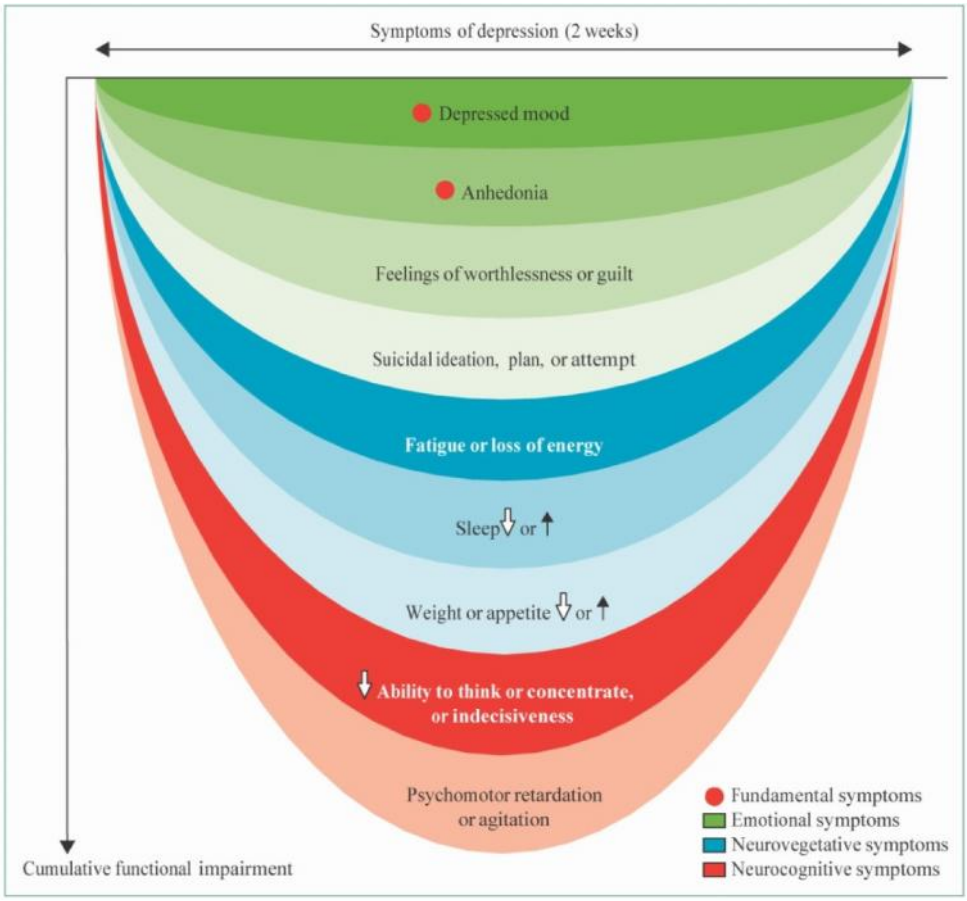
Guidance for the treatment of depression in primary care

DIAGNOSIS ICD-10



From The Lancet, published online November2, 2018

Core (Fundamental) symptoms should fulfil the following criteria:

- Present for at least 2 weeks and represent a change from normal mood
- Are not secondary to the effects of alcohol/drug misuse, medication, a medical disorder, or bereavement
- May cause significant distress and/or impairment of social, occupational, or general functioning

Severity

Mild

2 typical symptoms (depressed mood, anhedonia or fatigue) plus 2 other symptoms

Moderate

2 typical symptoms (depressed mood, anhedonia or fatigue) plus at least 3 other symptoms

Severe

3 typical symptoms (depressed mood, anhedonia or fatigue) plus at least 4 other symptoms

Differential diagnosis

- Standard tests to rule out treatable causes:

FBC, ESR, B12/folate, U&Es, LFTs, TFTs, glucose, Calcium

- Ask about episodes of mania or hypomania
- Establish if it is a mixed anxiety / depressive state

Antidepressants seem to be most effective at treating depressed mood, suicidal ideation and psychomotor retardation
They are less effective at treating insomnia, fatigue, concentration, lack of motivation, (multiple painful physical complaints)

NICE recommend

CBT for less severe depression
CBT in combination with SSRI or mirtazapine in moderate to severe depression

