Midazolam in the treatment of Status Epilepticus – Continue to Prescribe Epistatus®

Buccolam® (Midazolam) (5mg/ml) pre-filled syringes have recently been licensed and accepted for use by the Scottish Medicines Consortium (SMC) for use in status epilepticus in children from 3 months to 18 years of age.

After discussions with local consultants and specialist nurses the decision has been made that within NHS Fife the unlicensed product Epistatus® (10mg/ml) should continue to be used and prescribed instead of Buccolam®.

There are several reasons why this decision has been made, including the following –

1. Buccolam® is only licensed for use in children up to the age of 18 years of age and only for use in status epilepticus. Midazolam is also used in adults and for febrile convulsions. The use of different forms of midazolam for different indications may lead to prescribing/dispensing errors or the use of incorrect doses.
2. Patients/carers/school nurses are currently provided with training to ensure the appropriate use of midazolam. This is based on training with Epistatus®
3. The dose of midazolam required for administration when using Epistatus® (10mg/ml) is different from that required with Buccolam® (5mg/ml).
4. The Scottish Paediatric Epilepsy Network (SPEN) has recommended that patients continue to be prescribed Epistatus®.
5. All other health boards in Scotland have decided to continue to recommend the use of Epistatus®.
6. The potential resource and cost implications in patients switching from Epistatus® to Buccolam® in terms of training health care professionals, school nurses, parents and carers.
7. The manufacturer of Epistatus® has stated its intent to apply for a license for the use of Epistatus® as a pre-filled syringe later this year.

The ADTC have agreed to review this decision in 6 months time or earlier if Epistatus® is licensed and has progressed through the SMC process or if other health boards start switching to Buccolam® instead.

Key Messages

1. Epistatus® should continue to be prescribed/dispensed as the preferred midazolam preparation in patients with status epilepticus.
2. Patients should not be switched to or initiated on Buccolam®.

Rivaroxaban Preferred 1st Line Agent After a First Presentation of DVT

Rivaroxaban is now the first line oral anticoagulant for first presentation DVT. Treatment will be initiated in secondary care who will supply a three week course to the patient and will request that the patient’s GP prescribes the remainder of the course.

The dose is 15mg twice daily for three weeks, followed by 20mg daily for the rest of the course, which will be for a maximum of 6 months in total.

Warfarin remains the anticoagulant of choice in second and subsequent DVTs.

Further information on the appropriate prescribing of rivaroxaban can be found in Appendix 2H of the Fife Formulary.
Formulary Changes

Updated Fife Formulary Section - Ear, Nose & Oropharynx - Section 12

Section 12 of the Fife Formulary (Ear, nose & oropharynx) has recently been reviewed and updated. The revised section has been approved for use in NHS Fife by the Area Drugs & Therapeutic Committee.

Key changes to the section include –

- Clarification on treatment choices for otitis externa depending on if the eardrum is perforated or not.
- Fluticasone furoate (Avamys®) has replaced fluticasone propionate (Flixonase®) as a formulary option for treatment of nasal allergies. Beclomethasone is still the cheapest nasal spray. Mometasone and fluticasone furoate are now the formulary choice once daily nasal sprays. It should be noted that fluticasone furoate and fluticasone propionate are not interchangeable and the appropriate formulation should be prescribed and dispensed.
- Trimacrinolone, budesonide and azelastine nasal sprays are non-formulary.
- New subsection on formulary choices for the treatment of nasal polyps.
- Clarification that formulary choice PPIs for the treatment of laryngeal reflux are lansoprazole and omeprazole. Esomperazone is not recommended for this indication.

Ensuring compliance with the formulary choices is one of the ways that NHS Fife can ensure that the most cost-effective products are used for our patients.

Copies of the section have been distributed to all staff via e-mail. Copies of the formulary section can be accessed / downloaded from the ADTC website www.fifeadtcs.scot.nhs.uk/ by clicking on the link for Fife Formulary or via the Fife Formulary link on the NHS Fife intranet homepage.

Guidance

Updated Fife Formulary Appendices

Cardiovascular Section

The NHS Fife Formulary Appendices have been updated by the Vascular Disease MCN/Fife Stroke Network and have been approved for use in NHS Fife by the Fife Area Drugs & Therapeutics Committee (ADTC).

