Product Document Title: Tolterodine L-Tartrate
Trade Name: DETRUSITOL
Product Document No.:756
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QUALITATIVE AND QUANTITATIVE COMPOSITION

Tolterodine L-tartrate 2 mg corresponding 1.37 mg tolterodine (rINN) respectively.

PHARMACEUTICAL FORM

Film Coated Tablet

CLINICAL PARTICULARS

Therapeutic Indications

For the treatment of overactive bladder with symptoms of urinary urgency, frequency, or urge incontinence.

Posology and methods of administration

The recommended dose is 2 mg b.i.d. The dose may be reduced from 2 mg to 1 mg b.i.d., based on individual tolerability.

Safety and effectiveness in children have not yet been established. Therefore, Detrusitol is not recommended for children until more information is available.

Use in Impaired Renal Function
The recommended total daily dose is 2 mg (i.e., tolterodine tablets 1 mg twice daily) for patients with impaired renal function (see Section – **Special Warnings and Precautions for Use**).

Use in Impaired Hepatic Function
The recommended total daily dose is 2 mg (i.e., tolterodine tablets 1 mg twice daily) for patients with impaired hepatic function (see Section – **Special Warnings and Precautions for Use**).

Use with Potent CYP3A4 Inhibitors
The recommended total daily dose is 2 mg (i.e., tolterodine tablets 1 mg twice daily) for patients receiving concomitant ketoconazole or other potent CYP3A4 inhibitors (see Section – **Special Warnings and Precautions for Use, CYP3A4 inhibitors**, and Section – **Interactions with Other Medicinal Products and Other Forms of Interaction**).

After 6 months the need for further treatment should be considered.

Contraindications

Detrusitol is contraindicated in patients with:
- Urinary retention
- Uncontrolled narrow angle glaucoma

- Myastenia gravis
- Known hypersensitivity to tolterodine or excipients
- Severe ulcerative colitis
- Toxic megacolon

Special Warnings and Special Precautions for Use

Detrusitol shall be used with caution in patients with:

- Significant bladder outlet obstruction at risk for urinary retention.
- Gastrointestinal obstructive disorders, e.g. pyloric stenosis.
- Renal disease. (see Section – **Posology and Method of Administration, Use in Impaired Renal Function**, and Section **Pharmacokinetic Properties, *Specific patient group*s)**
- Hepatic disease. (see Section – **Posology and Method of Administration, Use in Impaired Hepatic Function,** and Section – **Pharmacokinetic Properties, *Specific patient group*s)**
- Autonomic neuropathy.
- Hiatus hernia.
- Organic reason for urgency and frequency and should be considered before treatment.
- With myasthenia gravis.

In a study of the effect of tolterodine immediate-release tablets on the QT interval, the effect on the QT interval appeared greater for 8 mg/day (two times the therapeutic dose) compared to 4 mg/day and was more pronounced in CYP2D6 poor metabolizers (PM) than extensive metabolizers (EMs) (see Section – **Pharmacodynamic Properties**).

The effect of tolterodine 8 mg/day was not as large as that observed after four days of therapeutic dosing with the active control moxifloxacin. However, the confidence intervals overlapped.

These observations should be considered in clinical decisions to prescribe tolterodine extended-release capsules for patients with:

- Congenital or documented acquired QT prolongation
- Patients who are taking Class IA (e.g., quinidine, procainamide) or Class III (e.g.,amiodarone, sotalol) antiarrhythmic medications

Patients on concomitant medication with potent CYP3A4 inhibitors, such as macrolide antibiotics (erythromycin and clarithromycin) or antifungal agents (ketoconazole, itraconazole and miconazole) should be treated with caution until further data are available.

Interaction with other medicaments and other forms of interaction

Concomitant medication with other drugs that possess antimuscarinic properties may result in more pronounced therapeutic effect and adverse-effects. Conversely, the therapeutic effect of Detrusitol may be reduced by concomitant administration of muscarinic receptor agonists. The effect of prokinetics like metoclopramide and cisapride on GI tract (increased lower esophageal sphincter pressure and improved gastroduodenal coordination) may be decreased by Detrusitol.

