Primary Care Interface+ Secondary Care

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NHS Blackburn with Darwen
NHS East Lancashire
East Lancashire Hospitals NHS Trust

A MONTHLY MEDICINES AND PRESCRIBING BULLETIN FOR HEALTHCARE PROFESSIONALS IN EAST LANCASHIRE FOCUSING ON NEW THERAPIES.

Depression

Pharmacological Treatments

Following on from the article in the previous edition of INTERFACE (issue 102 which can be found at www.elmmb.nhs.uk/newsletters/) on the Non-Pharmacological Treatments of Depression, here we now focus on the Pharmacological Treatments.

Definition of terms

SSRI selective serotonin reuptake inhibitor • **TCA** tricyclic antidepressant • **MAOI** monoamine oxidase inhibitor • **NSAID** non-steroidal anti-inflammatory drug

Choosing an antidepressant

All antidepressants have similar efficacy. Choice depends on:

- anticipated adverse effects and discontinuation symptoms,
- potential interactions with other medicines or illness; refer to appendix 1 of the BNF and appendix 16 of NICE CG91 (full guideline),
- efficacy and tolerability of other antidepressants tried.

First line – use a generic SSRI

Consider:

- the increased risk of bleeding with SSRIs; prescribe a gastro-protective drug for older people taking an NSAID or aspirin,
- the high risk of drug interactions with fluoxetine, fluvoxamine and paroxetine,
- the higher incidence of discontinuation symptoms with paroxetine,
- citalopram or sertraline for people with a chronic physical health problem as these cause fewer drug interactions.

Do **NOT** prescribe escitalopram for depression – Local MMB guidance (in line with that from Lancashire Care Foundation Trust).

Other antidepressants e.g. TCAs, MAOIs, venlafaxine

Consider:

- toxicity in overdose in patients at risk of suicide:
  - the greatest risk in overdose is with TCAs, except for Lofepramine,
  - venlafaxine is associated with a greater risk of death from overdose compared to other antidepressants used in primary care.
- the increased likelihood of discontinuation due to adverse effects; increase doses gradually with venlafaxine, duloxetine and TCAs,
- the specific cautions, contraindications and monitoring requirements for individual drugs,
- non-reversible MAOIs, combined antidepressants and lithium augmentation of antidepressants should only be prescribed by specialist mental health professionals.

Do **NOT** prescribe dosulepin.

Duloxetine (Cymbalta® is AMBER traffic light, specialist initiation only, with continued prescribing in primary care. Agomelatine is RED traffic lighted – all prescribing to be initiated and maintained by specialists only.

Cautions and counselling

When **starting treatment** inform patients:

- of the gradual development of full antidepressant effect,
- of the potential adverse effects and drug interactions,
- about the risk of discontinuation symptoms on stopping,
- to take medication regularly and continue beyond remission to reduce the risk of relapse,
- that antidepressants are **NOT** associated with addiction.

Monitoring

For patients at increased risk of suicide or younger than 30 years, review:

- after one week then frequently until the risk is no longer significant.

For patients **NOT** at increased risk of suicide, review:

- after two weeks, then regularly e.g. every 2 to 4 weeks in the first 3 months.

Response to treatment

- If no improvement is seen after 2 to 4 weeks, check patient compliance.
- If there is minimal or no response after 3 to 4 weeks of treatment with a therapeutic dose, consider:
  - increasing the dose, **OR**
  - switching to another antidepressant.
- If there is some improvement by 4 weeks, continue for another 2 to 4 weeks.

Consider switching antidepressants if:

- response is still not adequate, **OR**
- there are adverse effects, **OR**
- the person requests a change of drug.

If adverse effects occur:

- if mild, monitor symptoms closely, **OR**
- stop or switch to another antidepressant, **OR**
- if patient has significant symptoms of anxiety, agitation or insomnia add short-term treatment with a benzodiazepine (max 2 weeks); caution should be used if the person is at risk of falls.

Switching antidepressants

CARE is needed when switching between antidepressants.

Consider:

- initially, a different SSRI or a newer-generation antidepressant,
- subsequently an antidepressant of a different class such as venlafaxine, a TCA or an MAOI.

Do **NOT** switch to, or start dosulepin. Do **NOT** prescribe escitalopram for depression – Local MMB guidance (in line with that from Lancashire Care Foundation Trust).

- Further guidance on switching can be accessed at www.nelm.nhs.uk (see Medicines Q&A documents; Evidence section).

