There are long standing and well recognised safety concerns with all NSAIDs. The MHRA review on the cardiovascular safety of NSAIDs has highlighted further evidence that diclofenac is associated with cardiovascular risks that are higher than the other non-selective NSAIDs, and similar to the selective COX-2 inhibitors. Naproxen and low-dose ibuprofen are still considered to have the most favourable cardiovascular safety profiles of all non-selective NSAIDs.

It is acknowledged that whilst tablets and capsules are by far the most commonly used preparations, the route of administration and available formulations may restrict choice of drug in some situations.

It is recommended that prescribers consider the following strategies for reducing diclofenac and overall total NSAID use:

- Promotion of non-NSAID pain relief options wherever appropriate
- Promotion of Ibuprofen as first choice NSAID wherever possible
- Consideration of naproxen as second choice agent in preference to diclofenac

Plan for LTHT

- The new acute pain guidelines will state NSAID on the analgesic ladder recommending ibuprofen up to 1200mg/day in divided doses as first line and naproxen up to 1gram/day in divided doses as second line.
- Where rectal diclofenac is indicated, this must be used only for the shortest possible time until conversion to oral ibuprofen/ naproxen is possible. There are no licensed rectal dosage forms of ibuprofen or naproxen available.
- NSAIDs should be prescribed for the shortest possible course
- Oral diclofenac will be removed (including prepacks) from ward areas and replaced with suitable alternative
- Co-prescription of a gastroprotective agent should be considered according to individual risk factors
- Any LTHT Clinical Service Units wishing to continue using diclofenac must register it with their CSU clinical governance group and DTG.

The LTHT DTG considered the proposals below in December 2013 and January 2014. The CSU positions were supported, noting the plan to regularly review use of diclofenac and make any necessary changes in the light of new evidence.

DTG have also requested that clear communication is sent to GPs regarding their patients who should continue to receive diclofenac prescriptions. They request that this information includes the rationale for the decision to continue diclofenac in light of the MHRA advice, to avoid unnecessary switching or correspondence to confirm intention of use.

In The Rheumatology Department

Proposal

Selective and non-selective NSAIDs form an important part of the therapeutic strategy for the management of a number of inflammatory rheumatological conditions. The Rheumatology Department has considerable experience in the prescribing of these agents and is aware of the significant morbidity and mortality associated with their use. Differences in the anti-inflammatory effects of NSAIDs is small, but there is considerable variation in individual response and tolerance to these drugs. Patients may not respond to the first NSAID selected, but may gain full analgesic benefit when switched to an alternative NSAID. In view of this inter-patient variability, there may be a small number of patients where initiation or continued use of diclofenac may be appropriate. The Rheumatology Department will give full consideration to the increased cardiovascular risk associated with the use diclofenac and only in the following circumstances will consider prescribing diclofenac:
- Pre-existing patients established on diclofenac who have failed to gain therapeutic benefit or been intolerant of other NSAIDs.

- New patients who have failed to respond to an alternative NSAID or where there is intolerance/contraindications to an alternative NSAID after careful consideration of significant risk factors for cardiovascular disease (hypertension, hyperlipidaemia, diabetes mellitus and smoking).

The use of diclofenac in individual patients will be regularly reviewed and the lowest effective dose used for the shortest possible duration to control the patient’s symptoms.

Proposed by:
Dr Jane Freeston - Lead Clinician Rheumatology
Dr Jacqueline Andrews - Clinical Director, Chapel Allerton Clinical Service Unit
20th January 2013

**In Head and Neck patients**

There are several areas, where the withdrawal of Diclofenac would result in a poorer quality of care for patients:

- These are:

  1. Patients with head and neck cancer (particularly those undergoing radiotherapy or chemoradiotherapy) where analgesia is required for days to weeks. The combination of opiates with a NSAID is well known to be effective here, but frequently has to be given in a liquid form (perhaps even nasogastrically), because of difficulties in swallowing. Ibuprofen is not nearly as effective, and withdrawing Diclofenac would increase the need for opiates, with subsequent suppression of appetite, prolonging recovery.

  2. Adults having tonsillectomy or other throat procedures. These patients need combination analgesia for up to 2 weeks and we have normally used Paracetamol/Codeine mixtures with a NSAID, usually Diclofenac. We believe that Diclofenac offers greater anti-inflammatory action and subsequent better pain control, with faster recovery. We often have to use a liquid version initially.

  3. Children having tonsillectomy need combination analgesia again, more often in liquid form. While ibuprofen has been just satisfactory, we do believe that a combination with Diclofenac was our gold standard.

These are general areas, but there will be multiple other varying examples of the need for liquid versions of a NSAID, and where Ibuprofen is not as effective.

We believe that the ENT post-operative pain control patients are in a low risk group for cardiovascular effects, and whilst these risks are higher in our cancer patients, they warrant the best analgesic and anti-inflammatory drugs, for proper quality of analgesia, often when swallowing is difficult.

Proposal by Mr C J Woodhead. Clinical Director Head and Neck CSU and Consultant ENT and Head and Neck surgeon
In Paediatrics

In light of the MHRA alert in June 2013, and the subsequent confirmatory statement released in September 2013, a review of the use of diclofenac in paediatric patients was carried out.

The MHRA have stated that “Patients with serious underlying heart conditions, such as heart failure, heart disease, circulatory problems or a previous heart attack or stroke should no longer use diclofenac”.

It has been raised by a number of paediatric clinicians that this statement would not be applicable across the board in paediatrics, and that blanket removal of diclofenac use in paediatrics would be impractical.

The majority of the use of diclofenac in paediatrics is short term post-operative use as an analgesic. Occasionally it is used by some anaesthetists as a premedication for surgery.

It is also an important medication in the temporary management of long-term inflammatory conditions eg juvenile idiopathic arthritis. Especially so, when ibuprofen is ineffective or cannot be tolerated and a child cannot manage tablets (so naproen is not an option). Alternatives would be stronger NSAIDs eg piroxicam or systemic corticosteroids, both would have worse side effect profiles. Diclofenac is generally used in patients where ibuprofen has proved to be ineffective and a stronger NSAID is required. Occasionally it is the NSAID of choice in post-operative patients (this is based on experience of the anaesthetists responsible for the patient).

Diclofenac is currently available at LTHT as soluble tablets, enteric coated tablets, suspension, and suppositories. This wide range of formulations makes it the ideal choice of paediatric patients, where suspension and suppositories formulations are widely used.

With respect to the information about diclofenac increasing cardiovascular risk in patients with pre-existing severe cardiovascular risk, it has been highlighted that it should be avoided in patients with a high atherosclerotic risk (e.g. patients with Kawasaki Disease, thrombophilia, SLE and pre-existing severe heart failure).

There are also groups of patients in whom diclofenac should be used with caution (liver failure, renal failure, bleeding tendency, high risk of gastric/duodenal ulcer and patients taking long-term aspirin, obese patients)

Due to the lack of available formulations of naproen, and considering the general low incidence of increased cardiovascular amongst the paediatric population, continued use of diclofenac in paediatrics should pose no extra risk. This should be reviewed regularly in light of any new data that may become available.

Prady Gadaria
Advanced Clinical Pharmacist

Dr M Wood
Consultant Paediatric Rheumatologist
Date: December 2013

Summary Paper
Jane Otter Prescribing Advisor Pharmacist
March 2014