PRODUCT LITERATURE

BUSPAN TABLET 10 MG

Each tablets contains
Hyoscine Butylbromide BP 10 mg

Preservative
Sodium Benzoate BP 0.15% w/w

Description
Round flat white odourless tablet with score on one side and H11 embossed on the other side with score.

Pharmacodynamics/Pharmacokinetics
Mechanism of action/Effect:
Anticholinergic-The naturally occurring belladonna alkaloids, semisynthetic derivatives, quaternary ammonium compounds, and, to a lesser extent, the synthetic tertiary amines inhibit the muscarinic actions of acetylcholine on structures innervated by postganglionic cholinergic nerves as well as on smooth muscles that respond to acetylcholine but lack cholinergic innervation. These postganglionic receptor sites are present in the autonomic effector cells of the smooth muscle, cardiac muscle, sinostrial and a trioventricular nodes, and exocrine glands. Depending on the dose, anticholinergisc may reduce the motility and secretory activity of the gastrointestinal system, and the tone of the ureter and urinary bladder and may have a slight relaxant action on the bile ducts and gallbladder. In general, the smaller doses of anticholinergics inhibit salivary and bronchial secretions, sweating, and accommodation; cause dilatation of the pupil; and increase the heart rate. Larger doses are required to decrease motility of the gastrointestinal and urinary tracts and to inhibit gastric acid secretion.

Antispasmodic, gastrointestinal-Unproven. A local and direct action on smooth muscle, to reduce tone and motility of the gastrointestinal tract, has been suggested to explain the apparent gastrointestinal antispasmodic effect of the synthetic tertiary amine compounds.

Antidysmenorrheal-Effectiveness in relieving dysmenorrhea is due to spasmolytic action.

Antiarrhythmic-Inhibition of muscarinic actions of acetylcholine at postganglionic receptor sites present in the autonomic effector cells of the cardiac muscle, and sinostrial and a trioventricular nodes.

Antidote (to cholinesterase inhibitors; to muscarine; to organophosphate pesticides)-Atropine and hyoscyamine antagonize the actions of cholinesterase inhibitors at muscarinic receptor sites, including increased tracheobronchial and salivary secretion, bronchoconstriction, autonomic ganglionic stimulation, and, to a moderate extent, central actions.
Cholinergic adjunct (curariform block)-A tropine and hyoscyamine antagonize the actions, such as vagal and secretory enhancing effects, of cholinesterase inhibitors used in the treatment of non-depolarizing neuromuscular blockade.
Anesthesia adjunct-Scopolamine depresses the cerebral cortex; in large doses and in conjunction with analgesics, produces loss of memory.
Antiemetic-Belladonna and scopolamine act primarily by reducing the excitability of the labyrinthine receptors and by depressing conduction in the vestibular cerebellar pathway.
Antivertigo-The exact mechanism by which belladonna and scopolamine exert their antimotion sickness and antivertigo effects is unknown; however, they probably act either on the cortex or more peripherally on the maculae of the utricle and saccule.

Other actions/effects:
Scopolamine: Has peripheral action similar to that of atropine but, in contrast to atropine, is depressant to the CNS at therapeutic doses; it does not stimulate the medullary centers and therefore does not increase respiration or elevate blood pressure. Scopolamine has a more potent action than atropine on the sphincter muscle of the iris and the ciliary muscle of the lens, and on the secretory glands such as salivary, bronchial, and sweat glands.

Absorption:
Tertiary amines-Rapidly absorbed from gastrointestinal tract; also enter the circulation through the mucosal surfaces of the body.
Quaternary ammonium compounds-Gastrointestinal absorption is poor and irregular. Total absorption after an oral dose is about 10 to 25%.

Distribution:
Exact distribution of anticholinergic has not been fully determined. However, tertiary amines appear to be distributed throughout the entire body and readily cross the blood-brain barrier, while quaternary ammonium compounds exhibit minimal passage across the blood-brain barrier and into the eye.
Atropine, belladonna, and hyoscyamine are distributed into breast milk.

