ORPHENADRINE CITRATE ASPIRIN CAFFEINE- orphenadrine citrate, aspirin, caffeine tablet
Jerome Stevens Pharmaceuticals, Inc.

ORPHENADRINE
CITRATE
ASPIRIN
CAFFEINE
REGULAR AND
FORTE TABLETS

ACTIONS:

Orphenadrine citrate is a centrally acting (brain stem) compound which in animals selectively blocks facilitatory functions of the reticular formation. Orphenadrine does not produce myoneural block, nor does it affect crossed extensor reflexes. Orphenadrine prevents nicotine-induced convulsions but not those produced by strychnine.

Chronic administration of the regular formula to dogs and rats has revealed no drug-related toxicity. No blood or urine changes were observed, nor were there any macroscopic or microscopic pathological changes detected. Extensive experience with combinations containing aspirin and caffeine has established them as safe agents. The addition of orphenadrine citrate does not alter the toxicity of aspirin and caffeine.

The mode of therapeutic action of orphenadrine has not been clearly identified, but may be related to its analgesic properties. Orphenadrine citrate also possesses anticholinergic actions.

INDICATIONS:

1. Symptomatic relief of mild to moderate pain of acute musculoskeletal disorders.
2. The orphenadrine component is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomfort associated with acute painful musculoskeletal conditions.

The mode of action of orphenadrine has not been clearly identified, but may be related to its analgesic properties. These products do not directly relax tense skeletal muscles in man.

CONTRAINDICATIONS:

Because of the mild anticholinergic effect of orphenadrine, these products should not be used in patients with glaucoma, pyloric or duodenal obstruction, achalasia, prostatic hypertrophy or obstructions at the bladder neck. These products are also contraindicated in patients with myasthenia gravis and in patients known to be sensitive to aspirin or caffeine.

The drug is contraindicated in patients who have demonstrated a previous hypersensitivity to the drug.

WARNINGS:

Reye's syndrome may develop in individuals who have chicken pox, influenza, or flu symptoms.

Some studies suggest a possible association between the development of Reye's Syndrome and the use of medicines containing salicylate or aspirin. These products contain aspirin and therefore are not recommended for use in patients with chicken pox, influenza, or flu symptoms.

These products may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; ambulatory patients should therefore be cautioned accordingly.

Aspirin should be used with extra caution in the presence of peptic ulcers and coagulation abnormalities.

Fetal Toxicity

Premature Closure of Fetal Ductus Arteriosus:

Avoid use of NSAIDS, including Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets, in pregnant women at about 30 weeks of gestation and later. NSAIDs including Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets, increase the risk of premature closure of the fetal ductus arteriosus at approximately this gestational age.

Oligohydramnios / Neonatal Renal Impairment:

Use of NSAIDs including Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets, at about 20 weeks of gestation or later in pregnancy may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation.

Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may, for example, include limb contractures and delayed lung maturation. In some post marketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If NSAID treatment is necessary between about 20 weeks and 30 weeks gestation, limit Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets treatment extends beyond 48 hours. Discontinue Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets if oligohydramnios occurs and follow up according to clinical practice [see *PRECAUTIONS; Pregnancy*].

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as Orphenadrine Citrate Aspirin Caffeine Regular and Forte

Tablets. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets and evaluate the patient immediately.

Pregnancy:

Risk Summary

Withdrawal seizures were reported in a two-day-old male infant whose mother had taken a butalbital-containing drug during the last 2 months of pregnancy. Butalbital was found in the infant's serum. The infant was given phenobarbital 5 mg/kg, which was tapered without further seizure or other withdrawal symptoms.

Use of NSAIDs, including aspirin, can cause premature closure of the fetal ductus arteriosus and fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, limit dose and duration of Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets use between about 20 and 30 weeks of gestation, and avoid Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets use at about 30 weeks of gestation and later in pregnancy [see *WARNINGS; Fetal Toxicity].*

Premature Closure of Fetal Ductus Arteriosus

Use of NSAIDs, including aspirin, at about 30 weeks gestation or later in pregnancy increases the risk of premature closure of the fetal ductus arteriosus.

Oligohydramnios/Neonatal Renal Impairment

Use of NSAIDs at about 20 weeks gestation or later in pregnancy has been associated with cases of fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment.

Data from observational studies regarding other potential embryofetal risks of NSAID use in women in the first or second trimesters of pregnancy are inconclusive.

