**Prescribing Clinical Network**

**Surrey (East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG & Surrey Heath), Crawley CCG and Horsham & Mid-Sussex CCG**

**Application for change in colour classification**

|  |  |  |
| --- | --- | --- |
| **GREEN -** **Non-Specialist Drugs**  GPs (or non-medical prescribers in primary care) are able to take full responsibility for initiation and continuation of prescribing | | |
| **BLUE - Specialist Input WITHOUT Formal Shared Care Agreement**  Prescribing initiated and stabilised by specialist but has potential to transfer to primary care WITHOUT a formal shared care agreement | | |
| **AMBER - Specialist Initiation WITH Shared Care Guidelines**  Prescribing initiated and stabilised by specialist but has potential to transfer to primary care under a formal shared care agreement | | |
| **RED - Specialist ONLY drugs**  Treatment initiated and continued by specialist clinicians | | |
| **BLACK – NOT recommended**  Not recommended for use in any health setting across Surrey and NW Sussex health economy | | |
| **Medicine details** | | |
| **Name, brand name1** | * **Celecoxib - Celebrex®** * **Etoricoxib -** [**Arcoxia®**](https://www.evidence.nhs.uk/formulary/bnf/current/10-musculoskeletal-and-joint-diseases/101-drugs-used-in-rheumatic-diseases-and-gout/1011-non-steroidal-anti-inflammatory-drugs/etoricoxib#PHP6449)   Generics of both are available. | |
| **Manufacturer1** | * **Celecoxib -** [**Celebrex®**](https://www.evidence.nhs.uk/formulary/bnf/current/10-musculoskeletal-and-joint-diseases/101-drugs-used-in-rheumatic-diseases-and-gout/1011-non-steroidal-anti-inflammatory-drugs/celecoxib#PHP6416) **(Pfizer)** * **Etoricoxib -** [**Arcoxia®**](https://www.evidence.nhs.uk/formulary/bnf/current/10-musculoskeletal-and-joint-diseases/101-drugs-used-in-rheumatic-diseases-and-gout/1011-non-steroidal-anti-inflammatory-drugs/etoricoxib#PHP6449) **(**[**MSD**](https://www.evidence.nhs.uk/formulary/bnf/current/index-of-manufacturers#PHP10248)**)**   Numerous generic manufacturers. | |
| **Licensed indication1** | * **Celecoxib -** [**Celebrex®**](https://www.evidence.nhs.uk/formulary/bnf/current/10-musculoskeletal-and-joint-diseases/101-drugs-used-in-rheumatic-diseases-and-gout/1011-non-steroidal-anti-inflammatory-drugs/celecoxib#PHP6416)   Celebrex is indicated in adults for the symptomatic relief in the treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis.   * **Etoricoxib -** [**Arcoxia®**](https://www.evidence.nhs.uk/formulary/bnf/current/10-musculoskeletal-and-joint-diseases/101-drugs-used-in-rheumatic-diseases-and-gout/1011-non-steroidal-anti-inflammatory-drugs/etoricoxib#PHP6449)   Arcoxia is indicated in adults and adolescents 16 years of age and older for the symptomatic relief of osteoarthritis (OA), rheumatoid arthritis (RA), ankylosing spondylitis, and the pain and signs of inflammation associated with acute gouty arthritis.  Arcoxia is indicated in adults and adolescents 16 years of age and older for the short-term treatment of moderate pain associated with dental surgery. | |
| **Formulation1** | * **Celecoxib -** 100 mg, 200 mg capsules * **Etoricoxib -** 30 mg, 60mg, 90mg, 120mg film-coated tablets | |
