**New Zealand Datasheet**

# 1 PRODUCT NAME
Benztropine Omega 1mg/ml Solution for Injection

# 2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each mL of sterile clear colourless solution contains: 1 mg of Benztropine mesylate and 9 mg of Sodium chloride in Water for injection.

Hydrochloric acid and/or Sodium hydroxide may have been added to adjust the pH.

For the full list of excipients, see Section 6.1.

# 3 PHARMACEUTICAL FORM
Solution for injection

# 4 CLINICAL PARTICULARS
## 4.1 Therapeutic indications
Benztropine Omega is recommended for all etiologic groups of parkinsonism - arteriosclerotic, postencephalitic, idiopathic and drug-induced.

It can be effective at any stage of the disease, even when a patient has become bedridden. Often it is helpful in patients who have become unresponsive to other agents.
Though parkinsonism is chronic and usually progressive, its symptoms often can be controlled by suitable treatment. Therapy is directed toward control of disturbing symptoms to permit maximum integration of function and minimum discomfort.

In non-drug-induced parkinsonism, partial control of symptoms is the usual therapeutic accomplishment.

Benztropine Omega is a powerful anticholinergic agent, mainly effective in relieving tremor and rigidity. Many other troublesome signs and symptoms, including sialorrhoea, drooling, mask- like facies, oculogyric crises, speech and writing difficulties, dysphagia, gait disturbances, and pain and insomnia due to cramps and muscle spasm are also ameliorated.

Extensive muscle rigidity and spasm, often more disturbing than tremor, may be alleviated.
Improvement in muscle function relieves many stigmata of parkinsonism. During therapy with Benztropine Omega, the characteristic frozen facies, gait, and posture return toward normal; speech becomes freer; and sustained rigidity; discomfort, and restlessness during sleep usually are relieved.

Physiotherapy can be applied more easily and may be more effective.

**Drug-induced parkinsonism**
Benztropine Omega relieves manifestations of parkinsonism that may appear during treatment with phenothiazine derivatives and reserpine. Usually it is helpful in combatting tremulousness; restlessness; feelings of tension; ptyalism; urinary frequency, “lockjaw”; and acute dystonic reactions such as torticollis, oculogyric crises, and dysphagia.

## 4.2 Dose and method of administration
Benztropine Omega is available as an injection for intravenous and intramuscular use.

The injection is especially useful for psychotic patients with acute, dystonic reactions or other reactions that make oral medication difficult or impossible. It is recommended also when a more rapid response is desired than can be obtained with the tablets.

Since there is no significant difference in onset of effect after intravenous and intramuscular injection, usually there is no need to give Benztropine Omega intravenously. It is quickly effective after either route, with improvement sometimes noticeable a few minutes after injection. In emergency situations, when the condition of the patient is alarming, 1 to 2 mL of Benztropine Omega normally will provide quick relief. If the signs of parkinsonism begin to return, the dose can be repeated.

Because Benztropine Omega has cumulative action, therapy should be initiated with a low dose, which is increased gradually at five or six day intervals to the smallest amount necessary for optimal relief. Increases should be made in increments of 0.5 mg to a maximum of 6 mg, or until optimal results are obtained without excessive side effects.

**Arteriosclerotic, Idiopathic and Postencephalitic Parkinsonism**
The usual daily dosage of Benztropine Omega is 1 to 2 mg, with a range of 0.5 to 6 mg parenterally.

As with any agent used in parkinsonism, dosage must be individualised according to age and weight, and the type of parkinsonism being treated. Generally, older patients, thin patients, and patients with arteriosclerotic parkinsonism cannot tolerate large doses of Benztropine Omega. However, most patients with postencephalitic parkinsonism require fairly large doses and tolerate them well. Patients with a poor mental outlook are usually poor candidates for therapy.

In arteriosclerotic and idiopathic parkinsonism, therapy may be initiated with a single daily dose of 0.5 to 1 mg at bedtime. In some patients, this will be adequate; in others 4 to 6 mg a day may be required.

In postencephalitic parkinsonism, therapy may be initiated in most patients with 2 mg a day in one or more doses. In highly sensitive patients, therapy may be initiated with 0.5 mg at bedtime, and increased as necessary.

Some patients experience greatest relief by taking the entire dose at bedtime; others react more favourably to divided doses, two to four times a day. Frequently, one dose a day is sufficient, and divided doses may be unnecessary or undesirable.

The long duration of action of Benztropine Omega makes it particularly suitable for bedtime medication when its effects may last throughout the night. With Benztropine Omega patients are better able to turn in bed during the night and to rise in the morning.

When Benztropine Omega is started, do not terminate therapy with other antiparkinsonian agents abruptly; rather, reduce or discontinue them gradually. Many patients obtain greatest relief with a combination of Benztropine Omega and other medicines.

Benztropine Omega may be administered concomitantly with levodopa in which case the dose of each may need to be adjusted. However, if Benztropine Omega is continued when levodopa/carbidopa (in combination) is introduced, the dosage of Benztropine Omega may need to be adjusted.

