Current Recommendations (by Condition and Drug Class) [Feb 2025]

Depression

Selective Serotonin Reuptake Inhibitors (SSRIs): First-line antidepressants for moderate to severe depression

nhs.uk

nhs.uk
. SSRIs are favoured for their efficacy and relatively mild side-effect profile compared to older antidepressants
nhs.uk
. Common SSRIs include:

Generic (Brand)	Typical Dosage Range	Common Side Effects	Special Considerations
Sertraline (Lustral)	50–200 mg once daily nhs.uk	Nausea, headache, insomnia, dry mouth, sexual dysfunction nhs.uk .	Taper gradually to prevent withdrawal symptoms nhs.uk . Preferred SSRI for anxiety comorbidity; off-label first-line for GAD due to cost-effectiveness istituto-walden.it . Avoid grapefruit juice (raises sertraline levels) nhs.uk .
Fluoxetine (Prozac)	20–60 mg once daily nhs.uk	Nausea, insomnia, headache, diarrhoea, loss of appetite nhs.uk .	Long half-life (lowest risk of withdrawal). Only SSRI licensed for <18 (with specialist oversight) nhs.uk . Many drug interactions (potent CYP inhibitor).
Citalopram (Cipramil)	20–40 mg once daily nhs.uk	Nausea, dry mouth, tiredness, sweating, sexual dysfunction nhs.uk .	Dose-dependent QT prolongation risk – max 40 mg/day (20 mg in older adults) nhs.uk . Fewer drug interactions than fluoxetine/paroxetine. Taper to discontinue.
Escitalopram (Cipralex)	10–20 mg once daily nhs.uk	As per SSRIs: insomnia, nausea, dizziness,	Isomer of citalopram (max 20 mg/day; 10 mg in liver impairment) nhs.uk

Generic (Brand)	Typical Dosage Range	Common Side Effects	Special Considerations
		sexual dysfunction nhs.uk .	. Often well-tolerated.
Paroxetine (Seroxat)	20–40 mg once daily choiceandmedication.org	Drowsiness, weight gain, sexual dysfunction, dry mouth nhs.uk .	Short half-life – highest risk of withdrawal symptoms if stopped abruptly nhs.uk . Taper slowly. Not recommended in pregnancy (congenital risk).
Fluvoxamine (Faverin)	50–300 mg (divided doses)	Sedation, nausea, GI upset, dry mouth (similar to other SSRIs) nhs.uk .	Strong CYP inhibitor – significant drug interaction potential. Primarily used for OCD rather than depression.
Vortioxetine (Brintellix)	5–20 mg once daily choiceandmedication.org	Nausea, dizziness, abnormal dreams, constipation or diarrhoea nhs.uk .	**Multimodal** antidepressant. NICE recommends considering after 2 other antidepressants failed nhs.uk . Taper if discontinuing to avoid withdrawal.

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs): Used if SSRIs are ineffective or not tolerated

istituto-walden.it
. They increase serotonin and noradrenaline and may be more effective for some patients, but can raise blood pressure
nhs.uk
. Common SNRIs:

Generic (Brand)	Typical Dosage Range	Common Side Effects	Special Considerations
Venlafaxine (Efexor)	75–225 mg/day (XR formulation; up to 375 mg in severe cases) pmc.ncbi.nlm.nih.gov	Nausea, insomnia, dry mouth, sweating; dose-dependent ↑BP nhs.uk .	Monitor blood pressure (especially at higher doses) nhs.uk . Higher doses (>150 mg) also boost

Generic (Brand)	Typical Dosage Range	Common Side Effects	Special Considerations
			dopamine. Short half-life – taper to avoid withdrawal (similar to SSRIs; notable withdrawal if abrupt) istituto-walden.it istituto-walden.it .
Duloxetine (Cymbalta)	60–120 mg/day ema.europa.eu	Nausea, dizziness, dry mouth, constipation, fatigue pmc.ncbi.nlm.nih.gov .	Also licensed for GAD and neuropathic pain nhs.uk . Can cause modest ↑BP pmc.ncbi.nlm.nih.gov – check BP regularly. Avoid in heavy alcohol use (risk of liver injury).

