Treatment of Depression (based on NICE guidance and NHS Evidence update 13) Updated June 2012

Mild Depression

General measures – first line
- Watchful waiting AND

Refer toPCMHS for guided self help, exercise, sleep, anxiety management, stress control, CCBT and telephone therapy

Antidepressant Medication
Not recommended for the initial treatment of mild depression
- First line for patients who have a history of moderate or severe depression

Citalopram or Sertraline are recommended choices

Combine antidepressant medication with psychological therapies
- Where depression persists or is associated with psychosocial & medical problems

Moderate Depression

Antidepressant medication
First line in moderate depression in conjunction with psychological therapies

Patients should be offered psychology therapies with PCMHS

Citalopram or Sertraline are recommended choices

Psychological treatments such as CBT techniques, counselling if:
- Patient does not take or refuses to take antidepressant medication
- Had inadequate response to antidepressant

Severe Depression

Refer to secondary care service if patient considered to be at risk of suicide

Individual CBT & Case Management
- Combined with antidepressant medication in patients presenting with severe depression or patients with chronic depression (depression for at least 2 years)
- CBT alone in patients who do not take/refuse to take antidepressant treatment; or if avoiding the side effects is a clinical priority or a personal preference; or have not made an adequate response to other treatments for depression

Choice of Antidepressant Medication
- Citalopram or Sertraline are the most cost effective choices & have fewer discontinuation/withdrawal symptoms. Fluoxetine has more drug interactions.
- NICE recommend that when an antidepressant is prescribed, it should be an SSRI.
- Consider patient preference & the experience & outcome of previous treatment(s) when deciding on treatment.
  For older adults prescribe antidepressant at an age-appropriate dose for minimum of 6 weeks before considering if it is ineffective; if there is a partial response within this period, continue for a further 6 weeks. Consider the increased risk of drug interactions and monitor carefully for side effects, particularly with TCAs.
- Patients with dementia- consider as for older adults
- Patients with CV disease: sertraline has the best evidence base in IHD and is the drug of choice in patients with a recent MI or unstable angina; consider risks of TCAs in CV disease; an ECG and BP check should be performed before prescribing a TCA for a depressed patient at significant risk of CV disease.
- Consider toxicity in overdose: tricyclics (with the exception of lofepramine) are more dangerous in overdose.
- Women have a poorer tolerance of imipramine. Consider TCA in men with chronic depression who have not responded to an SSRI, as men can generally tolerate better
- St John's Wort may be of benefit in mild or moderate depression, but it should not be prescribed or advised. Tell patients taking St John's Wort about differences and uncertainties in potencies of preparations available, and interactions with other

Specialist Mental Health Services (RDaSH)

Only specialist mental healthcare professionals, including GPs with special interest in Mental Health should initiate the following:
- Phenelzine, Venlafaxine (see below) Combined antidepressants, Lithium augmentation of antidepressants.

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Antidepressant Initiation, Monitoring & Review

Initiation and Review

All patients initiated on antidepressants should be informed of:

- Nature and course of depression, length of treatment, the need to take medication as prescribed, delay in onset of effect, potential side effects, risk of discontinuation/withdrawal symptoms

See patients who are under 30 years old or considered to be at increased risk of suicide within one week of starting antidepressant treatment.

- Monitor frequently until risk no longer significant. Consider prescribing limited quantity of antidepressants if at high risk of suicide

See patients not considered to be at risk of suicide 2 weeks after starting anti-depressant.

- See regularly thereafter (for example every 2-4 weeks in the 1st 3 months). Reduce frequency of appointments if good response- record response in notes. Where management is shared between primary and secondary care, establish a clear agreement between all professionals on the responsibility for monitoring and treatment.

Monitor for signs of akathisia, suicidal ideas and increased anxiety or agitation with SSRIs:

- Review use of drug if patient develops marked and/or prolonged akathisia or agitation. If patients prefers, either switch to different antidepressant or consider brief period of concomitant treatment with a benzodiazepine. Review within 2 weeks.