Protein binding:
Scopolamine hydrobromide-Low

Biotransformation:
Most anticholinergics-Hepatic, by enzymatic hydrolysis

Half-life:
Elimination:
Scopolamine-8 hours.

Drug	Onset of action	Duration of action	Elimination (% excreted unchanged)
Scopolamine hydrobromide	Antisialagogue-Oral: 30-60 min Parenteral: 30 min	Oral: 4-6 hr Parenteral: 4 hr	Renal (1 of oral dose) (3.4 of SC dose)

Indication
Management of visceral spasm in GIT, billiary and genitourinary system.

Route of administration
Oral.

Recommended Dose
1 - 2 tablets every 8 hourly

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

Brain damage, in children (CNS effects may be exacerbated)
»Cardiac disease, especially cardiac arrhythmias, congestive heart failure, coronary artery disease, and mitral stenosis (increase in heart rate may be undesirable)
Down's syndrome (abnormal increase in pupillary dilation and acceleration of heart rate may occur)
»Esophagitis, reflux (decrease in esophageal and gastric motility and relaxation of lower esophageal sphincter may promote gastric retention by delaying gastric emptying and may increase gastroesophageal reflux through an incompetent sphincter)
Fever (may be increased through suppression of sweat gland activity)
» Gastrointestinal tract obstructive disease as in achalasia and pyloroduodenal stenosis (decrease in motility and tone may occur, resulting in obstruction and gastric retention)
» Glaucoma, angle-closure, or predisposition to (mydriatic effect resulting in increased intraocular pressure may precipitate an acute attack of angle-closure glaucoma)
» Glaucoma, open-angle (mydriatic effect may cause a slight increase in intraocular pressure; glaucoma therapy may need to be adjusted)
»Haemorrhage, acute, with unstable cardiovascular status (increase in heart rate may be undesirable)
Hepatic function impairment (decreased metabolism of anticholinergic)
» Hernia, hiatal, associated with reflux esophagitis (anticholinergics may aggravate condition)
Hypertension (may be aggravated)
Hyperthyroidism (characterized by tachycardia, which may be increased)
»Intestinal atony in the elderly or debilitated patient or
» Paralytic ileus (anticholinergic use may result in obstruction)
Lung disease, chronic, especially in infants, small children, and debilitated patients (reduction in bronchial secretion can lead to inspissation and formation of bronchial plugs)
» Myasthenia gravis (condition may be aggravated because of inhibition of acetylcholine action)
Neuropathy, autonomic (urinary retention and cycloplegia may be aggravated)
» Prostatic hypertrophy, nonobstructive or
»Urinary retention, or predisposition to or
»Uropathy, obstructive, such as bladder neck obstruction due to prostatic hypertrophy (urinary retention may be precipitated or aggravated)
»Pyloric obstruction (may be aggravated)
Renal function impairment (decreased excretion may increase the risk of side effects)
Sensitivity to any belladonna alkaloids or derivatives
Spastic paralysis, in children (response to anticholinergics may be increased)
»Tachycardia (may be increased)
Toxemia of pregnancy (hypertension may be aggravated)
»Ulcerative colitis (large anticholinergic doses may suppress intestinal motility, possibly causing paralytic ileus; also, use may precipitate or aggravate the serious complication, toxic megacolon)
Xerostomia (prolonged use may further reduce limited salivary flow)
Caution in use is also recommended in patients over 40 years of age because of the danger of precipitating undiagnosed glaucoma.

Warning and Precautions
Cross-sensitivity and/or related problems
For all anticholinergics-Patients sensitive to one belladonna alkaloid or derivative may be sensitive to the other belladonna alkaloids or derivatives also.