| **Usual dosage1** | * **Celecoxib -** [**Celebrex®**](https://www.evidence.nhs.uk/formulary/bnf/current/10-musculoskeletal-and-joint-diseases/101-drugs-used-in-rheumatic-diseases-and-gout/1011-non-steroidal-anti-inflammatory-drugs/celecoxib#PHP6416)   *Osteoarthritis*  The usual recommended daily dose is 200 mg taken once daily or in two divided doses. In some patients, with insufficient relief from symptoms, an increased dose of 200 mg twice daily may increase efficacy. In the absence of an increase in therapeutic benefit after two weeks, other therapeutic options should be considered.  *Rheumatoid arthritis*  The initial recommended daily dose is 200 mg taken in two divided doses. The dose may, if needed, later be increased to 200 mg twice daily. In the absence of an increase in therapeutic benefit after two weeks, other therapeutic options should be considered.  *Ankylosing spondylitis*  The recommended daily dose is 200 mg taken once daily or in two divided doses. In a few patients, with insufficient relief from symptoms, an increased dose of 400 mg once daily or in two divided doses may increase efficacy. In the absence of an increase in therapeutic benefit after two weeks, other therapeutic options should be considered.  The maximum recommended daily dose is 400 mg for all indications.   * **Etoricoxib -** [**Arcoxia®**](https://www.evidence.nhs.uk/formulary/bnf/current/10-musculoskeletal-and-joint-diseases/101-drugs-used-in-rheumatic-diseases-and-gout/1011-non-steroidal-anti-inflammatory-drugs/etoricoxib#PHP6449)   *Osteoarthritis*  The recommended dose is 30 mg once daily. In some patients with insufficient relief from symptoms, an increased dose of 60 mg once daily may increase efficacy. In the absence of an increase in therapeutic benefit, other therapeutic options should be considered.  *Rheumatoid arthritis*  The recommended dose is 60 mg once daily. In some patients with insufficient relief from symptoms, an increased dose of 90 mg once daily may increase efficacy. Once the patient is clinically stabilised, down-titration to a 60 mg once daily dose may be appropriate. In the absence of an increase in therapeutic benefit, other therapeutic options should be considered.  *Ankylosing spondylitis*  The recommended dose is 60 mg once daily. In some patients with insufficient relief from symptoms, an increased dose of 90 mg once daily may increase efficacy. Once the patient is clinically stabilised, down-titration to a 60 mg once daily dose may be appropriate. In the absence of an increase in therapeutic benefit, other therapeutic options should be considered.  *Acute pain conditions*  For acute pain conditions, etoricoxib should be used only for the acute symptomatic period.  *Acute gouty arthritis*  The recommended dose is 120 mg once daily. In clinical trials for acute gouty arthritis, etoricoxib was given for 8 days.  *Postoperative dental surgery pain*  The recommended dose is 90 mg once daily, limited to a maximum of 3 days. Some patients may require other postoperative analgesia in addition to ARCOXIA during the three day treatment period.  Doses greater than those recommended for each indication have either not demonstrated additional efficacy or have not been studied. Therefore:   * The dose for OA should not exceed 60 mg daily. * The dose for RA and ankylosing spondylitis should not exceed 90 mg daily. * The dose for acute gout should not exceed 120 mg daily, limited to a maximum of 8 days treatment. * The dose for postoperative acute dental surgery pain should not exceed 90 mg daily, limited to a maximum of 3 days. | |
| **Traffic Light Status** | **Current status** | **Proposed status** |
| 1. For pain and inflammation - BLACK. 2. For ankylosing spondylitis – BLUE 3. For use of the branded products, Celebrex® and Arcoxia® - BLACK | 1. For patients with pain and inflammation:   GREEN for both celecoxib and etoricoxib  Or  GREEN for both celecoxib and etoricoxib, with celecoxib as the preferred product.   1. For ankylosing spondylitis - GREEN 2. For use of the branded products, Celebrex® and Arcoxia® - BLACK |
| **Reason for requested change** | | |
