



**GREATER MANCHESTER INTERFACE
PRESCRIBING GROUP**



On behalf of the
GREATER MANCHESTER MEDICINES MANAGEMENT
GROUP

SHARED CARE GUIDELINE FOR THE PRESCRIBING OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs) FOR MAJOR DEPRESSION IN CHILDREN AND ADOLESCENTS BELOW 18 YEARS OF AGE		Reference Number Version 3
Scope: As above		Classification: SHARED CARE GUIDELINE
Issue date	1 November 2011	
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To be read in conjunction with the following documents	MM027 Guidelines on prescribing pharmacological treatment for depression in children and young people below 18 years of age. BNF 61 March 2011 cBNF 2011-2012 Summary of Product Characteristics (SPC)	
Authorised by	Drugs & Therapeutics Committee	21 October 2011 (then expiry date extended June 2015)
Review Date	31 December 2015	

1. Introduction

This shared care guideline covers prescribing of selective serotonin re-uptake inhibitors (SSRIs) for major depression in children and young people. Like many paediatric medicines, the prescribing for depression in children and young people is through the 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]

This Shared Care Guideline has been developed based on clinical decision making. There may be outstanding commissioning issues which are outside the remit of the document.

2. Background to the use of SSRIs for major depression in children and adolescents

a) Regulatory Framework

In December 2003, the Committee on Safety of Medicines advised that the balance of risks and benefits was favourable only for fluoxetine in treatment of major depression in under 18 year olds.

The CSM also went on to accept that on occasion, psychiatrists may use other SSRIs when patients have not tolerated or responded to fluoxetine. The risk versus benefit assessment and informed discussion with young person and carer would be managed by the responsible psychiatrist.

The lack of wider clinical trials on medicines for major depression in the childhood population is recognised as adding to the limitation in evaluating their safety and efficacy. *The CSM warnings apply only to major depression and not to other disorders treated with SSRIs.* [2]

b) Summary of the studies considered by the NICE Childhood Depression Working Group and by the Medicines and Health Products Regulatory Agency (MHRA) suggested:

- fluoxetine has consistent evidence of clinical improvement across a range of outcome measures.
- sertraline and citalopram have more limited and inconsistent evidence for clinical improvement, but the risk / benefit ratio is less unfavourable than for the remaining SSRIs.

3. Summary of NICE guidance covering medication for childhood and adolescent major depression

Medication is recommended for moderate to severe childhood depression only, which is unresponsive to psychological therapy after 4-6 sessions, and after specialist assessment. Concurrent psychological therapy and review is recommended alongside any medication. [3]

Antidepressant medication is recommended for children aged 12-18 years; fluoxetine may be prescribed to children from 5 years with extreme caution. However, it is licensed for children of 8 years of age and above.

1st line option – Fluoxetine

2nd line option – Sertraline or Citalopram

4. Prescribing and monitoring

Summary of dosage & formulations for use in major depression

SSRI	DOSAGE RANGE	FORMULATION
FLUOXETINE (LICENSED) 1st line	Child 8-18 years: 10mg once daily. Increased if necessary after one-two weeks. Max. 20mg once daily. NOTE: higher doses up to 40mg once daily may be considered in older children of higher body weight	Capsules Liquid
SERTRALINE (UNLICENSED) 2nd line	Child 12-18 years: 50mg once daily. Increased if necessary in steps of 50mg at intervals of at least a week. Max. 200mg once daily.	Tablets
CITALOPRAM (UNLICENSED) 2nd line	Child 12-18 years: Tablets: 10mg once daily. Increased if necessary over two-four weeks. Max. 60mg once daily Drops: 8mg once daily. Increased if necessary to 16mg over two-four weeks. Max. 48mg once daily. (8mg drops=10mg tablet)	Tablets Oral drops (can be mixed with water, orange or apple juice)

[4] [5]

Criteria for 2nd line treatment:

- persistent clinical severity.
- ineffective trial of 1st line treatment.
- reasonable exclusion of other likely causes of treatment resistance.
- following peer review or 2nd opinion from CAMHS specialist team.
- informed discussion with child/ carer, with latest regulatory information.
- written consent from young person /carer as appropriate.

Specialist Services will offer patients SSRIs for moderate to severe depression after assessment and where psychological therapy alone is insufficient (or unavailable). They will undertake informed discussion about risks and benefits of proposed treatment with young person and carers.

Specialist Services will provide advice on choice of drug, initiation, titration and monitoring. Monitoring clinical outcomes and side effects will generally take place in secondary care specialist mental health services

Paroxetine, venlafaxine, tricyclic antidepressants, mirtazapine, or St John's Wort are not recommended for treatment of major depression in children and adolescents.

Monitoring

Patients should be reviewed every 1–2 weeks at the start of antidepressant treatment. Treatment should be continued for at least 4 weeks before considering whether to switch antidepressant due to lack of efficacy. In cases of partial response, continue for a further 2–4 weeks.

Following remission, antidepressant treatment should be continued at the same dose for at least 6 months. Patients with a history of recurrent depression should receive maintenance treatment for at least 2 years.

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.

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. [4]

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

6. 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 SSRI to a suitable dose or supplying instructions/directions to the GP for initiation and titration of SSRI to a suitable dose.
- 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.
- Reporting suspected adverse drug reactions to the MHRA.
- Discontinuation of treatment, (or transfer if appropriate).

NB. For young people over 18 years on SSRIs, who are outside the current CAMHS age range, monitoring arrangements will be necessarily also subject to local agreement between primary care and working age adult specialist mental health services.

Aspects of care for which the GP is responsible:

- Replying to requests for shared care as soon as possible.
- Initiation and titration of SSRI / continued prescribing of SSRI in the community under guidance of Consultant/ Specialist Team.
- 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 noted adverse events to the Consultant/Specialist Team.

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

Please also refer to BNF and SPC [4] [5] [6]

Contra-indications – current episode mania

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.
- They 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 with depression.

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 or worsening of disease.

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. [2]

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 an 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.

8 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.

9 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.

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

10 Statement of Agreement between GP and Consultant.

This form 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.

11 Written information provided to patient

- Pennine Care NHS Foundation Trust Patient Information Leaflet
- CG28 Depression in children and young people: NICE guideline
- Patient information leaflet

12 References

1. Joint Royal College of Paediatrics and Child Health/Neonatal and Paediatric Pharmacists Group Standing Committee on Medicines, 2000.
2. MHRA – Overview of regulatory status and CSM advice relating to MDD in children and adolescents 2005
3. NICE Clinical Guideline 28: Depression in children and young people: Identification and management in primary, community and secondary care September 2005
4. BNF Number 61, March 2011
5. BNF for Children 2011- 2012
6. Summary of Product Characteristics. www.medicines.org.uk
7. MM 027 Pennine Care NHS Foundation Trust Guidelines for prescribing pharmacological treatment for depression in children and young people below 18 years of age.