

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## **1. NAME OF THE MEDICINAL PRODUCT**

Kentera 3.9 mg / 24 hours transdermal patch

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each transdermal patch contains 36 mg of oxybutynin. The area of the patch is 39 cm<sup>2</sup>, releasing a nominal 3.9 mg of oxybutynin per 24 hours.

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Transdermal patch

The patch is a clear plastic with an adhesive backing, protected by a release liner that is to be removed prior to application.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in adult patients with unstable bladder.

### **4.2 Posology and method of administration**

#### Posology

The recommended dose is one 3.9 mg transdermal patch applied twice weekly (every 3 to 4 days).

#### *Elderly*

Based on clinical trial experience no dose adjustment is considered necessary in this population. Nonetheless Kentera should be used with caution in elderly patients, who may be more sensitive to the effects of centrally acting anticholinergics and exhibit differences in pharmacokinetics (see section 4.4).

#### *Paediatric population*

The safety and efficacy of Kentera in the paediatric population has not been established. Kentera is not recommended for use in the paediatric population. Currently available data are described in section 4.8 but no recommendation on a posology can be made.

#### Method of administration

The patch should be applied to dry, intact skin on the abdomen, hip, or buttock immediately after removal from the protective sachet. A new application site should be selected with each new patch to avoid reapplication to the same site within 7 days. The patch must not be divided or cut into pieces. Patches that are damaged should not be used.

### **4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Kentera is contraindicated in patients with urinary retention, severe gastro-intestinal condition, myasthenia gravis or narrow-angle glaucoma and in patients who are at risk for these conditions.

#### **4.4 Special warnings and precautions for use**

Kentera should be used with caution in patients with hepatic or renal impairment. The use of Kentera in patients with hepatic impairment should be carefully monitored. Other causes of frequent urination (heart failure or renal disease) should be assessed before treatment with Kentera. If urinary tract infection is present, an appropriate antibacterial therapy should be started.

*Urinary retention:* Anticholinergic products should be administered with caution to patients with clinically significant bladder outflow obstruction because of the risk of urinary retention.

Kentera should be used with caution in elderly patients, who may be more sensitive to the effects of centrally acting anticholinergics and exhibit differences in pharmacokinetics.

In total 496 patients were exposed to Kentera in the randomised, double-blind, placebo-controlled 12-week and the 14-week safety extension studies. Of these 188 patients (38%) were 65 years of age and older and exhibited no overall differences in safety or effectiveness compared to younger patients. Thus based on current clinical evidence no need for dose adjustment in elderly patients is considered necessary.

Psychiatric and central nervous system (CNS) anticholinergic events like sleep disorders (e.g. insomnia) and cognitive disorders have been associated with oxybutynin use, especially in elderly patients. Caution should be exercised when oxybutynin is administered concomitantly with other anticholinergic medicinal products (see also section 4.5). If a patient experiences such events, drug discontinuation should be considered.

Other psychiatric events implying an anticholinergic mechanism have been reported during post-marketing use (see section 4.8).

Oral administration of oxybutynin may warrant the following cautionary statements, but these events were not observed during clinical trials with Kentera:

*Gastrointestinal disorders:* Anticholinergic medicinal products may decrease gastrointestinal motility and should be used with caution in patients with gastrointestinal obstructive disorders because of the risk of gastric retention. Also in conditions such as ulcerative colitis, and intestinal atony. Anticholinergic medicinal products should be used with caution in patients who have hiatus hernia/gastro-oesophageal reflux and/or who are concurrently taking medicinal products (such as bisphosphonates) that can cause or exacerbate oesophagitis.

Anticholinergic medicinal products should be used with caution in patients who have autonomic neuropathy, cognitive impairment or Parkinson's disease.

Patients should be informed that heat prostration (fever and heat stroke due to decreased sweating) can occur when anticholinergics such as oxybutynin are used in a hot environment.

Oxybutynin may exacerbate the symptoms of hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, tachycardia, hypertension and prostatic hypertrophy.

