Hertfordshire Partnership NHS
University NHS Foundation Trust

MEDICINES MANAGEMENT BRIEFING NOTE No 1

Increasing Cost-effective use of Quetiapine by Switching from quetiapine modified release (XL) to immediate release (IR)

NOVEMBER 2013

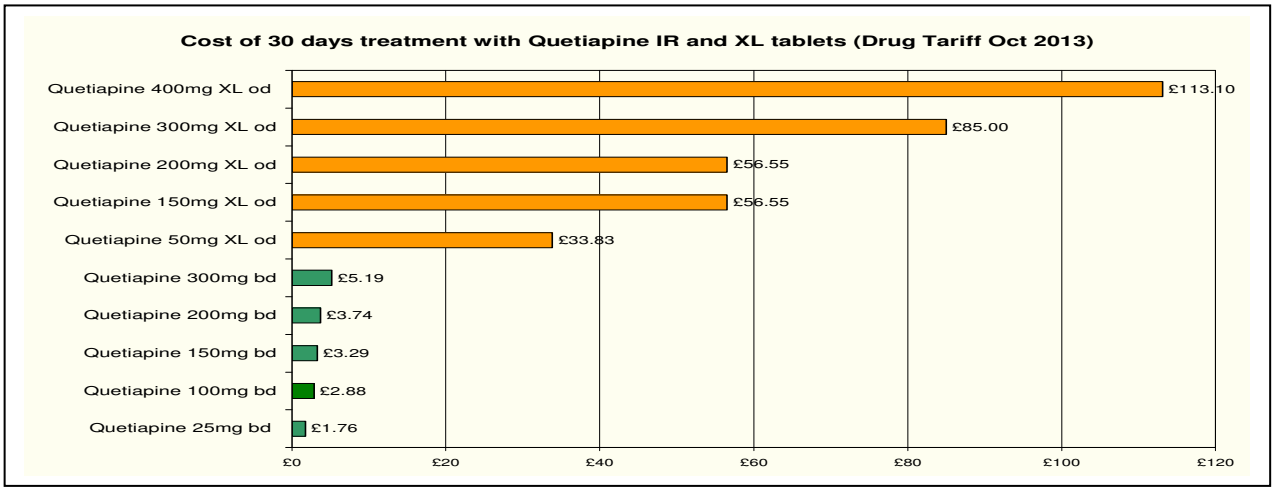
Quetiapine is available in two formulations: quetiapine immediate release (IR) and quetiapine modified release (XL). There are significant price differences between the two formulations and there is scope to achieve substantial cost savings by changing from use of XL to IR formulation. Prescribers are requested to prescribe quetiapine IR formulation when initiating quetiapine and switching existing patients stabilised on XL formulation to IR formulation where possible. If this change is managed carefully significant savings can be achieved for the Trust and the wider healthcare economy without any undue impact on the service we offer. This briefing note provides advice to prescribers on switching to IR formulation and the restrictions for the use of XL formulation.

Background

When the patent on quetiapine expired in March 2012 significant price reductions were expected for both IR and XL formulations with subsequent cost savings for HPFT and the wider health economy.

In reality the cost of IR formulation decreased by around 95% and although significant cost savings were generated by this price drop, similar price reductions were not seen with the XL formulation despite it being available as a generic preparation. The Drug Tariff price of generic quetiapine XL remains the same as that of the branded product Seroquel® XL. Graph 1 shows the current price differential between quetiapine IR and XL, which is significant.

Graph 1



HPFT annual spend on quetiapine is around £142k of which £104k is for the XL formulation. If the use of XL tablets could be minimised so that 80% of current XL usage was changed to IR then cost savings of around **£80K** could be generated.

Furthermore if this approach was extended to Primary Care, where annual spend is around £737k on quetiapine XL, the savings that could be generated for the wider healthcare economy would be in the region of **£560k.**

In the current financial climate every effort must be made to achieve the best possible value from generic quetiapine IR. Prescribers are requested to decrease the usage of quetiapine XL by initiating patients on IR preparations where appropriate and switching existing patients on XL to IR formulations where possible.

