28 January 2016
EMA/PRAC/1320/2016
Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 11-14 January 2016 PRAC

The product information wording in this document is extracted from the document entitled 'PRAC recommendations on signals' which contains the whole text of the PRAC recommendations for product information update, as well as some general guidance on the handling of signals. It can be found ***here*** (in English only).

New text to be added to the product information is underlined. Current text to be deleted is ~~struck through~~.

KENTERA (oxybutynin) – Psychiatric disorders (EPITT no 18342)

Summary of Product Characteristics

- **Applicable to all formulations: Kentera 3.9 mg / 24 hours transdermal patch, Kentera 90.7 mg/g gel in sachet and Kentera 90.7 mg/g gel in a metering pump**

4.2 Posology and method of administration

[...] Elderly population

There is no dose adjustment necessary in this population. 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.

~~There is no experience in children~~

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4.4 Special warnings and precautions for use

[…] 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.

Psychiatric and 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 administrated concomitantly with other anticholinergic medicines (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). […]

4.8 Undesirable effects

[…] 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 (≥ 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). 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.

[…]

MedDRA System Organ Class	**Incidence**	**Adverse reactions**
Psychiatric disorders	Uncommon	Anxiety, confusion, nervousness, agitation, insomnia
	Rare	Panic reaction#, delirium#, hallucinations#, disorientation#
Nervous system disorders	Rare	Memory impairment#, amnesia#, lethargy#, disturbance in attention#

[…]

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 known to be associated with anticholinergic therapy, such as oxybutynin, are anorexia, vomiting, reflux oesophagitis, decreased sweating, heat stroke, decreased lacrimation, mydriasis, tachycardia, arrhythmia, disorientation, poor ability to concentrate, fatigue, nightmares, restlessness, convulsion, intraocular hypertension and induction of glaucoma, confusion, anxiety, paranoia, hallucination, 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.

[…]

- **Applicable to Kentera 3.9 mg / 24 hours transdermal patch only**

4.8 Undesirable effects

[…]

MedDRA System Organ Class	Incidence	Adverse reactions
Nervous system disorders	Common	Headache, somnolence
Respiratory, thoracic and mediastinal disorders	Uncommon	Rhinitis
General disorders and administration site conditions	Common	[…], ~~headache~~, ~~Somnolence~~
	Uncommon	~~Rhinitis~~

Package leaflet

- **Applicable to all formulations: Kentera 3.9 mg / 24 hours transdermal patch, Kentera 90.7 mg/g gel in sachet and Kentera 90.7 mg/g gel in a metering pump**

4. POSSIBLE SIDE EFFECTS

[…]

Uncommon side effects:

[…]

- anxiety
- confusion
- nervousness
- agitation
- difficulty in sleeping

[…]

Rare side effects:

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

- poor concentration

[...]