Tricyclic Antidepressants (TCAs): Older antidepressants now usually **second-line** due to side effects and toxicity in overdose

hweclinicalguidance.nhs.uk
. Effective for severe or treatment-resistant depression. Examples:

Generic (Brand)	Typical Dosage Range	Common Side Effects	Special Considerations
Amitriptyline	50–150 mg at night (max ~200 mg)	Sedation, dry mouth, blurred vision, constipation, dizziness nhs.uk .	Strong anticholinergic effects (caution in glaucoma, elderly). **High overdose toxicity** – can cause cardiac arrhythmias hweclinicalguidance.nhs.uk . Often used at lower doses off-label for pain/insomnia.
Imipramine (Imipramil)	75– 200 mg/day (in divided doses)	Dry mouth, constipation, urinary retention, drowsiness, lightheadedness nhs.uk .	Similar profile to amitriptyline. Was historically used for depression and panic disorder. Risk of **cardiac toxicity** in overdose hweclinicalguidance.nhs.uk .
Clomipramine (Anafranil)	50– 250 mg/day (divided or once nightly)	Dry mouth, sweating, tremor, drowsiness, sexual dysfunction.	**Very effective for OCD**; in depression, reserved for treatment-resistant cases nice.org.uk

Generic (Brand)	Typical Dosage Range	Common Side Effects	Special Considerations
			. Higher serotonergic effect among TCAs. Requires slow titration. Toxic in overdose – limit supply dispensed nice.org.uk .

Other Antidepressants: Agents with unique mechanisms, used in specific scenarios or as add-on therapy.

Generic (Class)	Typical Dosage	Common Side Effects	Special Considerations
Mirtazapine (NaSSA)	15–45 mg at night hamad.qa	Sedation, increased appetite & weight gain, dry mouth nhs.uk .	Often chosen if insomnia or poor appetite (causes sedation & weight gain) nhs.uk . Low sexual side-effect burden. Can be combined with SSRIs for augmentation in resistant cases nhs.uk .
Lithium (mood stabilizer)	*Augmentation:* target serum 0.4–1.0 mmol/L nice.org.uk	Tremor, thirst, increased urination, weight gain.	**Augmentation therapy** in depression: added to antidepressant for treatment-resistant depression nice.org.uk nice.org.uk . Requires blood level monitoring (narrow therapeutic index – risk of toxicity) pmc.ncbi.nlm.nih.gov nice.org.uk . Monitor kidney & thyroid function every 6–12 months nice.org.uk .

Generic (Class)	Typical Dosage	Common Side Effects	Special Considerations
Augmenting Antipsychotics (e.g. quetiapine)	*Varies (low doses)*	Sedation, weight gain, metabolic effects.	In severe depression or depression with psychotic features, an atypical antipsychotic (e.g. quetiapine, aripiprazole) may be added as augmentation pmc.ncbi.nlm.nih.gov . Used under specialist guidance for treatment-resistant cases.
Note: *MAOIs* (e.g. **Phenelzine**, **Tranylcypromine**) – effective in atypical or resistant depression, but **not first-line** due to safety concerns (see historical section below for details on MAOIs being largely replaced mayoclinic.org).			

Anxiety Disorders

Generalized Anxiety Disorder (GAD): Pharmacotherapy is offered if anxiety is chronic and causing significant impairment. First-line are SSRIs

istituto-walden.it
(even if off-label) because of favourable risk/benefit. If SSRI is ineffective, another SSRI or an SNRI is tried
istituto-walden.it
. Pregabalin is recommended if SSRIs/SNRIs aren't tolerated
istituto-walden.it
. Benzodiazepines are **not** for routine long-term use (only short-term for crises)
istituto-walden.it
.

- **SSRIs (for GAD):** *e.g.* **Sertraline** (often first choice

  istituto-walden.it

  ), **Escitalopram**, **Paroxetine**. Doses are similar to depression (sertraline 50–150 mg, etc.). They reduce worry and are effective long-term. *Side effects:* transient increase in anxiety/restlessness at start, nausea, insomnia

istituto-walden.it

. *Special:* Start low to minimize initial jitteriness. Sertraline is cost-effective and recommended off-label first-line by NICE

istituto-walden.it

. Monitor for suicidal ideation in young adults as with any antidepressant.

- **SNRIs (for GAD):** *e.g.* **Duloxetine** 60–120 mg, **Venlafaxine XR** 75–225 mg. They are approved for GAD and help both psychic and somatic anxiety symptoms

  nhs.uk

  . *Side effects:* similar to SSRIs + possible blood pressure elevation

  nhs.uk

  . *Special:* Venlafaxine is used at extended-release doses for smoother delivery; taper off slowly to avoid withdrawal.

- **Pregabalin** (anticonvulsant) for GAD: 150–600 mg/day in divided doses. *Side effects:* dizziness, drowsiness, weight gain. *Special:* Considered if SSRIs/SNRIs unsuitable

  istituto-walden.it

  . Helps physical symptoms of anxiety. Now a controlled substance (Schedule C5 in UK) due to risk of misuse – use with caution

  istituto-walden.it

  .