Key Changes

- Appendix 2A - Guidance on Management of Hypertension - This appendix has been reviewed and updated to reflect the changes in NICE Clinical Guideline 127 - The Clinical Management of Primary Hypertension in Adults. The key changes in this appendix are -
  o The preferred drug at Step 1 in patients aged over 55 years is now a calcium channel blocker (CCB).
  o A thiazide diuretic should now only be considered at step 3 i.e. when a CCB and ACE inhibitor fail to get to target blood pressure.
  o Indapamide standard tablets is the preferred formulary thiazide diuretic. Bendroflumethiazide is now the 2nd line choice.
- Appendix 2B - Prevention of Cardiovascular Disease - Appendix updated to reflect changes in formulary choices for hypertension and to emphasise that antiplatelets should not routinely be used for primary prevention.
- Appendix 2C - Stroke Services in Fife - Appendix updated. Key change in terms of drugs choices is for patients who experience a stroke or TIA, the preferred anti-platelet is now clopidogrel for both indications. A combination of aspirin + dipyridamole M/R should now only be considered in patients where clopidogrel is contraindicated or not tolerated.
- Appendix 2F - Management of Cholesterol - Appendix updated. Key changes reflect the fact that atorvastatin is now available as a generic and atorvastatin is now recommended as the 2nd line choice in patients with stable angina (simvastatin remains the 1st line choice), and atorvastatin is now the 1st line choice in patients requiring intensive statin treatment. Rosuvastatin should now only be considered in patients who are unable to tolerate simvastatin / atorvastatin or in those not reaching target with maximum tolerated dose of atorvastatin.
- Appendix 2H - Newer Oral Anticoagulants - Appendix has been updated to reflect the fact rivaroxaban is the preferred newer oral anticoagulant in patients who are unable to tolerate or have an allergy to warfarin and other coumarins and in patients who are not remaining at target INR levels despite complying with warfarin/other coumarin treatment. Information is now also provided in this appendix on converting patients to and from warfarin or parenteral anticoagulants and rivaroxaban/dabigatran, how to manage bleeding in primary and secondary care settings and how to manage patients before surgery.
Contraceptive Prescribing in Primary Care, Emergency Contraception

The NHS Fife Formulary Appendices have been updated by Dr. Piegsa, Consultant in Sexual & Reproductive Health and have been approved for use in NHS Fife by Fife Area Drugs & Therapeutics Committee (ADTC).

Key Changes

Appendix 7B - Contraceptive Prescribing in Primary Care

This appendix has been updated to emphasise the preferred brands of contraceptives in NHS Fife.

<table>
<thead>
<tr>
<th>COC</th>
<th>Preferred brand</th>
<th>Equivalent to</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st line choices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Containing 30mcg ethinylestradiol</td>
<td>Rigevidon®</td>
<td>Micragnon® 30</td>
</tr>
<tr>
<td>Containing 20mcg ethinylestradiol</td>
<td>Loestrin® 20</td>
<td>N/A</td>
</tr>
<tr>
<td>Containing 35mcg ethinylestradiol</td>
<td>Ovysmen® or Cilest®</td>
<td>N/A</td>
</tr>
<tr>
<td>2nd line choices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Containing 30mcg ethinylestradiol</td>
<td>Gedarel® 30</td>
<td>Marvelon®</td>
</tr>
<tr>
<td>Containing 20mcg ethinylestradiol</td>
<td>Millenette® 30</td>
<td>Femodene®</td>
</tr>
<tr>
<td>Containing 20mcg ethinylestradiol</td>
<td>Gedarel® 20</td>
<td>Mercilon®</td>
</tr>
</tbody>
</table>

- There is also a reminder that Yasmin® and Qlaira® are not recommended for use in new patients without approval of an Individual Patient Treatment Request (IPTR).

Appendix 7C - Emergency Contraception

- Levonorgestrel (Levonelle®) is recommended as the preferred hormonal contraception in patients with unprotected sexual intercourse (UPSI) in the last 72 hours.

Ulipristal (EllaOne®) is the preferred hormonal contraception in the 72-120 hour window and may also be considered for use before the 72 hour window in teenagers or a patient presenting mid-cycle.

- Further changes in this appendix reflect recent changes in Guidelines from the Faculty of Sexual & Reproductive Health, including the following:
  - Advice on missed pills has been simplified, the same advice now applies to different strengths of combined oral contraceptives.
  - There is no longer a need to consider additional protection in patients prescribed a broad spectrum antibiotic as there is no conclusive evidence that the efficacy of the Pill is reduced if an antibiotic is co-prescribed.
  - The advice on the use of emergency contraception when a dose has been missed has also been updated to reflect when emergency contraception should be considered.

Further copies of any of the above appendices can be accessed / downloaded from the ADTC website www.fiteadtc.scot.nhs.uk/ by clicking on the link for Fife Formulary or via the Fife Formulary link on the NHS Fife intranet homepage.