| At present, on the Surrey PAD:   * Celecoxib and etoricoxib are BLACK for use in pain and inflammation * Celecoxib and etoricoxib are BLUE for use in ankylosing spondylitis * The use of the branded products, Celebrex® and Arcoxia® is BLACK   Use of COX-2 inhibitors is now included in the following:   * NICE Osteoarthritis: care and management Clinical guideline 1772 * CKS management of suspected rheumatoid arthritis in primary care3 and * CKS ankylosing spondylitis4.   The current BLACK status is limiting the use of COX-2 inhibitors which is included in national guidance, so the traffic light status on the Surrey PAD needs to be updated to reflect this guidance.  A GREEN status would allow the use of COX-2 inhibitors in appropriate patients in primary care to manage pain and inflammation, particularly while the patient is waiting for a referral.  For osteoarthritis2:  The NICE Osteoarthritis: care and management Clinical guideline 177, published: 12 February 20142 recommend the use of COX -2 inhibitors as follows:  NSAIDs and highly selective COX-2 inhibitors  Although NSAIDs and COX-2 inhibitors may be regarded as a single drug class of 'NSAIDs', these  recommendations use the two terms for clarity and because of the differences in side-effect profile.  1.5.6 Where paracetamol or topical NSAIDs are ineffective for pain relief for people with osteoarthritis, then substitution with an oral NSAID/COX-2 inhibitor should be considered. [2008]  1.5.7 Where paracetamol or topical NSAIDs provide insufficient pain relief for people with osteoarthritis, then the addition of an oral NSAID/COX-2 inhibitor to paracetamol should be considered. [2008]  1.5.8 Use oral NSAIDs/COX-2 inhibitors at the lowest effective dose for the shortest possible period of time. [2008]  1.5.9 When offering treatment with an oral NSAID/COX-2 inhibitor, the first choice should be either a standard NSAID or a COX-2 inhibitor (other than etoricoxib 60 mg). In either case, co-prescribe with a proton pump inhibitor (PPI), choosing the one with the lowest acquisition cost. [2008]  1.5.10 All oral NSAIDs/COX-2 inhibitors have analgesic effects of a similar magnitude but vary in their potential gastrointestinal, liver and cardio-renal toxicity; therefore, when choosing the agent and dose, take into account individual patient risk factors, including age. When prescribing these drugs, consideration  should be given to appropriate assessment and/or ongoing monitoring of these risk factors. [2008]  1.5.11 If a person with osteoarthritis needs to take low-dose aspirin, healthcare professionals should consider other analgesics before substituting or adding an NSAID or COX-2 inhibitor (with a PPI) if pain relief is ineffective or insufficient.[2008]  For rheumatoid arthritis3:  **Consider offering a nonsteroidal anti-inflammatory drug (NSAID) at the lowest effective dose for the shortest possible until a rheumatology appointment is available** — for example, a standard NSAID such as ibuprofen, naproxen, or diclofenac, or a coxib (such as celecoxib or etoricoxib).  For ankylosing spondylitis4:   * **Consider prescribing a nonsteroidal anti-inflammatory drug (NSAID)**such as ibuprofen or naproxen while waiting for referral. Take account of the person's risk of serious adverse effects, the safety profiles of individual standard NSAIDs or coxibs, the person's ability to tolerate individual NSAIDs, their other medications, and their preferences.   + If NSAIDs are contraindicated, prescribe a standard analgesic (paracetamol with or without codeine).   + If the person is at increased risk of gastrointestinal (GI) adverse effects, or is unable to tolerate NSAIDs because of GI adverse effects, prescribing options are:     - A standard NSAID together with a proton pump inhibitor (PPI).     - A coxib with a PPI.     - A standard analgesic (paracetamol with or without codeine).   Please note: Celecoxib and etoricoxib are both licensed for use in osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. Etoricoxib in addition is licensed for use in acute pain conditions, acute gouty arthritis and postoperative dental surgery pain. | | |