- **Benzodiazepines: Diazepam**, **Lorazepam**, etc. *Use:* **Short-term only** for acute anxiety spikes or crisis. Not routine for GAD due to dependence and tolerance risks

  istituto-walden.it

  . *Side effects:* sedation, psychomotor impairment, memory problems. *Special:* Limit to 2-4 weeks; do not discontinue abruptly after extended use to avoid withdrawal seizures

  istituto-walden.it

Panic Disorder: SSRIs are first-line here as well (e.g. **Sertraline**, **Paroxetine**, **Escitalopram**) to reduce panic frequency

nhs.uk
. *Side effects/special:* Start at low doses to prevent transient panic worsening when initiating (SSRIs can initially increase anxiety). **Imipramine** or **Clomipramine** (TCAs) are effective second-line for panic
nhs.uk
; use is limited by side effects. Benzodiazepines (e.g. alprazolam, clonazepam) can reduce panic acutely, but are generally reserved for short-term use or if other treatments fail, given dependence potential. Beta-blockers (e.g. propranolol 40 mg as needed) can help autonomic symptoms (racing heart, tremor) but do not stop panic attacks per se.

Social Anxiety Disorder (Social Phobia): SSRIs are first-line; NICE specifically recommends **Escitalopram or Sertraline** for adults

nice.org.uk
. *Dose:* Escitalopram 10–20 mg, Sertraline 50–150 mg. They reduce social fear and avoidance over weeks. *Side effects:* as per SSRIs (nausea, insomnia, sexual dysfunction). *Special:* SSRIs also help comorbid depression. If partial response, an alternative SSRI or **Venlafaxine XR** may be tried (venlafaxine is effective in social anxiety)
nice.org.uk
. **Phenelzine** (an MAOI) is a potent option for treatment-resistant cases – reserved for severe cases under specialist care due to dietary restrictions and side effects
nice.org.uk
. **Beta-blockers** (e.g. **Propranolol** 20–40 mg) taken 30–60 min before a performance situation can reduce tremors and heart racing (performance anxiety), though they do not alleviate cognitive anxiety
nhs.uk

nhsinform.scot
. Benzodiazepines are not routinely used long-term but may be prescribed short-term for infrequent anxiety-provoking events if necessary.

Obsessive-Compulsive Disorder (OCD): SSRIs at higher end of dose range are first-line (e.g. **Fluoxetine** 40–60 mg, **Sertraline** 100–200 mg, **Paroxetine** 40 mg, **Fluvoxamine** up to 300 mg)

pmc.ncbi.nlm.nih.gov
. *Side effects:* SSRIs are generally well-tolerated; at high doses watch for insomnia or GI upset. *Special:* OCD often requires doses at or above typical antidepressant doses and a longer trial (10–12 weeks) to see effect
nice.org.uk
. If two SSRIs fail, **Clomipramine** (TCA) is recommended next
nice.org.uk
, due to its potent serotonergic effect. Clomipramine (25–250 mg/day) often helps refractory OCD; side effects and precautions as listed under TCAs (notably, must monitor for cardiotoxicity in overdose and titrate slowly)
nice.org.uk

. For severe treatment-resistant OCD, augmentation of an SSRI or clomipramine with a low-dose **antipsychotic** (e.g. risperidone 0.5–2 mg) can be considered to reduce intrusive thoughts
nice.org.uk
. This is typically done under specialist supervision after other options exhausted.

Post-Traumatic Stress Disorder (PTSD): Antidepressants can be used if trauma-focused therapy is unavailable or symptoms are severe. **SSRIs** are first-line – notably **Sertraline** (50–150 mg) and **Paroxetine** (20–40 mg) are licensed for PTSD

pmc.ncbi.nlm.nih.gov
. They can alleviate core PTSD symptoms (intrusive thoughts, hyperarousal) over 8–12 weeks. *Side effects:* SSRIs as above. **Mirtazapine** (15–45 mg) is an alternative if SSRIs aren't tolerated, given some evidence in PTSD
nice.org.uk
. Older guidelines also supported **amitriptyline** or **phenelzine** for PTSD managed by specialists
nice.org.uk
, though these are now rarely used. Prazosin (an alpha-1 blocker) is sometimes used off-label to target PTSD-related nightmares (causes blood pressure lowering).
Special: Pharmacotherapy is usually continued for 12+ months if effective. Medication is **adjunct** to psychotherapy in PTSD; NICE emphasizes trauma-focused psychological therapy as first-line, using medication as a supplement or when therapy alone is insufficient.

