NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE
GUIDANCE EXECUTIVE (GE)

Review of TA98; Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents

This guidance was issued in March 2006.

The review date for this guidance is September 2011 to coincide with the Review of CG72 Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults. This was the recommendation of the previous review of TA98 in 2009. In November 2011, it was decided that CG72 should not be updated at this time.

1. Recommendation

The guidance should be transferred to the static list until such time as a decision is made to update CG72.

That we consult on this proposal.

2. Original remit(s)

To assess the clinical and cost effectiveness of methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents relative to other treatments in the NHS, and to update if and as necessary, guidance on the use of methylphenidate in ADHD issued to the NHS in England and Wales in October 2000.

3. Current guidance

1.1 Where drug treatment is considered appropriate, methylphenidate, atomoxetine and dexamfetamine are recommended, within their licensed indications, as options for the management of ADHD in children and adolescents.

1.2 The decision regarding which product to use should be based on the following:

- the presence of comorbid conditions (for example, tic disorders, Tourette’s syndrome, epilepsy)
- the different adverse effects of the drugs
- specific issues regarding compliance identified for the individual child or adolescent, for example problems created by the need to administer a mid-day treatment dose at school
- the potential for drug diversion (where the medication is forwarded on to others for non-prescription uses) and/or misuse
- the preferences of the child/adolescent and/or his or her parent or guardian.
1.3 If there is a choice of more than one appropriate drug, the product with the lowest cost (taking into account the cost per dose and number of daily doses) should be prescribed.

1.4 Drug treatment should only be initiated by an appropriately qualified healthcare professional with expertise in ADHD and should be based on a comprehensive assessment and diagnosis. Continued prescribing and monitoring of drug therapy may be performed by general practitioners, under shared care arrangements.

4. **Rationale**

The recommendations for TA98 have already been incorporated into CG72. No new evidence has been found to suggest that the recommendations require updating. In November 2011 a decision was made that CG72 should not be updated at this time; it will next be considered for review in June 2014. If transferred to the static list, TA98 will remain extant alongside the guideline with the consequence of preserving the funding direction for the technology appraisal recommendations. If, in the future, a decision is made to update CG72, a further review proposal for TA98 will be produced.

5. **Implications for other guidance producing programmes**

The proposal to transfer TA98 to the static list is consistent with the decision not to update CG72 at this time.

6. **New evidence**

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from March 2009 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the ‘Summary of evidence and implications for review’ section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. **Summary of evidence and implications for review**

The manufacturers have not made any changes to the current marketing authorisations or indicated that they are planning to extend the current marketing authorisations for methylphenidate, dexamfetamine and atomoxetine for the treatment of ADHD in children and adolescents. However the manufacturer of atomoxetine plans to [insert details]. The comparators in TA98 were placebo/usual care and either of the psychostimulant drugs licensed for this indication. Since the original guidance

1 A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

Confidential information has been removed.
Literature searches identified a number of new clinical trials since the publication of the original guidance. Of these a total of 14 were relevant, as they used a comparator specified in the TA96 scope (placebo/usual care and either of the psychostimulant drugs licensed for ADHD) and were in the population specified in the UK marketing authorisations for the technologies (i.e. aged 6 years and over). Two trials were excluded because they aimed to assess efficacy of the technologies in children and adolescents with ADHD and other co-morbidities (schizophrenia and substance abuse). The evidence base for methylphenidate, atomoxetine and dexamfetamine, does not appear to have substantially changed since guidance was published. Although two studies have been published which address the recommendations for further research into long term efficacy, these studies are only for atomoxetine. The new evidence identified is not likely to lead to a change in the recommendations of the original guidance.

Studies comparing technologies (n=1)

In TA98 the Committee was not able to differentiate between the drugs on the grounds of clinical effectiveness. One study (Faraone, 2010) was a meta-analysis of RCTs, comparing the efficacy of methylphenidate and amphetamine formulations in children with ADHD. A total of 23 trials were included. The results suggested that amphetamine products may be moderately more efficacious than methylphenidate products.

Studies evaluating Methylphenidate

*Trials with short-term follow-up (N=7)*

The populations in the trials were as follows: two were in children only (age range 6 to 12) four were on a mixed population of children and adolescents (age range 6 to 17 years) and one was in adolescents only (age range 13 to 16 years) and in one age was not reported. The trials had relatively short follow-up periods, ranging from 1 week to 5 weeks and none had a sample size of more than 50 participants. All of studies found a statistically significant improvement in ADHD symptoms with methylphenidate compared with placebo. None of these trials address research recommendations in the previous guidance.

