IN USE PRODUCT SAFETY ASSESSMENT REPORT FOR Onexila® XL (oxycodone once daily prolonged release tablets)

SUMMARY OF ASSESSMENT AND ITS FINDINGS

BACKGROUND

Onexila® XL prolonged release tablets (oxycodone hydrochloride) manufactured by Aspire Pharma Ltd was granted marketing authorisation in the UK on 25th August 2016. This is the first modified release oxycodone product in the UK market that has a **once daily** dosing regimen; all other modified release (MR) preparations of oxycodone are **twice daily** dosing regimens (1, 2). The addition of this new product to the UK market creates potential for confusion.

This review summarises practical in-use safety considerations associated with the introduction of Onexila® XL once daily.

DETAILS OF PRODUCT (S) ASSESSED

The products assessed using the validated UKMi product assessment tool (3) were:

- Onexila® XL (oxycodone prolonged release tablets) 10mg, 20mg, 40mg and 80mg by Aspire Pharma Ltd

Assessments were carried out with reference to: product packaging images, summaries of product characteristics (SmPC) (2) and packaging inserts (4).

There are currently at least ten of the oxycodone modified release (MR) twice daily preparations available in the UK from a variety of generic manufacturers ranging from 5mg to 120mg (1). We selected one of these (Oxylan®) and compared the product packaging to Onexila® XL. A formal assessment of Oxylan® was not undertaken.

CONCLUSION FOLLOWING APPLICATION OF VALIDATED ASSESSMENT TOOL

Onexila® XL is a once daily prolonged release preparation licensed for the management of severe pain (2). A once daily dosing preparation may be advantageous to patients on multiple medications as it reduces the number of the tablets taken over 24 hours. All other MR preparations of oxycodone in the UK are twice daily (1).

Onexila® XL pharmacokinetics are characterised by an increase of plasma concentration over 4 hours, a plateau for approximately 10 hours, followed by a gradual decline until 24 hours after dosing (2). The onset of analgesia is gradual over the first four hours after administration (5). Oxycodone MR twice daily preparations have a biphasic release mechanism with an initial relatively fast release providing an early onset of analgesia followed by a more controlled release (6). The maximal plasma concentration is achieved at 3 hours (6) which plateaus for approximately the first 4 hours (7). The onset of analgesia occurs within 1 hour in most patients (8).

Product packaging and literature

Overall the packaging of Onexila XL® was considered appropriate (see product images at the end of report). The brand and generic names are prominently displayed on 4 sides of the outer packaging and there is good use of colour to differentiate between the four strengths. 'Once Daily' is included on two sides of the outer packaging, however in our view, this may be easily missed as it is positioned at the bottom end of the front facing side, rather than beside the medicine name and formulation . The oxycodone MR twice daily preparation (Oxylan®) reviewed did not have 'twice daily' indicated on the packaging (see example images at the end of report).

Suitable patient and professional information is available in the form of summary of product characteristics and patient information leaflet. At the time of writing manufacturer risk minimisation material was not available.

Product selection

- Oxycodone modified release is listed in part VIIIA (Basic Prices of Drugs) of the Drug Tariff (9) and generic prescribing is common practice. The availability of Onexila® XL in the UK market introduces the potential for confusion if there is generic prescribing of modified release products.
- There is potential for error through incorrect product selection at the point of prescribing, dispensing/supply and administration.
- In the case of electronic prescribing and dispensing systems, there are risks associated with product selection based on drop down menus which in majority of cases are listed generically by strength or alphabetically by brand. This may lead to confusion between oxycodone once daily and twice daily preparations.
- It has also been noted reference sources widely used in the UK, such as the British National Formulary and

MIMS, do not sufficiently separate the oxycodone once daily and twice daily preparations which could lead to further confusion at the point of prescribing. In addition, the BNF does not list the once daily XL preparation as an option in the main part of the monograph.

- Mis-selection of the product could result in the wrong daily dose and/or frequency of oxycodone being received with potential serious adverse effects (too high a dose) or compromise of pain control (too low a dose).
- Onexila® XL is stored in a CD cupboard along with other oxycodone products adding to the risk of mis-selection of the product at the supply stage.
- The risk of the wrong product being supplied also exists at transitions of care between sectors, with the risk heightened by poor communication.
- Oxycodone is a schedule 2 controlled drug, and hence has specific legal requirements associated with it (10), including record keeping in a controlled drug register and prescription requirements (specify dose, formulation, strength and total quantity in words and figures). These legal requirements, in addition to other CD good practice techniques adopted by many NHS organisations e.g. second checks, may mitigate the risk of wrong product selection at the prescribing, dispensing and administration/supply points.

