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Diphenidol (Systemic)

INN:
Difenidol {05}

JAN:
Difenidol {05}

VA CLASSIFICATION
Primary: CN550
Secondary: GA609

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

*Not commercially available in the U.S.

†Not commercially available in Canada.

Category:

Antiemetic—

antivertigo agent—

Indications

Accepted

Vertigo (prophylaxis and treatment)—Diphenidol is indicated in the prevention and symptomatic treatment of peripheral (labyrinthine) vertigo and associated nausea and vomiting that occur in such conditions as Meniere's disease and surgery of the middle and inner ear. {03} {04}

Nausea and vomiting (prophylaxis and treatment) and
Nausea and vomiting, cancer chemotherapy–induced (prophylaxis and treatment)—Diphenidol is indicated also for the control of nausea and vomiting associated with postoperative states, malignant neoplasms, labyrinthine disturbances, antineoplastic agent therapy, radiation sickness, and infectious diseases. {03} {04}

Unaccepted
Diphenidol has been used in the treatment of ventricular tachyarrhythmias; however, the use of diphenidol as an antiarrhythmic is unwarranted because of the frequency and severity of adverse central nervous system (CNS) effects.

Diphenidol is *not* indicated for use in the nausea and vomiting of pregnancy.

Pharmacology/Pharmacokinetics

Physicochemical characteristics:
Molecular weight—
Diphenidol hydrochloride: 345.91 {05}

Mechanism of action/Effect:

The mechanism by which diphenidol exerts its antiemetic and antivertigo effects is not precisely known. It is thought to diminish vestibular stimulation and depress labyrinthine function. An action on the medullary chemoreceptive trigger zone may also be involved in the antiemetic effect. {03} {04}

Other actions/effects:

Diphenidol has no significant sedative, tranquilizing, or antihistaminic action. {03} It has a weak peripheral anticholinergic effect. {03} {04}

Absorption:

Well absorbed from gastrointestinal tract after oral administration {06}.

Half-life:

4 hours.

Time to peak concentration:

11/2 to 3 hours {06}.

Elimination:
Primarily renal (about 90% of drug) {03} {04}. Most of an oral dose is excreted within 3 to 4 days. {03}

Precautions to Consider

Pregnancy/Reproduction

Pregnancy—
Studies in humans and animals have not shown a significant difference in conception rate, litter size, live birth or viability, or birth abnormalities between diphenidol-treated and untreated control groups. {03}

Breast-feeding

Problems in humans have not been documented.

Pediatrics

Appropriate studies on the relationship of age to the effects of diphenidol used in the prophylaxis or treatment of vertigo have not been performed in the pediatric population. Also, appropriate studies with diphenidol used in the prophylaxis or treatment of nausea and vomiting in children weighing less than 22.8 kg have not been performed; use in these children is not recommended. {03}

Geriatrics

No information is available on the relationship of age to the effects of diphenidol in geriatric 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)—not necessarily inclusive (» = major clinical significance):

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

Anticholinergics or other medications with anticholinergic activity {04} (see **Appendix II**) (anticholinergic effects may be potentiated when these medications are used concurrently with diphenidol)

Apomorphine (prior ingestion of diphenidol may decrease the emetic response to apomorphine in the treatment of poisoning)

» CNS depression–producing medications (see **Appendix II**) (concurrent use may potentiate the effects of either these medications or diphenidol)

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)— not necessarily inclusive (» = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problem exists:
» Anuria {03}{04} (renal shutdown may increase risk of systemic accumulation of diphenidol)

Risk-benefit should be considered when the following medical problems exist
Gastrointestinal tract obstructive disease, such as stenosing peptic ulcer and pyloric or duodenal obstruction {03} {04} (decrease in motility and tone may occur, resulting in obstruction and gastric retention)

Genitourinary tract obstructive disease, such as prostatic hypertrophy {03}{04} (use may precipitate urinary retention)

Glaucoma {03}{04} (use may increase intraocular pressure)

» Hypotension {02} (may be exacerbated)

» Renal function impairment (decreased excretion may increase the risk of side effects {01})

Sensitivity to diphenidol {03}{04}

Caution is recommended when diphenidol is used, since signs of intestinal obstruction, brain tumor, or overdosage of toxic drugs may be obscured by its antiemetic action. {03}{04}

