LMMG New Medicine Recommendation

Change of RAG Rating for Lisdexamfetamine from Red to Amber1 when used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children and young adults

Recommendation

At the May 2018 meeting of the LMMG, members were asked to consider the RAG recommendation for lisdexamfetamine and to decide whether a new RAG classification of Amber1 was suitable, allowing shared care of lisdexamfetamine for the treatment of ADHD in children and young adults.

The LMMG approved the change from Red to Amber 1 for lisdexamfetamine and also prioritised the development of a Shared Care Guideline for the management of ADHD in children and young adults, incorporating lisdexamfetamine.

Background

A request was received from a Consultant in Child & Adolescent Psychiatry and a Paediatric Pharmacist based at East Lancashire Hospitals NHS Trust in November 2017 for lisdexamfetamine to be added to the shared care guidelines for the management of ADHD in children and young adults.

Lisdexamfetamine had a Red RAG rating whereas methylphenidate**,** dexamfetamine, atomoxetine and guanfacine all have an Amber1 RAG rating for the management of ADHD in children and adolescents aged 6 to 16 years.

Lisdexamfetamine is a pharmacologically inactive pro-drug of dexamfetamine - after oral administration, the drug is hydrolysed to dexamfetamine, which is responsible for the drug's activity.[i] Lisdexamfetamine has a once daily administration schedule which is felt to be advantageous by the requesting consultant when compared to dexamfetamine which at some doses is administered more than once daily.[ii]

Profile of Lisdexamfetamine

Lisdexamfetamine is indicated as part of a comprehensive treatment programme for attention deficit hyperactivity disorder in children and adolescents aged 6 years and over when response to previous methylphenidate treatment is considered clinically inadequate. Treatment must be under the supervision of a specialist in childhood and/or adolescent behavioural disorders. Lisdexamfetamine is not indicated in all children with ADHD and the decision to use the drug must be based on a very thorough assessment of the severity and chronicity of the child's symptoms in relation to the child's age and potential for abuse, misuse or diversion.[i]

Dosage should be individualised according to the therapeutic needs and response of the patient. Careful dose titration is necessary at the start of treatment with lisdexamfetamine.

The starting dose is 30 mg taken once daily in the morning. When in the judgment of the clinician a lower initial dose is appropriate, patients may begin treatment with 20 mg once daily in the morning. The dose may be increased by 10 or 20 mg increments, at approximately weekly intervals. Lisdexamfetamine should be administered orally at the

lowest effective dosage. The maximum recommended dose is 70 mg/day. Treatment must be stopped if the symptoms do not improve after appropriate dosage adjustment over a 1-month period.

Previous LMMG Position

Lisdexamfetamine when used for the treatment of ADHD in children and young adults had an LMMG Red RAG rating and therefore was not eligible for inclusion in a shared care guideline.

When used for the treatment of ADHD in adults aged 16 years or older, lisdexamfetamine has an LMMG Amber1 RAG rating (February 2016).

A new medicine review for Lisdexamfetamine for ADHD in children and young adults was originally considered by the LMMG in October 2013 and the drug was given a BLACK RAG rating.

In September 2014, following several separate requests from clinicians to review this recommendation, a further consultation document was circulated by MLCSU for comment. Following the LMMG meeting in October 2014 (and slight amendment in November 2014), the RAG rating was amended to RED for children and young adults who met the following criteria:

- extenuating circumstances exist which mean that a patient would not reliably receive all the required doses of dexamfetamine throughout the day and requires a once daily dose of lisdexamfetamine to support adherence
- treatment has been agreed through the internal governance arrangements of the trust.

Until May 2018 the drugs recommended by LMMG for the treatment of ADHD in children and young adults were:

- Methylphenidate – Amber 1
- Dexamfetamine – Amber 1
- Atomoxetine – Amber 1
- Guanfacine – Amber 1
- Lisdexamfetamine – Red

All of the Amber 1 drugs are covered by the LMMG shared care guideline for ADHD in children and adolescents aged 6 to 16 years.[iii]

The drugs currently recommended by LMMG for the treatment of ADHD in adults are:

- Methylphenidate – Amber 1
- Dexamfetamine – Amber 1
- Atomoxetine – Amber 1
- Lisdexamfetamine – Amber 1

All of the above drugs are covered by the LMMG shared care guideline for ADHD in adults.[iv] Guanfacine is not licensed in adults.[v]

There was an inconsistency in the RAG ratings for lisdexamfetamine, having a RED RAG rating for the treatment of children and young adults and an AMBER 1 RAG rating for the treatment of adults with an associated shared care guideline.

