Clonidine for Tic Disorders in Children and Young People

Traffic light classification - Amber 2
Information sheet for Primary Care Prescribers

Indications

Tic Disorders including:

- Chronic Motor Tic Disorder
- Chronic Vocal Tic Disorder
- Transient Tic Disorder
- Tourette Syndrome in children, young people and adults as part of a comprehensive treatment program

These are off-label (unlicensed) indications for both adults and children.

Therapeutic summary

Clonidine is a noradrenergic (a-2 agonist) treatment recommended by the European Clinical Guidelines for Tourette Syndrome and other Tic Disorder[1]. It is indicated as a treatment for tics particularly in children where the side effect profile is more benign compared to antipsychotic medication.

Clonidine is one of many medicines that have been tried in the management of Tourette's syndrome and tic disorders which are hypothesised to be related to disturbance of monoamine metabolism (including dopamine, noradrenaline, and serotonin) in the brain. Clonidine is thought to reduce central noradrenergic activity by stimulating a-2 receptors which are responsible for the regulation of noradrenaline by negative feedback.

Response to clonidine is usually seen within 4-6 weeks which families need to be made aware of and supported through this time.

Medicines Initiation

Treatment with clonidine should only be initiated by a specialist (child and adolescent psychiatrist, psychiatrist, paediatrician or appropriately qualified non-medical prescriber) with expertise in tic disorders following a comprehensive assessment and diagnosis.

Products available

Clonidine 25microgram tablets. Cost x 112 tablets = £5.01[2]
Clonidine 100microgram tablets. Cost x 100 tablets = £8.04[2]
Clonidine 50micrograms/5mL oral solution sugar-free. Cost x 100mL = £109.19[2] (non formulary and should not be used).

Dosages and route of administration

- Clonidine is given orally with or without food.
- It is usually given in two – three divided doses daily to reduce the risk of side effects.
- The initial dose and subsequent dosing will be determined by the specialist and stated in written communication.
- The usual starting dose is 25 microgram once daily at night with subsequent titrations of 25 microgram increments. Titrations should be weekly to fortnightly depending on response and tolerance to side effects where some children may prefer to be titrated more cautiously.

- The therapeutic window of clonidine, as described in the Maudsley Prescribing Guidelines[3], is 3-5 microgram per kg of body weight up to a maximum dose of 150-200 microgram daily.
- Most of the dose is usually administered at night to avoid sedation during the day. This also has the added benefit of treating co-morbid sleep difficulties.

Duration of treatment
Following an adequate treatment response, drug treatment should be continued for as long as it remains clinically effective with a regular 6 monthly review when stable. This includes 6 monthly physical monitoring (blood pressure, pulse, weight, and height).

In adolescents whose symptoms persist into adulthood, and who have shown clear benefit from treatment, it may be appropriate to continue treatment into adulthood. Often in later teenage years young people and adults find that their symptoms naturally reduce to a more tolerable level especially after moving into a more conducive education or work environment.

If symptoms reduce, or for any other reason the young person wishes to reduce and withdraw treatment, typically this is done by reducing the overall dose by 25 micrograms. This can be done every 2-4 days[4]. Some individuals prefer to reduce the dose slower than this to be able to judge any exacerbation in severity and frequency of symptoms. It is advisable not to decrease the dose any quicker than this due to the risk of rebound hypertension on abrupt withdrawal.

Treatment discontinuation
There is a risk of rebound hypertension on abrupt clonidine withdrawal. Clonidine should be reduced gradually in 25microgram increments every 2-4 days[4].

Monitoring Requirements and Responsibilities
Pre-treatment assessment to be performed by specialist and will include:
Assessment of Tics using the Yale Global Tic Severity Scale, descriptive reports from the service user/parents/school (if deemed necessary) to obtain longevity of symptoms, medical history, family history and review of physical health (including height, weight, baseline blood pressure and pulse).

Ongoing monitoring
Baseline monitoring will be performed by the specialist. Further monitoring may be performed by primary care and the results sent to the specialist for recording in the patients notes. If the monitoring can't be facilitated by primary care, it should be continued by the specialist and the results communicated to the GP in writing for recording in primary care notes.

Ongoing monitoring of the patient's response and assessment of continued need will be carried out by the specialist every 6 months.

Ongoing monitoring	Frequency
Heart Rate and Blood Pressure	Baseline and six monthly Before and after each dose change. Compare with previous measurements. Information on blood pressure and heart rate monitoring in children (including centile reference tables) is available on the Nottinghamshire Area Prescribing Committee website.
Weight and Height	Baseline and six monthly
ECG	Not recommended unless there is a clinical indication.

Blood monitoring	Not recommended unless there is a clinical indication.
Medication related side-effects*	At each visit

*Consider using standard symptom and side effect rating scales during treatment as an adjunct to clinical assessment.