Side/Adverse Effects

Note: Hallucinations, disorientation, and confusion have been reported with usual doses of diphenidol within the first 3 days of therapy. {03} {04} Upon cessation of therapy, symptoms disappeared within 3 days. {03} {04}
The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)—not necessarily inclusive:

Those indicating need for medical attention
Incidence rare
—less than 0.5%
Confusion *{03}{04}{06}*

hallucinations *{03}{04}{06}* (seeing, hearing, or feeling things that are not there)

Those indicating need for medical attention only if they continue or are bothersome
Incidence more frequent

Drowsiness *{03}{04}{06}*

Incidence less frequent or rare

Blurred vision *{03}{04}{06}*

dizziness *{03}{04}{06}*

dryness of mouth *{03}{04}{06}*

headache *{03}{04}{06}*

heartburn *{03}{04}{06}*

nervousness, restlessness, or trouble in sleeping *{03}{04}{06}*

skin rash *{03}{04}*

stomach upset or pain *{03}{04}*

unusual tiredness or weakness *{03}{04}*

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)–not necessarily inclusive:

Drowsiness, severe

hypotension (severe unusual tiredness or weakness)

respiratory depression (shortness of breath or troubled breathing)

Treatment of overdose
Treatment of overdosage is essentially supportive {03} {04}, including the following:

To decrease absorption—Early gastric lavage. {03} {04}

Supportive care—Maintenance of blood pressure and respiration {03} {04}. Patients in whom intentional overdose is confirmed or suspected should be referred for psychiatric consultation.

Patient Consultation
As an aid to patient consultation, refer to Advice for the Patient, Diphenidol (Systemic) .

In providing consultation, consider emphasizing the following selected information (» = major clinical significance):

Before using this medication
» Conditions affecting use, especially:
Sensitivity to diphenidol

Use in children—Not recommended for prophylaxis or treatment of nausea and vomiting in children weighing less than 22.8 kg

Other medications, especially CNS depressants
Other medical problems, especially anuria, hypotension, renal function impairment

Proper use of this medication
Taking with food, water, or milk to minimize gastric irritation

» Importance of not taking more medication than the amount prescribed

» Proper dosing
Missed dose: If on a regular dosing schedule—using as soon as possible; if almost time for next dose, not using at all; not doubling doses

» Proper storage

Precautions while using this medication
» Avoiding use of alcohol or other CNS depressants

» Caution if drowsiness or blurred vision occurs

Side/adverse effects
Signs of potential side effects, especially confusion and hallucinations

General Dosing Information
Because of its potential to cause hallucinations, disorientation, or confusion, use of diphenidol should be limited to patients who are hospitalized or under comparable continuous close professional supervision. {03} {04}

Diet/Nutrition
In the preventive treatment of vertigo and associated nausea and vomiting, diphenidol may be taken with food, water, or milk to minimize gastric irritation. However, if nausea and vomiting are present, the further intake of liquids or food may aggravate the condition.

Oral Dosage Forms

DIPHENIDOL HYDROCHLORIDE TABLETS

Usual adult and adolescent dose
Antiemetic and
Antivertigo
Oral, 25 to 50 mg every four hours as needed. {03} {04}

Usual adult prescribing limits
300 mg a day. {04}

Usual pediatric dose
Antiemetic
Oral, 880 mcg (0.88 mg) per kg of body weight or 25 mg per square meter of body surface area every four hours as needed {02}. If symptoms persist, dose may be repeated in one hour after initial dose; subsequent doses should be spaced four hours apart; or,

For children weighing 22.8 to 45.6 kg: Oral, 25 mg every four hours as needed. {03} {04}

Note: Children weighing up to 22.8 kg—Use is not recommended. {03} {04}

Usual pediatric prescribing limits
For children weighing 22.8 kg and over: 5.5 mg per kg of body weight a day. {04}

Strength(s) usually available
U.S.—
Not commercially available.

Canada—
Not commercially available.

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

Auxiliary labeling:
- May cause drowsiness.
- Avoid alcoholic beverages.

Revised: 01/29/1999

References

1. Vontrol product monograph. In: PDR. Physicians' desk reference. 40th ed. 1986. Oradell, NJ: Medical Economics Company; 1986. p. 1731.
2. Shirkey's Pediatric Textbook from the 1980's
3. Vontrol package insert (SKF—US), Rev 6/85, Rec 5/89.
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6. Reynolds JEF, editor. Martindale: the extra pharmacopeia. 27th ed. London: The Pharmaceutical Press; 1977. p. 1752.