PAPAVERINE (Systemic)

Introduction

VA CLASSIFICATION (Primary)¾CV500

Note: For information pertaining to the use of papaverine for impotence, see Papaverine (Intracavernosal) .
Commonly used brand name(s):Cerespan; Genabid; Pavabid; Pavabid HP; Pavacels; Pavacot; Pavagen; Pavarine; Pavased; Pavatine; Pavatym; Paverolan.

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

Category

Vasodilator.

Indications

Unaccepted

Although papaverine has previously been classed as a "grandfather drug" and exempted from FDA's DESI classification, the Peripheral and Central Nervous System Drugs Advisory Committee of the FDA has concluded after studies and hearings that, in spite of its proven vasodilating effects, the medication has not been shown to be effective for its claimed indications. These include use as a smooth muscle relaxant in the treatment of cerebral and peripheral ischemia associated with arterial spasm and myocardial ischemia complicated by arrhythmias; and for visceral spasm as in ureteral colic, biliary colic, or gastrointestinal colic.

Pharmacology/Pharmacokinetics

Physicochemical characteristics:

Molecular weight¾375.85

Mechanism of action/Effect:

Papaverine has a direct, nonspecific relaxant effect on vascular, cardiac, and other smooth muscle. 2

Absorption:

Variable; oral bioavailability is usually about 54%, but absorption from extended-release dosage forms is poor.

Protein binding:

Very high (approximately 90%).

Biotransformation:

Hepatic.

Half-life:

0.5 to 2 hours (variable; may be as long as 24 hours).

Elimination:

Renal (as metabolites).
In dialysis¾Removable by hemodialysis.

Precautions to Consider

Pregnancy/Reproduction

Pregnancy¾Studies have not been done in humans.
Studies have not been done in animals.
FDA Pregnancy Category C.

Breast-feeding

It is not known whether papaverine is distributed into breast milk. However, problems in humans have not been documented.

Pediatrics

Appropriate studies on the relationship of age to the effects of papaverine have not been performed in the pediatric population. However, pediatrics-specific problems that would limit the usefulness of this medication in children are not expected.

Geriatrics

Appropriate studies on the relationship of age to the effects of papaverine have not been performed in the geriatric population. However, the risk of papaverine-induced hypothermia may be increased in elderly patients.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.
Levodopa

(concurrent use may decrease the therapeutic effects of levodopa because of possible blockade of dopamine receptors by papaverine)

Smoking, tobacco

(heavy smoking may interfere with the therapeutic effect of papaverine because nicotine constricts blood vessels)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):
With physiology/laboratory test values

Alanine aminotransferase (ALT [SGPT]) concentration, serum and

Alkaline phosphatase concentration, serum and

Aspartate aminotransferase (AST [SGOT]) concentration, serum and

Bilirubin concentration, serum and

Eosinophil count

(may be increased; signs of hepatic hypersensitivity)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Except under special circumstances, this medication should not be used intravenously when the following medical problem exists

>> Atrioventricular (AV) heart block, complete

(large doses can depress AV and intraventricular conduction and produce serious arrhythmias)

Risk-benefit should be considered when the following medical problems exist

Angina or

Myocardial infarction, recent or

Stroke, recent

(ischemia may be exacerbated by a possible "steal effect" since papaverine has a greater effect on peripheral than cerebral and coronary vessels, leading to a further decrease in flow to ischemic areas)

Glaucoma

>> Myocardial depression

(large doses may cause further depression)

Sensitivity to papaverine 2

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):
Hepatic function tests

(may be indicated if patient develops gastrointestinal symptoms or jaundice suggesting hepatic hypersensitivity)

Intraocular pressure measurements

(recommended at periodic intervals in glaucoma patients who are receiving papaverine)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention

Incidence rare

Hepatic hypersensitivity (yellow eyes or skin)
With parenteral administration

Thrombosis (redness, swelling, or pain at injection site)
Those indicating need for medical attention only if they continue or are bothersome

With rapid parenteral administration

Deep breathing; fast heartbeat; flushing of face; hypotension (dizziness)

Overdose

For more information on the management of overdose or unintentional ingestion, contact a Poison Control Center (see Poison Control Center Listing).