Schizophrenia (and Psychotic Disorders)

Antipsychotics: The cornerstone of schizophrenia treatment. According to NICE, choice of antipsychotic should be individualized, considering side-effect profile and patient preference

ncbi.nlm.nih.gov
. **Second-Generation (Atypical) Antipsychotics** are usually preferred first-line due to lower risk of extrapyramidal side effects (EPS) compared to first-generation drugs
ncbi.nlm.nih.gov
. All antipsychotics are roughly comparable in efficacy (except clozapine in resistant cases), so selection hinges on side effects
ncbi.nlm.nih.gov
. Key drug classes and examples:

- **Atypical Antipsychotics:** These include **Risperidone** (Risperdal), **Olanzapine** (Zyprexa), **Quetiapine** (Seroquel), **Aripiprazole** (Abilify),

Amisulpride (Solian), **Paliperidone** (Xeplion/Invega), and **Clozapine** (Clozaril).

- *Dosing:* Risperidone 2–6 mg/day

  nhs.uk

  nhs.uk

  ; Olanzapine 5–20 mg/day; Quetiapine 300–750 mg/day (in divided or extended-release form); Aripiprazole 10–30 mg/day.

- *Side Effects:* Generally fewer EPS at therapeutic doses than older agents

  ncbi.nlm.nih.gov

  , but can cause weight gain and metabolic syndrome (notably with olanzapine and clozapine)

  pmc.ncbi.nlm.nih.gov

  . Sedation (quetiapine, olanzapine), elevated prolactin (risperidone, amisulpride causing breast symptoms), orthostatic hypotension, and QT prolongation (ziprasidone, higher doses of risperidone) are possible.

- *Special Considerations:*
  - **Clozapine:** reserved for **treatment-resistant schizophrenia** (after failure of ≥2 other antipsychotics)

    pmc.ncbi.nlm.nih.gov

    . It's the most effective for refractory cases

    pmc.ncbi.nlm.nih.gov

    , but requires regular blood monitoring due to risk of agranulocytosis (weekly CBC initially)

    pmc.ncbi.nlm.nih.gov

    . Also causes significant weight gain, sedation, hypersalivation, and seizure risk at high doses.

  - Many atypicals have long-acting injectable (depot) formulations (e.g. depot **Paliperidone** monthly, **Risperidone** long-acting), which are useful for adherence.
  - Metabolic monitoring (weight, glucose, lipids) is required for atypicals because of diabetes and lipid risk, especially with olanzapine and clozapine

pmc.ncbi.nlm.nih.gov

.

    - Aripiprazole is an atypical with partial dopamine agonism: less sedation and metabolic effect, but can cause akathisia (restlessness).
    - Amisulpride is effective for positive symptoms and causes dose-dependent prolactin elevation.
- **Typical (First-Generation) Antipsychotics:** e.g. **Haloperidol** (Haldol), **Chlorpromazine** (Largactil), **Flupentixol** (Depixol), **Zuclopenthixol** (Clopixol), **Perphenazine**, **Trifluoperazine**.
    - *Dosing:* Haloperidol 2–10 mg/day (may go higher in acute cases or depot form); Chlorpromazine 100–600 mg/day in divided doses. Long-acting injections (depots) like haloperidol decanoate or flupentixol are dosed every 2–4 weeks.
    - *Side Effects:* Higher risk of EPS (Parkinsonian tremor, stiffness, restlessness, dystonias)

      ncbi.nlm.nih.gov

      and **tardive dyskinesia** (involuntary movements with long-term use). Can also cause sedation and low blood pressure (especially chlorpromazine). Haloperidol causes relatively less sedation/weight gain but more EPS.

    - *Special:* These were the mainstay in the past, but are now often second-line due to side effects

      ncbi.nlm.nih.gov

      . However, they are still used, particularly **haloperidol**, which is very effective for acute psychosis or agitation (including emergency IM use) and in short-term treatment. Depot typical antipsychotics (e.g. flupentixol, zuclopenthixol) are options for patients with chronic schizophrenia who prefer injections or have adherence issues. Monitoring for movement disorders is essential (consider prophylactic anti-Parkinson medication if needed for EPS).

Bipolar Disorder (Mania and Bipolar Depression): Medication choice depends on phase (mania vs depression vs maintenance).

- **Mood Stabilizers:**
    - **Lithium:** Gold-standard maintenance treatment for bipolar and for acute mania/hypomania. Typical serum level target 0.6–0.8 mmol/L for maintenance (0.8–1.0 for acute mania)

nice.org.uk

. Reduces risk of suicide in bipolar patients

pmc.ncbi.nlm.nih.gov

. *Side effects:* tremor, thirst/polyuria (nephrogenic diabetes insipidus), hypothyroidism, renal impairment over time. *Special:* Requires regular blood level monitoring (narrow therapeutic range) and kidney/thyroid checks

nice.org.uk

nice.org.uk

. Avoid dehydration (toxicity risk). Interacts with NSAIDs, ACE inhibitors (raise lithium levels).