Pediatrics
For all anticholinergics:
Infants and young children are especially susceptible to the toxic effects of anticholinergics.
Close supervision is recommended for infants and children with spastic paralysis or brain damage since an increased response to anticholinergics has been reported in these patients and dosage adjustments are often required.
When anticholinergics are given to children where the environmental temperature is high, there is risk of a rapid increase in body temperature because of these medications" suppression of sweat gland activity
A paradoxical reaction characterized by hyperexcitability may occur in children taking large doses of anticholinergics.

Geriatrics
Geriatric patients may respond to usual doses of anticholinergics with excitement, agitation, drowsiness, or confusion.
Geriatric patients are especially susceptible to the anticholinergic side effects, such as constipation, dryness of mouth, and urinary retention (especially in males). If these side effects occur and continue or are severe, medication should probably be discontinued.
Caution is also recommended when anticholinergics are given to geriatric patients, because of the danger of precipitating undiagnosed glaucoma.
Memory may become severely impaired in geriatric patients, especially those who already have memory problems, with the continued use of anticholinergics since these drugs block the actions of acetylcholine, which is responsible for many functions of the brain, including memory functions.

Dental
Prolonged use of anticholinergic may decrease or inhibit salivary flow, thus contributing to the development of caries, periodontal disease, oral candidiasis, and discomfort.

Interactions with Other Medicaments
For all anticholinergics
Alkalizers, urinary, such as:

Antacids, calcium- and/or magnesium-containing
Carbonic anhydrase inhibitors
Citrates
Sodium bicarbonate (urinary excretion of anticholinergic may be delayed by alkalization of the urine, thus potentiating the anticholinergics' therapeutic and/or side effects)
» Antacids or
» Antidiarrheals, adsorbent (simultaneous use of these medications may reduce absorption of anticholinergics, resulting in decreased therapeutic effectiveness; doses of these medications should be spaced 2 or 3 hours apart from doses of anticholinergics)
» Anticholinergics or other medications with anticholinergic activity (concurrent use with anticholinergics may intensify anticholinergic effects; patients should be advised to report occurrence of gastrointestinal problems promptly since paralytic ileus may occur with concurrent therapy)
Antimyasthenics (concurrent use with anticholinergics may further reduce intestinal motility; therefore, caution is recommended; although atropine may be used to reduce or prevent the muscarinic effects of antimyasthenics, routine concurrent use is not recommended since the muscarinic effects may be the first signs of antimyasthenic overdose, and masking such effects with atropine may prevent early recognition of cholinergic crisis)
» Cyclopropane (concurrent intravenous administration of anticholinergics with Cyclopropane anesthesia may result in ventricular arrhythmias; however, if the anticholinergic used is glycopyrrolate, the risk is reduced if glycopyrrolate is given in increments of 100 mcg [0.1 mg] or less)
Haloperidol (antipsychotic effectiveness of haloperidol may be decreased in schizophrenic patients)
» Ketoconazole (anticholinergics may increase gastrointestinal pH, possibly resulting in a marked reduction in ketoconazole absorption during concurrent use with anticholinergics; patients should be advised to take these medications at least 2 hours after ketoconazole)
Metoclopramide (concurrent use with anticholinergics may antagonize metoclopramide's effects on gastrointestinal motility)
Opioid (narcotic) analgesics (concurrent use with anticholinergics may result in increased risk of severe constipation, which may lead to paralytic ileus, and/or urinary retention)
» Potassium chloride, especially wax-matrix preparations (concurrent use with anticholinergics may increase severity of potassium chloride-induced gastrointestinal lesions)

For scopolamine (in addition to interactions listed above)
» CNS depression-producing medications, other (concurrent use may potentiate the effects of either these medications or scopolamine, resulting in additive sedation)
Lorazepam, parenteral (concurrent use of scopolamine and parenteral lorazepam is reported to have no added beneficial effect and their combined effect may increase the incidence of sedation, hallucination, and irritational behavior)

Pregnancy and Lactation
Pregnancy
Scopolamine crosses the placenta. Studies with scopolamine have not been done in either animals or humans.

