SHARED CARE GUIDELINE

Pennine Care NHS
NHS Foundation Trust

Shared Care Guideline for the prescribing and monitoring of Selective Serotonin Reuptake Inhibitors (SSRIs) for the treatment of Anxiety in children and adolescents.	
Scope: Pennine Care NHS Foundation Trust NHS Bury NHS Oldham NHS Heywood, Middleton and Rochdale NHS Stockport NHS Tameside & Glossop	**Version:** Version 1
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To be read in conjunction with the following documents:	BNF 62 September 2011 BNF for children 2011-2012 Summary of Product Characteristics (SPC) Pharmaceutical company's patient information leaflet (PIL) **Pennine Care CL 16** The Prescribing, Supply and use of Unlicensed Medicines **Pennine Care CL17** The use of Licensed Medicines outside the conditions of their Product Licence
Authorised by:	Drugs and Therapeutics Committee, Pennine Care NHS Foundation Trust
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1. Scope

Pennine Care NHS Foundation Trust and associated Primary Care Trusts (PCTs). Acute Trust Service Level Agreement (SLA) partners.

2. Introduction

This shared care guideline covers prescribing of selective serotonin re-uptake inhibitors (SSRIs) for anxiety in children and young people for licensed indications, and for recommended or accepted off-label prescribing.

Like many paediatric medicines, some uses of SSRIs in this age group are with informed use of off-label prescribing.

In 2000, the Royal College of Paediatrics and Child Health issued a policy statement on the use of unlicensed medicines or the use of licensed medicines for unlicensed applications, in children and young people. This states clearly that such use is necessary in paediatric practice and that doctors are legally allowed to prescribe unlicensed medicines where there are no suitable alternatives and where the use is justified by a responsible body of professional opinion. [1]

Anxiety disorders in childhood and adolescence are highly prevalent about 5-18 percent of children and often debilitating and potentially disabling [2,3]. They can cause serious disruption to children's lives and are often persistent over time, leading to increased risks of anxiety disorders, major depression, substance misuse and educational underachievement in later life [3]. The anxiety disorders include panic attacks, phobias, social anxiety and generalised anxiety disorder. Many randomised controlled trials support cognitive behaviour therapy as an effective treatment in mild to moderately ill children. Hence medication is considered useful when the symptoms are affecting their day to day activities including education, social and family life.

The SCG recognises there are differences in commissioning of Child and Adolescent Mental Health Services across the Trust for 16 to 18 year olds and that there are differences in the practice of prescribing and supervision for 16 to 18 year olds by working age adult psychiatrists.

3. Supporting Information

Selective serotonin reuptake inhibitors (SSRIs) have been shown to have short-term efficacy and safety in the treatment of childhood anxiety disorders [4,5]. More recently however results have been published for an open label, long term extension to a controlled clinical trial in which fluoxetine was used to treat childhood anxiety disorders [6]

A Cochrane review looking at pharmacotherapy (SSRIs and other medications) for anxiety disorders in children and adolescents found that medication treatments can be effective in paediatric anxiety disorders, acting to reduce core symptoms, and should be considered as part of the treatment of these disorders [7]. The SSRIs fluoxetine, sertraline and citalopram are commonly used in practice. The latter two are already recommended by NICE for Obsessive Compulsive Disorder (OCD) for children and adolescents [8].

The Research Unit on Paediatric Psychopharmacology Anxiety Study Group conducted a well-designed, large-scale RCT that compared fluvoxamine (up to a maximum dose of 300 mg/day) with placebo in 128 children and adolescents with social phobia, separation anxiety disorder or generalised anxiety disorder, all of whom had failed to respond to 3 weeks of psychological therapy [4]. Children in the fluvoxamine group showed greater reductions on both the Paediatric Anxiety Rating Scale and the Clinical Global Impression of Improvement Scale than those receiving placebo. Few dropped out from either group as a result of adverse events, suggesting that

fluvoxamine (SSRI) is an efficacious and safe treatment for anxiety in this population [2].
A subsequent small RCT comparing sertraline at a dose of up to 50 mg/day against placebo in 22 children and adolescents with generalised anxiety disorder also reported significant global improvements and a decrease in anxiety symptoms beginning after 4 weeks of treatment [5].
Another RCT showed sertraline in combination with CBT resulted in similar results [9].

4. Prescribing and monitoring

The starting dose of medication for children and young people with anxiety should be low, especially in younger children. A half or quarter of the normal starting dose may be considered for the first week.

