NHS FORTH VALLEY
Drug Treatment of Depression

Endorsed by: Primary Care Prescribing Group
Primary Care Drug and Therapeutics Committee
Area Drug and Therapeutics Committee
Depression ICP Group

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Consultation and Change Record

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Change Record			
Date	**Author**	**Change**	**Version**
06/2007			1
06/2010	Tracey Main	Sertraline included as a suitable SSRI antidepressant for both adults and elderly patients. Addition of section on 'Other Prescribing Considerations'. Information on antidepressant use in pregnancy and lactation updated. Weblinks included for Moodjuice and SIDs Information on assessing the severity of depression in Primary Care updated	2

Change Record Continued			
Date	**Author**	**Change**	**Version**
08/2012	Tracey Main	Sections on Assessing the Severity of Depression in Primary Care and Stepped Approaches to Care have been removed. As these are now discussed in detail in the Depression ICP. Link to Depression ICP included Information on Risk of QTc prolongation added on Treatment algorithms AND section 4 added in relation to Citalopram and QTc prolongation Information on antidepressant use in pregnancy and lactation updated Information on antidepressant prophylaxis updated in line with West of Scotland Guideline on Antidepressant Prescribing and Efficiencies Work Reboxetine removed as antidepressant monotherapy. Referral to specialist services recommended after trial of two antidepressants in the treatment of elderly patients over 65 years L-tryptophan and Tri-iodythyronine removed as augmentation strategies in adults and elderly Swapping and stopping tables updated	3

Contents

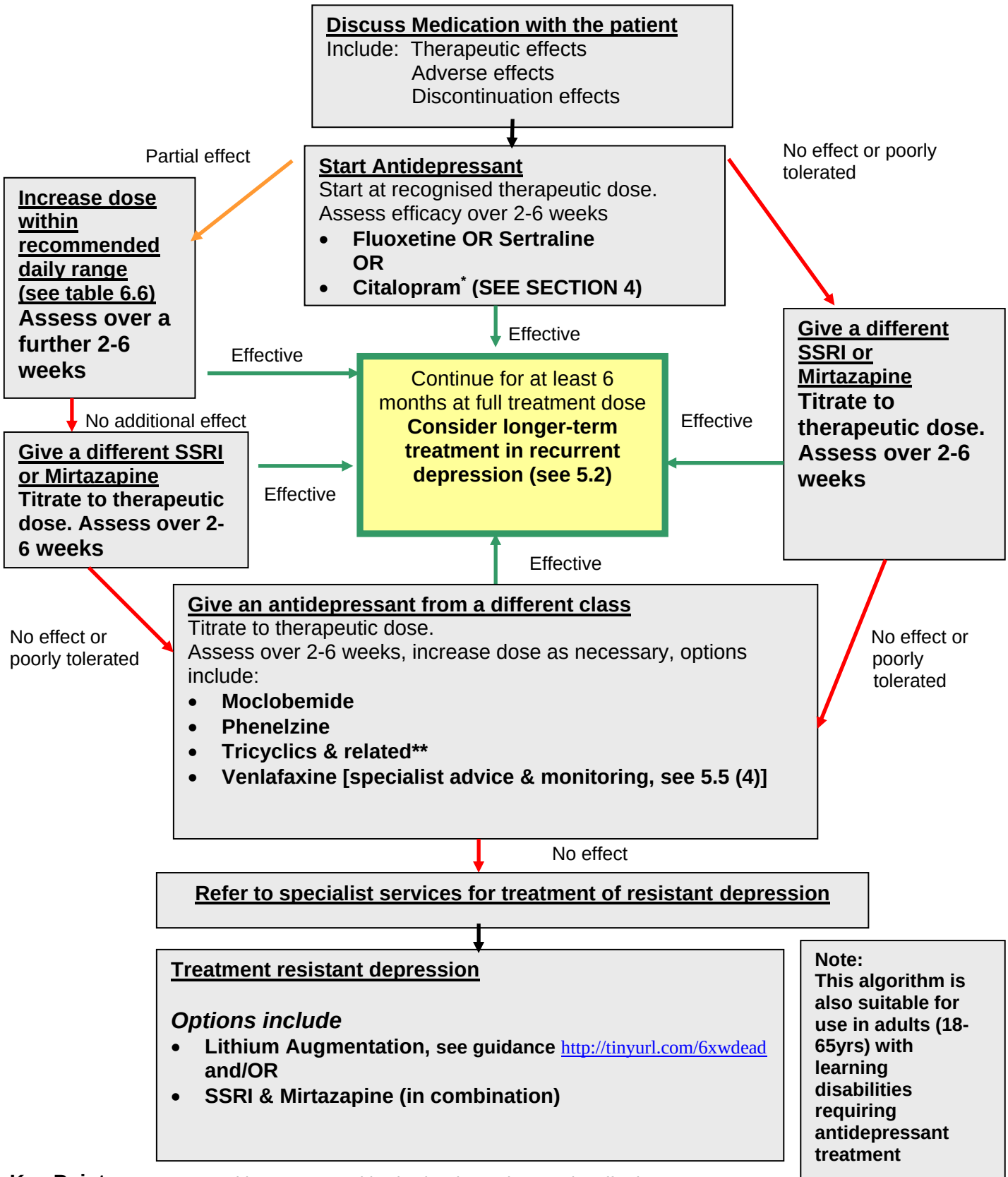
1. Introduction

A short-life working group was convened in 2006, by the Primary Care Drug and Therapeutics Committee, to review the evidence base for the drug treatment of depressive illness. Membership comprised a multidisciplinary group representing specialist services and general practice. The guideline produced was based primarily on the NICE Clinical Guideline 23. The guideline has since been reviewed in light of NICE Clinical Guideline 90[1] and 91[2] and as part of a consultation with the Depression ICP group as well as other Primary and Secondary Care colleagues.