- **Valproate** (valproic acid or semisodium valproate, e.g. Depakote): First-line for acute mania (except in women of childbearing age due to teratogenicity). Dose ~750–2500 mg/day (target blood level ~50–100 mg/L). *Side effects:* sedation, weight gain, tremor, hair loss, polycystic ovary syndrome, hepatotoxicity (rare). *Special:* Contraindicated in pregnancy (high risk of birth defects). Requires LFT and CBC monitoring. Often used in males or non-pregnant patients for mania or as a maintenance alternative to lithium.
- **Carbamazepine:** An anticonvulsant mood stabilizer, sometimes used for bipolar (especially bipolar with rapid cycling or lithium-refractory cases). Dose ~400–1600 mg/day. *Side effects:* drowsiness, dizziness, nausea, ataxia, hyponatremia. *Special:* Many drug interactions (strong inducer of liver enzymes). Not typically first-line per current NICE guidance, but an option for those not responding to lithium or valproate

  nice.org.uk

  . Requires periodic blood counts and LFTs.

- **Atypical Antipsychotics for Mania:** Many second-gen antipsychotics are effective for acute mania and are recommended by NICE as first-line treatments (often in combination with a mood stabilizer). **Haloperidol, Olanzapine, Risperidone, Quetiapine** and others can rapidly control manic symptoms

  cambridge.org

  . For example, haloperidol 5–10 mg or olanzapine 10–20 mg in acute mania. They are often used short-term during acute phases. *Side effects:* as noted above for antipsychotics (EPS or metabolic issues, depending on agent).

Special: Quetiapine and Lurasidone are also used in **bipolar depression** (quetiapine at 300 mg has evidence in bipolar depression). Maintenance treatment may involve continuing an atypical antipsychotic, often alongside lithium or valproate. Clozapine may be tried in refractory mania or for refractory bipolar disorder, but careful monitoring is needed.

- **Antidepressants in Bipolar:** Use with caution. NICE generally advises **not** to use antidepressant monotherapy in bipolar depression due to risk of switching to mania

  nice.org.uk

  . If used, always combine with a mood stabilizer or antipsychotic. Preferred choices for bipolar depression are quetiapine, olanzapine-fluoxetine combo (in some guidelines), or lamotrigine (especially for bipolar II depression). **Lamotrigine** (up to 200 mg) is effective for bipolar depression and maintenance, but not mania. It requires slow titration (risk of rash). Antidepressants like SSRIs may be used short-term for bipolar depression if needed, but should be discontinued once patient recovers to prevent mania relapse.

Attention-Deficit/Hyperactivity Disorder (ADHD): Medication is recommended for school-age children, adolescents, and adults with moderate-to-severe ADHD symptoms causing impairment

nice.org.uk
. Stimulant medications are first-line, with non-stimulants as alternatives. Dosing and choice may differ slightly for children vs adults, but core options overlap.

- **Stimulants (first-line):**
  - **Methylphenidate** (MPH) – e.g. Ritalin (immediate-release), Concerta XL or Equasym XL (extended-release). *Dose:* Children start ~5–10 mg twice daily (IR) titrated up; typical effective dose 20–30 mg/day (max ~60 mg/day)

    nhs.uk

    quizlet.com

    . Adults may require higher doses (up to 100 mg/day in some cases, usually as modified-release). *Side effects:* reduced appetite, insomnia, abdominal pain, headache

    pmc.ncbi.nlm.nih.gov

    , increased heart rate/BP. *Special:* Monitor weight and growth in children (MPH can slow growth slightly)

nice.org.uk

. BP and pulse checks for all ages. Consider drug holidays if appropriate to assess ongoing need. MPH has immediate and extended forms – extended-release once-daily formulations improve adherence and reduce midday dosing stigma or diversion risk

nice.org.uk

- **Lisdexamfetamine** (Elvanse) – a prodrug of dextroamphetamine. *Dose:* Start 30 mg qAM, usual range 30–70 mg daily

  nice.org.uk

  . *Side effects:* similar to MPH (insomnia, loss of appetite, weight loss, dry mouth) and can also cause irritability or tics in some. *Special:* Recommended by NICE as an option for children who do not respond sufficiently to methylphenidate

  nice.org.uk

  , and as first-line alongside MPH in adults

  nice.org.uk

  . Once daily dosing; lower abuse potential (must be converted to active form in body). If lisdexamfetamine works but its long duration causes issues, specialists may consider **dexamfetamine** (5–20 mg in divided doses) as an alternative for more flexible dosing

  nice.org.uk

  . (Dexamfetamine is essentially the active metabolite; it's used in adults who respond to lisdexamfetamine but need a shorter action window),

  nice.org.uk

- *Note:* Both MPH and lisdexamfetamine are Schedule 2 Controlled Drugs in the UK, requiring secure prescribing and monitoring for misuse. Caution in patients with history of substance misuse – use long-acting forms and involve specialists if needed

  nice.org.uk

  nice.org.uk

  . Contraindicated in those with serious heart problems – screen for cardiac risk (blood pressure, personal or family cardiac history) before starting stimulants

nice.org.uk

.