Pharmacokinetic interactions are possible with other drugs metabolized by or inhibiting cytochrome P450 2D6 (CYP2D6) or CYP3A4. However, concomitant treatment with fluoxetine (a potent CYP2D6 inhibitor which is metabolised to norfluoxetine, a CYP3A4 inhibitor) result in only minor increase in the combined exposure of unbound Detrusitol and the equipotent 5-hydroxymethyl metabolite. This does not result in a clinically significant interaction.

Ketoconazole, a potent inhibitor of CYP3A4, significantly increased plasma concentrations of tolterodine when coadministered to poor metabolizers (i.e., persons devoid of CYP2D6 (metabolic pathway). For patients receiving ketoconazole or other potent CYP3A4 inhibitors,the recommended total daily dose is 2 mg (see Section – **Posology and Method ofAdministration, Use with Potent CYP3A4 Inhibitors** and Section – **Special Warnings and Precautions for Use –CYP3A4 inhibitors**).

Clinical studies have shown no interactions with warfarin or combined oral contraceptives (ethinyl estradiol/levonorgestrel).

A clinical study with marker drugs for the major P450 isoenzymes has not shown any evidence that the activity of CYP2D6, 2C19, 2C9,3A4 or 1A2 will be inhibited by Detrusitol.

Pregnancy and lactation

No pregnant women have been included in the clinical studies. Therefore, Detrusitol should be used during pregnancy only after consideration of the potential benefits for the mother in the relation to the potential risk for the fetus.

Women of fertile age should be considered for treatment only if using adequate contraception.

Use of tolterodine during lactation should be avoided since no data on excretion into breast milk in humans are available.

Effects on Ability to Drive and Use Machines

The ability to drive and use machinery may be negatively affected. Patients should be advised to exercise caution.

Undesirable Effects

Tolterodine it may cause mild to moderate antimuscarinic effects, like dryness of the mouth, dyspepsia and reduced lacrimation.

Clinical Trials: Adverse events considered potentially drug-related from studies of tolterodine tablets and capsules are provided below.

Infections and Infestations: bronchitis
Immune System Disorders: allergic reactions
Psychiatric Disorders: confusion
Nervous System Disorders: dizziness, headache, somnolence
Eye Disorders: abnormal vision (including abnormal accommodation), dry eyes
Ear and Labyrinth Disorders: vertigo
Vascular Disorders: flushed skin
Gastrointestinal Disorders: dry mouth, abdominal pain, constipation, dyspepsia, flatulence, gastroesophageal reflux
Skin and Subcutaneous Tissue Disorders: dry skin
Renal and Urinary Disorders: dysuria, urinary retention
General Disorders and Administration Site Conditions: chest pain, fatigue
Investigations: increased weight

The following adverse events were reported during POST-MARKETING SURVEILLANCE:
Immune System Disorders: anaphylactoid reactions
Psychiatric Disorders: disorientation, hallucinations
Nervous System Disorders: memory impairment
Cardiac Disorders: tachycardia, palpitations
Gastrointestinal Disorders: diarrhea
Skin and Subcutaneous Tissue Disorders: angioedema
General Disorders and Administration Site Conditions: peripheral edema
Cases of aggravation of symptoms of dementia (e.g. confusion, disorientation, delusion) have been reported after tolterodine therapy was initiated in patients taking cholinesterase inhibitors for the treatment of dementia.

Reporting of Suspected Adverse Events:
Reporting suspected adverse events after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reaction via Pharmacovigilance Center/National MESO at e-meso.pom.go.id, and/or to pv@dexagroup.com and pharmacovigilance.id@aurobindo.com.

