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Etoricoxib for patients with inherited bleeding disorder

Amber Continuation Guideline

This guideline provides prescribing and monitoring guidance for etoricoxib therapy in the treatment of moderate to severe pain in patients with an inherited bleeding disorder. An Amber Continuation Guideline supports the transfer of prescribing to primary care following initiation or recommendation by specialist. It should be read in conjunction with the Summary of Product Characteristics (SPC) available on www.medicines.org.uk/emc and the BNF.

Specialist responsibilities prior to transfer of prescribing

- Complete pre-treatment assessment
- Initiate treatment and prescribe until the dose is stable or prescribe the first 28 days of treatment (whichever is most appropriate)
- Ensure the patients understand the nature and complications of drug therapy and their role in reporting adverse effects promptly
- Provide copy of patient information leaflet and drug monitoring card where appropriate
- Be available to give advice to GP and patient during treatment

GP responsibilities summary

- Prescribe medication as recommended below, once transfer of prescribing is complete
- Ensure all monitoring is completed in accordance with 'on-going monitoring' section.
- Monitor patient for adverse effects, contraindications and precautions as listed below.
- Take subsequent recommended actions as outlined below, including referral back to specialist if appropriate.

Patient's responsibilities

This section may be appropriate for some medicines but may also be omitted.

- To alert the haemophilia team if they suffer side effects, in particular gastrointestinal bleeding or chest pain

Background for Use

Haemophilia is an inherited bleeding disorder caused by mutations in the F8 or F9 genes that code for clotting factors. Haemophilia A and B are the most common forms. The severity of the haemophilia is linked to the magnitude of coagulation factor deficiency and is generally classified as mild (factor level 6% or more), moderate (1 - 5%) or severe (<1%). Standard treatment for haemophilia includes prophylaxis of regular administration of clotting factors to maintain plasma factor concentrations at levels sufficient to minimise recurrent bleeding into joints and muscles, as well as 'on-demand' treatment. Joint bleeding accounts

for over 90% of all serious bleeding episodes in a person with haemophilia, despite this management. Bleeding occurs in the ankles, knees, elbows, hips, and shoulders.

Recurrent bleeding into joints leads to a chronic inflammatory response and causes synovitis, chronic arthritis and joint destruction. This complication is known as haemophilic arthropathy. This arthropathy is debilitating and painful for patients. Management of pain and inflammation in this condition is difficult due to the lack of treatment options available. NSAIDs play a main role in the management of arthritis by providing analgesic and anti-inflammatory effects. However, the use of NSAIDs in those with haemophilia is limited by the increased risk of bleeding, mainly in the GI tract. This occurs due to the non-selectivity of COX inhibition, decreased platelet aggregation and inhibition of gastro protective prostaglandins. Therefore, the availability of COX-2 selective NSAIDs, which eliminates the inhibition of gastro protective prostaglandins, provides a more favorable treatment option. COX-2 inhibitors have significantly lower incidence of gastroduodenal ulcer complications and UGI bleeding. There appears to be no difference in the incidence of cardiovascular and renovascular adverse effects between NSAIDs and COX-2 inhibitors. When compared to the general population, patients with haemophilia are at an increased risk of GI bleeding (possibly by up to 10-fold) and renal disease, but cardiovascular disease and related deaths are lower. Monitoring of blood pressure is routinely undertaken for all haemophilia patients due to the increased potential for hypertension.

The main treatment group that we are likely to treat with etoricoxib are haemophilia patients with chronic painful arthropathy. However, we also treat other patient groups with inherited bleeding conditions, Von Willebrand disease (VWD) and disorders such as afibrinogenaemia. These patients may also develop similar types of arthropathy (albeit much less commonly) or may require anti-inflammatory medication in the short term for an acute injury. It is likely that a very small proportion of our prescribing of etoricoxib will be for a 7 - 14 day course of anti-inflammatory medication for a one-off injury or other musculoskeletal injury.

Supporting Information
World Federation of Haemophilia 'Guidelines for the management of haemophilia' (Srivastava, 2012): **https://www1.wfh.org/publication/files/pdf-1472.pdf**

Contraindications and Precautions

Contraindication	Action
Active peptic ulceration or active gastro-intestinal (GI) bleeding	Do not prescribe/Stop treatment
Pregnancy and lactation	
Severe hepatic dysfunction	
Children and adolescents under 16 years of age	
Inflammatory bowel disease	
Congestive heart failure (NYHA II-IV)	
Patients with hypertension whose blood pressure is persistently elevated above 140/90mmHg and has not been adequately controlled	
Established ischaemic heart disease, peripheral arterial	

disease, and/or cerebrovascular disease

Precautions	Action
Previous history of GI disease	Consider individual patient risk of GI bleeding
Risk factor for cardiovascular disease e.g. hyperlipidaemia and diabetes	Consider individual patient risks and minimise duration of use.
Renal impairment	Monitor renal function
Abnormal liver function tests	Investigate for underlying cause and if persistently abnormal review ongoing treatment
Cardiac failure/Left ventricular dysfunction	Monitor for fluid retention/oedema and potential hypertension

Dosage

Indication	Dose
moderate to severe pain in patients with an inherited bleeding disorder	30-90mg once daily titrated according to response

Time to Response
In general, the patient would be commenced on 30mg daily. If there was no change to symptoms (i.e. reduction in pain) after 1 month, then consideration would be given to increasing the dose to 60mg. There will be patient variation in the dose needed to provide sufficient symptom relief.

Pre-Treatment Assessment
BP monitoring is routinely undertaken for all haemophilia patients due to the increased potential for hypertension. This is carried out by the haemophilia team every 6 months and would also be checked prior to starting treatment with etoricoxib.

Ongoing Monitoring
Since etoricoxib has been associated with hypertension, it is recommended that blood pressure is checked by the GP prior to the prescription for continued usage (i.e. before month 2).

Actions to be taken
If blood pressure rises significantly, alternative treatment should be considered. The GP should inform the haemophilia team (contact details below) who will provide advice to the patient. All patients have direct access to the haemophilia team and are advised to contact them in the first instance.

Notable Drug Interactions (Refer to BNF and SPC)

- Diuretics, ACE inhibitors and Angiotensin II Antagonists
- Ciclosporin
- Tacrolimus
- Lithium

- Methotrexate
- Oral Contraceptives
- HRT
- Rifampicin

Back-up Information and Advice

Contact one of the coagulation and haemostasis team if further advice is required.

Dr Nicola Curry	nicola.curry@ouh.nhs.uk
Dr Susie Shapiro	susie.shapiro@ouh.nhs.uk
Coagulation and Haemostasis SpR	01865 225320 or 0300 304 7777, bleep 5529

References

Medicines.org.uk. (2018). Arcoxia 30 60 90 120mg film-coated tablets - Summary of Product Characteristics (SmPC) - (eMC). [online] Available at: https://www.medicines.org.uk/emc/product/3302/smpc [Accessed 8 Aug. 2018]

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