GUIDELINES INCLUDED IN THIS BOOKLET

UK NICE guideline:
Attention Deficit Hyperactivity Disorder: Diagnosis and Management¹

Canadian CADDRA guideline:
Canadian ADHD Practice Guidelines, Fourth Edition²

German guideline:
Interdisciplinary Evidence- and Consensus-based (S3) Guideline “Attention Deficit/Hyperactivity Disorder (ADHD) in Children, Young People and Adults”³ [in German]

Spanish guideline:
Clinical Practice Guideline on Therapeutic Interventions in Attention Deficit Hyperactivity Disorder (ADHD)⁴ [in Spanish]

The summaries in this booklet focus on recommendations for the pharmacological treatment of ADHD – for both children/adolescents and adults – from selected guidelines updated in 2017/2018

Pharmacological approaches are not indicated for every patient with ADHD. Treatment requires a comprehensive and multimodal approach, including non-pharmacological options, tailored to meet the needs of each individual patient with ADHD.

Please refer to the full guidelines, as this booklet is not intended to and does not contain an exhaustive list of all the treatment recommendations.

Also, please refer to the summaries of product characteristics for approved medications in your country before initiating treatment with these pharmacotherapies.
2018 UK NICE GUIDELINE
Attention Deficit Hyperactivity Disorder: Diagnosis and Management

Summary of principles for initiating pharmacotherapy in children (≥5 years*) and young people with ADHD

Following a full baseline assessment, medication should only be offered for children aged 5 years* and over and young people if their ADHD symptoms are still causing a persistent significant impairment in at least one domain (for example, interpersonal relationships, education and occupational attainment, and risk awareness) after they and their parents have received and discussed ADHD-focused information, group-based support has been offered, and environmental modifications have been implemented and reviewed.

Summary of recommendations for medication choice in children and young people with ADHD

<table>
<thead>
<tr>
<th>1ST-LINE OPTIONS</th>
<th>MPH</th>
<th>Does not derive enough benefit† after a 6-week trial of MPH at an adequate dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2ND-LINE OPTIONS</td>
<td>LDX</td>
<td>Responds to LDX, but cannot tolerate the longer effect profile</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cannot tolerate LDX or MPH, or their symptoms have not responded to separate 6-week trials of LDX and MPH‡</td>
</tr>
<tr>
<td>3RD-LINE OPTIONS</td>
<td>DEX</td>
<td>NICE now lists LDX as the 2nd-line medication choice in children and young adults who have ADHD</td>
</tr>
<tr>
<td></td>
<td>ATX</td>
<td>NICE now lists GXR as a 3rd-line medication choice in children and young adults who have ADHD</td>
</tr>
<tr>
<td></td>
<td>GXR</td>
<td></td>
</tr>
</tbody>
</table>

Figure created by Shire
Treatment recommendations in guidelines may not necessarily reflect approval statuses in different countries

*ADHD medicines are not licensed for the treatment of children with ADHD who are aged 5 years and under. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented
†In terms of reduced ADHD symptoms and associated impairment
‡Having considered alternative preparations and adequate doses

ATX, atomoxetine; DEX, dexamfetamine; GXR, guanfacine extended release; LDX, lisdexamfetamine dimesylate; MPH, methylphenidate; NICE, National Institute for Health and Care Excellence
2018 UK NICE GUIDELINE
Attention Deficit Hyperactivity Disorder: Diagnosis and Management

Summary of principles for initiating pharmacotherapy in adults with ADHD

Following a full baseline assessment, medication should only be offered to adult patients with ADHD if their ADHD symptoms are still causing a significant impairment in at least one domain (for example, interpersonal relationships, education and occupational attainment, and risk awareness) after environmental modifications have been implemented and reviewed.

Summary of recommendations for medication choice in adults with ADHD

Figure created by Shire

*Consider switching adults who have had a 6-week trial of either LDX or MPH at an adequate dose but have not derived enough benefit in terms of reduced ADHD symptoms and associated impairment

†Having considered alternative preparations and adequate doses

ATX, atomoxetine; DEX, dexamfetamine; LDX, lisdexamfetamine dimesylate; MPH, methylphenidate; NICE, National Institute for Health and Care Excellence
Summary of recommendations for medication choice in children and adolescents (6–17 years) with ADHD

Medications are part of an integrated and multimodal treatment plan that may include educational and psychosocial interventions. As with all pharmacological treatments in medicine, risk/benefit ratios need consideration before initiating any medication. Among the factors to be considered, the high morbidity of ADHD makes it important that we also weigh the risk of not treating ADHD.

