SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MYOCHOLINE-GLENWOOD® 25 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains 25 mg bethanechol chloride.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

MYOCHOLINE-GLENWOOD® 25 mg: Tablets with score line and imprint "MY25".

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Myocholine Glenwood is indicated in cases of postoperative urinary retention due to atony of the bladder in adults in diseases in which a stimulation of the bladder muscle is needed.

4.2 Posology and method of administration

Posology
The optimal dosage should be considered individually and depending on the type and severity of the disease.
Adults take 25-50 mg bethanechol chloride up to four times a day (4-8 MYOCHOLINE-GLENWOOD® tablets 25 mg per day).

Since there is no sufficient information on long term use of the product, if no improvement is observed within 30 days, stop the treatment and switch to alternative treatment.

Paediatric population
Myocholine Glenwood is not indicated for children and adolescents under 18 years old. The safety and efficacy of this drug in children have not yet been established.

Patients with impaired kidney and liver function
There is no information regarding this patient population.

Method of Administration
To avoid nausea and vomiting the tablets should be taken on an empty stomach about 1 hour before or two hours after a meal together with some liquid.
Treatment commences with a low dosage and is increased until an adequate effect is achieved.
The duration of treatment depends on the severity of the disease and the persistence of the symptoms. When the symptoms have subsided, medication with MYOCHOLINE-GLENWOOD® should be stopped.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- bronchial asthma;
- hypotension; hypertension; bradycardia; coronary heart disease; AV conduction disorders;
- epilepsy, Parkinson´s disease;

- external detrusor-sphincter-dyssynergia, if no effective relaxation of the external sphincter is evident at the same time;
- recent gastrointestinal operations due to the danger of a breakdown of suture;
- mechanical ileus or any other kind of obstruction in the urinary or gastrointestinal tract;
- hyperthyroidism;
- pronounced vagotonia;
- peritonitis; ulcer disease.

4.4 Special warnings and precautions for use

Particularly when commencing therapy, sudden changes of posture starting from the sitting position may lead to orthostatic hypotension.

Contraction of bladder muscles without open bladder sphincter due to hypertension can cause urinary reflux into the renal pelvis, followed by renal infection in case of bacteriuria.

Patients suffering from autonomic neuropathy (e.g. in the context of diabetes mellitus) could be more sensitive for side effects when MYOCHOLINE-GLENWOOD® tablets are administered. These patients should take a lower dose at the beginning of the therapy and they should be monitored closely regarding side effects.

4.5 Interactions with other medicinal products and other forms of interaction

Anticholinergic drugs (e.g. atropine) as well as quinidine and procainamide may antagonize the effect of bethanechol chloride.
Simultaneous administration of bethanechol chloride and other cholinergic drugs, especially cholinesterase inhibitors, may have additive effects of these substances and/or of bethanechol chloride up to toxic effects.
Simultaneous therapy with ganglion blocking agents may lead to a critical drop in blood pressure, with preceding severe abdominal pain.
Undesirable effects of tricyclic antidepressants, such as inactivation of salivation, sexual dysfunction, constipation and decreased bladder function, can be reduced by MYOCHOLINE- GLENWOOD® tablets.
Under therapy with MYOCHOLINE-GLENWOOD® tablets, changes in the following laboratory values can occur: serum amylase and serum lipase, SGOT (AST).

4.6 Fertility, pregnancy and lactation

Administration during pregnancy and lactation is not recommended.
In animal tests bethanechol chloride caused uterine contractions and passed into the mother’s milk.

4.7 Effects on ability to drive and use machines

Due to possible adverse effects like dizziness or giddiness, nausea, drop in blood pressure, blurred vision and changes in the accommodation ability, the ability to drive and use machines can be affected negatively.

4.8 Undesirable effects

Results from controlled clinical studies show undesirable effects with an overall frequency of 33% occuring during therapy. These are predominantly dose dependent and attributed to pharmacological effects of the medicament.
Undesirable reactions with supposed or possible interrelations with therapy are presented below considering system organ classes and overall frequencies.

The following incidences are used:
Very common (≥1/10)

Common	(≥1/100 to <1/10)
Uncommon	(≥1/1,000 to <1/100)
Rare	(≥1/10,000 to <1/1,000)
Very rare	(<1/10,000)
not known	(cannot be estimated from the available data)

Eye disorders:
Very rare: increased lacrimation, blurred vision, changes in accommodation ability.