This guideline aims to promote the safe and cost-effective prescribing of antidepressants in conjunction with the use of psychological approaches where appropriate. It is intended for use across primary and secondary care and compliments the Depression ICP which should be utilised for the full management of patients with depression.
The Depression ICP is available at
http://www.nhsforthvalley.com/__documents/qi/ce_guideline_depression/Depression-ICP.pdf

2. Drug Treatment of Depression 18 - 65 Yrs

This statement should be considered as a guideline only. The doctor will make the final judgement regarding the treatment plan, based on individual patient's clinical data, and the diagnostic and treatment options available.



Key Points: - CBT & Antidepressant combination has been shown to be effective

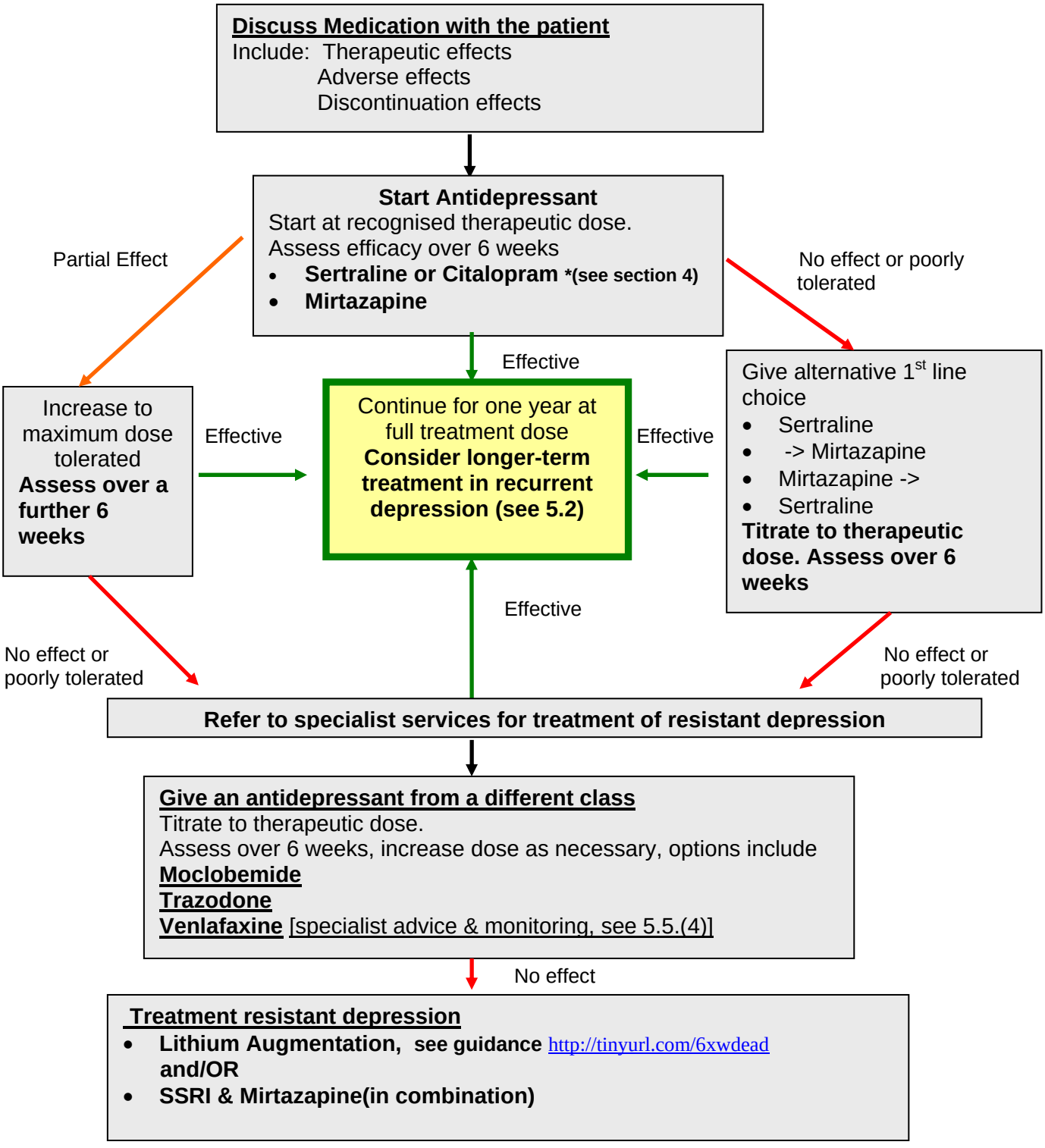
-For patients with psychotic depression, consider augmentation of the current treatment plan with antipsychotic medication

- MHRA safety advice for risk of QTc prolongation with citalopram – see section 4*

-**Amitriptyline; Clomipramine; Lofepramine(least cardiotoxic); Trazodone; (NB exclude Dosulepin)

3. Drug Treatment of Depression in Elderly Patients

This statement should be considered as a guideline only. The doctor will make the final judgment regarding the treatment plan, based on individual patient's clinical data, and the diagnostic and treatment options available.