- **Non-Stimulants (second-line or add-on):**
  - **Atomoxetine** (Strattera) – a selective noradrenaline reuptake inhibitor. *Dose:* weight-based in youth (around 0.5–1.2 mg/kg); in adults 40 mg daily titrated to 80–100 mg/day

    nice.org.uk

    . *Side effects:* insomnia or sedation (varies), decreased appetite, nausea, liver enzyme elevations (rarely severe hepatitis), and in adults, possible sexual dysfunction

    nice.org.uk

    . *Special:* Preferred if stimulants are not tolerated or contraindicated (e.g., severe tics, anxiety, or risk of misuse)

    nice.org.uk

    nice.org.uk

    . Takes several weeks for full effect. Monitor blood pressure and watch for mood changes – **suicidal ideation** risk is small but noted in youth

    nice.org.uk

    . Liver injury is rare but advise patients to report abdominal pain/jaundice.

  - **Guanfacine** (Intuniv) – an alpha-2A agonist. *Dose:* Children 6–12 start 1 mg daily, up-titrate weekly (typical 1–4 mg in kids; adolescents up to 7 mg). *Side effects:* sedation, fatigue, low blood pressure, slow heart rate

    nice.org.uk

    . *Special:* Usually used in children/adolescents with inadequate response to stimulants or intolerable side effects

    nice.org.uk

    . Particularly helpful for ADHD with tics or aggression. Not licensed for adults (off-label tertiary care use only)

    nice.org.uk

. Do not stop abruptly – risk of rebound hypertension, so taper to discontinue.

- **Clonidine** – another alpha-2 agonist, historically used off-label for ADHD (especially with tics or sleep problems). *Side effects:* more sedating than guanfacine, can cause rebound hypertension if stopped suddenly. *Special:* Current NICE guidance suggests clonidine only under specialist advice for children with ADHD + significant comorbid issues (like tics or sleep disturbance)

  nice.org.uk

  . Guanfacine has largely superseded clonidine in paediatric ADHD due to a cleaner side-effect profile.

- **Additional notes:** ADHD medication requires periodic monitoring: blood pressure, heart rate, weight, height (for kids) should be recorded at baseline and throughout treatment

  nice.org.uk

  nice.org.uk

  . Insomnia can often be managed by giving doses earlier in the day. If stimulant causes appetite suppression, high-calorie meals when medication effects are lowest (e.g. breakfast or late evening) can help. Medication breaks (with medical advice) can be considered to reassess continuing need, but in adults continuous treatment is often required. All ADHD meds should be initiated by an ADHD specialist, with shared care protocols for GPs to continue prescriptions

  nice.org.uk

  nice.org.uk

  .

Historical Recommendations (Previous First-line Treatments Now Less Used)

Over time, some medications have been replaced by newer ones due to safety or tolerability issues. Below is a list of such medications and **why they are no longer first-line**:

Antidepressants (Historical)

- **Monoamine Oxidase Inhibitors (MAOIs)** – e.g. **Phenelzine** (Nardil), **Tranylcypromine** (Parnate), **Isocarboxazid**. These were among the first antidepressants and are effective, especially for atypical depression and phobias. **Why replaced:** They have serious dietary and drug interaction risks. Tyramine-rich foods can trigger hypertensive crises (dangerously high blood pressure) in patients on MAOIs

  mayoclinic.org

  mayoclinic.org

  . Because of these safety concerns and the inconvenience of dietary restrictions, MAOIs have **"generally been replaced by antidepressants that are safer and cause fewer side effects."**

  mayoclinic.org

  . Now reserved for treatment-resistant cases under specialist care. (Moclobemide, a reversible MAOI, is an option for social anxiety or depression with fewer dietary issues, but its use is limited.)

- **Tricyclic Antidepressants (TCAs) – older agents: Dosulepin** (dothiepin) and **Trimipramine** are examples of TCAs that were widely used but now deprecated. **Dosulepin** in particular is almost never started in new patients. **Why:** NICE explicitly advises **do not prescribe dosulepin** because it's less safe – it's **highly toxic in overdose** and overall more dangerous than other antidepressants

  hweclinicalguidance.nhs.uk

  . (Deaths from dosulepin overdose can occur rapidly)

  hweclinicalguidance.nhs.uk

  Newer SSRIs and SNRIs are as effective and far safer in overdose. Thus dosulepin has been phased out in UK practice (existing patients are reviewed and encouraged to switch)

  hweclinicalguidance.nhs.uk

  . Other older TCAs like **Protriptyline** or **Amoxapine** have also fallen out of use due to side effects.