Cardiac disorders:
Common: bradycardia.
Not known: temporary periods with atrial fibrillation were noticed in patients suffering from thyroid dysfunction.

Vascular disorders:
Common: drop in blood pressure.
Rare: especially at the beginning of therapy feeling of dizziness or giddiness (orthostatic hypotension).

Respiratory, thoracic and mediastinal disorders:
Very rare: retrosternal pain, bronchospasm, dyspnoea, wheezing, especially in patients with tendency towards bronchial constriction.

Gastrointestinal disorders:
Common: diarrhoea.
Uncommon: nausea and vomiting, gastrointestinal disturbances.
Very rare: eructation, ulcer.

Skin and subcutaneous tissue disorders:
Very common: skin flushing.
Very rare: white heat rash (Miliaria cristallina).

Renal and urinary disorders:
Very common: urinary urgency.

General disorders and administration site conditions:
Very common: increased salivation and perspiration (as a result of the parasympathetic stimulation).
Common: hypothermia.
Very rare: heat sensation, feeling tense, headache.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

4.9 Overdose

Indication of overdose
Bethanechol chloride poisoning is characterized by typical parasympathomimetic symptoms: nausea, abdominal cramps, urinary urgency, involuntary bladder voiding and bowel evacuation, perspiration, shock, atrioventricular block, asthma, dyspnoea with bronchial secretion, salivation.
Therapy of overdose
Atropine 0.5-1.0 mg (adults) and 10 µg/kg bodyweight (children) subcutaneous injection. Repeated injection if required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Parasympathomimetics, Choline esters, Bethanechol, ATC-Code: N07AB02.

Mechanism of action
Bethanechol chloride is a parasympathomimetic active substance whose major pharmacologic effects result from direct and selective stimulation of cholinergic receptors of the smooth muscle, especially those of the bladder and the gastrointestinal tract. Bethanechol chloride is a synthetic choline ester, which is chemically and pharmacologically similar to the neurotransmitter acetylcholine. Compared with acetylcholine, bethanechol chloride acts mainly on muscarinic receptors and shows in therapeutic dosage negligible nicotinergic effects as well as a significantly longer effectiveness due to its low sensitivity to cholinesterase.

Pharmacodynamic effects
Bethanechol chloride increases the tonus of the bladder muscle (detrusor) and the vesical pressure and therefore supports spontaneous bladder voiding.
Bethanechol chloride stimulates muscle activity of the gastrointestinal tract and digestive glands. The food passage in the entire digestive tract is accelerated. The increased tonus of the lower oesophageal sphincter prevents reflux of acidic stomach contents. Secretion from the lacrimal, salivary and perspiratory glands is increased. Bronchial constriction and increased bronchial secretion can be observed.

Clinical efficacy and safety
Bethanechol chloride given orally shows only slight cardiovascular effects. In usual therapeutic doses, heart rate, blood pressure and peripheral blood circulation remain unchanged. The function of ganglia and skeletal muscles is not affected.

5.2 Pharmacokinetic properties

Resorption
Bethanechol chloride is poorly absorbed from the gastrointestinal tract.

Distribution and biotransformation
In therapeutic doses, it does not cross the blood-brain barrier. Its distribution in other compartments, the metabolism and the elimination are not known in detail.

Pharmacokinetic/pharmacodynamic relationship
The effects of bethanechol chloride on the gastrointestinal and the urinary tracts can sometimes be observed after 30 minutes, but usually start 60-90 minutes after administration and last for approximately 1 hour. The effects can last for up to 6 hours if a dose of 300 mg or more is administered.

5.3 Preclinical safety data

In tests on animals, LD_{50} of orally administered bethanechol chloride was 250 mg/kg in mice and 1,500 mg/kg in rats.
Information concerning chronic toxicity, reproductive toxicology and mutagenicity is not available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium sulfate dihydrate, maize starch, talcum.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on packaging materials.

6.4 Special precautions for storage

Store below 25ºC. Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Blister strips made of PVC/Aluminium foil in cartons;
50 tablets of 25 mg
100 tablets of 25 mg

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Propharm Ltd., P.O.Box 4046, 23 Ben-Gurion street, Zichron Yaacov 30900.

8. MANUFACTURER

GLENWOOD GmbH Pharmazeutische Erzeugnisse
Arabellastrasse. 17, 81925 Munich, Germany.

9. MARKETING AUTHORISATION NUMBER

167-20-35286-00

Revised in May 2021 according to MOHs guidelines.