Key Points:

- Psychological and pharmacological combination therapy has been shown to be effective
- For patients with psychotic depression, consider augmentation of the current treatment plan with antipsychotic medication
- ** MHRA safety advice for risk of QTc prolongation with citalopram – see section 4*

4. Association of Citalopram with Dose-dependent QT Interval Prolongation

Letters were sent to healthcare professionals in October 2011 to inform of new safety information and advice relating to **citalopram**. The new recommendations are a result of an assessment of a QT study and review of data which indicate that citalopram may cause a dose-dependent prolongation of the QT interval.

The summary of product characteristics for citalopram has been amended and your attention is drawn to the following changes:

- Recommended maximum dose in adults has been lowered to 40mg
- Recommended maximum dose in elderly has been lowered to 20mg
- Recommended maximum dose is 20mg in reduced hepatic function
- Caution is advised in patients at higher risk of developing Torsade de Pointes.
- Citalopram is now contraindicated in patients with known QT interval prolongation or congenital long QT syndrome. Co-administration with another medicinal product that can prolong the QT interval is also contraindicated

Many psychotropic medicines are associated with QT prolongation including antipsychotics (especially in 'high dose') and tricyclic antidepressants. Some non-psychotropic agents can also prolong the QT interval especially at higher doses, **methadone** is a specific example.

Escitalopram (NON-formulary) is also associated with dose dependent QT interval prolongation

Effects of **Psychotropic** Drugs on QTc				
No Effect	Low Effect	Moderate Effect	High Effect	Unknown Effect
Aripiprazole Paliperidone SSRIs (except citalopram and escitalopram) Reboxetine Mirtazepine MAOIs Carbamazepine Gabapentin Lamotrigine Valproate Benzodiazepine	Clozapine Flupentixol Fluphenazine Perphenazine Prochloperazine Olanzapine Risperidone Sulpiride Bupropion Moclobemide Venlafaxine Trazadone Lithium	Amisulpiride Chlorpromazine Quetiapine Citalopram TCAs	Any I.V antipsychotic Haloperidol Pimozide Sertindole Any drug or combination of drugs used in doses exceeding recommended maximum	Pipothiazine Trifluoperazine Zuclopenthixol Anticholinergic drugs (procyclidine, benzhexol etc)

Non- Psychotropic Drugs Known to effect QTc			
Antibiotics	Antiarrhythmics	Antimalarials	Others
Erythromycin Clarithromycin Ampicillin Co-trimoxazole Pentamidine (some 4 quinolones affect QTc – see Manufacturers literature)	Quinidine Disopyramide Procainamide Sotalol Amiodarone Bretylium	Chloroquine Mefloquine Quinine	Methadone Amantadine Cyclosporin Diphenhydramine Hydroxyzine Nicardipine Tamoxifen

Please note these tables (adapted from Maudsley[3]) are not exhaustive – and should be used as a guide only

5. Further Information

5.1 Discontinuing Antidepressants

All patients prescribed antidepressants should be informed that, although the drugs are not associated with tolerance and craving, discontinuation / withdrawal symptoms may occur on stopping, missing doses, or, occasionally on reducing the dose of the drug. These symptoms are usually mild and self-limiting but can occasionally be severe, particularly if the drug is stopped abruptly.

The symptoms of a discontinuation reaction may be mistaken for a relapse of illness or the emergence of a new physical illness leading to unnecessary investigations or reintroduction of the antidepressant. Symptoms may be severe enough to interfere with daily functioning.

Although anyone can experience discontinuation symptoms, the risk is increased in those prescribed short- half-life drugs (e.g. paroxetine, venlafaxine), particularly if they do not take them regularly.

	MAOIs	TCAs	SSRIs and related
Symptoms	**Common:** Agitation, irritability, ataxia, movement disorders, insomnia, somnolence, vivid dreams, cognitive impairment, slowed speech, pressured speech **Occasionally:** Hallucinations, paranoid delusions	**Common:** Flu-like symptoms (chills, myalgia, excessive sweating, headache, nausea), insomnia, excessive dreaming **Occasionally:** Movement disorders, mania, cardiac arrhythmia	**Common:** Flu-like symptoms, 'shock-like' sensations, dizziness exacerbated by movement, insomnia, excessive (vivid) dreaming, irritability, crying spells **Occasionally:** Movement disorders, problems with concentration and memory
Drugs most commonly associated with discontinuation symptoms	All	Amitriptyline Imipramine	Paroxetine Venlafaxine

Adapted from The Maudsley Prescribing Guidelines 11th Edition[3]

To avoid discontinuation symptoms, antidepressants should not be stopped abruptly. The antidepressant dose should be tapered down over at least 4 weeks. Fluoxetine is an exception to this rule.