Switching between oxycodone products

Conversion between Onexila® XL once daily and oxycodone MR twice daily preparations or oxycodone immediate release (IR) preparation is 1:1 of the total daily dose (5, 7, 8). However the differences in pharmacokinetics, highlighted previously, may have implications in pain control for patients who have been on long term treatment; appropriate monitoring of pain control and opioid adverse effects will be required.

POTENTIAL NEXT STEPS AND MITIGATION ACTIONS

To support safe use of Onexila® XL **all providers and commissioners of NHS healthcare** should consider:

- Risk assessments should be carried out as part of any local or area formulary applications for Onexila XL and should feed into any purchasing and procurement decisions made by trusts to stock this product. Consultation with the local/regional controlled drugs accountable officer (CDAO) should also form part of the risk assessment.
- Brand prescribing for Onexila® XL: it is recommended the product should be prescribed using the brand name to help select the intended product.
- Reviewing and amending prescribing and dispensing systems to ensure risk of mis-selecting product or strength is minimised.
- Raising awareness (pharmacy, nursing staff and prescribers) of the availability of Onexila® XL and the potential for errors by selecting the wrong product.
- Ensuring good practice techniques, such as second checks of controlled drugs, are used.
- Reviewing storage of the various oxycodone preparations and strengths in controlled drug cabinets to minimise the risks of wrong product selection.
- Ensuring record keeping for Onexila XL in CD registers is accurate and timely, by regular checks and audits
- Strategies to ensure safe prescribing of oxycodone across boundaries of care. This should include:
  - Clear communication on the dosage frequency of oxycodone and in the case of Onexila® XL, ensure it is prescribed using both brand and if possible generic name.
  - Healthcare professionals should confirm the brand and dosage frequency of oxycodone before prescribing.

In addition to actions for the NHS, this review also highlighted the below for, **Aspire Pharma Ltd, the manufacturer** of Onexila® XL to consider:

- Position the 'Once daily' in closer proximity to the medicine name and formulation.
- Develop risk minimisation material to highlight the difference in dosage frequency in comparison to other oxycodone modified release preparations.

Further action is suggested for **publishers/editors of medicine reference sources,** such as the British National Formulary and MIMS, to rectify issues noted in the 'product selection' section above to minimise the risk of confusion between oxycodone once daily and twice daily preparations**. Suppliers of electronic prescribing systems** in Trusts and primary care also need to consider how to minimise the risk of selecting the wrong product

within their systems.

This report was produced in November 2017 using photographic images (not physical products) and packaging artwork of licensed Onexila XL® available at the time of assessment. Images were obtained from pharmaceutical companies.

This report summarises product assessments undertaken by:
London Medicines Information Service (Northwick Park) and South West Medicines Information

For comments email lnwh-tr.medinfo@nhs.net

The UKMI product safety assessment group would appreciate your views on the usefulness of this report. We have devised a short survey which we would appreciate you completing, it should take approximately 10 minutes to complete. Click the following link to complete the survey:
https://www.surveymonkey.com/r/UKMiProductSafetyAssessments.

References:

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3. UKMI product assessment tool, full version. Accessed via https://www.sps.nhs.uk/articles/ukmi-product-assessment-tool/ on 12/07/2017
4. Patient information leaflet: Onexila® XL. Aspire Pharma Ltd. Date of revision of text: July 2016. Accessed via www.emc.medicines.org.uk on 12/07/2017
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7. Lux E.A, Janecki M, Maritz M.A. Clinical evaluation of the first oxycodone once daily prolonged release tablet in moderate to severe chronic pain: a randomised, double-blind, multicentre, cross-over, non-inferiority study to investigate efficacy and safety in comparison with an established oxycodone twice daily prolonged release tablet. Current Medical Research and Opinion 2017; 30 (11):2365-2375.
8. American Society of Health-System Pharmacists. AHFS Drug Information. Electronic edition. Bethesda, Maryland: American Society of Health-System Pharmacists. Accessed via http://www.medicinescomplete.com/ on 8/09/17
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10. Royal Pharmaceutical Society. Medicines, Ethics and Practice: The professional guide for pharmacists. Edition No. 41, July 2017.

PRODUCT PHOTOS

Onexila® XL prolonged-release tablets

Oxycodone MR twice daily preparations: Oxylan prolonged-release tablets