Oxybutynin may lead to suppressed salivary secretions which could result in dental caries, parodontosis or oral candidiasis.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

The concomitant use of oxybutynin with other anticholinergic medicinal products or with other agents that compete for CYP3A4 enzyme metabolism may increase the frequency or severity of dry mouth, constipation, and drowsiness.

Anticholinergic agents may potentially alter the absorption of some concomitantly administered medicinal products due to anticholinergic effects on gastrointestinal motility. As oxybutynin is metabolised by cytochrome P 450 isoenzyme CYP3A4, interactions with medicinal products that inhibit this isoenzyme cannot be ruled out. This should be borne in mind when using azole antifungals (e.g. ketoconazole) or macrolide antibiotics (e.g. erythromycin) concurrently with oxybutynin.

The anticholinergic activity of oxybutynin is increased by concurrent use of other anticholinergics or medicinal products with anticholinergic activity, such as amantadine and other anticholinergic antiparkinsonian medicinal products (e.g. biperiden, levodopa), antihistamines, antipsychotics (e.g. phenothiazines, butyrophenones, clozapine), quinidine, tricyclic antidepressants, atropine and related compounds like atropinic antispasmodics, dipyridamole.

Patients should be informed that alcohol may enhance the drowsiness caused by anticholinergic agents such as oxybutynin (see section 4.7).

Oxybutynin may antagonize prokinetic therapies.

#### **4.6 Fertility, pregnancy and lactation**

##### Pregnancy

There are no adequate data on the use of oxybutynin transdermal patch in pregnant women. Studies in animals have shown minor reproductive toxicity (see section 5.3). Kentera should not be used during pregnancy unless clearly necessary.

##### Breast-feeding

When oxybutynin is used during breast-feeding, a small amount is excreted in the mother's milk. Use of oxybutynin while breast-feeding is therefore not recommended.

#### **4.7 Effects on ability to drive and use machines**

No studies on the effects on the ability to drive and use machines have been performed.

Because Kentera may produce drowsiness, somnolence, or blurred vision, patients should be advised to exercise caution when driving or using machinery (see section 4.5).

#### **4.8 Undesirable effects**

##### Summary of the safety profile

The most commonly reported adverse drug reactions were application site reactions, occurring in 23.1% of patients. Other commonly occurring adverse drug reactions reported were dry mouth (8.6%), constipation (3.9%), diarrhoea (3.2%), headache (3.0%), dizziness (2.3%) and blurred vision (2.3%).

##### Tabulated list of adverse reactions

Adverse reactions from phase 3 and 4 clinical studies are listed below by system organ class and frequency grouping. Frequencies are defined as: very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ ). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Post-marketing adverse reactions not seen in clinical trials are also included.

<b>System Organ Class (MedDRA)</b>	<b>Frequency</b>	<b>Adverse reaction</b>
<b>Infections and infestations</b>	Common	Urinary tract infection
	Uncommon	Upper respiratory tract infection, fungal infection
<b>Psychiatric disorders</b>	Uncommon	Anxiety, confusion, nervousness, agitation, insomnia

	Rare	Panic reaction#, delirium#, hallucinations#, disorientation#
<b>Nervous system disorders</b>	Common	Headache, somnolence
	Rare	Memory impairment#, amnesia#, lethargy#, disturbance in attention#
<b>Eye disorders</b>	Common	Blurred vision
<b>Ear and labyrinth disorders</b>	Common	Dizziness
<b>Cardiac disorders</b>	Uncommon	Palpitations
<b>Vascular disorders</b>	Uncommon	Urticaria, hot flushes
<b>Respiratory, thoracic and mediastinal disorders</b>	Uncommon	Rhinitis
<b>Gastrointestinal disorders</b>	Common	Dry mouth, constipation, diarrhoea, nausea, abdominal pain
	Uncommon	Abdominal discomfort, dyspepsia
<b>Musculoskeletal and connective tissue disorders</b>	Uncommon	Back pain
<b>Renal and urinary disorders</b>	Uncommon	Urinary retention, dysuria
<b>General disorders and administration site conditions</b>	Very common	Application site pruritis
	Common	Application site erythema, application site reaction, application site rash
<b>Injury, poisoning and procedural complications</b>	Uncommon	Inflicted injury

# post-marketing adverse reactions from post-marketing reports only (not seen in clinical trials), with the frequency category estimated from clinical trial safety data, and reported in association with oxybutynin topical use (anticholinergic class effects).