If discontinuation symptoms are mild, the patient should be reassured that these symptoms are not uncommon after discontinuing an antidepressant and will pass in a few days. If symptoms are severe, reintroduce the original antidepressant (or another with a longer half-life from the same class) and taper gradually while monitoring for symptoms.

5.2 Antidepressant Prophylaxis

A single episode of depression should be treated for at least 6 months after recovery. If antidepressant therapy is stopped immediately on recovery, 50% of patients experience a return of their depressive symptoms.
Once a patient has taken antidepressants for 6 months after remission, the need for continued antidepressant treatment should be reviewed. This review may include consideration of the number of previous episodes, presence of residual symptoms, and concurrent psychosocial difficulties[1].

Of those patients who have one episode of major depression, 50-85% will go on to have a second episode and 80-90% of those who have a second episode will go on to have a third. Many factors are known to increase the risk of recurrence, including a family history of depression, recurrent dysthymia, concurrent non-affective psychiatric illness, chronic medical illness and social factors (e.g. lack of confiding relationships and psychosocial stressors). Some prescription drugs may precipitate depression.

Patients who have had two or more depressive episodes in the recent past, and who have experienced significant functional impairment during episodes, should be advised to continue antidepressant for at least 2 years[1]. Adults should receive the same dose for prophylaxis as used for acute treatment.

People with multiple episodes of depression, and who have had a good response to treatment with an antidepressant and an augmenting agent, should remain on this combination after remission if they find the side effects tolerable and acceptable. If one medication is stopped, it should usually be the augmenting agent. Lithium should not be used as a sole agent to prevent recurrence[1].

Patients on maintenance treatment should be re-evaluated by the GP, taking into account age, co-morbid conditions and other risk factors in the decision to continue the treatment beyond two years. The following table can be utilised when considering stopping antidepressant therapy.

	Stop after 6 months of recovery	Stop after 12 months of recovery	Stop at 24+ months of recovery
Prompt, uncomplicated recovery			
1 or more risk factors			
2 or more risk factors			

	Stopping appropriate: Low risk or relapse
	Caution when stopping: Moderate risk of relapse
	Advise continue medicines: High risk of relapse

Risk factors:

- Current episode was severe, prolonged or treatment-resistant
- History of previous episodes (take a careful history)
- Continuing residual symptoms
- Elderly patients
- Ongoing physical health problems and psychosocial difficulties
- The consequences of relapse are likely to be severe.

The above table and risk factor are adapted from The West of Scotland Guidance on Cost Effective Treatment of Depression where drugs are indicated.

5.3 Switching Antidepressant

When switching from one antidepressant to another, abrupt withdrawal should usually be avoided. Cross-tapering is preferred, in which the dose of the ineffective or poorly tolerated drug is slowly reduced while the new drug is slowly introduced.
Note that the co-administration of some antidepressants, even when cross-tapering, is absolutely contraindicated. In other cases theoretical risks or lack of experience preclude recommending cross-tapering.

Therefore, when switching from one antidepressant to another, be aware of interactions between antidepressants, and the risk of serotonin syndrome when combinations of serotonergic antidepressants are prescribed. Features of the serotonin syndrome include confusion, delirium, shivering, sweating, changes in blood pressure, and myoclonus.

The advice given in the following tables (see 5.7) should be treated with caution and patients should be very carefully monitored when switching.

5.4 Pregnancy and Lactation

There is sufficient evidence to show that leaving severe depression untreated can have adverse effects on the pregnancy outcome, especially if the mother is in danger of self harm and it can adversely affect the mother-child relationship. Treatment with antidepressants may be required throughout pregnancy and during the first couple of months or so after the birth. Therefore, it is important to assess the potential adverse effects of medication on the foetus and on the neonate and child who may continue to be exposed via the breast milk. There is a diversity of opinion based on limited data on the antidepressant of choice during lactation[4].

It is important to ensure that maternal mental health is treated appropriately. Tricyclic antidepressants such as amitriptyline and imipramine have been considered appropriate choices in terms of teratogenic risk to the foetus but are associated with increased risks of maternal cardiotoxicity, particularly in overdose. Furthermore, available data on tricyclic antidepressant use in pregnancy do not prove that they are less teratogenic than SSRIs. SSRIs, including fluoxetine, may therefore be appropriate for use in pregnancy but risks and benefits of use must be considered on a case by case basis[4].

Up to date information on antidepressant use during pregnancy and lactation can be accessed through the National Teratology Information Service (NTIS) by phoning 0844 892 0909 or via www.toxbase.com (username and password required)

It should be noted that the use of SSRIs later in pregnancy may be associated with an increased risk of persistent pulmonary hypertension of the newborn[4].

MAOIs should be avoided if at all possible because of their inherent maternal toxicity and lack of published data[4].

Chronic use, or the use of high doses of antidepressants near term, has been associated with neonatal withdrawal symptoms in some cases[4]. Further advice is available from NTIS.