Overdose

The highest dose tolterodine given to human volunteers is 12.8 mg as single dose. The most severe adverse events observed were accommodation disturbances and micturition difficulties.

In the event of tolterodine overdose, standard supportive measures for managing QT prolongation should be adopted (see Section – **Special Warnings and Precautions for Use**, and Section – **Pharmacodynamic Properties**).

Treat symptoms as follows:

- Severe central anticholinergic effects (e.g. hallucinations, severe excitation): treat with physostigmine
- Convulsions or pronounced excitation: treat with benzodiazepines
- Respiratory insufficiency: treat with artificial respiration
- Tachycardia: treat with beta-blockers
- Urinary retention: treat with catheterization
- Mydriasis: treat with pilocarpine eye drops. If the daylight is unpleasant place patient in dark room.

Pharmacology

Pharmacodynamic properties

Tolterodine is a competitive, specific muscarinic receptor antagonist with a selectivity for the urinary bladder over salivary glands in vivo. One of the tolterodine metabolites (5-hydroxymethyl derivative) exhibits a pharmacological profile similar to that of the parent compound. In extensive metabolisers this metabolite contributes significantly to the therapeutic effect. (see Section – **Pharmacokinetic Properties**).

Effect of treatment with Detrusitol 2 mg twice daily after 4 and 12 weeks, respectively, compared with placebo (pooled data). Absolute change and percentage change relative to baseline.

A total of 710 pediatric patients (486 on tolterodine extended-release capsules, 224 on placebo) aged 5-10 with urinary frequency and urge incontinence were studied in two phase 3 randomized, placebo-controlled, double-blind, 12-week studies. The percentage of patients with urinary tract infections was higher in patients treated with tolterodine extended-release capsules (6.6%) compared to patients who received placebo (4.5%). Aggressive, abnormal and hyperactive behavior and attention disorders occurred in 2.9% of children treated with tolterodine extended-release capsules compared to 0.9% of children treated with placebo.

Table 1. Effect of treatment with tolterodine 2 mg twice daily after 4 and 12 weeks, respectively, compared with placebo (pooled data). Absolute change and percentage change relative to baseline.

Variable	4-week studies			12-week studies		
	Detrusitol 2 mg b.i.d.	Placebo	Statistical significance vs. placebo	Detrusitol 2 mg b.i.d.	Placebo	Statistical significance vs. placebo
Number of micturitions per 24 hours	-1.6 (-14%) n=392	-0.9 (-8%) n=189	*	-2.3 (-20%) n=354	-1.4 (-12%) n=176	**
Number of incontinence episodes per 24 hours	-1.3 (-38%) n=288	-1.0 (-26%) n=151	n.s.	-1.6 (-47%) n=299	-1.1 (-32%) n=145	*
Mean volume voided per micturition (ml)	+25 (+17%) n=385	+12 (+8%) n=185	***	+35 (+22%) n=354	+10 (+6%) n=176	***
Number of patients with no or minimal bladder problems after treatment (%)	16% n=394	7% n=190	**	19% n=356	15% n=177	n.s.

n.s.=not significant; *=p≤0.05; **= p≤0.01; ***= p≤0.001

The effect of tolterodine was evaluated in patients, examined with urodynamic assessment at baseline and, depending on the urodynamic result, they were allocated to a urodynamic positive (motor urgency) or a urodynamic negative (sensory urgency) group. Within each group, the patients were randomized to receive either tolterodine or placebo. The study could not provide convincing evidence that tolterodine had effects over placebo in patients with sensory urgency.

The effect of 2 mg BID and 4 mg BID of tolterodine immediate-release (tolterodine IR) tablets on the QT interval was evaluated in a 4-way crossover, double-blind, placebo- and active-controlled (moxifloxacin 400 mg QD) study in healthy male (N=25) and female (N=23) volunteers aged 18-55 years. There was an approximately equal representation of CYP2D6 extensive metabolizers (EMs) and poor metabolizers (PMs). The 4 mg BID dose of tolterodine IR (two times the highest recommended dose) was chosen because this dose results in tolterodine exposure similar to that observed upon co-administration of tolterodine 2 mg BID with potent CYP3A4 inhibitors in patients who are CYP2D6 poor metabolizers (see Section – **Special Warnings and Precautions for Use**, and Section – **Overdose**).

