

First-choice antidepressant use in adults with depression or generalised anxiety disorder

Key therapeutic topic

Published: 15 January 2015

[nice.org.uk/guidance/ktt8](https://www.nice.org.uk/guidance/ktt8)

Options for local implementation

- Non-drug interventions are the mainstay of treatment for many people with depression or generalised anxiety disorder, with drugs generally reserved for more severe illness or when symptoms have failed to respond to non-drug interventions.
- Review and, if appropriate, revise prescribing of antidepressants in adults to ensure that it is in line with NICE guidelines on [depression in adults](#), [depression in adults with a chronic physical health problem](#) and [generalised anxiety disorder and panic disorder in adults](#).

Evidence context

The use of antidepressants in adults with depression or generalised anxiety disorder (GAD) has been addressed by the NICE guidelines on [depression in adults](#) (which is being updated; publication expected May 2017), [depression in adults with a chronic physical health problem](#) and [GAD and panic disorder in adults](#). The NICE guideline on [common mental health disorders](#) brings these recommendations together and can be used to help clinicians, commissioners and managers develop effective local care pathways for such people.

See the NICE Clinical Knowledge Summaries on [depression](#) and [GAD](#) for general overviews of these conditions. The NICE pathways on [depression](#) and [GAD](#) bring together all related NICE guidance and associated products on antidepressants in a set of interactive topic-based diagrams. See also specific NICE guidelines on [antenatal and postnatal mental health](#), [depression in children and young people](#) (recommendations on psychological therapies and antidepressants were

updated in March 2015) and [social anxiety disorder](#). The NICE quality standards on [depression in adults](#), [depression in children and young people](#), and [anxiety disorders](#) describe concise sets of prioritised statements designed to drive measurable quality improvements within these areas.

NICE advocates a stepwise approach to managing common mental health disorders. It recommends offering, or referring people for, the least intrusive and most effective intervention first. Therefore, non-drug interventions (such as cognitive behavioural therapy [CBT]) should be the mainstay of treatment for many people with depression or GAD, with drugs generally reserved for more severe illness or when symptoms have failed to respond to non-drug interventions.

Prescribing data suggest that there is variation in antidepressant prescribing across localities. In view of the NICE guideline on [common mental health disorders](#), a review of local antidepressant prescribing is advised. This should be considered alongside the local availability of non-drug treatments, such as CBT.

If an antidepressant is indicated for an adult with depression, the NICE guideline on [depression in adults](#) recommends that it should normally be a selective serotonin reuptake inhibitor (SSRI) in generic form. SSRIs are equally effective as other antidepressants and have a favourable risk–benefit ratio. Similarly, if drug treatment is indicated for GAD, and an adult chooses to take medication, the NICE guideline on [GAD in adults](#) recommends offering an SSRI with sertraline as the first-line option because it is the most cost-effective drug for this condition. However, prescribers should note that sertraline does not currently have a UK marketing authorisation for GAD, so prescribing would be off-label^[1]. The NICE guideline on [depression in adults](#) recommends that dosulepin should **not** be prescribed for adults with depression because evidence supporting its tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose.

The full guideline on [depression in adults](#) concluded that antidepressants have largely equal efficacy and that choice should mainly depend on side-effect profile, people's preference and previous experience of treatments, propensity to cause discontinuation symptoms, safety in overdose, interactions and cost. However, a generic SSRI is recommended as first-choice because SSRIs have a favourable risk–benefit ratio. Neither escitalopram nor any of the available 'dual action' antidepressants, such as venlafaxine and duloxetine, were judged to have any clinically important advantages over other antidepressants. Results from meta-analyses ([Gartlehner et al. 2011](#) and 3 Cochrane reviews: [Cipriani et al. 2012, CD006534](#), [Cipriani et al. 2012, CD006533](#) and [Purgato et al. 2014, CD006531](#)) have provided no evidence to depart from NICE guidance when selecting antidepressants for people with depression.

The full guideline on [GAD and panic disorder in adults](#) found that of the antidepressants available, there were sufficient clinical-effectiveness data and an acceptable harm-to-benefit ratio for escitalopram, duloxetine, paroxetine, sertraline and venlafaxine XL. However, the economic analysis concluded that sertraline was the most cost-effective drug for people with GAD because it was associated with the highest number of quality-adjusted life years (QALYs) gained and the lowest total costs among all treatments assessed, including no treatment. As with depression, drug choice in GAD should also be influenced by several other factors relating to the individual person, including their previous experience of treatments, likely drug interactions, safety and tolerability.

Drug safety warnings on antidepressants that have been issued by the MHRA should be considered. The MHRA has issued [guidance on the use and side effects of SSRIs and serotonin and noradrenaline reuptake inhibitors \(SNRIs\)](#), their safety, use in pregnancy and the risk of suicidal behaviour (published December 2014). See the [December 2007 edition of Drug Safety Update](#) for information on measures to reduce risk of fatal overdose with dosulepin and the [December 2011 edition of Drug Safety Update](#) for details about the association of dose-dependent QT interval prolongation with citalopram and escitalopram. In addition, the [November 2014 edition of Drug Safety Update](#) issued a reminder to test liver function before and during treatment with agomelatine.