NICE have produced a useful guideline on this topic entitled 'Antenatal and Postnatal Mental Health'[5] available at http://www.nice.org.uk/nicemedia/pdf/CG045NICEGuidelineCorrected.pdf

5.5 Other Prescribing considerations

Adapted from NICE Clinical Guideline 90[1] and 91[2]

(1) When an antidepressant is to be prescribed for a patient with depression and a chronic physical health problem, take into account the following:

- the presence of additional physical health disorders
- the side effects of antidepressants, which may impact on the underlying physical disease (e.g. antidepressants, SSRIs notably but all antidepressants, may result in or exacerbate hyponatraemia, especially in older people)
- Antidepressants can cause prolongation of QT interval, notably TCAs and citalopram – see section 4 for more details. This should be considered where other medicines which can prolong QT interval are coadministered.
- Interactions with other medications.

(2) Interactions of SSRIs with other medication (NOT exhaustive see BNF Appendix 1 for full list of interactions)

- Do not normally offer SSRIs to patients taking non-steroidal anti-inflammatory drugs (NSAIDs) because of the increased risk of gastrointestinal bleeding. Consider offering an antidepressant with a lower propensity for, or a different range of, interactions e.g mirtazapine.
- If no suitable alternative antidepressant to an SSRI can be identified for a patient receiving a NSAID then consideration should be given to offering gastroprotection with, for example, proton-pump inhibitors.
- Do not normally offer SSRIs to patients taking warfarin or heparin because of their anti-platelet effect.
- Use SSRIs with caution in patients taking aspirin. If no suitable alternative antidepressant can be identified, consideration should be given to offering gastroprotection with, for example, proton-pump inhibitors.
- Do not offer SSRIs to patients receiving 'triptan' drugs for migraine. Offer a safer alternative such as mirtazapine.

(3) Take into account toxicity in overdose when choosing an antidepressant for patients at significant risk of suicide. Be aware that:

- compared with other equally effective antidepressants recommended for routine use in primary care, 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.

(4) Use of venlafaxine is contraindicated in those patients with conditions associated with a high risk of cardiac arrhythmia and in patients with uncontrolled hypertension.

(5) For further advice on the use of particular agents in co-morbid conditions refer to The Maudsley Prescribing Guidelines[3] or contact the Clinical Pharmacy Team (Mental Health) on 01324 566728 or 566729

(6) For full advice on the treatment of depression and information on medicines which can precipitate depression please see the Depression ICP which is available at http://www.nhsforthvalley.com/__documents/qi/ce_guideline_depression/Depression-ICP.pdf

5.6 Tables of formulary antidepressants

Adapted, from Maudsley Prescribing Guidelines 11th Edition[3]. Further information from the BNF[6] and SPC[7].

Antidepressant drugs – SSRI's (formulary choices)					
SSRI	Licensed Indication	Licensed Doses	Main Adverse Effects **(not exhaustive –See BNF)**	Major Interactions (**not exhaustive - See BNF**)	Approx. half-life
Citalopram	Depression- Treatment of the initial phase and as maintenance therapy against potential relapse or recurrence Panic disorder +/- agoraphobia	Adult (>18yrs) 20-40mg/day Use lowest dose – evidence for higher doses poor 10mg/day for 1 week, increasing up to 40mg/day Elderly Doses (>65 yrs) (regardless of indication) Usual maintenance 20mg/day increased to Max 40mg/day	Nausea, vomiting, dyspepsia, abdominal pain, diarrhoea, rash, sweating, agitation, anxiety, headache, insomnia, tremor, sexual dysfunction (male and female), hyponatraemia, cutaneous bleeding disorders. **See section 4 on QTc prolongation – specific to Citalopram** May alter insulin/oral hypoglycamic requirements Discontinuation symptoms may occur (please refer to Maudsley[1] or SPC [2] for more information.	**Co-administration of citalopram with other medicinal products that can prolong the QT interval is contraindicated - see section 4** Not a potent inhibitor of most cytochrome enzymes MAOI's - Avoid Pimozide – Avoid Selegiline - Avoid St Johns Wort – Avoid Caution with Alcohol (although no interaction seen) Caution with NSAIDs/ tryptophan/warfarin.	33hours (although may be longer in elderly patients) Has weak metabolites.
Fluoxetine	Depression OCD Bulimia Nervosa	20mg/day Dose can be increased after 3 weeks if non-responsive Max 60mg/day 20-60mg/day (review after 3 months) 60mg/day Elderly (>65 yrs) Caution recommended when increasing dose. Recommended daily dose should not exceed 20mg/day.	As for citalopram but currently no evidence of dose dependent QTc prolongation with Note insomnia and agitation more common. Rash may occur more frequently. May alter insulin requirements	Inhibits CYP2D6, CYP3A4. Increases plasma levels of some antipsychotics, some benzodiazepines, carbamazepine, ciclosporin, phenytoin, tricyclics. MAOI's- Never Avoid selegiline Avoid Pimozide Avoid St John's Wort Caution – alcohol (although no interaction seen) NSAIDs/tryptophan/ warfarin	4-6 days 4-16 days Active metabolite (norfluoxetine)
Sertraline Sertraline (continued)	Depression +/- anxiety and prevention of relapse or recurrence of depression +/- anxiety OCD (under specialist supervision in children)	50-200mg/day 50-100mg recommended as poor evidence for higher doses. 50-200mg/day (adults and children over 12years. 6-12 yr: 25 mg/day, may be increased to 50mg/day after 1 week then in steps of 50 mg at intervals of one week MAX 200mg/d	As for citalopram but currently no evidence of dose dependent QTinterval prolongation with sertraline	Inhibits CYP2D6 (more likely to occur at doses ≥ 100mg/day). Increases plasma levels of some antipsychotics/tricyclics. Avoid – Pimozide Avoid - Selegiline Avoid - St John's Wort Caution: alcohol(although no interaction seen) Caution: litium/tryptophan/warfarin.	≈ 26 hours Has a weak metabolite.