Explicit criteria for review and/or discontinuation of clonidine

Sustained resting bradycardia	Consider dose reduction and discuss with the specialist team. Seek cardiology input if necessary.
Orthostatic hypotension	Consider dose reduction if there are immediate concerns. Discuss with the specialist team.
Dry mouth	Discuss with specialist team.
Sedation	Discuss with specialist team.
Repeated sudden withdrawal of clonidine	Sudden withdrawal places patient at risk of rebound hypertension. Discuss with specialist.
Patient/family requesting dose change	Discuss with specialist as a review will be needed. Physical observations could be obtained in primary care.
Failure to attend for physical monitoring checks	There is a risk of rebound hypertension on abrupt clonidine withdrawal. It may be appropriate to provide repeat prescriptions if a patient misses one physical health monitoring appointment and a follow up appointment can be arranged. If multiple appointments are missed, repeat prescriptions should not be issued and the specialist should be informed. The patient and carer should be informed of the safest way to reduce clonidine to avoid the risk of rebound hypertension.

For a full list of Side Effects refer to the BNF/BNFC or Summary of Product Characteristics (SPC).

IF YOU ARE IN ANY DOUBT ABOUT ANY POTENTIAL ADVERSE REACTION, PLEASE CONTACT THE SPECIALIST TEAM.

Contraindications[4,5]

- Severe bradyarrhythmia resulting from either sick-sinus syndrome or AV block of 2nd or 3rd degree.
- Known hypersensitivity to the active substance or to any of the excipients listed in SPC.

Precautions[4,5]

- Cerebrovascular disease, coronary insufficiency, and heart failure
- Mild to moderate bradyarrhythmia
- Occlusive peripheral vascular disorders such as Raynaud's disease
- Polyneuropathy
- Constipation
- History of depression
- Renal insufficiency
- Abrupt withdrawal should be avoided; it is associated with rebound hypertension, agitation, restlessness, tremor, palpitations, headache, and nausea.
- May cause decreased lacrimation.

Pregnancy and Breast-Feeding[4,5]

There is a limited amount of data on the use of clonidine in pregnant women. Clonidine passes the placental barrier and may lower fetal heart rate. Clonidine should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

Clonidine is excreted in human breast milk and therefore should be avoided in breast feeding[4].

Clinically Relevant Medicine Interactions and their Management[4,5]

- Antihypertensive agents – concurrent use may lead to an increased hypotensive effect
- Diuretics - concurrent use may lead to an increased hypotensive effect
- Vasodilators - concurrent use may lead to an increased hypotensive effect
- Beta blockers – concurrent use can cause bradycardia, dysrhythmia, and hypotension
- Cardiac glycosides - concurrent use can cause bradycardia or dysrhythmia
- Mirtazapine – may antagonize the antihypertensive effect of clonidine (but note that antihypertensive effect is not the desired clinical effect of clonidine)
- Tricyclic antidepressants – may reduce or abolish the antihypertensive effects of clonidine (but note that antihypertensive effect is not the desired clinical effect of clonidine)
- Monoamine oxidase inhibitors (MAOIs) - concurrent use may lead to an increased hypotensive effect
- Antihistamines – additive CNS depressant effects
- Antipsychotics – concurrent use with phenothiazine antipsychotics may lead to an increased hypotensive effect
- Anxiolytics and hypnotics – additive CNS depressant effects
- Guanfacine - concurrent use may lead to an increased hypotensive effect

For a full list of contraindications, precautions and drug interactions refer to the BNF/BNFC and SPC.

Information Given to Patient / Carer

- The specialist will provide relevant, age-appropriate written information to people with tic disorder and their families and carers about diagnosis, assessment, support groups, self-help, psychological treatment, drug treatment and possible side-effects.
- Written information sheets can be found at:

Medicines for Children – Clonidine for Tourette's syndrome, ADHD and sleep-onset disorder

Specialist contact details

Patients prescribed clonidine for the treatment of tic disorders are likely to be under community or hospital paediatric services or child and adolescent mental health services (CAMHS). Contact the relevant clinic from the information provided in individual patient correspondences.

References and Version Control

1. Roessner V, Plessen KJ, Rothenberger A, Ludolph AG, Rizzo R, Skov L, Strand G, Stern JS, Termine C, Hoekstra PJ; ESSTS Guidelines Group. European clinical guidelines for Tourette syndrome and other tic disorders. Part II: pharmacological treatment. Eur Child Adolesc Psychiatry. 2011 Apr;20(4):173-96.
2. The Electronic Drug Tariff https://www.drugtariff.nhsbsa.nhs.uk/#/00798052-DC/DC00798043/Home [Accessed on 10/02/2022].
3. Taylor, DM., Barnes, TRE., Young, AH. 2021. The Maudsley Prescribing Guidelines in Psychiatry (14th ed.). John Wiley & Sons.
4. Clonidine Hydrochloride 25microgram Tablets - Accord-UK Ltd. Summary of Product Characteristics (last updated 07/12/21). www.medicines.org.uk [Accessed on 14/02/2022].

5. Paediatric Formulary Committee. *BNF for Children* (online) London: BMJ Group, Pharmaceutical Press, and RCPCH Publications. www.medicinescomplete.com [Accessed on 14/02/2022].

Version Control- Clonidine for Tics Information Sheet			
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