Concerns have been raised regarding the over-use of psychotropic medicines such as antipsychotics and antidepressants in people with learning disabilities. This is addressed in 3 reports published in 2015 by the [Care Quality Commission](#), [Public Health England](#) and [NHS Improving Quality](#).

^[1] In line with the [guidance from the General Medical Council \(GMC\)](#), it is the responsibility of the prescriber to determine the clinical need of the patient and the suitability of using a medicine outside its authorised indications. Informed consent should be obtained and documented.

Prescribing data

Three [prescribing comparators](#) are available to support this key therapeutic topic^[2]:

- **Antidepressant (selected): ADQ/STAR PU (ADQ based):** the total number of average daily quantities (ADQs) for selected antidepressant prescribing per Antidepressants (BNF 4.3 sub-set) ADQ based Specific Therapeutic Group Age-sex weightings Related Prescribing Unit (STAR-PU).

- **Antidepressants: first choice % items:** the number of prescription items for SSRIs (sub-set of BNF 4.3.3) prescribed by approved name as a percentage of the total number of prescription items for 'selected' antidepressants (sub-set of BNF 4.3).
- **Dosulepin % items:** the number of prescription items for dosulepin as a percentage of the total number of prescription items for 'selected' antidepressants (sub-set of BNF 4.3).

Antidepressants: ADQ/STAR-PU

- Data for the quarter April to June 2015 show a 3.7 fold variation in prescribing rates at Clinical Commissioning Group (CCG) level, from 0.14 to 0.50 ADQ/STAR-PU.
- Between Q2 2013/14 (July to September 2013) and Q1 2015/16 (April to June 2015) there was an 11.5% increase in the comparator value for England (total prescribing) from 0.30 to 0.33 ADQ/STAR-PU.
- Over the same period there was a 17.4% increase in the variation between CCGs, as measured by the inter-decile range, an absolute increase of 0.03 ADQ/STAR-PU. The inter-decile range is the difference between the highest and lowest values after the highest and lowest 10% of values have been removed.

Antidepressants: first choice % items

- Data for the quarter April to June 2015 show a 1.3 fold variation in prescribing rates at CCG level, from 59.7% to 79.3%.
- Between Q2 2013/14 (July to September 2013) and Q1 2015/16 (April to June 2015) there was a 0.53% decrease in the comparator value for England (total prescribing) from 69.6% to 69.2%.
- Over the same period there was a 2.55% increase in the variation between CCGs, as measured by the inter-decile range, an absolute increase of 0.23%. The inter-decile range is the difference between the highest and lowest values after the highest and lowest 10% of values have been removed.

Dosulepin % items

- Data for the quarter April to June 2015 show a 10.2 fold variation in prescribing rates at CCG level, from 0.56% to 5.66%.

- Between Q2 2013/14 (July to September 2013) and Q1 2015/16 (April to June 2015) there was a 28.2% decrease in the comparator value for England (total prescribing) from 3.14% to 2.25%.
- Over the same period there was a 26.7% decrease in the variation between CCGs, as measured by the inter-decile range, an absolute decrease of 0.77%. The inter-decile range is the difference between the highest and lowest values after the highest and lowest 10% of values have been removed.

The [medicines optimisation dashboard](#), which brings together a range of medicines-related quality indicators from across sectors, includes several mental health metrics related to this key therapeutic topic. These include 2 of the prescribing comparators outlined above (Antidepressant [selected]: ADQ/STAR PU [ADQ based] and Antidepressants: first choice % items) plus:

- Depression (DEP002) % achieving upper threshold or above, which is the percentage of practices in a CCG that achieve upper threshold or above (80% or more inclusive of exceptions) for QOF indicator DEP002.
- Depression (DEP002) % underlying achievement, which is the percentage underlying achievement at CCG level for QOF indicator DEP002 inclusive of exceptions.

^[2] The comparator and associated data presented here are based on the previous Key therapeutic topics publication (January 2015). Data provided by the [Health and Social Care Information Centre](#) (October 2015; source: [Information Services Portal](#), Business Services Authority). For details of any update to the comparators refer to the [Health and Social Care Information Centre](#) website and the [Information Services Portal](#), Business Services Authority.

Update information

February 2016 This topic was retained for the 2016 update of Medicines optimisation: key therapeutic topics. The evidence context has been updated in the light of new guidance and important new evidence as appropriate.

About this key therapeutic topic

This document summarises the evidence base on this key therapeutic topic which has been identified to support Medicines Optimisation. It is not formal NICE guidance.

For information about the process used to develop the Key therapeutic topics, see the [integrated process statement](#).

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ISBN: 978-1-4731-0941-4