**1ST-LINE OPTIONS**

- **LONG-ACTING PSYCHOSTIMULANTS**
  - LDX
  - MPH
  - AMF mixed salts
  
  An adequate trial of MPH and AMF is recommended before moving to 2nd-line treatment.
  
  Non-stimulants may also be used in combination with 1st-line agents as a potential augmentation for 1st-line treatment suboptimal responders.

  If patients have significant side effects, suboptimal response, lack of access to 1st-line medications, or if stimulant agents are contraindicated (e.g., high risk of misuse).

- **SHORT- AND INTERMEDIATE-ACTING PSYCHOSTIMULANTS**
  - MPH
  - DEX

- **LONG-ACTING NON-STIMULANTS**
  - GXR
  - ATX

**2ND-LINE ADJUNCTIVE OPTIONS**

- **LONG-ACTING PSYCHOSTIMULANTS**
  - LDX remains a 1st-line medication option in children and adolescents who have ADHD.

- **SHORT- AND INTERMEDIATE-ACTING PSYCHOSTIMULANTS**
  - GXR is now a 2nd-line medication option in both children and adolescents who have ADHD.

*Only GXR has been approved by Health Canada for the adjunctive treatment of ADHD in combination with psychostimulants.

AMF, amphetamine; ATX, atomoxetine; CADDRA, Canadian ADHD Resource Alliance; DEX, dexamfetamine; GXR, guanfacine extended release; LDX, lisdexamfetamine dimesylate; MPH, methylphenidate.

Figure created by Shire

Treatment recommendations in guidelines may not necessarily reflect approval statuses in different countries.
### 2018 CANADIAN CADDRA GUIDELINE

Canadian ADHD Practice Guidelines, Fourth Edition

#### Summary of recommendations for medication choice in adults with ADHD

Medications are part of an integrated and multimodal treatment plan that may include educational and psychosocial interventions. As with all pharmacological treatments in medicine, risk/benefit ratios need consideration before initiating any medication. Among the factors to be considered, the high morbidity of ADHD makes it important that we also weigh the risk of not treating ADHD.

<table>
<thead>
<tr>
<th>1&lt;sup&gt;ST&lt;/sup&gt;-LINE OPTIONS</th>
<th>2&lt;sup&gt;ND&lt;/sup&gt;-LINE OPTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LONG-ACTING PSYCHOSTIMULANTS</strong></td>
<td><strong>SHORT- AND INTERMEDIATE-ACTING PSYCHOSTIMULANTS</strong></td>
</tr>
<tr>
<td>LDX</td>
<td>MPH</td>
</tr>
<tr>
<td>AMF mixed salts</td>
<td></td>
</tr>
<tr>
<td>An adequate trial of MPH and AMF is recommended before moving to 2&lt;sup&gt;nd&lt;/sup&gt;-line treatment</td>
<td></td>
</tr>
<tr>
<td>If patients have significant side effects, suboptimal response, lack of access to 1&lt;sup&gt;st&lt;/sup&gt;-line medications, or if stimulant agents are contraindicated (e.g., high risk of misuse)</td>
<td></td>
</tr>
<tr>
<td><strong>LONG-ACTING NON-STIMULANTS</strong></td>
<td><strong>MPH</strong></td>
</tr>
<tr>
<td><strong>DEX</strong></td>
<td>ATX</td>
</tr>
</tbody>
</table>

LDX remains a 1<sup>st</sup>-line medication option in adults who have ADHD

Figure created by Shire

Treatment recommendations in guidelines may not necessarily reflect approval statuses in different countries.
Summary of recommendations for medication choice in children (≥6 years) and adolescents with ADHD

The treatment of ADHD shall be delivered in the context of a multimodal treatment plan, which can combine psychosocial (including psychotherapeutic) and pharmacological and supplementary interventions, according to the individual symptoms, the level of functioning, participation and the preferences of the patient and their social network.

<table>
<thead>
<tr>
<th>STIMULANTS</th>
<th>NON-STIMULANTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st choice:</td>
<td></td>
</tr>
<tr>
<td>MPH</td>
<td>GXR</td>
</tr>
<tr>
<td>Immediate or delayed release</td>
<td>If stimulants not suitable, not tolerated or ineffective*</td>
</tr>
<tr>
<td>Inadequate response to MPH</td>
<td>Both LDX and GXR are recommended and indicated for the pharmacotherapy of ADHD in children and adolescents</td>
</tr>
<tr>
<td>LDX</td>
<td>ATX</td>
</tr>
<tr>
<td>Immediate release</td>
<td></td>
</tr>
<tr>
<td>DEX</td>
<td></td>
</tr>
<tr>
<td>Immediate release</td>
<td></td>
</tr>
</tbody>
</table>

*GXR can be used without prior prescription of other ADHD medications if there are medical reasons against the use of stimulants or concomitant conditions that support the use of GXR.