	PTSD/social anxiety disorder/ panic disorder	25-200mg/day Elderly doses: no specific precautions are required. Usual adult doses are recommended.			

Antidepressant drugs – other (formulary choices)

Antidepressant	Licensed Indication	Licensed Doses	Main Adverse Effects **(not exhaustive – see BNF)**	Major Interactions **(not exhaustive – see BNF)**	Approx. half-life (h)
Mirtazapine	Depression	15-45 mg/day Elderly Dose: same as adult dose however dose increases should be done under close supervision.	Increased appetite, weight gain, drowsiness, oedema, dizziness, headache. Reversible white blood cell disorders including agranulocytosis, leukopenia and granulocytopenia have been reported as a rare occurrence with Mirtazapine. Nausea/sexual dysfunction relatively uncommon	MAOI's – Avoid Minimal effect on CYP2D6/1A2/3A. Caution : alcohol/sedatives. Increased clearance of mirtazapine with carbamazepine and phenytoin.	20-40. 25 Active metabolite (demethyl-mirtazepine).
Trazodone	Depression +/- anxiety Anxiety	150-300mg mg/day (up to 600mg/day in hospitalised patients). b.d dosing recommended for doses above 300mg/day. Elderly : very elderly/frail initially 100mg/day in divided doses or as a single night-time dose. 75-300mg/day	Sedation, dizziness, headache, nausea, vomiting, tremor, . postural hypotension, tachycardia, priapism (discontinue immediately), Blood dyscrasias – have been reported. Not anticolinergic, less cardiotoxic than tricyclics.	Caution: sedatives/alcohol/other antidepressants/digoxin/ Phenytoin. MAOIs: avoid.	5-13 (biphasic) 4-9 Active Metabolite
Venlafaxine.	Depression +/- anxiety. Also prevention of relapse or recurrence of depression. GAD/social Anxiety disorder	75mg-375mg/day (b.d) with food. XL prep ONLY 75mg XL daily (discontinue in GAD if no response after 8 weeks)	Nausea, insomnia, dry mouth, somnolence, dizziness, sweating, Nervousness, headache, sexual dysfunction. Elevation of blood pressure at higher doses. Avoid in those at risk of cardiac arrhythmia and in uncontrolled hypertension. Discontinuation symptoms common – withdraw slowly.	Metabolised by CYP2D6/3A4 – caution with drugs known to inhibit both isoenzymes. Minimal effects on CYP2D6. MAOIs – avoid. Selegiline – Avoid Caution – Entacapone Caution – St Johns Wort Caution: alcohol (although no interaction seen). Caution: clozapine/haloperidol/lithium/ warfarin/cimetidine. Caution: NSAIDs/aspirin Caution: Tramadol	5 11 Active metabolite (O-desmehyl-venlafaxine)

Antidepressant drugs – Tricyclics (formulary choices)					
Antidepressant	Licensed Indication	Licensed Doses	Main Adverse Effects **(not exhaustive see BNF)**	Major Interactions (**not exhaustive see BNF**)	Approx. half-life (h)
Amitriptyline	Depression	150-200mg/day. Initially 75mg daily in divided doses Or as single dose at bedtime Elderly Dose: Initial dose of 30-75mg. No other changes required.	Sedation, often with hangover, dry mouth, blurred vision, constipation, urinary retention. Cardiovascular side-effects – postural hypotension, tachycardia, arrhythmias.	MAOI's – avoid. SSRI's Alcohol Antimuscarinics Antipsychotis (esp pimozide. Also phenothiazines, clozapine – increased risk of antimuscarinic side-effects) Analgesics – opioids e.g Tramadol. Antiarrhythmics Cimetidine.	9-25 18-96 Active metabolites (nortriptyline)
Clomipramine	Depression Phobic and obsessional states.	30-250mg/day Normal maintenance 30-150mg/day Elderly: initially 10mg increased to 30-75mg/day 10-50mg/day	As for amitriptyline Also diarrhoea.	As for amitriptyline	12-36 36 Active metabolites (desmethyl-clomipramine)
Lofepramine	Depression	140-210mg mg/day Elderly: May respond to lower doses	As for amitriptyline but less sedative/ anticholinergic/ cardiotoxic. Constipation may be problematic.	As for amitriptyline	1.5-6 12-24 Active metabolite (desipramine)