Studies evaluating Atomoxetine

*Trials with short-term follow-up (N=4).*

The populations in three of the trials were a mixed population of children and adolescents (age range 6 to 16 years), and in one age was not reported. The follow-up periods in the trials ranged from 6 to 12 weeks, and the sample sizes ranged from 48 to 156 participants. All of studies found a statistically significant improvement in ADHD symptoms with atomoxetine compared with placebo.

*Studies with long term follow-up (N=2).*
TA98 contained the following recommendations for further research: “Given that ADHD is a chronic condition which may require long-term treatment, there is a need for further data on long-term outcomes of drug treatments”.

One study (Donnelly, 2009) evaluated the long term safety and tolerability of atomoxetine using pooled data from 13 double bind placebo-controlled trials and 3 open label extension studies. A total of 714 children and adolescents with ADHD were treated with atomoxetine for 3 years or more (mean 4.8 years, S.D 1.1). The study found that atomoxetine was safe and well tolerated for children and adolescents with 3 or more than 4 years of treatment.

One study (Hammerless, 2009) was a systematic review which examined short- and long-term efficacy, the moderating effect of comorbid disorders, and short- and long-term safety and tolerability of atomoxetine for the treatment of paediatric ADHD. The literature search identified one meta-analysis which found that over a two year period, 25.7% of children and 16.5% of adolescents discontinued treatment due to lack of effectiveness. Another study found 16% of children discontinued treatment due to lack of efficacy over a 5 year period.

Studies evaluating Dexamfetamine

No studies identified

8. Implementation

A submission from Implementation is included in Appendix 3.

Since the original guidance the published, it appears that NICE guidance is being adhered to and current practice has not changed.

9. Equality issues

No equalities issues were raised in the original guidance.

GE paper sign off: Janet Robertson, 22 February 2012

Contributors to this paper:
Information Specialist: Mike Raynor
Technical Lead: Helen Tucker
Implementation Analyst: Rebecca Lea
Project Manager: Andrew Kenyon
CPP input Caroline Keir
Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

<table>
<thead>
<tr>
<th>Options</th>
<th>Consequence</th>
<th>Selected – ‘Yes/No’</th>
</tr>
</thead>
<tbody>
<tr>
<td>A review of the guidance should be planned into the appraisal work programme.</td>
<td>A review of the appraisal will be planned into the NICE’s work programme.</td>
<td>No</td>
</tr>
<tr>
<td>The decision to review the guidance should be deferred to [specify date or trial].</td>
<td>NICE will reconsider whether a review is necessary at the specified date.</td>
<td>No</td>
</tr>
<tr>
<td>A review of the guidance should be combined with a review of a related technology appraisal.</td>
<td>A review of the appraisal(s) will be planned into NICE’s work programme as a Multiple Technology Appraisal, alongside the specified related technology.</td>
<td>No</td>
</tr>
<tr>
<td>A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE.</td>
<td>A review of the appraisal(s) will be planned into NICE’s work programme as a Multiple Technology Appraisal, alongside the newly referred technology.</td>
<td>No</td>
</tr>
</tbody>
</table>
| The guidance should be incorporated into an on-going clinical guideline. | The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review.  

This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal. | No                  |
| The guidance should be updated in an on-going clinical guideline. | Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn.  

Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation). | No                  |
<table>
<thead>
<tr>
<th>Options</th>
<th>Consequence</th>
<th>Selected – ‘Yes/No’</th>
</tr>
</thead>
<tbody>
<tr>
<td>The guidance should be transferred to the ‘static guidance list’</td>
<td>The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.</td>
<td>Yes</td>
</tr>
</tbody>
</table>

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include:
   - Spending on a treatment for the indication which was the subject of the appraisal continues to rise
   - There is evidence of unjustified variation across the country in access to a treatment
   - There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed
   - The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.
Appendix 2 – supporting information

Relevant Institute work

Published

CG72 Attention deficit hyperactivity disorder: Diagnosis and management of ADHD in children, young people and adults. Issued Sep 2008. Review date: Jul 2014 (review decision November 2011 guideline should not be updated at this time).