Offer psychological therapy for mild depression
If moderate /severe offer combination of CBT and an antidepressant

Discuss choice of drug with the patient

Include:
Review of response / side effects to previous antidepressant
Potential therapeutic effects
Possible side effects (including an increase in suicidal thoughts)
Likelihood of discontinuation symptoms
Likely time to show any response (1- 2 weeks)

SSRI as first choice, mirtazapine if sedation required

Start antidepressant
Assess efficacy after 2 weeks (or 1 week if currently suicidal)

No effect

Effective

Poorly tolerated

Assess weekly for a further 1 -2 weeks
If still no response
Review diagnosis
Review adherence
Increase dose as necessary

Continue for 6 – 9 months at full treatment dose
Consider longer-term treatment in recurrent depression

Switch to different antidepressant
Assess over 3-4 weeks, increase dose as necessary

No effect

Effective

Poorly tolerated or no effect

Switch to different antidepressant (alternative SSRI, venlafaxine, mirtazapine)
Assess over 3-4 weeks, increase dose as necessary. Refer to comparison table

No effect

Review diagnosis, review adherence
Consider third-choice options
Mirtazapine (in combination with SSRI/SNRI), agomelatine, duloxetine, trazadone, vortixetine. Refer to comparison table for more information

No effect

Consult with specialist for treatment for refractory depression

Minimum therapeutic daily dose	
Agomelatine	25mg
Citalopram	20mg
Escitalopram	10mg
Fluoxetine	20mg
Mirtazapine	30mg
Paroxetine	20mg
Sertraline	50mg
Trazadone	150mg
Venlafaxine	75mg
Vortioxetine	10mg

Guidance for the treatment of depression for primary care, comparison of medications

This is a guide and reference should be made to the BNF or SPC for more detailed information

Medication	Licensed indications	Risk in co-morbidities					Main side effects						How to stop it*	Other information
		Cardiac problems	Mild / Moderate Hepatic impairment	Narrow-angle Gluacoma	Mild / Moderate Renal Impairment	Risk of bleed	Dry Mouth	Insomnia	Nausea	Sedation	Sexual problems	Weight gain		
FIRST LINE														
Citalopram	Depressive illness & panic disorder	Prolongs QTc, max dose 20mg in > 65 years Use with caution if at risk of serious arrhythmia	Dose reduction required			High	●	●	●●●	●	●●●	●	Slowly over about 4 weeks	ECG recommended at baseline and 1 week after initiation and every dose increase if at risk of serious arrhythmia
Escitalopram	Depressive illness, GAD, OCD, social anxiety disorder & panic disorder	Prolongs QTc, max dose 10mg in > 65 years Use with caution if at risk of serious arrhythmia	Dose reduction required			High	●	●	●●●	●	●●●	●	Slowly over about 4 weeks	ECG recommended at baseline and 1 week after initiation and every dose increase if at risk of serious arrhythmia
Fluoxetine	Major depression & OCD	Moderate effect on QTc	High		High	High	●	●	●●●	●	●●●	●	Should be no problems	May initially increase anxiety Long half-life: advantage for people who forget doses, withdrawal symptoms less likely
Sertraline	Depressive illness, PTSD, OCD, social anxiety disorder & panic disorder	Considered safest post MI	Dose reduction required		High	High	●	●	●●●	●	●●●	●	Slowly over about 4 weeks	May initially increase anxiety