The Health Minds Website contains information and leaflets with contact details for services in each locality.
www.eastlancshealthyminds.nhs.uk

Combining and augmenting antidepressants

Do **NOT** combine or augment antidepressants in primary care without advice from a consulting psychiatrist.

After providing information about increased adverse effects, consider combining or augmenting an antidepressant with:

- lithium – see full guideline for monitoring requirements, and the shared care protocol which can be found at www.elmmb.nhs.uk/shared-care/,
- an antipsychotic such as aripiprazole*, olanzapine*, quetiapine* or risperidone*,
- another antidepressant such as mianserin or mirtazepine,
- do NOT routinely augment an antidepressant with:
  - buspirone*, carbamazepine*, lamotrigine*, valproate*, pindolol* or thyroid hormones*,
  - a benzodiazepine for more than 2 weeks.

** These agents do not have a UK marketing authorisation for this indication. See individual Summary of Product Characteristics for full prescribing information.*

Stopping or reducing antidepressants

- Advise patients that discontinuation symptoms may occur on stopping, missing doses or when reducing the dose; these are usually mild and self-limiting, but can be severe if the drug is stopped abruptly.
- Gradually reduce over 4 weeks (this is not necessary with fluoxetine) or over longer periods for drugs with a short half-life (e.g. paroxetine, venlafaxine).

If discontinuation symptoms occur:

- if symptoms are mild, monitor,
- if symptoms are severe, re-introduce the original antidepressant (or a similar antidepressant with a longer half-life) at the dose that was effective, and reduce the dose gradually while monitoring symptoms.

Continuation and prevention of relapse

At remission - patients who have benefited with antidepressant treatment should continue this for at least 6 months.

6 months after remission – review the need to continue medication. If there is a significant risk of relapse or a history of recurrent depression consider the following options:

- continuing medication for another 2 years,
- augmenting medication,
- psychological intervention.

See full guideline for details.

Acknowledgement: NICE Bites, Issue 11, November 2009.

CONTENTS:

MMB Guidance

Please see the Medicines Management Board website for prescribing information on the following;
www.elmmb.nhs.uk

GREEN LIST

Pioglitazone (Actos®) – First line choice of glitazone.

Use of rosiglitazone is steadily declining year on year, whilst pioglitazone use in preference is increasing. Further to this pioglitazones patent will expire in ~Jan 2011, meaning less expensive generic pioglitazone will be available at this time. This is in contrast to rosiglitazone which is patent protected until ~Sept 2014, and will continue to attract a much higher price. In addition, prescribers will be aware that pioglitazone has a less restrictive license when used in diabetics with established heart disease compared to rosiglitazone. Therefore, the MMB is recommending the use of pioglitazone in preference to rosiglitazone where a glitazone is recommended by NICE. A proactive review of all current rosiglitazone prescribing and a move to pioglitazone use first line for new patients could realise an additional £90,000 per year after patent expiry of pioglitazone across both PCTs. Prescribers are asked to move to using pioglitazone as their first line glitazone, where glitazones are indicated by NICE and local guidance.

Lercanidipine – Second line calcium channel blocker.

The MMB approved the use of lercanidipine as a second line calcium channel blocker when amlodipine is not tolerated (e.g. where patients develop significant ankle oedema). This is now available generically and is a category M product in the drug tariff.

BLACK LIST

Prucalopride (Resolor®) – Chronic and laxative refractory constipation in women.

The MMB reviewed the evidence for this treatment in its licensed indication, and decided it should not be recommended for prescribing, as it is a low priority for NHS resources. This was due to several uncertainties that remain in the research base for this new drug. The MMB noted there are some moderate benefits at best for a restricted group of women with severe constipation, however there are a number of concerns including:

- Short studies (mostly of 12 weeks duration) mean that long-term effects (both benefits & harms) are currently unknown.
- There is a lack of published long-term safety data. The MMB was particularly aware that rare, fatal cardiac arrhythmias led to the withdrawal of cisapride (same drug class) from the GI market in 2001
- At present there are no comparative data against alternative. treatments because trials to date have all been placebo-controlled.

With these uncertainties, and at a usual price of almost £60/month, the MMB was also not convinced that this was a cost effective use of NHS resources. NICE will rule on this drug in December 2010.

TRAFFIC LIGHT DEFINITIONS

GREEN - Primary or Secondary care (+/- recommendations)

BLACK - Non-Formulary. Not recommended for prescribing in primary or secondary care

See website for more information on these recommendations.