PH12 Promoting children's social and emotional wellbeing in primary education. Issued: Mar 2008

Commissioning guide. **Specifying a service for the diagnosis and management of attention deficit hyperactivity disorder in children and young people.** Issued: Mar 2010

*In progress*

Clinical guideline. **Conduct disorder in children and young people: Recognition, identification and management of conduct disorder in children and young people.** Due to be published April 2013.

*Suspended/terminated*

Nothing found

*In topic selection*²

Nothing found

² Information held by the NICE Topic Selection Team is treated as being potentially commercially sensitive by default. Details of the topics considered by NICE's Consideration Panels may be available on the NICE website, providing the manufacturers of the technologies under discussion have consented to the release of this information.
## Details of changes to the indications of the technology

<table>
<thead>
<tr>
<th>Indication considered in original appraisal</th>
<th>Proposed indication (for this appraisal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylphenidate is a CNS stimulant. It is licensed as part of a comprehensive treatment programme for ADHD, under specialist supervision, where remedial measures alone prove insufficient. It is a Schedule 2 controlled drug and is not currently licensed for use in children less than 6 years old. It is available in immediate-release tablets (Ritalin, Cephalon; Equasym, UCB Pharma) that are usually given in two or three daily doses. Methylphenidate is also available in modified-release formulations that enable once-daily dosing (Concerta XL, Janssen-Cilag; Equasym XL, UCB Pharma).</td>
<td>Unchanged</td>
</tr>
</tbody>
</table>

Dexamfetamine (Dexedrine, UCB Pharma) is a CNS stimulant. It is licensed as an adjunct in the management of refractory hyperkinetic states in children, under specialist supervision. It is a Schedule 2 controlled drug and is not currently licensed for use in children less than 3 years old.

Atomoxetine (Strattera, Eli Lilly) is licensed for the treatment of ADHD in children 6 years and older and in adolescents, under specialist supervision. It is a selective noradrenaline reuptake inhibitor, although the precise mechanism by which it works on ADHD is unknown.

Note this drug is now generic. According to BNF62 it is still indicated for ADHD.

Eli Lilly plan to submit to the EMA for Strattera to initiate treatment in adult ADHD. Currently the licence permits the continuation of Strattera treatment if it has been initiated in childhood or adolescence when it has shown benefit and is appropriate to continue.
### Details of new products

<table>
<thead>
<tr>
<th>Drug (manufacturer)</th>
<th>Details (phase of development, expected launch date, )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonidine hydrochloride (Addrenex Pharmaceuticals)</td>
<td>Licensed in US. No UK launch plans</td>
</tr>
<tr>
<td>Dextmethylphenidate hydrochloride (Novartis)</td>
<td>Launched in US. No UK launch plans</td>
</tr>
<tr>
<td>Droxidopa (Chelsea Therapeutics)</td>
<td>Phase II (study has reported). UK launch plans 2016.</td>
</tr>
<tr>
<td>Guanfacine (Shire)</td>
<td>Phase III. UK launch plans Q1 2014</td>
</tr>
<tr>
<td>Lisdexamfetamine dimesylate (Shire)</td>
<td>Phase III. Pre-registration filed in EU. UK launch plans Q4 2012</td>
</tr>
<tr>
<td>JNS001 (Janssen)</td>
<td>Phase III. Due to report May 2013</td>
</tr>
</tbody>
</table>