Adverse reactions considered associated with anticholinergic therapy, in general or observed with oral administration of oxybutynin, but as of yet not with Kentera in clinical trials or post-marketing, are: anorexia, vomiting, reflux oesophagitis, decreased sweating, heat stroke, decreased lacrimation, mydriasis, tachycardia, arrhythmia, nightmares, restlessness, convulsion, intraocular hypertension and induction of glaucoma, paranoia, photosensitivity, erectile dysfunction.

#### Paediatric population

During post-marketing use in this age group, cases of hallucinations (associated with anxiety manifestations) and sleep disorders correlated with oxybutynin have been reported. Children may be more sensitive to the effects of the product, particularly the CNS and psychiatric adverse reactions.

#### 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. Healthcare professionals are asked to report any suspected adverse reactions **via the national reporting system** listed in [Appendix V](#).

## **4.9 Overdose**

Plasma concentration of oxybutynin declines within 1 to 2 hours after removal of transdermal system(s). Patients should be monitored until symptoms resolve. Overdosage with oxybutynin has been associated with anticholinergic effects including CNS excitation, flushing, fever, dehydration, cardiac arrhythmia, vomiting, and urinary retention. Ingestion of 100 mg oral oxybutynin chloride in association with alcohol has been reported in a 13 year old boy who experienced memory loss, and in a 34 year old woman who developed stupor, followed by disorientation and agitation on awakening,

dilated pupils, dry skin, cardiac arrhythmia, and retention of urine. Both patients recovered fully with symptomatic treatment.

No cases of overdose have been reported with Kentera.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: urinary antispasmodic, ATC code: G04B D04.

#### Mechanism of action

Oxybutynin acts as a competitive antagonist of acetylcholine at post-ganglionic muscarinic receptors, resulting in relaxation of bladder smooth muscle.

#### Pharmacodynamic effects

In patients with overactive bladder, characterised by detrusor muscle instability or hyperreflexia, cystometric studies have demonstrated that oxybutynin increases maximum urinary bladder capacity and increases the volume to first detrusor contraction. Oxybutynin thus decreases urinary urgency and the frequency of both incontinence episodes and voluntary urination.

Oxybutynin is a racemic (50:50) mixture of R- and S-isomers. Antimuscarinic activity resides predominantly in the R-isomer. The R-isomer of oxybutynin shows greater selectivity for the M<sub>1</sub> and M<sub>3</sub> muscarinic subtypes (predominant in bladder detrusor muscle and parotid gland) compared to the M<sub>2</sub> subtype (predominant in cardiac tissue). The active metabolite, N-desethyloxybutynin, has pharmacological activity on the human detrusor muscle that is similar to that of oxybutynin *in vitro* studies, but has a greater binding affinity for parotid tissue than oxybutynin. The free base form of oxybutynin is pharmacologically equivalent to oxybutynin hydrochloride.

#### Clinical efficacy

A total of 957 patients with urge urinary incontinence were evaluated in three controlled studies comparing Kentera to either placebo, oral oxybutynin and/or tolterodine long acting capsules. Reductions in weekly incontinence episodes, urinary frequency, and urinary void volume were evaluated. Kentera led to consistent improvements in overactive bladder symptoms compared with placebo.