Table 2 summarizes the mean change from baseline to steady state in corrected QT interval (Fridericia's QTcF and population-specific QTcP) relative to placebo at the time of peak tolterodine (1

hour) and moxifloxacin (2 hour) concentrations. QT interval was measured manually and by machine, and data from both are presented. The reason for the difference between machine and manual read of QT interval is unclear.

Table 2: Mean (CI) change in QTc from baseline to steady state (Day 4 of dosing) at T_{max} (relative to placebo)

Drug/Dose	**N**	**QTcF (msec) (manual)**	**QTcF (msec) (machine)**	**QTcP (msec) (manual)**	**QTcP (msec) (machine)**
Tolterodine 2 mg BID[1]	48	5.01 (0.28, 9.74)	1.16 (-2.99, 5.30)	4.45 (-0.37, 9.26)	2.00 (-1.81, 5.81)
Tolterodine 4 mg BID[1]	48	11.84 (7.11, 16.58)	5.63 (1.48, 9.77)	10.31 (5.49, 15.12)	8.34 (4.53, 12.15)
Moxifloxacin 400 mg QD[2]	45	19.26[3] (15.49, 23.03)	8.90 (4.77, 13.03)	19.10[3] (15.32, 22.89)	9.29 (5.34, 13.24)

[1]At T_{max} of 1 hr; 95% Confidence Interval
[2]At T_{max} of 2 hr; 90% Confidence Interval
[3]The effect on QT interval with 4 days of moxifloxacin dosing in this QT trial may be greater than typically observed in QT trials.

The QT effect of tolterodine immediate-release tablets appeared greater for 8 mg/day (two times the therapeutic dose) compared to 4 mg/day. The effect of tolterodine 8 mg/day was not as large as that observed after four days of therapeutic dosing with the active control moxifloxacin.

There appeared to be a greater QTc interval increase in PMs than in EMs after tolterodine treatment in this study (see Section – **Special Warnings and Precautions for Use**, and Section – **Overdose**).

Pharmacokinetic properties

Tolterodine is rapidly absorbed. Both tolterodine and the 5-hydroxymethyl metabolite reach maximal serum concentrations 1-3 hours after dose. The average peak serum concentrations of tolterodine and the metabolite increase proportionally in the dose interval 1 to 4 mg. Tolterodine is mainly metabolized by the polymorphic enzyme CYP2D6 leading to the formation of a pharmacologically active 5-hydroxymethyl metabolite. The systemic serum clearance of tolterodine in extensive metabolisers about 30 L/h and the terminal half life is 2 to 3 hours. The half life of the hydroxymethyl metabolite is 3 – 4 hours. In poor metabolisers (deficient of CYP2D6) tolterodine is dealkylated via CYP3A isoenzymes whereby N-dealkalylated tolterodine is formed. This metabolite does not contribute to the clinical effect. The reduced clearance and prolonged half life (about 10 hours) of the parent compound in poor metabolisers lead to increased concentration of tolterodine (about 7 fold) associated with undetectable concentrations of the 5-hydroxymethyl metabolite. As a result, the exposure (AUC) of unbound tolterodine in poor metabolisers is similar to the combined exposure of unbound tolterodine and 5-hydroxymethyl metabolite in patients with CYP2D6 activity given the same dosage regimen. The safety, tolerability and clinical response are similar irrespective of phenotype. Steady state concentrations are reached within 2 days.

The absolute bioavailability of tolterodine is 65% in poor metabolisers (devoid of CYP2D6) and 17% in extensive metabolisers (the majority of the patients).