If a lower dose of medication for children and young people with anxiety is ineffective, the dose should be increased until a therapeutic response is obtained, with careful and close monitoring for adverse events.

4.1 Summary of indications, dosage & formulations

Drug	Licensing	Formulations	Dose range (daily)
Fluvoxamine	Unlicensed	Tablets	50mg once daily Age 6-11yrs max. 200mg/day Age 12yrs or over max. 300mg
Sertraline	Unlicensed	Tablets	25mg – 200mg daily Max. 200mg
Citalopram	Unlicensed	Tablets Oral solution 40mg/ml	10mg – 20mg once daily Max. 40mg 4 drops (8mg) is equivalent to a 10mg tablet
Fluoxetine	Unlicensed	Tablets Liquid	10mg – 20mg Max. 20mg

[6, 8-12]

4.2 Monitoring

Patients should be reviewed every 1–2 weeks at the start of antidepressant treatment.

Hyponatraemia has been associated with all types of antidepressants; however, it has been reported more frequently with SSRIs than with other antidepressants. Hyponatraemia should be considered in all patients who

develop drowsiness, confusion, or convulsions while taking an antidepressant. [13]

Suicidal behaviour and antidepressant therapy
The use of antidepressants has been linked with suicidal thoughts and behaviour; children, young adults, and patients with a history of suicidal behaviour are particularly at risk. Where necessary patients should be monitored for suicidal behaviour, self-harm, or hostility, particularly at the beginning of treatment or if the dose is changed.
For those patients at a high risk of suicide, a limited quantity of medication should be prescribed. [14]

(Please also see CSM advice on suicidal behaviour on page 6)

5. Regimen Management

Aspects of care for which the Specialist is responsible. The term Specialist includes Child and Adolescent Psychiatrist, Paediatrician, or nominated Advanced Practitioner/ Non Medical Prescriber (in agreement with their medical supervisor):

- Direct assessment or supervision of specialist team assessment, evaluation of prior treatment, and rationalisation of treatment with appropriate SSRI.
- Informing patient/ carer of diagnosis, care plan, treatment including side effects and use of unlicensed product. Use of Patient Information Leaflets (PILs), user-friendly information leaflets for children/ adolescents.
- Treatment decisions should be shared between patient, carer and the Specialist.
- Informing young person/ carers of the latest regulatory advice.
- Ascertaining patient/ family's commitment to safe storage and handling of medication.
- Asking General Practitioners (GP) if they are willing to participate in shared care.
- Initiation and titration of medication to a suitable dose or provide instructions/directions to the GP for initiation and titration of medication to a suitable dose where agreed.

- Written correspondence to GP from Specialist Team, summarising progress and recommendations for continued treatment.
- Ensure clear arrangements for GP back up, advice and support.
- To inform young person/ carer of the risk of mood or physical side effects, particularly around initiation and cessation of treatment.
- Monitoring response to treatment, and adverse effects.
- Ensure patients are monitored for suicidal behaviour, self-harm or hostility particularly at the beginning of treatment. . A person with depression started on antidepressants who is considered to present an increased suicide risk should normally be reviewed after one week and frequently thereafter as appropriate until the risk is no longer considered clinically significant.
- Ensuring concurrent psychological therapy is offered.
- If one is needed, use a recognised self-report rating scale such as the Mood and Feelings Questionnaire (MFQ).
- Promoting access to any appropriate supporting therapies, carer education, and appropriate school liaison.
- Minimum 6 monthly Specialist review appointments 'once established on treatment'
- Reporting suspected adverse events to the GP and the MHRA via the Yellow Card scheme to www.mhra.gov.uk/yellowcard
- Discontinuation of treatment, (or transfer if appropriate).

Aspects of care for which the GP is responsible:

- Replying to requests for shared care as soon as possible.
- Initiation and titration of SSRI where agreed / continued prescribing of SSRI in the community under guidance of Consultant/ Specialist Team.
- To undertake appropriate investigations, during treatment if requested to do so by the Consultant.
- Refer to the Consultant/Specialist Team for queries regarding treatment/side effects, and concerns about compliance or suspected drug misuse.

- To be aware of the risk of mood or physical side effects, particularly around initiation and cessation of treatment.
- Ensure compatibility of SSRI with concomitant prescribed medication.
- Stopping treatment on the advice of the Consultant/Specialist team.
- Continuation without specialist review is not recommended.
- Reporting suspected adverse events to the Specialist team and the MHRA via the Yellow Card scheme to www.mhra.gov.uk/yellowcard

6. Summary of cautions, contra indications, side effects & interactions

Please refer to the current edition of the BNF and BNF for Children and Summary of Product Characteristics (SPCs) of the individual drugs for the latest list of contraindication, cautions, side effects and interactions.