### **5.2 Pharmacokinetic properties**

#### Absorption

Kentera has a concentration of oxybutynin sufficient to maintain continuous transport over the 3 to 4 day dosing interval. Oxybutynin is transported across intact skin and into the systemic circulation by passive diffusion across the stratum corneum. Following the application of Kentera, oxybutynin plasma concentration increases for approximately 24 to 48 hours, reaching average maximum concentrations of 3 to 4 ng/ml. Steady-state conditions are reached during the second application of the transdermal patch. Thereafter, steady concentrations are maintained for up to 96 hours. The difference in AUC and C<sub>max</sub> of oxybutynin and the active metabolite N-desethyloxybutynin following transdermal administration of Kentera on either the abdomen, buttocks or hip is not clinically relevant.

#### Distribution

Oxybutynin is widely distributed in body tissues following systemic absorption. The volume of distribution was estimated to be 193 l after intravenous administration of 5 mg oxybutynin hydrochloride.

#### Biotransformation

Oxybutynin administered orally is metabolised primarily by the cytochrome P450 enzyme systems, particularly CYP3A4, found mostly in the liver and gut wall. Metabolites include phenylcyclohexylglycolic acid, which is pharmacologically inactive, and N-desethyloxybutynin,

which is pharmacologically active. Transdermal administration of oxybutynin bypasses the first-pass gastrointestinal and hepatic metabolism, reducing the formation of the N-desethyl metabolite.

#### Elimination

Oxybutynin is extensively metabolised by the liver, see above with less than 0.1% of the administered dose excreted unchanged in the urine. Also, less than 0.1% of the administered dose is excreted as the metabolite N-desethyloxybutynin.

### **5.3 Preclinical safety data**

Pre-clinical data reveal no special hazard for humans based on studies for acute toxicology, repeat dose toxicity, genotoxicity, carcinogenic potential and local toxicity. At a concentration of 0.4 mg/kg/day oxybutynin administered subcutaneously, the occurrence of organ anomalies is significantly increased, but is observed only in the presence of maternal toxicity. Kentera delivers approximately 0.08 mg/kg/day. However, in the absence of understanding the association between maternal toxicity and developmental effect, the relevance to human safety cannot be addressed. In the subcutaneous fertility study in rats, while no effects were reported in males, in females, fertility was impaired and a NOAEL (no observed adverse effect level) of 5 mg/kg was identified.

#### Environmental risk assessment (ERA)

The active substance oxybutynin is persistent in the environment.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

#### Backing film

Clear polyester/ethylene-vinyl acetate (PET/EVA)

#### Middle layer

Triacetin

Acrylic copolymer adhesive solution containing 2-ethylhexyl acrylate N-vinyl pyrrolidone and hexamethyleneglycol dimethacrylate polymer domains

#### Release Liner

Siliconised polyester

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

3 years.

### **6.4 Special precautions for storage**

Do not refrigerate or freeze.

### **6.5 Nature and contents of container**

The transdermal patches are individually contained in LDPE/paper laminate sachets and supplied in patient calendar boxes of 2, 8 or 24 patches.

Not all pack sizes may be marketed.

## **6.6 Special precautions for disposal and other handling**

Apply immediately upon removal from the protective sachet. After use the patch still contains substantial quantities of active ingredients. Remaining active ingredients of the patch may have harmful effects if reaching the aquatic environment. Hence, after removal, the used patch should be folded in half, adhesive side inwards so that the release membrane is not exposed, placed in the original sachet and then discarded safely out of reach of children. Any used or unused patches should be disposed of according with local requirements or returned to the pharmacy. Used patches should not be flushed down the toilet nor placed in liquid waste disposal systems.

Activities that may lead to excessive sweating, or exposure to water or extreme temperature may contribute to adhesion problems. Do not expose the patch to the sun.