Food does not influence the exposure to the unbound tolterodine and the active 5-hydroxymethyl metabolite in extensive metabolisers, although the tolterodine levels increase when taken with food. Clinically relevant changes are likewise not expected in poor metabolisers.

Tolterodine and the 5-hydroxymethyl metabolite bind primarily to orosomucoid. The unbound fractions are 3.7% and 36%, respectively. The volume of distribution of tolterodine is 113 L.

The excretion of radioactivity after administration of [^{14}C]-tolterodine is about 77% in urine and 17% in faeces. Less than 1% of the dose is excreted as unchanged drug and about 4% as the 5-hydroxymethyl metabolite. The carboxylated metabolite and the corresponding dealkylated metabolite account for about 51% and 29% of the urinary recovery, respectively.

About 2-fold higher exposure of unbound tolterodine and the 5-hydroxymethyl metabolite is found in liver cirrhosis subjects.

The pharmacokinetics is linear in the therapeutic dosage range.

Specific patient groups:

Impaired hepatic function: About 2-fold higher exposure of unbound tolterodine and the 5-hydroxymethyl metabolite is found in subjects with liver cirrhosis (see Section – **Posology and Method of Administration, Use in Impaired Hepatic Function**, and **Special Warnings and Precautions for Use**).

Impaired renal function: The mean exposure of unbound tolterodine and its 5-hydroxymethyl metabolite is doubled in patients with severe renal impairment (inulin clearance GFR =30 ml/min). The plasma levels of other metabolites were markedly (up to 12-fold) increased in these patients. The clinical relevance of the increased exposure of these metabolites is unknown. There is no data in mild to moderate renal impairment (see Section **Posology and Method of Administration – Use in Impaired Renal Function** and **Special Warnings and Precautions for Use).**

Preclinical safety data

In toxicity, genotoxicity, carcinogenicity and safety pharmacology studies no clinically relevant effects have been observed, except those related to the pharmacological effect of the drug.

Reduced foetal weight, embryolethality and increased incidence of foetal malformations have been observed in pregnant mice treated with high doses. No effect were observed at a systemic exposure (measured as C_{max} or UAC for unbound tolterodine and its major active metabolite) 9 – 50 times higher than in humans after the highest recommended dose.

In conscious dogs, a slight prolongation (10% to 20%) of the QT interval has been observed at a toxic dose (4.5 mg/kg/day) of tolterodine. This dose results in very high serum consentrations both of tolterodine and its major active metabolite. No QT interval prolongation has been found in clinical studies with tolterodine.

Reproduction studies have been performed in mice and rabbits.
In mice, there was no effect of tolterodine on fertility or reproductive function. Tolterodine produced embryo death and malformations at plasma exposures (C_{max} or AUC) 20 or 7 times higher than those seen in treated humans.

In rabbits, no malformative effect was seen, but the studies were conducted at 20 or 3 times higher plasma exposure (C_{max} or AUC) than those expected in treated humans.

Studies in pregnant mice have shown that high doses of Detrusitol cause reduced foetal weigt, embryolethality and increased incidence of foetal malformations.

Tolterodine, as well as its active human metabolites prolong action potential duration (90% repolarization) in canine purkinje fibers (14 - 75 times therapeutic levels) and block the K+-current in cloned human ether-a-go-go-related gene (hERG) channels (0.5 - 9.8 times therapeutic levels). In dogs prolongation of the QT interval has been observed after application of tolterodine and its human metabolites (3.1 - 42 times therapeutic levels).

Pharmaceutical Particulars

List of excipients

Core:
Cellulose, microcrystalline
Calcium hydrogen phosphate dihydrate
Sodium starch glycollate (Type B)
Magnesium stearate
Colloidal anhydrous silica

Film coating:
Coating granules containing:
Methylhydroxypropylcellulose (Hypromellose)
Cellulose, microcrystalline
Stearic acid
Titanium dioxide

Incompatibilities

No incompatibilities are known.