Medication	Licensed indications	Risk in co-morbidities					Main side effects						How to stop it*	Other information
		Cardiac problems	Mild / Moderate Hepatic impairment	Narrow-angle Gluacoma	Mild / Moderate Renal Impairment	Risk of bleed	Dry Mouth	Insomnia	Nausea	Sedation	Sexual problems	Weight gain		
Mirtazapine	Major depression		Dose reduction required		Dose reduction may be required	High	○	●	○	●●●	○	●●●	Should be no problems	Can be combined with SSRI or SNRI Discuss likelihood of weight gain with patient
SECOND LINE														
Paroxetine	Major depression, GAD, OCD, PTSD, social anxiety disorder & panic disorder		Lower		Dose reduction may be required	High	•	•	•••	•	•••	•	Slowly over several weeks, high risk of w/d symptoms	Rarely used as likely to cause withdrawal symptoms. However is used by liver disease specialists
Venlafaxine	Major depression, GAD & social anxiety disorder	Moderate, increases BP Mild effect on QTc Use with caution if at risk of serious arrhythmia	Dose reduction required		High	High	●●	●●●	●●●	●	●●●	●	Slowly over at least 4 weeks, high risk of w/d symptoms	ECG recommended at baseline and 1 week after initiation and every dose increase if at risk of serious arrhythmia
THIRD LINE														
Agomelatine	Major depression		High	Lower	Lower	Lower	○	○	○	○	○	○	No known problems	Monitor LFTs at baseline, 3, 6, 9, 12 and 24 weeks
Duloxetine	Major depressive disorder & GAD	Caution in hypertension & post MI	High			High	●	●●	●●●	●	●●	●	Slowly over at least 4 weeks	
Trazadone	Depressive illness	Mild effect on QTc	High		Lower	Unknown	○	○	●●	●●●	●	●	Slowly over about 4 weeks	
Vortioxetine	Major depression		Lower	Lower	Lower	Unknown	●	○	●●	○	○	○	No known problems	

Medication	Licensed indications	Risk in co-morbidities					Main side effects						How to stop it*	Other information
		Cardiac problems	Mild / Moderate Hepatic impairment	Narrow-angle Gluacoma	Mild / Moderate Renal Impairment	Risk of bleed	Dry Mouth	Insomnia	Nausea	Sedation	Sexual problems	Weight gain		
AUGMENTATION – initiation in specialist setting or after consulting with a specialist														
Aripiprazole, Lamotrigine, Lithium, Olanzapine, Quetiapine, Risperidone														
N.B. Monitoring required for lithium: levels 3 monthly. Calcium, Thyroid function, Urea and electrolytes, creatinine or estimated GFR 6 monthly Annual health check for all patients on these medications to include: BP & pulse, Fasting blood glucose and HbA1c, Lipids (fasting if possible), FBC, LF, Urea & electrolytes, eGFR, waist circumference, weight														

Key	Side effect frequency			
Mild effect on QTC = >5 and < 9ms	•••	Most people will get this side effect	•	Only a few people will get this side effect
Moderate effect on QTC = >9 and < 16ms	••	Quite a few people will get this side effect	○	This is very rare or not known

Stopping antidepressants

*A general rule is that the withdrawal should take a few days if the drug has been taken for weeks, a few weeks if taken for months, and a few months if the drug has been taken for years. Tapering is not usually required for agomelatine, fluoxetine or mirtazapine

Switching antidepressants (taken from the Maudsley guidelines, 13th edition). This does not include guidance for MAOIs

To agomelatine: cross taper cautiously

From agomelatine: stop agomelatine and then start

To Fluoxetine: Direct switch to other SSRI/SNRI and vortioxetine possible, cross taper cautiously with mirtazapine and trazadone

From fluoxetine: cross taper cautiously with agomelatine and mirtazapine, stop and wait 4 – 7 days before initiating another SSRI/SNRI or vortixetine

To other SSRI/SNRI/vortioxetine: Stop agomelatine then start, cross taper cautiously with mirtazapine and trazodone, direct switch possible within this group

From other SSRI/SNRI/vortioxetine: cross taper cautiously with agomelatine , mirtazapine and trazodone, direct switch possible within this group

To mirtazapine: cross taper cautiously with agomelatine, SSRI/SNRI, trazadone and vortioxetine

From mirtazapine: cross taper cautiously with agomelatine, SSRI/SNRI, trazadone and vortioxetine

Additional information

Pregnancy or breast feeding: discuss options with MIMHS: 01227 768928

All antidepressants can cause l**ow sodium**, risk is considered lower with mirtazapine and agomelatine

All antidepressants can **increase suicide risk**

Risk of bleed is increased with concomitant use of NSAIDs , NOACs, warfarin or anti-platelets, PPIs reduce this risk. Risk highest during first 30 days of treatment

Caution in concomitant use of medications affecting heart rhythm to avoid Torsades de Point

Please contact KMPT via your established local route for advice regarding a specific patient

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