AIIRAs associated with an increased risk of cancer

A meta-analysis of RCTs has found that the diagnosis of new cancer was increased in patients randomised to receive angiotensin-II receptor antagonists (AIIRAs), compared with control. The absolute increase in the risk of cancer was small (1.2%) but statistically significant. However, because of the large number of people taking AIIRAs, even a small absolute increase would, if true, produce a large number of additional cancers.

Action

This meta-analysis provides a safety signal about a possible increased risk of cancer in people who are taking AIIRAs. However, due to the inherent limitations of the data, this cannot be regarded as definitive. The authors point out that the clinical significance of the excess cancer risk they found is unclear, and the finding of a 1.2% increase in the absolute risk of new cancer diagnosis over an average of four years needs to be interpreted in view of the estimated 41% lifetime risk of cancer.

Acknowledgement: MeReC Rapid Review 24th June 2010

We anticipate that regulatory authorities will be examining this data. In the meantime, this safety concern adds weight to the argument that ACE inhibitors, not AIIRAs, are the first-line choice when a renin-angiotensin system drug is indicated. ACE inhibitors have a more robust evidence base than AIIRAs for all indications in terms of evidence for efficacy, safety and most patient factors. The major benefit of AIIRAs over ACE inhibitors is a lower rate of cough. Hence, AIIRAs are an alternative where a renin-angiotensin system drug is indicated, but an ACE inhibitor has to be discontinued because of an intolerable ACE inhibitor induced cough.

How should **hay fever** be managed in pregnancy and breastfeeding?

Hay fever season is upon us and we have received a number of calls asking about the choice of agent for managing symptoms in patients who are pregnant or breastfeeding.

Topical therapies such as eye drops and nasal sprays are preferred where possible as these lead to limited systemic absorption, reducing exposure to the foetus or breastfed infant.

If an oral antihistamine is required during pregnancy, loratadine is preferred; of the non-sedating antihistamines it is the most studied in pregnancy. Although the BNF notes that toxicity has been reported in studies of high-dose loratadine in animals, human data do not suggest a teratogenic risk, and loratadine is the oral agent recommended in CKS guidance for treating hay fever in pregnancy and breastfeeding.

Cetirizine is also suitable for use during pregnancy and breastfeeding; there are fewer data than for loratadine.

Chlorpheniramine may be used during pregnancy but its sedative effect may limit its usefulness. It is not suitable for use in breastfeeding women as exposure via breast milk can lead to drowsiness and poor feeding in the breastfed infant.

Two Medicines Q&A articles provide further information:

- Which medicines can be used to treat intermittent allergic rhinitis during pregnancy? **www.nelm.nhs.uk/en/NeLM-Area/Evidence/Medicines-Q--A/Which-medicines-can-be-used-to-treat-intermittent-allergic-rhinitis-during-pregnancy2/**
- How should seasonal allergic rhinitis (hay fever) be treated in a breast feeding mother? **www.nelm.nhs.uk/en/NeLM-Area/Evidence/Medicines-Q--A/How-should-seasonal-allergic-rhinitis-hay-fever-be-treated-in-a-breastfeeding-mother/**

Acknowledgement:
Primary Care Talk, No. 102, June 2010

Patient group Directions

Legislation has been amended to allow dental hygienists and dental therapists to administer and supply medicines under Patient Group Directions (PGDs). Examples where this may be useful include the administration of local anaesthetics and the supply of fluoride preparations to patients.

A summary document briefly describes the role of dental hygienists and dental therapists, and provides information on drawing up PGDs for use in dental practice:
www.nelm.nhs.uk/en/NeLM-Area/Evidence/Medicines-Q--A/Patient-Group-Directions-in-dental-practice/

An updated version of the NPC document – A Practical Guide and Framework of Competencies for all Professionals using Patient Group Directions can be found on the elmmb website:
www.elmmb.nhs.uk/patient-group-direction/

Acknowledgement:
Primary Care Talk, No. 102, June 2010

Mixing medicines

The National Prescribing Centre has published practical guidance for organisations and practitioners on the mixing of medicines. Medicines legislation was amended in December 2009 allowing prescribers to mix medicines themselves or direct others to do so. The guidance includes examples of clinical areas where mixing of medicines is accepted practice. It notes that the supply and administration of unlicensed medicines, including those produced by mixing, under a PGD is unlawful.

The 29 page guidance can be found at: **www.npc.co.uk/policy/resources/mixing_of_medicines.pdf**

The NPC document also supports a series of guidance points issued by the Department of Health:
www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/documents/digitalasset/dh_116360.pdf

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Comments and feedback
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