Contra-indications –
current episode mania

Citalopram has been found to cause a dose-dependent increase in the QT interval on the electrocardiogram (ECG).
Citalopram is:

- contraindicated in patients with known QT prolongation or congenital long QT syndrome
- contraindicated in patients taking other medicines known to prolong the QT interval
- to be used with caution in patients at risk of developing Torsades de Pointes [11].

Cautions

SSRIs should be used with caution in patients with epilepsy (avoid if poorly controlled, discontinue if convulsions develop)

cardiac disease

diabetes mellitus

susceptibility to angle-closure glaucoma

a history of mania

history of bleeding disorders (especially gastro-intestinal bleeding), and if used with other drugs that increase the risk of bleeding

SSRIs should also be used with caution in those receiving concurrent electroconvulsive therapy (prolonged seizures reported with fluoxetine).

SSRIs may also impair performance of skilled tasks (e.g. driving)

CSM advice on risk of suicidal behaviour in young adults treated with SSRIs.

Careful and frequent patient monitoring by healthcare professionals, and where appropriate other carers, is important in the early stages of treatment, particularly if a patient experiences worsening of symptoms or if new symptoms arise after starting treatment.

If a patient is not doing well after starting treatment the possibility of an adverse reaction to the drug should be considered. Patients should be monitored for signs of restlessness or agitation, particularly at the beginning of treatment. Increasing the dose in these circumstances may be detrimental.

Patients should be monitored around the time of dose changes for any new symptoms.

To minimise withdrawal reactions on stopping SSRIs, the dose should be tapered gradually over a period of several weeks, according to the patient's need [15]

Side Effects

Gastro-intestinal effects (dose-related and fairly common—include nausea, vomiting, dyspepsia, abdominal pain, diarrhoea, constipation),

Anorexia with weight loss (increased appetite and weight gain also reported)

Hypersensitivity reactions

Dry mouth, urinary retention, sweating

Nervousness, anxiety

Headache, insomnia, hallucinations, drowsiness

Dizziness, asthenia

Galactorrhoea, sexual dysfunction

Hypomania or mania (see Cautions above),

Convulsions (see Cautions above), movement disorders and dyskinesia

Visual disturbance

Hyponatraemia should be suspected in anyone with drowsiness, confusion, nausea, cramps or seizures.

Bleeding disorders

Interactions

Anti-epileptics

An SSRI or related antidepressant should not be started until 2 weeks after stopping a monoamine oxidase inhibitor (MAOI). Conversely, an MAOI should not be started until at least a week after an SSRI or related antidepressant has been stopped (2 weeks in the case of sertraline, at least 5 weeks in the case of fluoxetine).

St John's Wort.

Fluoxetine inhibits the hepatic cytochrome P450 2D6 enzyme. Concomitant therapy with drugs also metabolised by this enzyme system may lead to drug interactions.

Sertraline and citalopram are weak inhibitors of cytochrome P450 enzyme, so interactions with other drugs are possible.

7. Special Considerations

Handover for shared care largely by written agreement. Individual consideration of patients to occur when issues of tolerance, inconsistent response to treatment, pre-existing medical conditions or issues of patient compliance.

8. Back-up care available to GP from Hospital, including emergency contact procedures and help line numbers.

Written correspondence following Consultant/ Specialist Team appointments, specifically detailing the next review date and any dose adjustments.

Telephone advice/ information from the Consultant / Specialist Team during office hours, and plans for earlier review by team if necessary.

Dr [insert text here]_____

Contact number: [insert text here] _____

Hospital: [insert text here]_____

Out of hours on call/ emergency mental health service contactable through hospital switchboards.

9. Statement of Agreement between GP and Consultant

This document outlines the suggested care pathway of your patient. If you are unable to agree to the sharing of care and prescribing the suggested medication, please make this known to the Consultant within 14 days stating the nature of your concern.

10. Written information provided to patient

- Pennine Care NHS Foundation Trust Patient Information Leaflet
- Patient information leaflet

11. Supporting references

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13. BNF 63, March 2012 and BNF for Children 2011- 2012

14. Overview of regulatory status and CSM advice relating to major depressive disorder (MDD) in children and adolescents. Medicines and Healthcare products Regulatory Agency (MHRA). 2005

15. Summary of Product Characteristics. www.medicines.org.uk