If poor/no response to anti-depressant, and there are no significant side effects:

- Check compliance; Consider gradual dose increase; Consider switch to another drug if no response after one month or if antidepressant is poorly tolerated.
- If partial response, postpone switch until 6 weeks. Consider range of other treatment options before switching to another single antidepressant

Switching to an Alternative Antidepressant

Alternative anti-depressants: If switching due to poor tolerance or lack of effectiveness with 1st choice a different SSRI or mirtazepine, moclobemide, reboxetine or TCA (except dosulepin)

Switching to a new TCA: Start on a low dose and, if there is a clear clinical response, maintain on that dose with careful monitoring. Gradually increase dose if lack of efficacy and no major side effects

Length of Treatment and Stopping Treatment

- **A remission date should be recorded in the patient's notes**
- **Continue antidepressants for 6 months after remission** (to minimise risk of relapse) in patients with moderate or severe depressive episode; then review need for continued antidepressant treatment.
- **Continue antidepressant for 2 yrs if:** if patient has have had 2 or more depressive episodes in the recent past, and have experienced significant functional impairment during these episodes
- **Reduce doses gradually** over a 4-week period (6 months in patients who have been on long-term maintenance treatment). Dosage tapering is usually not necessary when stopping fluoxetine.
- **Discontinuation/ withdrawal symptoms**: if mild, reassure patient and monitor. If severe symptoms, consider re-introducing antidepressant at the effective dose (or another antidepressant with a longer half-life from the same class) and reduce gradually; monitor symptoms
- **Record if the patient has completed a full course of treatment**

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Choice of antidepressant should be influenced by:	Choice of antidepressant should be based on:
• Duration of episode • Symptoms • Previous course of depression • Previous response to treatment • Likelihood of adherence • Potential side effects • Patient preference and priorities • Course and treatment of any physical health problems	• Co-morbidity • Side effects/acceptability • Patient's perception of efficacy and tolerability of any previous treatment • Potential for interactions • Risk of discontinuation symptoms • Toxicity in overdose

	Group	**Drug**	**Reason**	**Comment**
First Choice	SSRI	Citalopram	Most cost effective	• Citalopram maximum dose: The maximum daily dose has been reduced from 60mg to 40mg owing to the risk of dose-dependent QT interval prolongation. In the elderly (65 years and over) and in patients with reduced hepatic function, the maximum dose is lowered to 20mg daily. Patients who are on higher doses will need to be identified, reviewed and doses gradually reduced. • Sertraline should be prescribed first line in patients with established heart disease as onlySSRI recommended post MI and in CVD • Fluoxetine, fluvoxamine, paroxetine have greater potential for drug-drug interaction • Paroxetine associated with higher incidence of discontinuation symptoms • Increased risk of bleeding with SSRIs
Second Choice	Another SSRI even if no response to first SSRI	Sertraline		
	or	Mirtazepine		Only licensed for major depressive disorder
	or TCA	Lofepramine (low dose = 70mg)	Safest TCA including safety in overdose and cardiotoxicity	• Caution in patients with IHD. • Drowsiness, dry mouth& blurred vision may reduce tolerability • Other TCAs have greatest toxicity in overdose

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- Phenelzine, ; Venlafaxine (see below) ; Combined antidepressants ; Lithium augmentation of antidepressants.

Venlafaxine: Venlafaxine should not be prescribed for patients with pre-existing heart disease, those with electrolyte imbalance, or who are hypotensive. An ECG and BP measurement should be performed before starting venlafaxine. Monitor BP regularly thereafter, particularly for patients on high doses; consider monitoring cardiac function. Patients currently doing well on treatment with venlafaxine previously initiated by the GP can continue to the end of their treatment programme

Dosulepin: is not recommended for any indication and SHOULD NOT BE PRESCRIBED

Duloxetine and Reboxetine should not be prescribed based on lower efficacy and cost

Medications Associated with Depression

- NSAIDs
- Antihypertensives
- Digoxin
- Sedatives
- Corticosteroids
- Anti YTB drugs
- Antineoplastic drugs
- Interferon

Interactions of SSRIs with other medication

Refer to current BNF

Most common with fluoxetine, fluvoxamine, paroxetine

Avoiding Adverse Effects

Suicide - Risk is greater in 18 – 30 year old. Careful monitoring and risk assessment is required. Avoid in under 18s.

Falls/Hip Fractures – risk is greatest in the first two weeks of commencing an antidepressant. This applies to all antidepressants equally and extra care is required in the elderly

Reduced Toxicity (Cardiac toxicity) - Avoid using venlafaxine and dosulepin; Use TCAs with caution, except lofepramine (always use low dose)

Patients with Established Heart Disease - NICE guidance recommends sertraline as the first line choice.

Bleeding - Increased risk of bleeding with SSRIs. Same potential as low dose ibuprofen to cause GI bleed.

Avoid using SSRIs in:

- Elderly (over 80)
- Patients on Aspirin
- Patients on NSAID

Consider gastro-protection (Lansoprazole) if using SSRI in patients with one of the above conditions

Discontinuation Symptoms - higher incidence with paroxetine

Overdose – greater risk of death with venlafaxine