**Drug-Induced parkinsonism**

When treating extrapyramidal disorders due to central nervous system medicines such as phenothiazine derivatives or reserpine, the recommended dosage is 1 to 4 mg once or twice a day orally or parenterally. Dosage must be individualised according to the needs of the patient. Some patients require more than recommended; others do not need as much.

In acute dystonic reactions, 1 to 2 mg of Benztropine Omega intravenously quickly relieves the condition. After that, 1 to 2 mg given orally twice a day, usually prevents recurrence.

Extrapyramidal disorders that develop soon after initiation of treatment with phenothiazines or reserpine, are likely to be transient. One to 2 mg of benztropine mesyalte orally, two or three times a day, usually provides relief within one or two days. After one or two weeks of administration, Benztropine Omega should be withdrawn to determine the continued need for it. If parkinsonism recurs, Benztropine Omega can be reinstituted.

Certain extrapyramidal disorders which develop slowly, such as tardive dyskinesia, usually do not respond to Benztropine Omega.

Patients must be closely observed for severe reactions and Benztropine Omega discontinued temporarily if they appear. (See Sections 4.4 and 4.8).

Benztropine Omega should not be used beyond the period necessary to counteract the extrapyramidal manifestations. Although medication with the medicine causing parkinsonism can frequently be continued without change of dosage when adjunct therapy with Benztroprine Omega is used, a reduction in dosage of the psychotropic agent might be indicated.

## 4.3 Contraindications

Because of its atropine-like side effects, this medicine is contraindicated in children under three years of age, and should be used with caution in older children.

The use of the medicine is contraindicated in the presence of glaucoma. (see Section 4.4).

Benztropine Omega is contraindicated in patients who are hypersensitive to any component of this product.

## 4.4 Special warnings and precautions for use

**PRECAUTIONS**

**General**

Since Benztropine Omega has cumulative action, continued supervision is advisable.
Patients with a tendency to tachycardia, and patients with prostatic hypertrophy, should be closely observed during treatment. Dysuria may occur, but rarely becomes a problem.
The physician should be aware of the possible occurrence of glaucoma. Although the medicine does not appear to have any adverse effect on simple glaucoma, it should not be used in narrow-angle glaucoma.

In large doses, the medicine may cause complaints of weakness and inability to move particular muscle groups. For example, if the neck has been rigid and suddenly relaxes, it may feel weak, causing some concern. In this event, dosage adjustment is required.

Mental confusion and excitement may occur with large doses, or in susceptible patients. Visual hallucinations have been reported occasionally. Furthermore, in the treatment of

extrapyramidal symptoms due to central nervous system medicines, such as phenothiazines, and reserpine in patients with a mental disorder, occasionally there may be intensification of mental disorders. Although benztropine mesylate need not be discontinued when this occurs, the psychotogenic potential of antiparkinsonian medicines should be considered when planning the management of patients with mental disorders. Also, when using benztropine mesylate in these patients they should be kept under careful observation especially at the beginning of treatment or if dosage is increased. In such cases, at times, increased doses of antiparkinsonian medicines can precipitate a toxic psychosis.

Tardive dyskinesia may appear in some patients on long-term therapy with phenothiazines and related agents, or may occur after therapy with these medicines has been discontinued. Antiparkinsonism agents usually do not alleviate the symptoms of tardive dyskinesia, and in some instances may aggravate or unmask such symptoms. Benztropine Omega is not recommended in tardive dyskinesia.

Benztropine mesylate contains structural features of atropine and may produce anhidrosis. For this reason, it should be given with caution during hot weather, especially when given concomitantly with other atropine-like medicines to the chronically ill, the alcoholic, those who have central nervous system disease and those who do manual labour in a hot environment. Anhidrosis may be anticipated to occur more readily when some disturbance of sweating already exists. If there is evidence of anhidrosis, the possibility of hyperthermia should be considered. Dosage should be decreased at the discretion of the physician so that the ability to maintain body heat equilibrium by perspiration is not impaired. Severe anhidrosis and fatal hyperthermia have occurred.

**Use in Children**
See Section 4.3.

## 4.5 Interaction with other medicines and other forms of interaction

When Benztropine Omega is given concomitantly with phenothiazines, haloperidol or other medicines with anticholinergic or antidopaminergic activity, patients should be advised to report gastrointestinal complaints fever or heat intolerance promptly. Paralytic ileus, sometimes fatal, has occurred in patients taking anticholinergic-type antiparkinsonism medicines, including Benztropine Omega, in combination with phenothiazines and/or tricyclic antidepressants.

## 4.6 Fertility, pregnancy and lactation

**Pregnancy:** The safe use of this medicine in pregnancy has not been established.

**Nursing Mothers:** It is not known whether this medicine is excreted in human milk. Because many medicines are excreted in human milk, caution should be exercised when Benztropine Omega is administered to a nursing mother.

