
OLD MATERIAL CODE	1035837
REQUEST TYPE	Change
WORKFLOW	Change Control Export Flow
STRENGTH	250 mg /350 mg
PACK SIZE	---
CUSTOMER APPROVAL	Yes

FINALIZATION SUMMARY

ACTION	DEPARTMENT	ACTION BY	ACTION ON
Initiate,User Authorization ,CustomerCopy/Artw ork Documents Upload	Packaging Development-AW	Viswanathan Sakthivelan	08/14/2019 12:00 PM
Checklist Approval/Reject	Packaging Development-AW	Viswanathan Sakthivelan	08/14/2019 12:11 PM
Checklist Approva/Reject	Packaging Development-Tech	Anil Kumar	08/23/2019 03:01 PM
Checklist Approva/Reject	Marketing/BD	Selvaraj Admin	08/23/2019 05:18 PM
Checklist Approva/Reject	FDD/TTD	Santhosh	08/23/2019 05:47 PM
Checklist Approva/Reject	Regulatory Affairs	Mamta Yogendra Chahar	08/23/2019 06:10 PM
Checklist Approva/Reject	Quality Assurance	Bharathi Raj	08/24/2019 02:55 PM
Checklist Approva/Reject	Production	Mohandoss Subramanian	08/26/2019 09:38 AM

Harmony elabel