Information and Advice to Prescribers

- The pharmacokinetic parameters of the 2 formulations are similar. IR and XL formulations reach the same peak plasma concentration (Cmax); however the time taken to reach Cmax is 1.5 hours and 6 hours respectively.
- All patients who are to be initiated on quetiapine should receive quetiapine IR except for acutely unwell patients in whom the simplified titration regime with XL formulation can be used for the first 3 days, after which the IR formulation must be used.
- Patients currently stabilised on XL formulation should where possible be switched to IR formulation, unless there are significant clinical reasons not to do so, such as side-effects. If adherence with twice a day treatment regime with IR formulation is likely to be a problem then a once a day regime using IR tablets could be considered. See table 1 for suggested dose conversions.
- The switch may be associated with a slightly higher risk of sedation and postural hypotension. If sedation and postural hypotension are a concern then a larger proportion of the dose could be given at night eg 600mg XL at night could be changed to 200mg IR in the morning and 400mg IR at night (see table 1 below).
- Quetiapine IR is usually administered twice a day, however, it is licensed to be used once a day for the treatment of depressive episodes in bi-polar disorder. There have been some small, short-term studies[2,3,4] supporting quetiapine IR once daily for schizophrenia and this is occasionally done in practice. It would therefore not be unreasonable to consider using IR preparations once a day for other licensed indications when compliance with twice a day is likely to be a problem, although this would be considered off-label use.
- If the IR formulation is to be used once a day, then this should be taken at night to minimise side-effects such as hypotension. For reasons of safety it is recommended that the maximum single dose of IR formulation should not exceed 400mg.
- For those patients who are not suitable to change from XL to IR, the clinical reasons for this must be documented in the patient's records and a full explanation provided to the GP. It is important that this information is communicated to GPs so that they do not attempt to switch unsuitable patients and can highlight this on their records.
- There is very little difference in terms of side-effects between quetiapine XL and quetiapine IR. There may however be patients who do not tolerate quetiapine IR but are able to tolerate quetiapine XL, which could justify the use of XL formulation.
- GPs may switch patients currently on quetiapine XL to IR, however they should seek approval from the relevant psychiatrist for each patient before doing so. Otherwise they can refer to patients to HPFT clinicians for review and who can then make the decision to switch.
- All changes to medication must be fully discussed, explained and agreed with the patient (and or their carer as appropriate). A patient information leaflet is available to help explain the reasons for the switch.
- It is important that all prescriptions and any communication clearly indicate which formulation is intended by using the abbreviations XL and IR. This is especially important when IR is prescribed once a day as it may be incorrectly assumed that the XL version is required.
- The first dose of IR formulation should be given approximately 24 hours after the last dose of the XL formulation.
- **XL tablets should only be prescribed for:**
  - **acutely unwell patients for first 3 days after which IR tablets should be prescribed**
  - **those who cannot tolerate the switch to IR tablets once or twice a day**
  - **those in whom it would be clinically inappropriate to use or switch to IR tablets – a valid reason must be provided.**

Table 1 Suggested dose conversions when switching from quetiapine XL to IR

Current dose quetiapine XL	Quetiapine IR dosing options		
	For those who are tolerating quetiapine well and do not have compliance concerns	For those who are (or at risk of) experiencing sedation or postural hypotension following the switch*	For those who are tolerating quetiapine well but have compliance concerns. Note: IR not licensed once a day except for those with depressive episode in bipolar
100mg XL OD	50mg BD	25mg AM, 75mg ON	100mg ON
200mg XL OD	100mg BD	50mg AM, 150mg ON	200mg ON
300mg XL OD	150mg BD	100mg AM, 200mg ON	300mg ON
400mg XL OD	200mg BD	150mg AM, 250mg ON	400mg ON
600mg XL OD	300mg BD	200mg AM, 400mg ON	-
800mg XL	400mg BD	-	-

***** Those at increased risk of experiencing sedation or postural hypotension following the switch to quetiapine IR may include: the elderly, those with learning disabilities, adolescents, concurrent cardiac medication and concurrent CNS depressants.

Table 2 Current licensed Indications for quetiapine IR and XL (see SPC for further information)

	Current licensed Indication	No of daily doses
Quetiapine XL	• Schizophrenia including prevention of relapse • Mania or depression in bipolar disorder • Prevention of relapse in bipolar • Add on treatment (to an antidepressant) in major depressive disorder	ONCE daily
Quetiapine IR	• Schizophrenia including prevention of relapse • Mania in bipolar disorder • Prevention of relapse in bipolar disorder	TWICE daily
	• Depression in bipolar	ONCE daily

*Although unlicensed in schizophrenia as a once daily preparation there are 3 small, short term studies supporting quetiapine IR once daily and this is occasionally done in practice[2,3,4].

Reference

1. Seroquel (Quetiapine) Summary of Product Characteristics last updated on the eMC: Nov 2012.Astra Zeneca. Electronic Medicines Compendium: http://emc.medicines.org.uk/
2. Chengappa et al (2003) A random-assignment, double-blind, clinical trial of once vs twice daily administration of quetiapine fumarate in patients with schizophrenia or schizoaffective disorder: A pilot study. Can J Psychiatry; 48: 187-194
3. Ohlsen et al (2004) Clinical response after switching from twice to once daily quetiapine in first episode schizophrenic patients. Schizophrenia research: 67(1Suppl S): 169-70, Abs 336B
4. Tauscher-Wisniewski et al (2002) Quetiapine: an effective antipsychotic in first pisode schizophrenia despite only transiently high dopamine 2 receptor blocade. J Clin Psychiatry: 63; 992-997