Medicines Optimisation Update
Antidepressants

Partners in improving local health

NHS North Cumbria Clinical Commissioning Group

What this includes:

1. Total number of all antidepressants (ADQs/STAR-PU*). LOWER THE BETTER.
2. Number of prescription items for all Selective Serotonin Reuptake Inhibitors (SSRIs - citalopram, sertraline, escitalopram, fluoxetine, fluvoxamine, paroxetine) prescribed (generically) as a percentage of the total number of items for all antidepressant group. (Excludes selected tricyclic and related antidepressants where there are significant levels of prescribing (70% or more) for indications other than depression or anxiety disorder). HIGHER THE BETTER.

Identifying the problem:

Review and if appropriate, revise prescribing of antidepressants in adults to ensure that it is in line with NICE guidelines on depression in adults, depression in adults with a chronic physical health problem, and generalised anxiety disorder and panic disorder in adults. (Links in "Resources")

Suggested actions:

Treating depression

- **Persistent subthreshold depressive symptoms or mild to moderate depression:** Do NOT routinely prescribe antidepressants as the risk-benefit ratio is poor. Actively monitor and provide advice on sleep hygiene and offer low intensity psychosocial interventions e.g. cognitive behavioral therapy (CBT), guided CBT type self-help, group support programmes or structured group physical activity programme.
- **Persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial intervention:** Offer an antidepressant (usually an SSRI) OR a high-intensity psychological intervention (see full NICE CG90 guideline for details).
- **Moderate and severe depression:** Combine an antidepressant (usually an SSRI) with a high intensity psychological intervention.
- **Complex and severe depression:** Refer to specialist mental health services.
- **Also consider an antidepressant** for people with a past history of moderate or severe depression OR initial presentation of subthreshold depressive symptoms present for at least 2 years OR mild depression that complicates the care of a physical health problem.

Choosing an antidepressant

- When an antidepressant is to be prescribed, it should normally be an SSRI in a generic form: SSRIs are equally effective as other antidepressants and have a favourable risk–benefit ratio.
- First line choices are sertraline, fluoxetine, citalopram, escitalopram, fluvoxamine, paroxetine. Choice will depend on: contraindications, anticipated adverse effects and discontinuation symptoms, potential interactions with other medicines or illness, efficacy and tolerability of other antidepressants tried. Refer to appendix 16 of NICE CG91 (full guideline).
- Citalopram and escitalopram should not be used in patients with congenital long QT syndrome or known pre-existing QT interval prolongation or in combination with other medicines known to prolong the QT interval. Maximum daily doses in people >65 years are: citalopram 20mg, escitalopram 10mg.
- None of the 'dual action' antidepressants, such as venlafaxine and duloxetine, have been judged to have any clinically important advantages over other antidepressants.
- Venlafaxine is best avoided due to its higher risk of cardiovascular adverse effects than with most SSRI antidepressants.
- Compared with other equally effective antidepressants venlafaxine is associated with a greater risk of death from overdose
- Tricyclic antidepressants (TCAs), except for lofepramine, are associated with the greatest risk in overdose.
- Mirtazapine may be effective for some people who are unable to take SSRIs. The side effects are similar to those of SSRIs, it may cause more drowsiness initially but it is thought to cause fewer sexual problems.
- Do not start dosulepin due to its established link with a number of adverse cardiovascular effects (hypotension, tachycardia/arrhythmia and QT segment prolongation), and toxicity in overdose (less than 1 weeks' supply may cause serious toxicity or death); never prescribe if a risk of suicide identified.
- Doxepin should not be prescribed – it has similar cardiotoxicity to dosulepin and has major cost implications. It is occasionally used as third line choice by dermatology for its antihistamine effects.
- Specialists should justify their choice of antidepressants especially when recommending a non-first line antidepressant, when there are significant risks, cautions, contraindications or where there are significant acquisition costs.