National and Regional Context

The applicants partly justified the request for a re-classification as a number of regions have added lisdexamfetamine to their shared care guidelines for children and young people. Lisdexamfetamine is included in the shared care guidelines of both the Greater Manchester Medicines Management Group[vi] and Pan Mersey Area Prescribing Committee[vii] for the

treatment of ADHD in children and young adults. The Scottish Medicines Consortium and All Wales Medicines Strategy Group have both accepted lisdexamfetamine as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in children aged six years of age and over when response to previous methylphenidate treatment is considered clinically inadequate.[viii,ix]

NICE NG87 - Attention deficit hyperactivity disorder: diagnosis and management states:

Medication choice – children aged 5 years and over and young people

1.7.7 Offer methylphenidate (either short or long acting) for children aged 5 years[1] and over and young people if their ADHD symptoms are still causing a persistent significant impairment in at least one domain after their parents have received ADHD-focused information, group-based support has been offered and environmental modifications have been implemented and reviewed.

1.7.8 Consider switching to lisdexamfetamine[1] for children aged 5 years and over and young people who have had a 6-week trial of methylphenidate at an adequate dose and not derived enough benefit in terms of reduced ADHD symptoms and associated impairment.

1.7.9 Consider dexamfetamine[1] for children aged 5 years and over and young people whose ADHD symptoms are responding to lisdexamfetamine but who cannot tolerate the longer effect profile.

1.7.10 Offer atomoxetine or guanfacine[1] to children aged 5 years and over and young people if:

- they cannot tolerate methylphenidate or lisdexamfetamine or
- their symptoms have not responded to separate 6-week trials of lisdexamfetamine and methylphenidate, having considered alternative preparations and adequate doses.[x]

NICE NG87 also states:

6.8.1.1 Mental health trusts, and children's trusts that provide mental health/child development services, should form multidisciplinary specialist ADHD teams and/or clinics for children and young people and separate teams and/or clinics for adults. These teams and clinics should have expertise in the diagnosis and management of ADHD, and should:

- put in place systems of communication and protocols for information sharing among paediatric, child and adolescent, forensic, and adult mental health services for people with ADHD, including arrangements for transition between child and adult services
- produce local protocols for shared care arrangements with primary care providers, and ensure that clear lines of communication between primary and secondary care are maintained.[xi]

NICE CG72 - Attention deficit hyperactivity disorder: diagnosis and management, which was updated by NG87, was more detailed regarding shared care arrangements stating:

- Drug treatment should only be initiated by an appropriately qualified healthcare professional with expertise in ADHD and should be based on a comprehensive

[1] At the time of publication, methylphenidate, lisdexamfetamine, dexamfetamine, guanfacine and atomoxetine did not have a UK marketing authorisation for this indication in children aged 5 years. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented.

> assessment and diagnosis. Continued prescribing and monitoring of drug therapy may be performed by general practitioners, under shared care arrangements.[xii]

This issue is discussed in the supporting evidence section of NG87 - evidence report H – 'other factors the committee took into account', as follows:

> The evidence identified that some people with ADHD experienced delays in care and problems with monitoring when their primary healthcare professionals were uncomfortable prescribing medication for ADHD. The committee noted that this was a common theme in their own experience and reinforced the previous recommendation that while primary care practitioners should not start medication, after titration and dose stabilisation prescribing should be carried out under a shared care arrangement between primary and secondary care. The committee also emphasised that healthcare providers should ensure continuity of care for people with ADHD.[xiii]

Shared care prescribing is therefore recommended for all the ADHD drugs listed in NG87 and this includes lisdexamfetamine.

Cost implications

Lisdexamfetamine is given as a once daily dose, with a usual dosage range of 30-70mg / day.[i]

Dexamfetamine is given in divided daily doses, with a usual dosage range of 5-40mg / day.[ii]

Atomoxetine[xiv] is given either as a once daily dose or as divided doses if the patient does not achieve a satisfactory clinical response when taking as a single daily dose. The usual dosage range is 10-120mg / day (dependent on weight).

Drug	Dosage Range	Annual Cost
Lisdexamfetamine	30-70mg / day	£757 – £1081
Dexamfetamine	5-40mg / day	£306 - £1909
Atomoxetine	10-120mg / day	£690 - £1380*

*120mg cost calculated as 2 x 60mg capsules. Prices taken from NHS Electronic Drug Tariff December 2017

The cost implication of prescribing lisdexamfetamine vs its comparators would therefore not appear to be significant.

References

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