## **7. MARKETING AUTHORISATION HOLDER**

Teva B.V.  
Swensweg 5  
2031 GA Haarlem  
The Netherlands

## **8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/03/270/001	8 transdermal patches
EU/1/03/270/002	24 transdermal patches
EU/1/03/270/003	2 transdermal patches

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 15 June 2004  
Date of latest renewal: 30 April 2009

## **10. DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency (EMA) <http://www.ema.europa.eu>



## **ANNEX II**

- A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

**A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer(s) responsible for batch release

Merckle GmbH  
Ludwig-Merckle-Straße 3  
89143 Blaubeuren  
Germany

Teva Pharmaceuticals Europe B.V.  
Swensweg 5  
2031 GA Haarlem  
The Netherlands

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Medicinal product subject to medical prescription.

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

**D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

- **Risk management plan (RMP)**

Not applicable.

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****CARTON****1. NAME OF THE MEDICINAL PRODUCT**

Kentera 3.9 mg / 24 hours transdermal patch  
oxybutynin

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each transdermal patch releases 3.9 mg of oxybutynin per 24 hours. Each patch of 39 cm<sup>2</sup> contains 36 mg of oxybutynin.

**3. LIST OF EXCIPIENTS**

Excipients: triacetin; acrylic adhesive (containing 2-ethylhexyl acrylate; N-vinyl pyrrolidone and hexamethyleneglycol dimethacrylate polymer domains).  
Backing: polyester/ethylene-vinyl acetate film; siliconised polyester film.

**4. PHARMACEUTICAL FORM AND CONTENTS**

2 transdermal patches  
8 transdermal patches  
24 transdermal patches

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

For transdermal use only.  
Do not use if seal on sachet is broken

Apply immediately upon removal from sachet.  
Read the package leaflet before use.

Sun/Wed  
Mon/Thu  
Tue/Fri  
Wed/Sat  
Thu/Sun  
Fri/Mon  
Sat/Tue

Apply a new Kentera patch twice weekly (every 3 to 4 days).

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY****8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Do not refrigerate or freeze.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE****11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Teva B.V.  
Swensweg 5  
2031 GA Haarlem  
The Netherlands

**12. MARKETING AUTHORISATION NUMBER (S)**

EU/1/03/270/001	8 transdermal patches
EU/1/03/270/002	24 transdermal patches
EU/1/03/270/003	2 transdermal patches

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY****15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

Kentera

<b>17.      UNIQUE IDENTIFIER – 2D BARCODE</b>
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2D barcode carrying the unique identifier included.

<b>18.      UNIQUE IDENTIFIER - HUMAN READABLE DATA</b>
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PC  
SN  
NN

<b>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</b> <b>SACHET</b>
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<b>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</b>
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Kentera 3.9 mg / 24 hours transdermal patch  
oxybutynin

For transdermal use only.

<b>2. METHOD OF ADMINISTRATION</b>
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Apply immediately upon removal from sachet.  
Read the package leaflet before use.

<b>3. EXPIRY DATE</b>
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EXP

<b>4. BATCH NUMBER</b>
------------------------

Lot

<b>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</b>
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Contains 1 transdermal patch.

<b>6. OTHER</b>
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Do not refrigerate or freeze.



## **B. PACKAGE LEAFLET**

## **Package leaflet: Information for the user**

### **Kentera 3.9 mg / 24 hours transdermal patch** oxybutynin

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet**

1. What Kentera is and what it is used for
2. What you need to know before you use Kentera
3. How to use Kentera
4. Possible side effects
5. How to store Kentera
6. Contents of the pack and other information

#### **1. What Kentera is and what it is used for**

Kentera is used in adults to control the symptoms of urge incontinence and/or increased urinary frequency and urgency.

Kentera works by allowing the bladder to expand and accommodate more urine.

#### **2. What you need to know before you use Kentera**

##### **Do not use Kentera**

- if you are allergic to oxybutynin or any of the other ingredients of this medicine (listed in section 6).
- if you have a rare condition called myasthenia gravis that makes the muscles in the body become weak and tire easily.
- if you experience incomplete bladder emptying during urination, the use of oxybutynin may increase this problem. You should discuss this problem with your doctor before using Kentera.
- if you have digestion problems caused by reduced emptying of the stomach after a meal you should consult your doctor before using Kentera.
- if you have glaucoma or a family history of glaucoma, tell your doctor.