Store at temperature below 25°C.

Nature and content of container

Tablets are packed in either blister package made of PVC/PVDC and aluminium foil with a heat seal coating of PVDC or plastic containers made of polyethylene provided with screw caps of polypropylene.

How Supplied

Detrusitol Tablets 2 mg (white, round, biconvex film-coated tablets engraved with arcs above and below the letters DT) in carton containing 2 blisters @ 14 tablets.

Reg. No. DKIxxxxxxxxxxx

HARUS DENGAN RESEP DOKTER

Manufactured by:
Pfizer Italia S.r.l., Ascoli, Italy

Imported by:
PT Ferron Par Pharmaceuticals, Bekasi, Indonesia

Marketed by:
PT Aurogen Pharma Indonesia, Jakarta, Indonesia

Leaflet kemasan: Informasi untuk pengguna

Detrusitol®
2 mg Tablet Salut Selaput
Tolterodine L-Tartrate

Baca semua bagian leaflet ini dengan cermat sebelum mulai menggunakan obat ini karena berisi informasi penting bagi Anda.
- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan memberikannya kepada orang lain. Obat ini dapat membahayakan mereka, sekalipun tanda-tanda penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 13.

Isi leaflet ini:

1. Nama obat
Detrusitol®

2. Bentuk sediaan
Tablet Salut Selaput

3. Deskripsi obat

Detrusitol® mengandung zat aktif tolterodine L-tartrate. Detrusitol® tersedia dalam tablet salut selaput berbentuk bulat, cembung, berwarna putih dengan ukiran bentuk busur di atas dan di bawah huruf DT.

4. Apa kandungan obat ini?

Setiap tablet mengandung 2 mg tolterodine L-tartrate, setara dengan 1,37 mg tolterodine.

Bahan lainnya adalah:
Inti: Selulosa mikrokristalin, kalsium hidrogen fosfat dihidrat, natrium pati glikolat (Tipe B), magnesium stearat, dan silika anhidrat koloid.

Salut selaput: Hipromelosa, selulosa mikrokristalin, asam stearat, dan titanium dioksida.

5. Kekuatan obat

2 mg.

6. Apa kegunaan obat ini?

Detrusitol® digunakan untuk mengobati gejala sindrom kandung kemih terlalu aktif (beser). Jika Anda mengalami sindrom kandung kemih terlalu aktif, Anda akan mendapati bahwa:

- Anda tidak dapat mengendalikan buang air kecil,
- Anda harus bergegas ke kamar kecil tanpa peringatan sebelumnya dan/atau harus sering ke toilet.

7. Berapa banyak dan seberapa sering Anda seharusnya menggunakan obat ini? Apa yang harus dilakukan jika ada dosis yang terlewat?

Dosis

Selalu gunakan obat ini dengan tepat sesuai anjuran dokter atau apoteker Anda. Tanyakan kepada dokter atau apoteker jika Anda merasa tidak yakin.

Dosis normalnya adalah satu tablet 2 mg dua kali sehari, kecuali untuk pasien yang menderita penyakit ginjal atau hati atau mengalami efek samping yang mengganggu sehingga dokter Anda harus menurunkan dosis Anda.

Detrusitol® tidak dianjurkan untuk anak-anak.

Durasi pengobatan

Dokter Anda akan memberi tahu berapa lama Anda harus menjalani pengobatan dengan Detrusitol®. Selesaikan rangkaian pengobatan yang telah diresepkan oleh dokter Anda. Jika sesudahnya Anda belum melihat efek apa pun, konsultasikan dengan dokter Anda.

Manfaat pengobatan harus dievaluasi kembali setelah 6 bulan.

Konsultasikan selalu dengan dokter Anda jika Anda bermaksud menghentikan pengobatan.