- **Reboxetine** – a selective noradrenaline reuptake inhibitor introduced in the late 1990s. It was briefly considered for depression but is now rarely used. **Why:** Reboxetine showed inferior efficacy in many trials (it was found significantly less effective than other antidepressants) and can cause side effects like dry mouth, insomnia, urinary retention. NICE guidelines did not recommend it as a first-line option due to questionable risk–benefit.
- **Agomelatine** (Valdoxan) – a novel melatonergic antidepressant. **Why:** Never established in NICE guidance as first-line. The manufacturer did not provide evidence for NICE appraisal, so NICE was *"unable to recommend the use of agomelatine"* on the NHS

  nice.org.uk

  . Additionally, agomelatine requires liver function monitoring (risk of hepatic injury) and its efficacy relative to SSRIs remains debated. Thus it has not supplanted older treatments and is used only sparingly.

Anxiolytics and Hypnotics (Historical)

- **Barbiturates** (e.g. **Phenobarbital**, **Secobarbital**, **Amobarbital**) – These sedative drugs were used in the mid-20th century for anxiety and insomnia. **Why replaced:** Barbiturates have a **very narrow therapeutic index** – the dose causing coma and death is only slightly above the therapeutic dose

  villaoasissandiego.com

  . They presented unacceptably high risks of lethal overdose and caused tolerance and addiction. **Benzodiazepines emerged as a safer alternative**, with a much better safety margin

  villaoasissandiego.com

  villaoasissandiego.com

  . By the 1970s, benzodiazepines had largely replaced barbiturates for anxiety/sleep. Now barbiturates are obsolete for these uses (used only in anaesthesia or refractory epilepsy).

- **Meprobamate** – An older anxiolytic (1950s) once popular for anxiety. **Why:** It has similar risks to barbiturates (sedation, dependence, overdose potential) and was replaced by benzodiazepines by the 1970s.
- **Chloral Hydrate** – a sedative/hypnotic used historically for insomnia or agitation. **Why:** Very limited use now; causes gastric irritation and has safer modern alternatives.
- **Long-term Benzodiazepines** – Benzodiazepines themselves (e.g. **Diazepam**, **Alprazolam**) were once commonly prescribed long-term for

anxiety or insomnia. Now it's recognized that chronic use leads to tolerance, dependence, and withdrawal syndrome. **Why reduced:** Guidelines (including NICE) now advise against long-term benzodiazepines for anxiety

istituto-walden.it

. They are reserved for short durations (2–4 weeks) or intermittent use. For chronic anxiety, SSRIs and therapy are preferred. This represents a shift from earlier decades when benzodiazepines were liberally given; concerns about addiction (the "Valium problem") have made prescribers more cautious.

Antipsychotics (Historical)

- **First-Generation Antipsychotics** (FGAs or "typicals") – e.g. **Chlorpromazine**, **Thioridazine**, **Trifluoperazine**, **Haloperidol** (partially). In the 1950s–70s, these were the only antipsychotics available and were standard for schizophrenia. **Why less used now:** The introduction of **atypical antipsychotics in the 1990s** (e.g. risperidone, olanzapine) provided effective treatment with **fewer extrapyramidal side effects**

  ncbi.nlm.nih.gov

  . Older agents, especially high-potency ones, caused high rates of drug-induced Parkinsonism, akathisia, and tardive dyskinesia (a potentially permanent movement disorder). For example, **Thioridazine** was withdrawn entirely due to cardiotoxicity (QT prolongation causing arrhythmias) and eye toxicity risk. **Chlorpromazine**, while still used occasionally for its sedative properties, is no longer first-line because of sedation, weight gain, and hypotension, and its higher risk of causing tardive dyskinesia with long-term use. **Haloperidol** remains in use (especially for acute psychosis or as a depot), but even it is often second-line to atypicals unless urgent tranquilization is needed. In summary, most patients are now started on atypical antipsychotics, with typicals reserved for specific cases, due to the **lower EPS risk and improved tolerability of atypicals**

  ncbi.nlm.nih.gov

  .

- **Combination Antipsychotic Therapy:** Historically, patients who partially responded might be put on two antipsychotics together or antipsychotics plus

high-dose anticholinergics, etc. Modern practice strives for monotherapy where possible – combining antipsychotics is not routine due to unclear benefit and increased side effects (this is reflected in NICE guidance discouraging routine polypharmacy).