##### **Warnings and precautions**

Talk to your doctor or pharmacist before using Kentera if you have any of the following.

- Liver problems
- Kidney problems
- Difficulty urinating
- Intestinal blockage
- Bloody stools
- Generalized muscle weakness
- Painful swallowing

Since treatment with oxybutynin may cause decreased perspiration, there is an increased risk of fever and heat stroke if you are exposed to high environmental temperatures.

### **Children and adolescents**

Kentera is not recommended for use in children or adolescents.

### **Other medicines and Kentera**

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Applying the Kentera patch at the same time as taking other medicines that have similar side effects such as dry mouth, constipation and drowsiness, may increase how often and how severe these side effects are experienced.

Oxybutynin may slow the digestive tract and thereby influence the adsorption of other oral medicines, or the use of this medicine together with other medicines may increase the effect of oxybutynin, especially:

- Ketoconazole, itraconazole or fluconazole (used for the treatment of fungal infections).
- Erythromycin a macrolide antibiotic (used to treat bacterial infections).
- Biperiden, levodopa, or amantadine (used to treat Parkinson's disease).
- Antihistamines (used in the treatment of allergies such as hay fever).
- Phenothiazines or clozapine (used to treat mental illness).
- Tricyclic antidepressants (used to treat depression).
- Dipyridamole (used to treat blood clotting problems).
- Atropine and other anticholinergic medicines (used for treatment in stomach disorders such as irritable bowel syndrome).

### **Kentera with alcohol**

Oxybutynin may cause drowsiness or blurred vision. Drowsiness may be increased by consumption of alcohol.

### **Pregnancy and breast-feeding**

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Kentera should not be used during pregnancy unless clearly necessary.

When oxybutynin is used during breast-feeding, a small amount is excreted in the mother's milk. Use of oxybutynin while breast-feeding is therefore not recommended.

### **Driving and using machines**

Because Kentera may produce drowsiness, somnolence, or blurred vision, patients should be advised to exercise caution when driving or using machinery.

## **3. How to use Kentera**

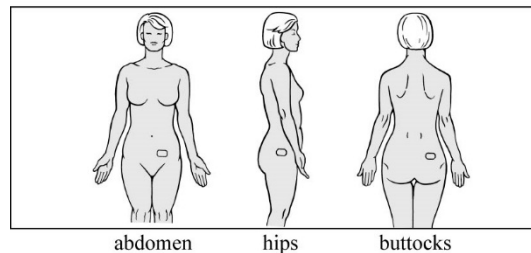
Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Apply a new Kentera patch twice weekly (every 3 to 4 days) according to the instructions for use. Change the patch on the same two days every week, for example, every Sunday and Wednesday or Monday and Thursday.

Printed on the inside flap of your Kentera package, you will find a Kentera calendar checklist that will help you to remember your dosing schedule. Mark the schedule you plan to follow and remember always to change your patch on the same two days of the week you have chosen on your calendar. Make sure to wear only one patch at a time and wear your patch continuously, until it is time to apply a new one.

### Where to apply

Apply the patch to a clean, dry, smooth area of skin on your abdomen, hips or buttocks. Avoid placing the patch in the waistline area to prevent tight clothing from rubbing against the patch. Do not expose the patch to the sun. Place the patch underneath your clothing. Rotate application sites with each new application. Do not apply a patch to the same place on your body for at least 1 week.



### How to apply

Each patch is individually sealed in a protective sachet. Please read all the information below before you begin to apply Kentera.

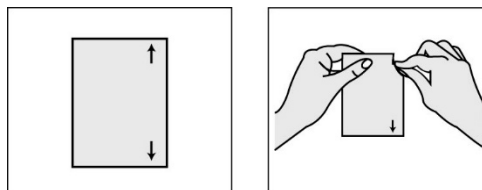
### **To apply Kentera**

#### **Step 1: Choose a spot for the patch that is:**

- Freshly washed, but dry and cool (wait a few minutes after taking a hot bath or shower).
- Free of body powder, lotion, and oil.
- Free of cuts, rashes or any other skin irritation.