## 4.7 Effects on ability to drive and use machines

**Occupational Hazards**: Benztropine mesylate may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle.

## 4.8 Undesirable effects

Adverse reactions most of which are anticholinergic or antihistaminic in nature, are listed below by body system in order of decreasing severity:

**Cardiovascular**

Tachycardia.

**Digestive**
Constipation, dry mouth, nausea, vomiting.

Adjustment of dosage or time of administration sometimes helps to control these reactions. If dry mouth is so severe that there is difficulty in swallowing or speaking, or loss of appetite and weight, reduce dosage, or discontinue the medicine temporarily.

Nausea unaccompanied by vomiting usually can be disregarded. Slight reduction in dosage may control the nausea and still give sufficient relief of symptoms. Vomiting may be controlled by temporary discontinuation, followed by resumption at a lower dosage.

**Nervous system**
Toxic psychosis including confusion, disorientation, memory impairment, visual hallucinations; exacerbation of pre-existing psychotic symptoms; nervousness; depression; listlessness; numbness of fingers.

**Special Senses**
Blurred vision, dilated pupils.

**Urogenital**
Urinary retention, dysuria

**Metabolic/Immune and Skin**
Occasionally, an allergic reaction, e.g. skin rash, develops. Sometimes this can be controlled by reducing dosage, but occasionally benztropine mesylate has to be discontinued.

**Other**
Heart stroke, hyperthermia, fever.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

## 4.9 Overdose

**Manifestations:** May be any of those seen in atropine poisoning or antihistamine overdosage: CNS depression, preceded or followed by stimulation; confusion; nervousness; listlessness; intensification of mental symptoms or toxic psychosis in patients with mental illness being treated with phenothiazine derivatives or reserpine; hallucinations (especially visual); dizziness; muscle weakness; ataxia; dry mouth; mydriasis; blurred vision; palpitations; nausea; vomiting; dysuria; numbness of fingers; dysphagia; allergic reactions, e.g., skin rash; headache; hot, dry, flushed skin; delirium; coma; shock; convulsions; respiratory arrest; anhidrosis; hyperthermia; glaucoma; constipation.

**Treatment:** Physostigmine salicylate, 1 to 2 mg, s.c. or i.v., reportedly will reverse symptoms of anticholinergic intoxication (Duvoisin, R.C., Katz R., J. Amer. Med. Ass. 1968, 206: 1963- 1965). A second injection may be given after 2 hours if required. Otherwise treatment is symptomatic and supportive. Induce emesis or perform gastric lavage (contraindicated in precomatose, convulsive, or psychotic states). Maintain respiration. A short-acting barbiturate may be used for CNS excitement, but with caution to

avoid subsequent depression; supportive care for depression (avoid convulsant stimulants such as picrotoxin, pentylenetetrazol, or bemegride); artificial respiration for severe respiratory depression; a local miotic for mydriasis and cycloplegia; ice bags or other cold applications and alcohol sponges for hyperpyrexia, a vasopressor and fluids for circulatory collapse. Darken room for photophobia.

In case of overdose, immediately contact the Poisons Information Centre, call 0800 764 766 for advice.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiparkinson agents, ATC codes N04AC01
Benztropine Omega is a synthetic compound resulting from the combination of the active portions of atropine and diphenhydramine. Benztropine possesses both anticholinergic and antihistaminic effects, although only the former have been established as therapeutically significant in the management of parkinsonism.

Benztropine antagonizes the effect of acetylcholine. This decreases the imbalance between the neurotransmitters, acetylcholine and dopamine, which may improve the symptoms of early Parkinson's disease.

## 5.2 Pharmacokinetic properties

In a clinical study measuring serum levels of neuroleptics and anticholinergics via radioreceptor assay, the correlation between total daily dose of benztropine and serum concentration was extremely poor (r=0.281). Serum concentrations varied nearly 100-fold with given doses between 2 and 6 mg/day. A markedly non-linear relationship between daily dose and serum anticholinergic medicine levels was observed with an increasing oral dosage of benztropine. In most cases, 2 mg increments in oral dose were associated with several-fold increases in the serum level of anticholinergic activity.

It has been reported that the duration of action for benztropine may persist for up to 24 to 48 hours following a single 2 mg IM injection. Benztropine binds extensively, approximately 95%, with serum proteins. Benztropine crosses the blood-brain barrier.

## 5.3 Preclinical safety data

Not supplied.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Sodium Chloride
Sodium hydroxide (for pH adjustment) Water for Injections

## 6.2 Incompatibilities

Not applicable.

## 6.3 Shelf life

36 months

## 6.4 Special precautions for storage

Do not store above 30°C. Protect from freezing.

## 6.5 Nature and contents of container

Benztropine Omega is supplied in glass vials of 2mL, contained within a carton pack of 10 vials.

## 6.6 Special precautions for disposal

Single use vial. Discard unused portion.

# 7 MEDICINE SCHEDULE

Prescription Medicine.

# 8 SPONSOR

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# 9 DATE OF FIRST APPROVAL

Provisional consent 22 June 2017

# 10 DATE OF REVISION OF THE TEXT

15 March 2019