Mood Stabilizers (Historical)

- **Older treatments for mania:** Before modern antipsychotics, sedation for acute mania sometimes involved **barbiturates** or heavy sedation with **chlorpromazine** or **paraldehyde** in asylums. These have fallen away with the advent of specific anti-manic drugs.
- **Carbamazepine** was a go-to for bipolar in the 1980s (especially for those not tolerating lithium). It's still used, but **Valproate** (Depakote) largely replaced it from the 1990s due to broader efficacy in mania and simpler dosing (carbamazepine's interactions and need for blood monitoring made it trickier). Carbamazepine is now a second- or third-line option in bipolar (or for certain subtypes like rapid cycling), rather than first-line.
- **Psychosurgery/ECT**: While not a medication, it's worth noting that prior to modern meds, treatments like continuous barbiturate sedation or even insulin coma were used for severe mental illness. Electroconvulsive therapy (ECT) was overused for chronic schizophrenia in mid-20th century; today it's reserved mainly for severe depression or catatonic schizophrenia, reflecting a historical shift.

ADHD Treatments (Historical)

- **Pemoline** (Cylert) – a stimulant for ADHD used in past decades. **Why no longer used:** Pemoline was withdrawn from the market due to **serious liver toxicity.** The UK stopped using it in 1997 (US in 2005) after cases of acute liver failure

  en.wikipedia.org

  . Safer stimulants (methylphenidate, amphetamines) meant pemoline's risk was unacceptable.

- **Immediate-release stimulants** as sole therapy – In earlier practice, children often took immediate-release methylphenidate or dextroamphetamine 2–3 times daily. This is inconvenient and has higher misuse potential (tablets can be crushed and abused). **Now, long-acting once-daily formulations are preferred** to improve adherence and reduce abuse risk

  nice.org.uk

  . Short-acting formulations are still available, but the trend is toward extended-release unless short action is specifically needed.

- **Clonidine (for ADHD)** – Before **Guanfacine** was approved, clinicians used clonidine off-label for ADHD (especially with tics or severe aggression). Clonidine is effective for some symptoms but causes more sedation and has a

risk of rebound hypertension. Guanfacine, a similar but more selective alpha-2 agonist, was developed as a better option. Now guanfacine (for kids) has largely supplanted clonidine for ADHD, and **clonidine's use is now limited to specialist recommendations** only

nice.org.uk

- **Dietary interventions** – Not a medication, but historically, things like the Feingold diet (artificial colour/preservative-free diet) were popular "treatments" for ADHD in the 1970s/80s. These have fallen out of favour as primary treatment as evidence for effectiveness is weak; modern NICE guidelines emphasize proven medications and behavioural therapy, noting that dietary modifications (other than addressing any overt food sensitivities or deficiencies) are not first-line treatments.

Other Notable Mentions

- **Older antipsychotic use in anxiety/insomnia:** In the past, low-dose **antipsychotics** like **Levomepromazine** or **Chlorpromazine** were sometimes prescribed off-label for anxiety or as sleep aids. Now, due to their side effects, this practice is uncommon (except possibly short-term in acute psychiatric settings). Safer options (non-habit-forming sleep aids or SSRIs for anxiety) are favoured.
- **Ergot Derivatives for dementia or old antidepressants (e.g. Tryptophan):** These saw historical use (tryptophan augmentation for depression, ergoloid mesylates for cognitive impairment), but have no role now due to lack of proven benefit.
- **Parenteral sedative cocktails:** Historically, combinations like "chloral hydrate + promethazine + haloperidol" were used for rapid tranquilization in hospitals. Now we have standardized intramuscular injections (like lorazepam or IM haloperidol plus promethazine) for acute agitation – a refinement of practice.

In summary, **medications fall out of favour when newer therapies offer equal efficacy with improved safety or tolerability.** The above examples show a common theme: drugs with lethal overdose potential, severe side effects, or heavy monitoring needs have been replaced by safer or more convenient options. For instance, benzodiazepines replaced barbiturates for anxiety due to a better safety margin

villaoasissandiego.com
, and atypical antipsychotics replaced many uses of typicals due to fewer movement side effects
ncbi.nlm.nih.gov
. Similarly, within classes, refinement happens – e.g. newer SSRIs over older TCAs for depression
hweclinicalguidance.nhs.uk
, or long-acting stimulants over short-acting in ADHD. The evolution of psychopharmacology is guided by improving patient safety, adherence, and overall outcomes. (Patients who do well on older drugs may continue them, but new patients will usually be started on the modern preferred treatments.)

Sources: The information above is based on the latest NICE guidelines and related authoritative sources, with key points referenced accordingly.

nhs.uk

hweclinicalguidance.nhs.uk

istituto-walden.it

ncbi.nlm.nih.gov