SMC Recommendations

**Medicines not recommended by SMC**

- **Abiraterone acetate 250mg tablets (Zytiga®)** is not recommended for use with prednisone or prednisolone for the treatment of metastatic castration-resistant prostate cancer (mCRPC) in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen. Lack of benefits compared to cost.

- **Asenapine (Sycrest®)** is not recommended for treatment of moderate to severe manic episodes associated with bipolar I disorder, in adults. Lack of evidence of economic benefits.

- **Fingolimod (Gilenya®)** is not recommended as single disease modifying therapy in highly active relapsing remitting multiple sclerosis (RRMS). Lack of evidence of economic benefits.

- **Tocilizumab (RoActemra®)** is not recommended for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease-modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists. Lack of evidence of clinical and cost-effective benefits.

- **Belimumab (Benlysta®)** is not recommended as add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g. positive anti-dsDNA and low complement) despite standard therapy. Lack of evidence of cost-effective benefits.

- **Catumaxomab (Removab®)** is not recommended as intraperitoneal treatment of malignant ascites in patients with EpCAM-positive carcinomas where standard therapy is not available or no longer feasible. Non-submission by the manufacturer.

- **Everolimus (Votuba®)** is not recommended for treatment of patients aged 3 years and older with subependymal giant cell astrocytoma (SEG A) associated with tuberous sclerosis complex (TSC) who require therapeutic intervention but are not amenable to surgery. Non-submission by the manufacturer.

- **Fampridine (Fampyra®)** is not recommended for improvement of walking in adult patients with multiple sclerosis with walking disability. Non-submission by the manufacturer.
Medicines accepted for use by SMC

**Formulary Choices** – Products that are recommended within Fife and should be used in the majority of patients.

**Restricted Use** – Products that have been approved by the SMC for a limited indication or for a niche group of patients. Appropriate for them to be prescribed for patient groups that have been approved by the SMC / Fife ADTC.

**Not Preferred** – Products that have been approved by the SMC but agreed in Fife that suitable Formulary choices are already available. These products should only be used when Formulary products have been ineffective, not tolerated or are contra-indicated.

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication assessed</th>
<th>Fife ADTC decisions &amp; comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catibant acetate, 30mg, solution for injection in prefilled syringe (Firazyr®)</td>
<td>Symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults (with C1-esterase-inhibitor deficiency).</td>
<td>Add to restricted list.</td>
</tr>
<tr>
<td>Atorvastatin 10 and 20mg chewable tablets (Lipitor®)</td>
<td>As an adjunct to diet for reduction of elevated total cholesterol (total-C), LDL-cholesterol (LDL-C), apolipoprotein B, and triglycerides in adults, adolescents and children aged 10 years or older with primary hypercholesterolaemia including familial hypercholesterolaemia (heterozygous variant) or combined (mixed) hyperlipidaemia (Corresponding to Types IIa and IIb of the Fredrickson classification) when response to diet and other nonpharmacological measures is inadequate; to reduce total-C and LDL-C in adults with homozygous familial hypercholesterolaemia as an adjunct to other lipid-lowering treatments (e.g. LDL apheresis) or if such treatments are unavailable; prevention of cardiovascular events in adult patients estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors.</td>
<td>Not preferred.</td>
</tr>
<tr>
<td>Bupivacaine HCL 1.0mg/mL and 1.25mg/mL plus fentanyl (as citrate) 2 microgram/mL solution for infusion (Bufyl®)</td>
<td>Epidural analgesia to relieve pain during labour and to control post operative pain.</td>
<td>Not preferred.</td>
</tr>
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Dates for 2012 ADTC Meetings

<table>
<thead>
<tr>
<th>ADTC meeting</th>
<th>Deadline for submission of papers and agenda items</th>
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</thead>
<tbody>
<tr>
<td>27th June</td>
<td>11th June</td>
</tr>
<tr>
<td>15th August</td>
<td>30th July</td>
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<tr>
<td>17th October</td>
<td>28th September</td>
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<tr>
<td>19th December</td>
<td>3rd December</td>
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</table>

Contact the Clinical Effectiveness Pharmacist on 01592 226915 for advice on making a formulary submission or for clarification on the process for approval of guidance documents.

The information provided in this bulletin is correct at the time of publishing but is subject to change as new clinical information becomes available.

If you require this newsletter in alternative formats please telephone 01592 226915

Produced By: Ishiaq Mohammed, Clinical Effectiveness Pharmacist
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