Antidepressant Drugs – MAOI's (formulary choices)					
MAOI	Licensed Indication	Licensed Doses	Main Adverse Effects **(not exhaustive see BNF)**	Major Interactions (**not exhaustive see BNF**)	Approx. half-life (h)
Phenelzine	Depression	15 mg t.d.s – q.d.s (hospital patients: max 30mg t.d.s). Considering reducing to lowest possible maintenance dose. Elderly: no specific recommended dose but caution should be exerted as this group is especially susceptible to side-effect of postural hypotension	Postural hypotension (especially in the elderly), dizziness, drowsiness, insomnia, headaches, oedema, anticholinergic adverse effects, nervousness, paraesthesia, weight gain, hepatotoxicity, leucopenia, hypertensive crisis.	Tyramine in food, sympathomimetics, alcohol, opioids, antidepressants, levodopa, $5HT_1$ agonists. Probably safest of the MAOI's and is the one that should be used if combinations are considered.	1.5
Moclobemide (Reversible inhibitor of MAO-A)	Depression Social phobia	150-600mg/day administered in 2 divided doses after food. Recommended initial dose is 300mg/day. Dose may be reduced to 150mg/day, depending on individual response. 300-600mg/day administered in 2 divided doses after food. Last dose before 3 pm Elderly patients: no specific dose adjustments required.	Sleep disturbances, nausea, agitation, confusion, headache, dizziness, skin reactions.	Tyramine interactions rare and mild but possible if high doses (>600mg/day) used or if large quantities of tyramine ingested. CNS excitation/depression with dextromethorphan and pethidine- Avoid Avoid: clomipramine/ levodopa/ selegiline/ sympathomimetics and SSRI's Caution with Fentanyl/ morphine/ tricyclics. Cimetidine – half the dose of moclobemide.	2-4

5.7 Tables 'Swapping and Stopping' (Adapted from Maudsley 11th Edition[3])

Table Antidepressants - swapping and stopping* (Adapted from The Maudsley Prescribing Guidelines 11th Edition[2].)

To From	MAOIs-hydrazines	Tranyl-cypromine	Tricyclics	Citalopram/ escitalopram	Fluoxetine	Paroxetine	Sertraline	Trazodone	Moclobemide	Reboxetine[g]	Venlafaxine	Mirtazapine	Duloxetine
MAOIs-hydrazines	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks[a]	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks
Tranyl-Cypromine	Taper, stop and wait for 2 weeks	-	Taper, stop and wait for 2 weeks[a]	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks	Taper, stop and wait for 2 weeks
Tricyclics	Taper, stop and wait for 2 weeks[a]	Taper, stop and wait for 2 weeks[a]	Cross-taper cautiously	Halve dose and add citalopram then slow withdrawal[b]	Halve dose and add fluoxetine then slow withdrawal[b]	Halve dose and add paroxetine then slow withdrawal[b]	Halve dose and add sertraline then slow withdrawal[b]	Halve dose and add trazodone then slow withdrawal	Taper and stop and wait at least 1 week	Cross-taper cautiously	Cross-taper cautiously, starting with venlafaxine 37.5 mg/day[b]	Cross-taper cautiously	Cross-taper cautiously, start at 30mg/day increase very slowly[b]
Citalopram/ escitalopram	Taper, stop and wait for 1 week	Taper, stop and wait for 1 week	Cross-taper cautiously[b]	-	Taper, stop then start fluoxetine at 10 mg/day	Taper, stop and start paroxetine at 10 mg/day	Taper, stop and start sertraline at 25 mg/day	Cross-taper cautiously starting with low dose trazodone	Taper, stop and wait at least 1 week	Cross-taper cautiously	Cross taper cautiously Start venlafaxine 37.5 mg/day and increase very slowly	Cross-taper cautiously	Abrupt switch possible. Start at 60mg/day
Paroxetine	Taper, stop and wait for 2 weeks	Taper, stop and wait for 1 week	Cross-taper cautiously with very low dose of tricyclic[b]	Taper, stop and start citalopram at 10mg/day	Taper, stop then start fluoxetine at 10mg/day	-	Taper, stop and start sertraline at 25 mg/day	Cross-taper cautiously starting with low dose trazodone	Taper, stop and wait at least 1 week	Cross-taper cautiously	Cross taper cautiously Start venlafaxine 37.5 mg/day and increase very slowly	Cross-taper cautiously	Abrupt switch possible. Start at 60mg/day
Fluoxetine[c]	Taper, stop and wait for 5-6 weeks	Taper, stop and wait for 5-6 weeks	Taper and stop fluoxetine. Wait 4-7 days Start tricyclic at very low dose and increase very slowly[b]	Taper and stop fluoxetine. Wait 4-7 days Start citalopram at 10 mg/day and increase slowly	-	Taper and stop fluoxetine. Wait 4-7 days then start paroxetine at 10 mg/day	Taper and stop fluoxetine. Wait 4-7 days then start sertraline at 25 mg/day	Cross-taper cautiously starting with low dose trazodone	Taper and stop and wait at least 5 weeks	Cross-taper cautiously	Taper and stop. Start venlafaxine 37.5 mg/day Increase very slowly	Cross-taper cautiously. Start at 15mg/day	Abrupt switch possible. Start at 60mg/day

*Note: Advice given in this table is partly derived from manufacturers' information and partly theoretical. Caution is required in every instance.

Table Antidepressants - swapping and stopping - (contd.)