Based on animal data, prostaglandins have been shown to have an important role in endometrial vascular permeability, blastocyst implantation, and decidualization. In animal studies, administration of prostaglandin synthesis inhibitors such as aspirin, resulted in increased pre- and post-implantation loss. Prostaglandins also have been shown to have an important role in fetal kidney development. In published animal studies, prostaglandin synthesis inhibitors have been reported to impair kidney development when administered at clinically relevant doses.

The estimated background risk of major birth defects and miscarriage for the indicated population(s) 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 2-4% and 15-20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Premature Closure of Fetal Ductus Arteriosus:

Avoid use of NSAIDs in women at about 30 weeks gestation and later in pregnancy, because NSAIDs, including Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets, can cause premature closure of the fetal ductus arteriosus *(see WARNINGS; Fetal Toxicity).*

Oligohydramnios/Neonatal Renal Impairment

If an NSAID is necessary at about 20 weeks gestation or later in pregnancy, limit the use to the lowest effective dose and shortest duration possible. If Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets treatment extends beyond 48 hours, consider monitoring with ultrasound for oligohydramnios. If oligohydramnios occurs, discontinue Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets and follow up according to clinical practice *(see WARNINGS; Fetal Toxicity).*

Data

Human Data

Premature Closure of Fetal Ductus Arteriosus:

Published literature reports that the use of NSAIDs at about 30 weeks of gestation and later in pregnancy may cause premature closure of the fetal ductus arteriosus.

Oligohydramnios/Neonatal Renal Impairment:

Published studies and post marketing reports describe maternal NSAID use at about 20 weeks gestation or later in pregnancy associated with fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. In many cases, but not all, the decrease in amniotic fluid was transient and reversible with cessation of the drug. There have been a limited number of case reports of maternal NSAID use and neonatal renal dysfunction without oligohydramnios, some of which were irreversible. Some cases of neonatal renal dysfunction required treatment with invasive procedures, such as exchange transfusion or dialysis.

Methodological limitations of these post marketing studies and reports include lack of a control group; limited information regarding dose, duration, and timing of drug exposure; and concomitant use of other medications. These limitations preclude establishing a reliable estimate of the risk of adverse fetal and neonatal outcomes with maternal NSAID use. Because the published safety data on neonatal outcomes involved mostly preterm infants, the generalizability of certain reported risks to the full-term infant exposed to NSAIDs through maternal use is uncertain.

USAGE IN CHILDREN:

The safe and effective use of this drug in children has not been established. Usage of this drug in children under 12 years of age is not recommended.

PRECAUTIONS:

Confusion, anxiety and tremors have been reported in a few patients receiving propoxyphene and orphenadrine concomitantly. As these symptoms may be simple due to an additive effect, reduction of dosage and/or discontinuation of one or both agents is recommended in such cases.

Safety of continuous long-term therapy with these products has not been established; therefore, if they are prescribed for prolonged use, periodic monitoring of blood, urine and liver function values is recommended.

Pregnancy

Embryo-Fetal Toxicity

Inform pregnant women to avoid use of aspirin and other NSAIDs starting at 30 weeks gestation because of the risk of the premature closing of the fetal ductus arteriosus. If treatment with Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets is needed for a pregnant woman between about 20 to 30 weeks gestation, advise her that she may need to be monitored for oligohydramnios, if treatment continues for longer than 48 hours [see *WARNINGS; Fetal Toxicity, PRECAUTIONS; Pregnancy*].

Serious Skin Reactions, including DRESS

Advise patients to stop taking Orphenadrine Citrate Aspirin Caffeine Regular and Forte Tablets immediately if they develop any type of rash or fever and to contact their healthcare provider as soon as possible [see *Warnings*].

ADVERSE REACTIONS:

Side effects of these products are those seen with aspirin and caffeine or those usually associated with mild anticholinergic agents. These may include tachycardia, palpitation, urinary hesitancy or retention, dry mouth, blurred vision, dilation of the pupil, increased intraocular tension, weakness, nausea, vomiting, headache, dizziness, constipation, drowsiness, and rarely, urticaria and other dermatoses. Infrequently, an elderly patient may experience some degree of confusion. Mild central excitation and occasional hallucinations may be observed. These mild side effects can usually be eliminated by reduction in dosage. One case of aplastic anemia associated with the use of the regular formula has been reported. No causal relationship has been established. Rare G.I. hemorrhage due to aspirin content may be associated with the administration of these products. Some patients may experience transient episodes of lightheadedness, dizziness or syncope.

To report SUSPECTED ADVERSE REACTIONS, contact Jerome Stevens Pharmaceuticals Inc. at 1-844-686-1019 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DOSAGE AND ADMINISTRATION:

REGULAR: Adults 1 to 2 tablets 3 to 4 times daily.