Jika Anda lupa meminum Detrusitol®

Jika Anda lupa meminum satu dosis pada waktu yang seharusnya, segera minum saat Anda ingat kecuali jika sudah hampir masuk waktu untuk dosis berikutnya. Dalam kondisi ini, abaikan dosis yang terlewatkan dan ikuti jadwal dosis yang normal.

Jangan menggunakan dosis ganda untuk mengganti dosis yang terlupa.

Jika Anda memiliki pertanyaan lebih lanjut seputar penggunaan obat ini, tanyakan kepada dokter atau apoteker Anda.

8. Kapan seharusnya Anda tidak menggunakan obat ini?

Jangan menggunakan Detrusitol®

- jika Anda alergi (hipersensitif) terhadap tolterodine atau bahan apa pun lainnya dalam obat ini
- jika Anda tidak dapat mengeluarkan air seni dari kandung kemih (retensi air seni)
- jika Anda menderita glaukoma sudut sempit yang tidak terkontrol (tekanan tinggi di dalam mata disertai hilangnya penglihatan yang tidak mendapatkan perawatan yang memadai)
- jika Anda menderita miastenia gravis (kelemahan otot yang berlebihan)
- jika Anda menderita kolitis ulseratif berat (ulserasi dan peradangan usus besar)
- jika Anda menderita megakolon toksik (pelebaran akut pada usus besar).

9. Apa yang harus dipertimbangkan saat menggunakan obat ini?

Konsultasikan dengan dokter atau apoteker Anda sebelum memulai pengobatan dengan Detrusitol® jika Anda merasa mengalami kondisi mana pun berikut ini.

- Jika Anda mengalami kesulitan dalam berkemih dan/atau aliran air seni yang tidak lancar
- Jika Anda memiliki penyakit pencernaan
- Jika Anda menderita gangguan ginjal (insufisiensi ginjal)
- Jika Anda mengidap penyakit hati
- Jika Anda menderita kelainan saraf yang memengaruhi tekanan darah, fungsi usus, atau fungsi seksual (neuropati sistem saraf otonom)
- Jika Anda menderita hiatus hernia (herniasi bagian atas perut)
- Jika Anda mengidap penyakit jantung

10. Apa saja obat lain atau makanan yang harus dihindari selama menggunakan obat ini?

Beri tahu dokter atau apoteker jika Anda meminum, baru saja meminum, atau mungkin meminum obat-obatan lain, termasuk obat-obatan yang diperoleh tanpa resep.

Tolterodine, zat aktif dalam Detrusitol®, dapat berinteraksi dengan produk medisinal lainnya.

Detrusitol® harus digunakan dengan hati-hati jika dikombinasikan dengan:

- obat-obatan yang memengaruhi pergerakan makanan (misalnya metoklopramid dan cisaprid)
- obat-obatan untuk mengobati detak jantung tidak teratur (misalnya amiodaron, sotalol, kuinidin, prokainamida)
- obat-obatan lainnya dengan mekanisme kerja yang sama dengan Detrusitol® (sifat antimuskarinik) atau obat-obatan dengan mekanisme kerja yang berlawanan dengan Detrusitol® (sifat kolinergik). Tanyakan kepada dokter Anda jika Anda merasa ragu.
- beberapa antibiotik (misalnya eritromisin, klaritromisin)
- produk medisinal yang digunakan untuk mengobati infeksi jamur (misalnya ketokonazol, itrakonazol, mikonazol)

Detrusitol® bersama makanan dan minuman
Detrusitol® dapat diminum sebelum, sesudah, atau saat makan.

11. Apakah obat ini aman bagi ibu hamil dan menyusui?
Kehamilan
Anda tidak boleh menggunakan Detrusitol® jika sedang hamil. Jika Anda mengira diri Anda sedang hamil, atau berencana untuk hamil, Anda harus memberi tahu dokter sebelum meminum Detrusitol®.

Menyusui
Tidak diketahui apakah tolterodine dikeluarkan bersama ASI. Tidak dianjurkan untuk menyusui selama pengobatan dengan Detrusitol®.