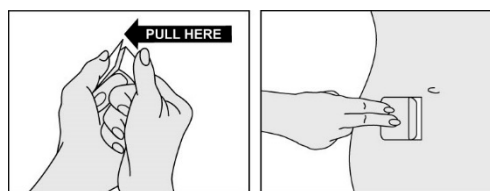
#### **Step 2: Open the sachet that contains the patch.**

- Tear open along arrows marked on the right side of the sachet as shown in drawing below.
- Do not cut the sachet with scissors, which might damage the patch inside.
- Pull the patch out.
- Do not cut or divide the patch, do not use damaged patches.
- Apply immediately to your skin; do not keep or store the patch outside the sealed sachet.



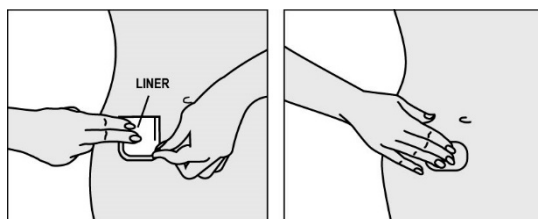
#### **Step 3: Apply one half of the patch to your skin.**

- Gently bend the patch and remove the first piece of protective liner, which covers the sticky surface of the patch.
- Without touching the sticky surface, firmly press the patch, adhesive face down, onto the part of the abdomen, hips or buttocks you have selected for application.



#### **Step 4: Apply the second half of the patch to your skin.**

- Bend the patch back over itself. Press down on the liner firmly.
- Push the liner forward a little to loosen the edge.
- Grab the loose edge at either corner and peel off the second piece of the liner. Try not to touch the sticky surface of the patch.
- Press the entire patch firmly onto the skin with your fingertips. Press for at least 10 seconds to make sure the patch will stay in place. Be sure all of it sticks to your skin, even around the edges.
- Discard the protective liners.



#### **Bathing, showering, swimming and exercise**

You should wear each patch all the time until you apply a new one. Baths, showers, swimming and exercise should not affect the patch as long as you don't rub the patch as you wash. Avoid soaking in a hot bath for a long period of time, which can make the patch come off.

#### **If the patch comes off**

If the patch starts to lift off your skin, apply a little bit of pressure using your fingertips. The patch is designed to re-stick. Very rarely will the patch come off completely. If it does, try putting the same patch back on the same spot. If it sticks firmly all over, leave it on. If not, take it off and put a new patch on a new spot. No matter what day this happens, continue with the twice-a-week schedule that you have marked on your patch box.

#### **If you forget to change the patch after 3-4 days**

As soon as you remember, remove the old patch and apply a new one to a new spot on your abdomen, hips or buttocks. No matter what day this happens, continue with the same twice-a-week schedule for your next patch, even if it means changing the new patch before 3 to 4 days have elapsed.

#### **How to remove**

When changing the patch, remove the old patch slowly. Fold it in half (sticky sides together) and throw it away to keep out of the reach of children and pets. Mild redness may be present at the application site. This redness should disappear within several hours after removal of the patch. If irritation persists, please contact your doctor.

Gently washing the application site with warm water and a mild soap should remove any adhesive that remains on your skin after removal of the patch. A small amount of baby oil may also be used to remove any excess residue. Rings of adhesive that become soiled may require a medical adhesive removal pad that should be available from your pharmacist. Alcohol or other strong solvents may cause skin irritation and should not be used.

After use the patch still contains substantial quantities of active ingredients. Remaining active ingredients of the patch may have harmful effects if reaching the aquatic environment. Hence, after removal, the used patch should be folded in half, adhesive side inwards so that the release membrane is not exposed, placed in the original sachet and then discarded safely out of reach of children. Any used or unused patches should be discarded according to local requirements or returned to the pharmacy. Used patches should not be flushed down the toilet nor placed in liquid waste disposal systems.