FORTE: Adults ½ to 1 tablet 3 to 4 times daily.

HOW SUPPLIED:

Regular tablets can be identified as a round, multi-layered tablet embossed JSP 554 on one side, and contains orphenadrine citrate (2-dimethylaminoethyl 2-methylbenzhydryl ether citrate) 25 mg, aspirin 385 mg, and caffeine 30 mg.

Forte tablets are exactly twice the strength of the regular. They are identified by their scored capsule shape. Each multi-layered tablet is embossed JSP 555 on one side and contains orphenadrine citrate 50 mg, aspirin 770 mg, and caffeine 60 mg.

Products also contain: lactose, starch, D&C yellow #10 and FD&C blue #1.

Regular: Bottles of

100 tablets	NDC 50564-554-01
500 tablets	NDC 50564-554-05

Forte: Bottles of

100 tablets	NDC 50564-555-01
500 tablets	NDC 50564-555-05

Store below 30°C (86°F)

Caution:

Federal law prohibits dispensing without prescription.

Manufactured by:
Jerome Stevens Pharmaceuticals, Inc.
Bohemia, NY 11716

Rev. 03/21
MG # 11584

Principal Display Panel - 25 mg Bottle Label

JSP INC.

NDC 50564-554-01

**ORPHENADRINE CITRATE,
ASPIRIN, CAFFEINE**

**Caution: Federal law prohibits
dispensing without prescription.**

100 TABLETS

Principal Display Panel - 50 mg Bottle Label

JSP INC.

NDC 50564-555-01

**ORPHENADRINE CITRATE,
ASPIRIN, CAFFEINE
FORTE**

**Caution: Federal law prohibits
dispensing without prescription.**

100 TABLETS

ORPHENADRINE CITRATE ASPIRIN CAFFEINE

orphenadrine citrate, aspirin, caffeine tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50564-554
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
orphenadrine citrate (UNII: X0A40N8I4S) (orphenadrine - UNII:AL805O9OG9)	orphenadrine citrate	25 mg
aspirin (UNII: R16CO5Y76E) (aspirin - UNII:R16CO5Y76E)	aspirin	385 mg
caffeine (UNII: 3G6A5W338E) (caffeine - UNII:3G6A5W338E)	caffeine	30 mg

Inactive Ingredients

Ingredient Name	Strength
lactose, unspecified form (UNII: J2B2A4N98G)	
starch, corn (UNII: O8232NY3SJ)	
d&c yellow no. 10 (UNII: 35SW5USQ3G)	
fd&c blue no. 1 (UNII: H3R47K3TBD)	

Product Characteristics

Color	green (green) , white (white) , yellow (yellow)	**Score**	no score
Shape	ROUND (ROUND)	**Size**	11mm
Flavor		**Imprint Code**	JSP;554
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50564-554-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	04/30/1999	
2	NDC:50564-554-05	500 in 1 BOTTLE; Type 0: Not a Combination Product	04/30/1999	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA074988	04/30/1999	

ORPHENADRINE CITRATE ASPIRIN CAFFEINE

orphenadrine citrate, aspirin, caffeine tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:50564-555
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
orphenadrine citrate (UNII: X0A40N8I4S) (orphenadrine - UNII:AL805O9OG9)	orphenadrine citrate	50 mg
aspirin (UNII: R16CO5Y76E) (aspirin - UNII:R16CO5Y76E)	aspirin	770 mg
caffeine (UNII: 3G6A5W338E) (caffeine - UNII:3G6A5W338E)	caffeine	60 mg

Inactive Ingredients

Ingredient Name	Strength
lactose, unspecified form (UNII: J2B2A4N98G)	
starch, corn (UNII: O8232NY3SJ)	
d&c yellow no. 10 (UNII: 35SW5USQ3G)	
fd&c blue no. 1 (UNII: H3R47K3TBD)	

Product Characteristics

Color	green (green) , white (white) , yellow (yellow)	**Score**	2 pieces
Shape	CAPSULE (CAPSULE)	**Size**	19mm
Flavor		**Imprint Code**	JSP;555
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50564-555-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	04/30/1999	
2	NDC:50564-555-05	500 in 1 BOTTLE; Type 0: Not a Combination Product	04/30/1999	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA074988	04/30/1999	

Labeler - Jerome Stevens Pharmaceuticals, Inc. (021130638)

Establishment

Name	Address	ID/FEI	Business Operations
Jerome Stevens Pharmaceuticals, Inc.		021130638	MANUFACTURE(50564-554, 50564-555) , PACK(50564-554, 50564-555)

Revised: 4/2021 Jerome Stevens Pharmaceuticals, Inc.