NECS medicines optimisation website. Available at http://medicines.necsu.nhs.uk/guidelines/cumbria-guidelines/
Date updated: August 2017; **Review**: August 2019; **Author**: Jeanette Pieri

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Suggested actions

Patients currently prescribed an antidepressant

- Check if any patient is currently being seen by mental health specialists as an outpatient or a current inpatient. If so please liaise with these teams before making any changes.
- Review non-first line and higher risk antidepressants: e.g. venlafaxine, dosulepin, doxepin, trazadone.
- Citalopram and escitalopram: review treatment in patients who currently take doses higher than recommended daily maximum (see "choosing an antidepressant").
- Citalopram and escitalopram should not be used in:
    - Patients with congenital long QT syndrome or known pre-existing QT interval prolongation
    - In combination with other medicines known to prolong the QT interval
- The balance of benefits and risks of citalopram and escitalopram should be considered carefully, particularly at higher doses, in patients with pre-existing risk factors for QT interval prolongation—including significant bradycardia, recent acute myocardial infarction or decompensated heart failure.
- Review patients on venlafaxine and explain the risks (Patients should be given enough information to make an informed choice about their treatment and this should be documented in notes):
    - High dose venlafaxine, is contraindicated in patients who have a very high risk of serious cardiac ventricular arrhythmia (e.g. those with a significant left ventricular dysfunction (NYHA Class III/IV)) and in patients with uncontrolled hypertension. It can exacerbate existing arrhythmia.
    - The cost of formulations of venlafaxine vary widely. Prescribers should choose the most cost effective formulation unless there are exceptional circumstances
- Dosulepin patients should be reviewed and the risks and benefits explained. to the patient, (Patients should be given enough information to make an informed choice about their treatment and this should be documented in notes) a limited number of tablets should be prescribed for all patients to reduce the risk of overdose, this is especially important for those at risk of suicide.
- Switching antidepressants: CARE is needed when switching between antidepressants, see guidance on switching in resources.
- Doxepin: review patients with the aim of switching to safer alternatives where possible, including patients prescribed doxepin for dermatological indications.

Resources:

National Institute for Health and Care Excellence (NICE): CG90: Depression in adults: recognition and management. Oct 2009/ updated: April 2016. http://guidance.nice.org.uk/CG90

CG91: Depression in adults with a chronic physical health problem: recognition and management. http://guidance.nice.org.uk/CG91

CG113: Generalised anxiety disorder and panic disorder in adult https://www.nice.org.uk/guidance/CG113

NICE Clinical Knowledge Summaries (CKS). Switching antidepressants. http://cks.nice.org.uk/depression#!prescribinginfosub:2

Dosulepin Prescribing Guidance. NECS/Cumbria Clinical Commissioning Group http://medicines.necsu.nhs.uk/download/cumbria_dosulepin_prescribing_guidance_aug151-docx/

NICE Key therapeutic topics: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-advice/Key-therapeutic-topics/medicines-optimisation-ktt-feb-16.pdf

References:

- The Maudsley Prescribing Guidelines. 10th Edition. THE SOUTH LONDON AND MAUDSLEY NHS FOUNDATION TRUST and THE OXLEAS NHS FOUNDATION TRUST.
- NICE Clinical Knowledge Summaries (CKS). Depression. http://cks.nice.org.uk/depression#!management
- Venlafaxine: more dangerous than most "selective" serotonergic antidepressants. Prescrire Int. 2016 Apr;25(170):96-9. http://www.ncbi.nlm.nih.gov/pubmed/27186622
- Medicines and Healthcare products Regulatory Agency (MHRA: Citalopram and escitalopram: QT interval prolongation. https://www.gov.uk/drug-safety-update/citalopram-and-escitalopram-qt-interval-prolongation
- NHS Choices: http://www.nhs.uk/conditions/Antidepressant-drugs/Pages/Introduction.aspx
- Medicines and Healthcare products Regulatory Agency (MHRA): Dosulepin: measures to reduce risk of fatal overdose.http://webarchive.nationalarchives.gov.uk/20141205150130/http://www.mhra.gov.uk/home/groups/pl-p/documents/publication/con2033217.pdf
- Toxicity of antidepressants: rates of suicide relative to prescribing and non-fatal overdose. The British Journal of Psychiatry Apr 2010, 196 (5) 354-358; DOI: 10.1192/bjp.bp.109.070219.http://bjp.rcpsych.org/content/196/5/354