**If you use more Kentera than you should**

Do not apply more than one patch at a time.

**If you forget to use Kentera**

Apply a Kentera patch as soon as you realise your patch is missing, or you have missed a scheduled day of application.

**If you stop using Kentera**

Your urge incontinence may return and you may have increased urinary frequency if you decide to stop using the patch. Continue to use Kentera as long as your doctor tells you to.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

**4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

**Very common** side effect (may affect more than 1 in 10 people)

- itching around the site of patch application

**Common** side effects (may affect up to 1 in 10 people)

- redness or rash at the site of patch application
- dry mouth
- constipation
- diarrhoea
- upset stomach
- stomach pain
- headache or sleepiness
- urinary tract infections
- blurred vision
- dizziness

**Uncommon** side effects (may affect up to 1 in 100 people)

- upper respiratory tract or fungal infections
- anxiety
- confusion
- nervousness
- agitation
- difficulty in sleeping
- palpitations
- hot flushes
- back pain
- urinary retention
- difficulty urinating
- common cold
- accidental injury

**Rare** side effects (may affect up to 1 in 1,000 people)

- panic reaction
- mental confusion
- hallucinations
- disorientation
- memory impairment
- loss of memory
- abnormal tiredness

- poor concentration

### **Reporting of side effects**

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

## **5. How to store Kentera**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the sachet and the carton. The expiry date refers to the last day of that month.

Do not refrigerate or freeze.

The used patches should be folded in half, adhesive side inwards so that the release membrane is not exposed, placed in the original sachet and then discarded safely out of the reach of children. Any used or unused patches should be discarded according to local requirements or returned to the pharmacy. Used patches should not be flushed down the toilet nor placed in liquid waste disposal systems.

## **6. Contents of the pack and other information**

### **What Kentera contains**

- The active substance is oxybutynin.  
Each transdermal patch releases 3.9 mg of oxybutynin per 24 hours. Each patch of 39 cm<sup>2</sup> contains 36 mg of oxybutynin.
- The other ingredients are: Each patch contains triacetin, and acrylic adhesive solution. The oxybutynin, triacetin and acrylic adhesive are coated on clear PET/EVA backing film and covered with a siliconised polyester release liner.

### **What Kentera looks like and contents of the pack**

Kentera is a transdermal patch and it is packaged in cartons containing 2, 8, and 24 patches. Each patch consists of a clear backing film that has the pharmaceutical ingredients coated on the side containing the protective backing film. The backing film is to be removed prior to patch application.

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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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Detailed information on this medicine is available on the European Medicines Agency web site:  
<http://www.ema.europa.eu>

**ANNEX IV**  
**SCIENTIFIC CONCLUSIONS AND GROUNDS FOR THE VARIATION TO THE TERMS**  
**OF THE MARKETING AUTHORISATION(S)**

## **Scientific conclusions**

Taking into account the PRAC Assessment Report on the PSUR(s) for oxybutynin, the scientific conclusions of the CHMP are as follows:

### **Oral formulation**

In view of available data on risk of palpitations from spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge, the PRAC considers a causal relationship between Oxybutynin as per EURD list and Palpitation is at least a reasonable possibility. The PRAC concluded that the product information of oral formulations containing oxybutynin should be amended accordingly.

### **Transdermal formulation**

In view of available data on medication errors concerning patients cutting the patches into smaller pieces, the PRAC considers that, in the current SmPC and PIL, it is not clear enough that the transdermal patches should not be cut or divided in any way. The PRAC concluded that the product information of the transdermal formulation containing oxybutynin should be amended accordingly.

The CHMP agrees with the scientific conclusions made by the PRAC.

## **Grounds for the variation to the terms of the marketing authorisation(s)**

On the basis of the scientific conclusions for oxybutynin the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing oxybutynin is unchanged subject to the proposed changes to the product information.

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.