To / From	MAOIs-hydrazines	Tranyl-cypromine	Tricyclics	Citalopram/ escitalopram	Fluoxetine	Paroxetine	Sertraline	Trazodone	Moclobemide	Reboxetine[f]	Venlafaxine	Mirtazapine	Duloxetine
Sertraline	Taper, stop and wait for 1 week	Taper, stop and wait for 1 week	Cross-taper cautiously with very low dose of tricyclic[b]	Taper, stop then start citalopram at 10 mg/day	Taper, stop then start fluoxetine at 10 mg/day	Taper, stop then start paroxetine at 10 mg/day	-	Cross-taper cautiously starting with low dose trazodone	Taper, stop and wait for 1 week	Cross-taper cautiously	Cross-taper cautiously Start venlafaxine at 37.5 mg/day increase very slowly	Cross-taper cautiously	Abrupt switch possible. Start at 60mg/day
Trazodone	Taper, stop and wait for at least 1 week	Taper, stop and wait for at least 1 week	Cross-taper cautiously with very low dose of tricyclic	Cross-taper cautiously. Start citalopram at 10 mg/day	Cross-taper cautiously. Start fluoxetine at 10 mg/day	Cross-taper cautiously. Start paroxetine at 10 mg/day	Cross-taper cautiously. Start sertraline at 25 mg/day	-	Taper, stop and wait for at least 1 week	Cross-taper cautiously	Cross-taper cautiously Start venlafaxine at 37.5 mg/day	Cross-taper cautiously	Cross-taper cautiously Start at 30mg/day. Increase slowly
Moclobemide	Withdraw and wait 24 hours	Withdraw and wait 24 hours	Withdraw and wait 24 hours	Withdraw and wait 24 hours	Withdraw and wait 24 hours	Withdraw and wait 24 hours	Withdraw and wait 24 hours	Withdraw and wait 24 hours	-	Withdraw and wait 24 hours	Withdraw and wait 24 hours	Withdraw and wait 24 hours	Withdraw and wait 24 hours
Reboxetine	Taper, stop and wait for at least 1 week	Taper, stop and wait for at least 1 week	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Taper, stop and wait for at least 1 week	-	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously
Venlafaxine	Taper, stop and wait for at least 1 week	Taper, stop and wait for at least 1 week	Cross-taper cautiously with very low dose of tricyclic[b]	Cross-taper cautiously Start citalopram at 10 mg/day	Cross-taper cautiously Start at 10 mg/day fluoxetine	Cross-taper cautiously Start with 10 mg/day	Cross-taper cautiously Start with 25 mg/day	Cross-taper cautiously	Taper, stop and wait for at least 1 week	Cross-taper cautiously	-	Cross-taper cautiously	Cross-taper cautiously Start at 30mg/day. Increase slowly
Mirtazapine	Taper, stop and wait for at 2 weeks	Taper, stop and wait for at 2 weeks	Cross-taper cautiously with very low dose of tricyclic	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Cross-taper cautiously	Taper, stop and wait for at least 1 week	Cross-taper cautiously	Cross-taper cautiously	-	Cross-taper cautiously Start at 30mg/day. Increase slowly
Duloxetine	Taper, stop and wait at least 5 days	Taper, stop and wait at least 5 days	Cross-taper cautiously with very low dose of tricyclic[b]	Cross-taper cautiously Start with 10 mg/day	Taper, stop then start fluoxetine	Taper, stop then start paroxetine		Cross-taper cautiously Starting with low dose trazadone	Taper, stop and wait at least 5 days	Cross-taper cautiously	Taper and stop then start venlafaxine	Cross-taper cautiously	-
Stopping[d]	Reduce over 4 weeks	Reduce over 4 weeks	Reduce over 4 weeks	Reduce over 4 weeks	At 20 mg/day, just stop. At higher doses reduce over 2 weeks	Reduce over 4 weeks or longer, if necessary[f]	Reduce over 4 weeks	Reduce over 4 weeks	Reduce over 4 weeks	Reduce over 4 weeks	Reduce over 4 weeks or longer, if necessary[e]	Reduce over 4 weeks	Reduce over 4 weeks

Notes

[a] Three weeks in case of imipramine and clomipramine

[b] Do not co-administer clomipramine and SSRIs, venlafaxine or duloxetine.

[c] Beware: interactions with fluoxetine may still occur for 5 weeks after stopping fluoxetine because of its long half-life.

[d] See general guidelines (Maudsley p270)

[e] Withdrawal effects seem to be more pronounced. Slow withdrawal over 1-3 months may be necessary. Some patients may prefer abrupt withdrawal (to shorten overall duration of discontinuation effects)

[f] Switching to reboxetine as antidepressant monotherapy is no longer recommended.

5.8 References

1. National Institute for Clinical Excellence (NICE) Clinical Guideline 90 (Oct 2009) – Depression: Treatment and management of depression in Adults

2. National Institute for Clinical Excellence (NICE) Clinical Guideline 91 (Oct 2009) – Depression: Treatment and management of depression in adults with a chronic physical health problem

3. The Maudsley Prescribing Guidelines (2012) 11th Edition

4. National Teratology Information Service, Regional Drug and Therapeutic Centre – Treatment of Depression in Pregnancy [accessed June 2012]

5. National Institute for Clinical Excellence (NICE) Clinical Guideline 45 (Feb 2007) – Antenatal and postnatal mental health

6. The British National Formulary (March 2010), 59th Edition

7. www.Medicines.org.uk – Summary of Product Characteristics (SPC) for Individual Drugs

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