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Blurred or double vision; drowsiness; weakness
Treatment of overdose

Treatment of acute poisoning consists of: Removal or delay of absorption of papaverine by administration of tap water, milk, or activated charcoal, and removal of stomach contents by gastric lavage or emesis, followed by catharsis; appropriate measures for treatment of coma or respiratory depression and maintenance of blood pressure; hemodialysis may be useful.

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Papaverine (Systemic).
In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):
Before using this medication

>> Conditions affecting use, especially:

Sensitivity to papaverine
Use in the elderly¾Increased risk of hypothermia
Other medical problems, especially complete atrioventricular heart block (for intravenous administration only) and myocardial depression
Proper use of this medication

Taking with or following meals, milk, or antacids, to reduce nausea

Proper administration of extended-release capsules: Swallowing whole without crushing, breaking, or chewing before swallowing or, if too large to swallow, mixing contents with jam or jelly and swallowing without chewing

>> Proper dosing
Missed dose: Taking as soon as possible; not taking if almost time for next dose; not doubling doses
>> Proper storage
Precautions while using this medication

Checking with physician before discontinuing medication

Avoiding smoking because nicotine constricts blood vessels

>> Caution when getting up from a lying or sitting position or when climbing stairs

Side/adverse effects

Signs of potential side effects, especially hepatic hypersensitivity and (for parenteral administration only) thrombosis

General Dosing Information

Dosage of papaverine should be reduced if drowsiness occurs.
If signs of hepatic hypersensitivity occur, it is recommended that papaverine therapy be withdrawn.
For oral dosage forms only

Oral papaverine may be administered with or following meals, milk, or antacids to reduce stomach upset.
For parenteral dosage forms only

The intra-arterial route should be used only by those experienced in the procedure.
Intravenous administration may be used when an immediate effect is desired, but should be done slowly over 1 or 2 minutes to avoid adverse effects (arrhythmias and fatal apnea).

Oral Dosage Forms

PAPAVERINE HYDROCHLORIDE EXTENDED-RELEASE CAPSULES

Usual adult dose

Vasospastic therapy adjunct¾
Oral, 150 mg every twelve hours, 2 the dosage being increased to 150 mg every eight hours or 300 mg every twelve hours if necessary. 2

Strength(s) usually available

U.S.¾150 mg (Rx)[Cerespan] [Genabid] [Pavabid (sucrose)] [Pavacels] [Pavacot] [Pavagen] [Pavarine] [Pavased] [Pavatine] [Pavatym] [Paverolan] [Generic]

Canada¾Not commercially available.

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), in a well-closed container, unless otherwise specified by manufacturer.

PAPAVERINE HYDROCHLORIDE TABLETS USP

Usual adult dose

Vasospastic therapy adjunct¾
Oral, 100 to 300 mg three to five times a day.

Strength(s) usually available

U.S.¾30 mg (Rx) [Generic]

60 mg (Rx)[Pavacot] [Generic]

100 mg (Rx)[Pavacot] [Generic]

200 mg (Rx) [Generic]

300 mg (Rx)[Pavabid HP] [Generic]

Canada¾100 mg (OTC) [Generic]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Store in a tight container.

Parenteral Dosage Forms

PAPAVERINE HYDROCHLORIDE INJECTION USP

Usual adult dose

Vasospastic therapy adjunct¾
Intra-arterial, 40 mg, administered slowly over a one- to two-minute period.
Intramuscular or intravenous, 30 to 120 mg every three hours, administered slowly over a one- to two-minute period. 2 In the treatment of cardiac asystole, two doses may be given ten minutes apart.

Usual pediatric dose

Intramuscular or intravenous, 1.5 mg per kg of body weight four times a day.

Strength(s) usually available

U.S.¾30 mg per mL (Rx) [Generic]

Canada¾32.5 mg per mL (OTC) [Generic]

Packaging and storage:

Store below 40 °C (104 °F), preferably between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

Incompatibilities:

Papaverine hydrochloride injection is physically incompatible with lactated Ringer's injection (precipitate will form).