12. Apakah pasien diperbolehkan mengemudi dan mengoperasikan mesin selama menggunakan obat ini?
Kemampuan Anda untuk mengemudi dan mengoperasikan mesin dapat terpengaruh.

13. Apa saja potensi efek yang tidak diinginkan dari penggunaan obat ini?
Seperti obat-obatan lainnya, obat ini dapat menimbulkan efek samping, sekalipun tidak semua orang mengalaminya.

Anda harus segera mengunjungi dokter Anda atau mendatangi unit gawat darurat jika mengalami gejala-gejala angioedema seperti
- wajah, lidah, atau faring membengkak
- kesulitan untuk menelan
- kaligata dan kesulitan bernapas

Anda juga harus mencari pertolongan medis jika mengalami reaksi hipersensitivitas (misalnya gatal-gatal, ruam, kaligata, kesulitan bernapas).

Berikut ini efek samping yang teramati selama pengobatan dengan Detrusitol®.
- mulut kering
- gangguan pencernaan (dispepsia)
- mata kering, penglihatan kabur
- radang saluran yang menuju ke paru-paru
- pusing, sakit kepala, mengantuk
- gangguan ingatan
- peningkatan detak jantung, detak jantung berdebar-debar
- vertigo
- sakit perut, sembelit, udara atau gas berlebihan di dalam lambung atau usus, aliran mundur isi perut ke kerongkongan, diare
- kulit kering
- kesakitan atau kesulitan saat berkemih, tidak dapat mengosongkan kandung kemih
- sakit dada, keletihan (kelelahan)
- peningkatan berat badan

Reaksi tambahan yang dilaporkan mencakup reaksi alergi berat, kebingungan, halusinasi, kulit memerah, angioedema, dan disorientasi. Juga telah dilaporkan adanya perburukan gejala demensia pada pasien yang menjalani pengobatan untuk demensia.

Beri tahu dokter atau perawat Anda jika teramati adanya efek samping yang tercantum di atas.

Melaporkan efek samping
Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter, apoteker, atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Anda dapat melaporkan efek samping tersebut melalui pv@dexagroup.com dan pharmacovogilance.id@aurobindo.com. Dengan melaporkan efek samping, Anda bisa membantu memberikan informasi lebih lanjut mengenai keamanan obat ini.

14. Tanda-tanda dan gejala-gejala overdosis

Jika meminum tablet terlalu banyak, Anda akan mengalami gejala-gejala berikut:

- halusinasi, eksitasi berat
- kejang atau eksitasi hebat
- sulit bernapas
- meningkatnya detak jantung
- kesulitan berkemih
- dilatasi berlebihan pada pupil mata

15. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?

Jika Anda tanpa sengaja meminum terlalu banyak tablet Detrusitol®, segera hubungi dokter Anda atau datangi unit gawat darurat di rumah sakit terdekat.

Bawa selalu kemasan obat berlabel, baik yang masih ada tablet Detrusitol® yang tersisa di dalamnya atau tidak.

Jangan meminum tablet lagi hingga dokter Anda memerintahkan Anda.

16. Bagaimana cara menyimpan obat ini?

Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan gunakan obat ini setelah melewati tanggal kedaluwarsa yang tertera pada wadahnya.

Simpan di tempat kering pada suhu kurang dari 25 °C.

17. Nomor izin edar

Detrusitol® 2 mg tablet, No. Reg DKIxxxxxxxxxxx

18. Nama dan alamat produsen/importir/Pemilik Izin Edar

Diproduksi oleh:
Pfizer Italia S.r.l., Ascoli, Italia

Diimpor oleh:
PT Ferron Par Pharmaceuticals, Bekasi, Indonesia

Dipasarkan oleh:
PT Aurogen Pharma Indonesia, Jakarta, Indonesia

19. Tanggal revisi
08/2025

20. Peringatan khusus
HARUS DENGAN RESEP DOKTER