### Registered and unpublished trials

<table>
<thead>
<tr>
<th>Trial name and registration number</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Versus Combination Medication Treatment for Children With Attention Deficit Hyperactivity Disorder NCT00429273</td>
<td>Phase IV. Completed c. October 2011. Currently analysing results Estimated enrolment 180</td>
</tr>
<tr>
<td>Treatment of College Students With Attention-Deficit/Hyperactivity Disorder (ADHD) Using OROS Methylphenidate NCT000931398</td>
<td>Phase IV. Not yet recruiting. Estimated completion date June 2014 Estimated enrolment 110</td>
</tr>
<tr>
<td>Comparing Treatment With Melatonin to Treatment With Stimulants (Methylphenidate) in Children With Attention Deficit Hyperactivity Disorder and Sleep Difficulties NCTNCT01393574</td>
<td>Phase IV. Recruiting. Estimated completion date June 2012 Estimated enrolment 46</td>
</tr>
<tr>
<td>International Study to Predict Optimised Treatment in Attention Deficit/Hyperactivity Disorder NCT863499</td>
<td>Phase IV non-random parallel assignment. Recruiting. Estimated completion date July 2013 Estimated enrolment 1344</td>
</tr>
<tr>
<td>Trial name and registration number</td>
<td>Details</td>
</tr>
<tr>
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</tr>
<tr>
<td>Time Course of Response to Methylphenidate HCl ER Capsules in Children 6 to 12 Years With ADHD in Classroom Setting NCT01269463</td>
<td>Phase III. Estimated completion date August 2011. Recruiting. Estimated enrolment 24</td>
</tr>
<tr>
<td>Efficacy and Safety Study of Methylphenidate Hydrochloride Modified Release in Adults With Childhood-onset Attention Deficit/Hyperactivity Disorder (ADHD) NCT01259492</td>
<td>Phase III. Recruiting. Estimated completion date August 2012 Estimated enrolment 700.</td>
</tr>
<tr>
<td>Stimulant Versus Nonstimulant Medication for Attention Deficit Hyperactivity Disorder in Children NCT183391</td>
<td>Phase III. Completed currently analysing results. Estimated enrolment 160.</td>
</tr>
<tr>
<td>Cost-Effectiveness Study Of The Treatment Of Attention Deficit/Hyperactivity Disorder In Brazil NCT01228604</td>
<td>Phase IV. Recruiting. Estimated completion date December 2012. Estimated enrolment 50.</td>
</tr>
<tr>
<td>Comparison of Lisdexamfetamine Dimesylate With Atomoxetine HCl in Attention-Deficit/Hyperactivity Disorder (ADHD) Subjects With an Inadequate Response to Methylphenidate NCT01106430</td>
<td>Phase III. Recruiting. Estimated completion date January 2014 Estimated enrolment 262</td>
</tr>
<tr>
<td>Effects of Atomoxetine on Brain Activation During Attention and Reading Tasks in Patients With ADHD &amp; Comorbid Dyslexia. NCT00716274</td>
<td>Phase IV. Recruiting. Estimated completion date January 2016. Estimated enrolment 90</td>
</tr>
<tr>
<td>Open-Label Study of the Long Term Tolerability and Safety of Atomoxetine in Children With FASD and ADD/ADHD. NCT00418262</td>
<td>Phase III. Recruiting. Non-randomised safety/efficacy. Estimated completion date June 2011. Can find no evidence from Manufacturer’s website that this study has reported. Estimated enrolment 60</td>
</tr>
<tr>
<td>Effectiveness of Atomoxetine in Treating ADHD Symptoms in Children and Adolescents With Autism NCT00498173</td>
<td>Phase III. Recruiting. Estimated completion date July 2012 Estimated enrolment 86</td>
</tr>
<tr>
<td>Trial name and registration number</td>
<td>Details</td>
</tr>
<tr>
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</tr>
<tr>
<td>Associated Genes With Atomoxetine Response in Attention Deficit Hyperactivity Disorder (ADHD) NCT01339286</td>
<td>Phase III. Recruiting. Estimated completion date December 2011 Estimated enrolment 100</td>
</tr>
<tr>
<td>Comparison of Lisdexamfetamine Dimesylate With Atomoxetine HCl in Attention-Deficit/Hyperactivity Disorder (ADHD) Subjects With an Inadequate Response to Methylphenidate NCT01106430</td>
<td>Phase III. Recruiting. Estimated completion date January 2014 Estimated enrolment 262</td>
</tr>
<tr>
<td>Effectiveness of ATMX in Treating Adolescents With ADHD and SUD NCT00218322</td>
<td>Phase IV. Recruiting. Estimated completion date September 2012 Estimated enrolment 108</td>
</tr>
<tr>
<td>Efficacy and Safety of Extended-release Guanfacine Hydrochloride in Children and Adolescents Aged 6-17 Years With Attention-Deficit/Hyperactivity Disorder (ADHD) NCT01244490</td>
<td>Phase III. Recruiting. Estimated completion date August 2013 Estimated enrolment 333</td>
</tr>
<tr>
<td>Interventions for Children With Attention and Reading Disorders (ICARD) NCT01133847</td>
<td>Phase IV. Recruiting. Estimated completion date April 2015 Estimated enrolment 216</td>
</tr>
<tr>
<td>Effectiveness of Combined Medication Treatment for Aggression in Children With Attention Deficit With Hyperactivity Disorder (The SPICY Study) NCT00794625</td>
<td>Phase IV. Recruiting. Estimated completion date April 2013 Estimated enrolment 270</td>
</tr>
<tr>
<td>Dimesylate 2-year Safety Study in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder (ADHD) NCT 01328756</td>
<td>Phase IV. Recruiting. Non-randomised safety study. Estimated completion date February 2015 Estimated enrolment 300</td>
</tr>
<tr>
<td>Phase 4, Open Label, Multicentre, 2 Year Safety Study of Lisdexamfetamine Dimesylate in Children/Adolescents With ADHD (SPD489-404)</td>
<td>Phase IV. Non-randomised efficacy study. Not yet recruiting. Estimated completion date December 2013 Estimated enrolment 12</td>
</tr>
<tr>
<td>Trial name and registration number</td>
<td>Details</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>The effects of Concerta® on the brain structures of children with attention deficit hyperactivity disorder, measured by optimised Voxel-Based Morphometry (VBM) and Tract-Based Spatial Statistics (TBSS) of Diffusion Tensor Imaging (DTI). ISRCTN44227400</td>
<td>No information about stage or phase. Ongoing. Estimated completion date December 2012. Estimated enrolment 80</td>
</tr>
<tr>
<td>Open label trial of Atomoxetine for attention deficit hyperactivity disorder (ADHD) in children with special educational needs. ISRCTN25691213</td>
<td>Study type interventional open label. Ongoing. Estimated completion date December 2012 Estimated enrolment 40.</td>
</tr>
</tbody>
</table>