| **Key Considerations** | | |
| **Cost implications to the local health economy** | | |
| **Cost of product5 :**  **Celecoxib**  Capsules, celecoxib 100 mg, [net price](https://www.evidence.nhs.uk/formulary/bnf/current/general-information-and-changes/how-to-use-the-bnf/prices-in-the-bnf) 60-cap pack = £2.72; 200 mg, 30-cap pack = £1.01  **Etoricoxib**  Etoricoxib 30mg tablets x 28 = £9.59  Etoricoxib 60mg tablets x 28 = £3.53  Etoricoxib 90mg tablets x 28 = £3.03  Etoricoxib 120mg tablets x 28 = £13.82    **Monthly cost per patient:**   |  |  |  |  | | --- | --- | --- | --- | | **COXII** | **Indication** | **Dose** | **Generic** | | **Celecoxib** | **Osteoarthritis** | 200 mg taken once daily or in two divided doses | £1.01 - £2.72 | |  |  | 200 mg twice daily | £ 2.02 | |  | **RA** | 200mg taken in two divided doses | £ 2.72 | |  |  | 200mg twice daily | £ 2.02 | |  |  |  |  | | **Etoricoxib** | **Osteoarthritis** | 30 mg once daily | £ 9.59 | |  |  | 60 mg once daily | £ 3.53 | |  | **RA** | 60mg once daily | £ 3.53 | |  |  | 90mg once daily | £ 3.03 |   **Availability of PAS and details (if appropriate):** Not applicable.  **Availability of homecare service (if appropriate):** Not applicable. | | |
| **Impact to current prescriber or medication initiator** | | |
| * Current status is BLACK (or BLUE for ankylosing spondylitis), so prescribing and initiation in primary care is not currently recommended. | | |
| **Impact to proposed prescriber or medication initiator** | | |
| * Extend care of patient in primary care by extending prescribing options * Prescriber able to follow NICE and CKS guidance * Primary care prescribers may feel more comfortable when PAD reflects national guidance. | | |
| **Impact to patients** | | |
| * Another option to manage pain and inflammation symptoms, particularly while waiting for referral. | | |
| **Additional comments** | | |
| **Introduction:**  Cyclo-oxygenase-2 (COX-2) inhibitors are a type of non-steroidal anti-inflammatory drug (NSAID) that specifically block COX-2 enzymes.  There are two main types of COX enzymes: COX-1 and COX-2. Both types produce prostaglandins which have a number of different effects, one of which is to regulate inflammation.  By specifically only blocking COX-2 enzymes, COX-2 inhibitors relieve inflammation and pain with less adverse gastrointestinal effects than NSAIDs that inhibit both COX-1 and COX-2 enzymes. However, they are not devoid of gastrointestinal effects entirely, and their use (like all NSAIDs) has been associated with a higher risk of stroke and heart attack.   1. **GP contract:**   The GP contract for this year directs prescribers to the NICE CKS on NSAID prescribing advice when performing specific elements of the quality improvement activity.  Advice from CKS – NSAIDS prescribing issues is available at: <https://cks.nice.org.uk/nsaids-prescribing-issues#!scenario>   * **Do not prescribe COX-2 inhibitors, diclofenac, aceclofenac or high dose ibuprofen (more than 2400 mg daily)** **to people with**: * Ischaemic heart disease. * Inflammatory bowel disease (COX-2 inhibitors only). * Peripheral arterial disease. * Cerebrovascular disease. * Congestive heart failure (New York Heart Association [NYHA] classification II–IV). * **Do not prescribe etoricoxib or high dose ibuprofen to** people with uncontrolled hypertension (persistently above 140/90 mmHg).   