FDA Pregnancy Category C.

Labor
For scopolamine: Parenteral administration of scopolamine before the onset of labor may cause CNS depression in the neonate and may contribute to neonatal hemorrhage due to reduction in vitamin K-dependent clotting factors in the neonate.

Breast-feeding
For all anticholinergics-Anticholinergics may inhibit lactation.
For quaternary ammonium compounds- It is unlikely that these drugs are excreted in breast milk since they are incompletely absorbed from the gastrointestinal tract and have poor lipid solubility.

Side Effects
Allergic reaction (skin rash or hives)
Confusion
Increased intraocular pressure (eye pain)
Orthostatic hypotension (dizziness, feeling faint or continuing lightheadedness)
Medical attention needed only if continuing or bothersome
Bloated feeling
Constipation
Decreased flow of breast milk
Decreased salivary secretion (difficulty in swallowing)
Decreased sweating
Difficult urination
Difficulty in accommodation of the eye (blurred vision)
Drowsiness
Dryness of mouth, nose, throat, or skin
False sense of well-being
Headache
Lightheadedness, temporary-with parenteral administration
Loss of memory
Mydriatic effect (increased sensitivity of eyes to light)
Nausea or vomiting
Paradoxical reaction (trouble in sleeping)
Redness or other signs of irritation at injection site
Unusual tiredness or weakness
Symptoms and Treatment of Overdose
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:

Blurred vision, continuing, or changes in near vision
clumsiness or unsteadiness
confusion
difficulty in breathing-may lead to respiratory paralysis with quaternary ammonium compounds because of curare-like effects
dizziness
drowsiness, severe

dryness of mouth, nose, or throat, severe
fast heartbeat
fever
hallucinations
muscle weakness, severe-may lead to respiratory paralysis with quaternary ammonium compounds because of curare-like effects
seizures
slurred speech
tiredness, severe-may lead to respiratory paralysis with quaternary ammonium compounds because of curare-like effects
unusual excitement, nervousness, restlessness, or irritability
unusual warmth, dryness, and flushing of skin

Treatment of overdose
Recommended treatment for anticholinergic overdose includes the following:
To decrease absorption:
Emesis or gastric lavage with 4% tannic acid solution.
Administration of an aqueous slurry of activated charcoal.

Specific treatment:
To reverse severe anticholinergic symptoms, slow, intravenous administration of physostigmine in doses of 0.5 to 2 mg (0.5 to 1 mg in children, up to a total dose of 2 mg), at a rate not to exceed l mg per minute; may be given in repeated doses of 1 to 4 mg as needed, up to a total dose of 5 mg in adults.
Or, neostigmine methyl sulfate administered intramuscularly in doses of 0.5 to 1 mg, repeated every 2 to 3 hours; or intravenously in doses of 0.5 to 2 mg, repeated as needed.
To control excitement or delirium, administration of small doses of a short-acting barbiturate (100 mg thiopental sodium) or benzodiazepines, or rectal infusion of 2% solution of chloral hydrate.
To restore blood pressure, infusion of norepinephrine bitartrate or Metaraminol.

Supportive care:
Artificial respiration with oxygen if needed for respiratory depression.
Adequate hydration.
Symptomatic treatment as necessary.
Patients in whom intentional overdose is confirmed or suspected should be referred for psychiatric consultation.

Packing
Packed in blister-packs of 3x10's , 10x10's , 50x10's and 100x10's tablets in a paper box.

Storage Conditions
Store below 30°C in a dry place, protected from direct light.
Keep away from reach of children.

Expiry Date
3 years from date of manufacture

Name and Address of Distributor
ZONTRON PHARMACEUTICALS SDN BHD.
(445695-T)
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Lorong IKS Simpang Ampat B,
14100 Simpang Ampat, S.P.S.,
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Malaysian Drug Registration No. :
MAL19900043ACZ

Date of Revision:
24/06/2025