References


Appendix 3 – Implementation submission

Implementation feedback: review of NICE technology appraisal guidance 98

<table>
<thead>
<tr>
<th>NICE Technology Appraisal 98 Attention deficit hyperactivity disorder (ADHD) - methylphenidate, atomoxetine and dexamfetamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implementation input required by 19/12/2011</td>
</tr>
</tbody>
</table>
| Please contact Rebecca Lea regarding any queries
  rebecca.lea@nice.org.uk                                             |
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Appendix A: Healthcare activity data definitions .....................24
1 Routine healthcare activity data

NICE implementation uptake reports provide information on national trends and activity associated with recommendations in NICE guidance. The NICE implementation programme has looked at the following data to determine the uptake of NICE technology appraisal guidance 98.

- NICE implementation uptake report: *Attention deficit hyperactivity disorder (ADHD), management of ADHD in children, young people and adults*

1.1 Uptake report summary

Guidance published in March 2006 stated “It is not anticipated that this guidance will result in a major increase over current trends in the rate of prescribing for ADHD.” The latest prescribing data confirms this is the case. Methylphenidate, which accounts for around eighty percent of prescribing for drugs used to treat ADHD, is steadily increasing as part of a long term trend (figure 2). Atomoxetine prescriptions are increasing (figure 3). There was a slight upturn in dexamfetamine prescriptions during mid-2006 (figure 4). Nearly sixty percent of usage for ADHD drugs is attributable to general practitioners indicating widespread use of shared cared arrangements as recommended in the NICE guidance (figure 6).
1.2 Hospital Pharmacy Audit Index data

This section presents recent HPAI data on the cost and volume of methylphenidate, atomoxetine and dexamfetamine.

Figure 1 Volume of dexamphetamine dispensed in hospitals between July 200 and March 2011

![Dexamphetamine Volume Graph]

Source: IMS Health Hospital Pharmacy Audit Index
Figure 2 Cost of dexamphetamine dispensed in hospitals between July 2000 and March 2011

![Cost of dexamphetamine dispensed in hospitals between July 2000 and March 2011](image)

Source: IMS Health Hospital Pharmacy Audit Index

Figure 3 Volume of atomoxetine dispensed in hospitals between July 2000 and March 2011

![Volume of atomoxetine dispensed in hospitals between July 2000 and March 2011](image)

Source: IMS Health Hospital Pharmacy Audit Index
Figure 4 Cost of atomoxetine dispensed in hospitals between July 2000 and March 2011

![Graph showing cost of atomoxetine dispensed in hospitals between July 2000 and March 2011. The graph has a y-axis labeled 'Cost (£)' and an x-axis labeled 'Year by quarter'. The line graph shows a peak in 2005 followed by a decline. The graph includes a note indicating 'TA98 Attention deficit hyperactivity disorder (ADHD) - methylphenidate, atomoxetine and dexamfetamine (March 2006)' and is sourced from IMS Health Hospital Pharmacy Audit Index.]