There is also advice on the use of PPIs for co-prescription with NSAIDs available on CKS at: <https://cks.nice.org.uk/nsaids-prescribing-issues#!scenario>   1. **Monitoring requirements (as per SPC):**  |  |  | | --- | --- | | **Etoricoxib** | **Celecoxib** | | **4.3 Contraindications** |  | | • **Patients with hypertension whose blood pressure is persistently elevated above 140/90 mmHg and has not been adequately controlled.** |  | |  |  | | **4.4 Special warnings and precautions for use** | **4.4 Special warnings and precautions for use** | | *Fluid retention, oedema and hypertension* | *Hypertension* | | Etoricoxib may be associated with more frequent and severe hypertension than some other NSAIDs and selective COX-2 inhibitors, particularly at high doses. Therefore, **hypertension should be controlled before treatment with etoricoxib (see section 4.3) and special attention should be paid to blood pressure monitoring during treatment with etoricoxib. Blood pressure should be monitored within two weeks after initiation of treatment and periodically thereafter. If blood pressure rises significantly, alternative treatment should be considered.** | As with all NSAIDS, celecoxib can lead to the onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of cardiovascular events. **Therefore, blood pressure should be monitored closely during the initiation of therapy with celecoxib and throughout the course of therapy**. |  1. **Traffic light status within local formularies:**  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | |  | **SURREY PAD** | **CHMS CCG** | **Brighton and Hove Joint Formulary** | **G&W Joint Formulary** |  | | **Celecoxib** | BLUE – AS\*, BLACK - all other indications | GREEN | GREEN | BLUE – AS\*, BLACK - all other indications |  | | **Etoricoxib** | BLUE – AS\*, BLACK - all other indications | GREEN | GREEN - Third line agent | BLUE – AS\*, BLACK - all other indications |  | |  |  |  |  |  |  | |  | **SASH** | **ESHUT** | **Ashford and St Peter's Hospitals** | **Croydon University Hospital** | **Kingston Hospital** | | **Celecoxib** | BLUE – AS\*, BLACK - all other indications | On formulary | Restricted: Rheumatology | On formulary | GREEN | | **Etoricoxib** | BLUE – AS\*, BLACK - all other indications | Non formulary | Restricted: Rheumatology | Non formulary | Non formulary |   \*ankylosing spondylitis | | |
| **Proposals for APC consideration** | | |
| **Option 1:**  Amend the BLACK status of both celecoxib and etoricoxib to GREEN, for use in pain and inflammation.  And  Amend the BLUE status of both celecoxib and etoricoxib for ankylosing spondylitis to GREEN.  **Option 2:**  Amend the BLACK status of both celecoxib and etoricoxib to GREEN, for use in pain and inflammation with celecoxib as the preferred choice of COX-2 inhibitor  And  amend the BLUE status of both celecoxib and etoricoxib for ankylosing spondylitis to GREEN with celecoxib as the preferred choice of COX-2 inhibitor  Preference of celecoxib is due to:   * Contraindication for use of etoricoxib in people with uncontrolled hypertension (persistently above 140/90 mmHg). * The specific requirement for blood pressure to be monitored within two weeks after initiation of treatment with etoricoxib and periodically thereafter. * NICE (use in osteoarthritis) recommends that ‘When offering treatment with an oral NSAID/COX-2 inhibitor, the first choice should be either a standard NSAID or a COX-2 inhibitor (other than etoricoxib 60 mg).’ so the only first choice for the use of etoricoxib is etoricoxib 30mg, which is much more expensive than celecoxib (see table above).   Etoricoxib is marginally more expensive than celecoxib | | |
| **Identified lead for development of necessary documents e.g. shared care agreement** | | |
| **Name:** Tejinder Bahra  **Designation:** Lead Commissioning Pharmacist  **Organisation:** Surrey Downs CCG  **Estimated date of preparation:** | | |

