

## IN USE PRODUCT SAFETY ASSESSMENT REPORT FOR Ketamine hydrochloride and esketamine hydrochloride injections

### SUMMARY OF ASSESSMENT AND ITS FINDINGS

#### BACKGROUND

Pfizer have announced that they will not be able to supply the UK market with Ketalar (ketamine); 10mg/mL and 100mg/mL preparations will not be available until March 2015 but they are hoping to supply 50mg/mL strength preparations as soon as possible. It is likely that hospitals will need to maintain a supply by using imported ketamine products that are unlicensed in the UK. This review assesses some of the safety issues with this approach. Esketamine (sometimes called s-ketamine), the S-enantiomer of ketamine, is marketed overseas (e.g. as Ketanest-S) and is also considered in this summary.

#### DETAILS OF PRODUCTS ASSESSED

Where possible photographs of packaging and package inserts were reviewed. However obtaining a complete set of information for all presentations of each potential import has not been possible.

The specific products considered in this assessment were –

##### Ketamine hydrochloride

1. Ketalar - 10mg/mL (20mL), 50mg/mL (10mL), 100mg/mL (10mL); (Pfizer UK),
2. Ketamin-Actavis - 10mg/mL (5mL amp); (Actavis GmbH)
3. Ketamin-Inresa 50mg/mL (2mL amp and 10mL vial) (Inresa Arzneimittel GmbH)

Other strengths of the above products may be available

##### Esketamine hydrochloride

1. Ketanest S - 5mg/mL (5mL amp and 20mL vial), 25mg/mL (2mL + 10mL amps and 10mL and 50mL vials) (Pfizer GmbH),

This selection is not exhaustive as there are other ketamine hydrochloride and possibly esketamine hydrochloride products available. Additional strengths and volumes of the above products may also be available. If these are imported then the product should also be assessed through the product safety in use process to highlight any additional concerns.

#### CONCLUSION FOLLOWING APPLICATION OF VALIDATED ASSESSMENT TOOL

The risks associated with imported ketamine/esketamine products are -

##### 1. Imported ketamine –

- variation in the strength/volume of products compared to UK licensed Ketalar that prescribers are familiar with.
- non-English labelling and packaging,
- lack of prescribing and administration information in English at point of use (i.e. on vials, ampoules and package inserts)

##### 2. Imported esketamine

- New guidelines/local policies would have to be developed for the use of esketamine in clinical practice which highlight the approximate two fold difference in potency between the racemic mixture (ketamine hydrochloride) and the S-enantiomer (esketamine). A switch to using the more potent S-enantiomer will require careful management in order to avoid dosing and administration errors in high risk settings such as theatres and ITU.
- Practitioners will not be familiar with using esketamine in practice. This will impact on prescribing and supply and introduces a risk of confusion and selection errors with ketamine and esketamine if

both products are in use within an organisation.

- There are a number of different volumes and strengths of esketamine available,
- Lack of prescribing and administration information in English at point of use (i.e. on vials, ampoules and package inserts)

Ketamine is mainly used in secondary care/theatres however there may be use in the ambulance services and in palliative care, some of which may be in community settings, so there needs to be consideration of how these risks are communicated in that setting. There could be compatibility issues if esketamine is used in a syringe driver in place of ketamine given its greater concentration of the s-isomer. Ketamine is used for off-label indications – clinicians should consider the risks of continuing this with unlicensed, imported versions of ketamine.

#### POTENTIAL NEXT STEPS AND MITIGATION ACTIONS

Despite the availability of esketamine, it seems sensible to attempt to maintain a supply of ketamine using imported, overseas licensed products (ideally with English translations of product information) where possible. Esketamine remains an alternative in the absence of ketamine.

##### Local actions

- **Review current use** of ketamine hydrochloride to ensure that use is prioritised for indications where alternatives are limited.
- **If using imported ketamine hydrochloride** consider the strength(s) available and amend prescribing guidance/policies. Communicate this to all those involved in the purchase, supply, dispensing, prescribing and administration of ketamine hydrochloride.
- **If using imported esketamine hydrochloride**, decide which areas will use this product, amend all prescribing guidance and ensure all professionals involved in prescribing, supply and administration of esketamine know that it is approximately twice as potent as ketamine hydrochloride.
- **If using esketamine hydrochloride as well as ketamine hydrochloride** then storage and supply needs to be risk assessed particularly for the risk of confusing the two products during prescribing, storage, supply, dispensing and administration.

## FULL ASSESSMENT REPORT

This report was produced in June 2014 using photographic images (not physical products) of licensed ketamine hydrochloride, as well as non-UK ketamine hydrochloride and esketamine hydrochloride available at the time of assessment. Images were obtained primarily from pharmaceutical companies, but also from the Commercial Medicines' Unit PharmaQC database (<http://cmu.dh.gov.uk/medicines/pharmaqc-database/>), importers and from various sources within the NHS.

This report summarises product assessments undertaken by:

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