Figure 5 Volume of methylphenidate dispensed in hospitals between July 2000 and March 2011

![Graph showing volume of methylphenidate dispensed in hospitals between July 2000 and March 2011. The graph has a y-axis labeled 'Volume' and an x-axis labeled 'Year by quarter'. The line graph shows a peak in 2005 followed by a decline. The graph includes a note indicating 'TA98 Attention deficit hyperactivity disorder (ADHD) - methylphenidate, atomoxetine and dexamfetamine (March 2006)' and is sourced from IMS Health Hospital Pharmacy Audit Index.]

Confidential information has been removed.
1.3 ePACT data

This section presents the cost and volume of dexamphetamine, atomoxetine and methylphenidate prescribed in primary care and hospitals and dispensed in the community between March 2006 and July 2011. Unfortunately ePACT prescribing data prior to September 2006 are not available.
Figure 7 Cost and volume of dexamphetamine prescribed in primary care and hospitals dispensed in the community

Source: IMS Health Hospital Pharmacy Audit Index
Figure 8 Cost and volume of atomoxetine prescribed in primary care and hospitals dispensed in the community.
Figure 9 Cost and volume of methylphenidate prescribed in primary care and hospitals dispensed in the community

2 Implementation studies from published literature

Information is taken from the uptake database (ERNIE) website.


Clinical records of all open ADHD cases (296) in three English child and adolescent mental health services were examined. Following the introduction of NICE guidance, the median time to start prescribing medication fell from 1262 to 526 days: the minimum realistic time to complete a routine assessment was approximately 70 days. Overall 70% were prescribed medication.

3 Qualitative input from the field team

The implementation field team has recorded the following feedback in relation to this guidance:
Two comments have been received about this TA since 2009. One person commented that they had managed to significantly reduce prescribing costs for Ritalin (methylphenidate) in collaboration with their NHS partners. Another person suggested that NICE could consider more non-pharmacological drug approaches such as psychological therapies, for conditions such as ADHD.

Appendix A: Healthcare activity data definitions

*Prescribing analysis and cost tool system*

This information comes from the electronic prescribing analysis and cost tool (ePACT) system, which covers prescriptions by GPs and non-medical prescribers in England and dispensed in the community in the UK. The Prescription Services Division of the NHS Business Services Authority maintains the system. PACT data are used widely in the NHS to monitor prescribing at a local and national level. Prescriptions written in hospitals but dispensed in the community (FP10 [HP]) are not included in PACT data. Prescriptions dispensed in hospitals or mental health units, and private prescriptions, are not included in PACT data.
**Measures of prescribing**

Prescription Items: Prescriptions are written on a prescription form. Each single item written on the form is counted as a prescription item. The number of items is a measure of how many times the drug has been prescribed.

Cost: The net ingredient cost (NIC) is the basic price of a drug listed in the drug tariff, or if not in the drug tariff, the manufacturer's list price.

**Data limitations (national prescriptions)**

PACT data do not link to demographic data or information on patient diagnosis. Therefore the data cannot be used to provide prescribing information by age and sex or prescribing for specific conditions where the same drug is licensed for more than one indication.

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**IMS HEALTH Hospital Pharmacy Audit Index (IMS HPAI)**

IMS HEALTH collects information from pharmacies in hospital trusts in the UK. The section of this database relating to England is available for monitoring the overall usage in drugs appraised by NICE. The IMS HPAI database is based on issues of medicines recorded on hospital pharmacy systems. Issues refer to all medicines supplied from hospital pharmacies: to wards; departments; clinics; theatres; satellite sites and to patients in outpatient clinics and on discharge.

**Measures of prescribing**

Volume: The HPAI database measures volume in packs and a drug may be available in different pack sizes and pack sizes can vary between medicines.

Cost: Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Costs based on the drug tariff provide a degree of standardization allowing comparisons of prescribing data from different sources to be made. The costs stated
in this report do not represent the true price paid by the NHS on medicines. The estimated costs are used as a proxy for utilization and are not suitable for financial planning.

**Data limitations**
IMS HPAI data do not link to demographic or to diagnosis information on patients. Therefore, it cannot be used to provide prescribing information on age and sex or for prescribing of specific conditions where the same drug is licensed for more than one indication.