**References:**

1. eMC (electronic Medicines Compendium). DataPharm.

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1. Osteoarthritis: care and management Clinical guideline Published: 12 February 2014. NICE. Available at: <https://www.nice.org.uk/guidance/cg177> Accessed <30.5.19>
2. CKS Rheumatoid arthritis. Scenario: Suspected rheumatoid arthritis. Available at: <https://cks.nice.org.uk/rheumatoid-arthritis#!scenario> Accessed <10.6.19>
3. CKS Ankylosing spondylitis. Scenario: Suspected ankylosing spondylitis. Available at: <https://cks.nice.org.uk/ankylosing-spondylitis#!scenario> Accessed <10.6.19>
4. May 2019 Drug Tariff. Available at: <http://www.drugtariff.nhsbsa.nhs.uk/#/00703110-DB/DB00703105/Home> Accessed <30.5.19>

**Prepared by:**

Tejinder Bahra, Lead Commissioning Pharmacist, Surrey Downs CCG

Declaration of Interest:

Indirect shareholder – Pfizer.

Date: 11.6.19

**Reviewed by: Sarah Watkin, Associate Director of Pharmaceutical Commissioning**

Declaration of Interest: None to declare

Date: 11/6/19

**VERSION CONTROL SHEET**

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| **Version** | **Date** | **Author** | **Status** | **Comment** |
| v.1 | 4.6.19 | T. Bahra | Draft | Out for consultation |
| v.2 | 10.6.19 | T. Bahra | Draft | Comments incorporated.  Change of status for AS from BLUE to GREEN incorporated. |
| v.3 | 25.6.10 | S. Watkin | Final | Comments from consultation added |

**Comments on proposal to change traffic light status of celecoxib and etoricoxib**

**Supportive**

1. This seems good

Will increase mx options and come into line with NICE

I thought we did not use Diclofenac but it is included here has this policy changed?

Potentially this cd make quite a difference possibly even lower referral rates

Really appreciate your involving us in the discussion too

***Rose Block – Ashford and St Peter’s Hospitals***

Diclofenac is outside the scope of this proposal. Mention is made in the document only as it is appears in NICE guidance for rheumatoid arthritis. There is no policy change

1. I would support taking them off "black" for these indications. I have not seen any research showing  improved outcome with etoricoxib vs celecoxib so generic celecoxib make sense as the first choice.

***Andy King – Ashford and St Peter’s Hospital***

1. The proposed changes would be very helpful

***Sian Griffith – Surrey and Sussex Healthcare***

1. Sounds a sensible change

***Rod Hughes – Ashford and St Peter’s Hospital***

1. Sounds sensible

***Mark Lloyd – Frimley Park Hospital***

**For consideration**

1. I would like to see etoricoxib kept as blue status, and only celecoxib green, because of the safety issues regarding raising blood pressure and the burden for primary care of needing to monitor BP regularly.

***Helen Marlow – Surrey Downs CCG***

Similar safety and monitoring requirements from SPC.

* Etoricoxib is contraindicated in uncontrolled hypertension
* Both should only be used after careful consideration in patients with significant risk of cardiovascular events (e.g. hypertension) Initial monitoring for etoricoxib specified for blood pressure within two weeks then periodically
* For celecoxib blood pressure should be monitored closely during initiation and throughout the course

There is no indication of monitoring frequency given for either drug after initiation phase

1. I can see that on a cost basis the COX2 are no longer inhibitory and there are a number of guidelines that include their use with the specific addition of their use as an option for GPs in the new QOF Quality Improvement work to reduce GI bleed.

I agree that they can be green status as you suggest with celecoxib second line [after NSIAD] but bearing in mind the fact that I am sure we do not monitor BP in the cases of other NSAID such as Naproxen and Ibuprofen and the conclusion is that they are all of similar efficacy then should we consider promoting Ibuprofen and Naproxen as first line NSAID subject to another perceived increased risks of GI bleeding?

Regarding GI bleed would we still recommend Ibup/naproxen plus PPI over Celecoxib +PPI?

Secondly how does the relative CVS risk compare if we were to look at all the options here?

I ask this as it may be helpful for targeting the lowest risk drugs to patients.

***Andreas Pitsiaeli – Surrey Downs CCG***

The proposal is aiming to support prescribers access a COXII when the clinical decision has been made that it would be more appropriate than a NSAID. There is CKS guidance on when to use a COXII in preference to a NSAID – those at moderate or high gastrointestinal risk (without cardiovascular risk).