ATX, atomoxetine; DEX, dexamfetamine; GXR, guanfacine extended release; LDX, lisdexamfetamine dimesylate; MPH, methylphenidate.
Summary of recommendations for medication choice in adults with ADHD

The treatment of ADHD shall be delivered in the context of a multimodal treatment plan, which can combine psychosocial (including psychotherapeutic) and pharmacological and supplementary interventions, according to the individual symptoms, the level of functioning, participation and the preferences of the patient and their social network.

1ST-LINE OPTIONS

MPH
Delayed or extended release*

MPH is not sufficiently effective or not tolerated

2ND-LINE OPTIONS

ATX
In the context of a differentiated treatment plan

Figure created by Shire

Treatment recommendations in guidelines may not necessarily reflect approval statuses in different countries

*Use of OROS-MPH (extended release) is possible as continuation of a therapy initiated in childhood and adolescence

ATX, atomoxetine; MPH, methylphenidate; OROS-MPH, osmotic release oral system-methylphenidate
Summary of recommendations for medication choice in children (6 years) and adolescents with ADHD

Pharmacological treatment in school-aged children and adolescents is recommended only when psychotherapy and/or psychosocial therapy has not given any results, or in severely affected individuals. The medications indicated for school-aged children and adolescents with ADHD are LDX, MPH, GXR and ATX.

Summary of evidence for the recommendations

- **LDX**: Effective treatment in children that also improves quality of life and functioning.
- **MPH**: Seems to improve symptoms and general behavior in children with ADHD.
  - Prolonged-release MPH significantly improves symptoms in children aged 6-8 years with ADHD.
- **GXR**: Effective in reducing symptoms of ADHD in children.
  - Minor to moderate effect on oppositional behavior of young people with ADHD.
- **ATX**: Effective treatment in children and young people.
  - Significantly improves quality of life domains most affected in children with ADHD.

Efficacy

LDX: Effective treatment in children that also improves quality of life and functioning.

MPH: Seems to improve symptoms and general behavior in children with ADHD.

GXR: Effective in reducing symptoms of ADHD in children.

ATX: Effective treatment in children and young people.

Both LDX and GXR are recommended and indicated for the pharmacotherapy of ADHD in children and adolescents.

Safety

LDX: Can produce minor changes to heart rate in children.

MPH: The guideline’s summary of evidence does not include safety of MPH in children and adolescents.

GXR: Favorable risk/benefit profile in children.

ATX: Relatively well tolerated by children and young people.

Figure created by Shire

Treatment recommendations in guidelines may not necessarily reflect approval statuses in different countries.

*The quality of the evidence makes it difficult to estimate the magnitude of the effect
†Throughout the day, regardless of when it is administered

ATX, atomoxetine; GXR, guanfacine extended release; LDX, lisdexamfetamine dimesylate; MPH, methylphenidate
Summary of recommendations for medication choice in adults with ADHD

Although there is a choice between psychological and pharmacological treatment in adults with minor cases of ADHD, pharmacological treatment is the treatment of first choice for adults with moderate or severe cases. The guideline states that LDX, MPH, ATX and GXR can be used in the treatment of adults with ADHD.*

Summary of evidence for the recommendations

<table>
<thead>
<tr>
<th></th>
<th>LDX</th>
<th>MPH</th>
<th>ATX</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EFFICACY</strong></td>
<td>Effective in treating ADHD</td>
<td>MPH is effective in the short term</td>
<td>Modest beneficial effect on reduction of symptoms</td>
</tr>
<tr>
<td></td>
<td>Provides improvement in executive function and quality of life</td>
<td>OROS-MPH is effective</td>
<td>There is little evidence to support use in adults</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prolonged-release MPH is associated with symptom reduction</td>
<td></td>
</tr>
<tr>
<td><strong>SAFETY</strong></td>
<td>Tolerability is similar to that of placebo</td>
<td>High rate of treatment interruption due to adverse events</td>
<td>Benefit may not compensate for adverse effects that result in adult patients ceasing treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OROS-MPH is well tolerated</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prolonged-release MPH is well tolerated, but may have minor effects on heart rate</td>
<td></td>
</tr>
</tbody>
</table>

*In Spain, only ATX is approved for treatment of ADHD in adults. OROS-MPH and LDX can continue to be used in patients who were prescribed these in childhood and need to continue their use into adulthood. The guideline provides no evidence summary for use of GXR in adults with ADHD.

ATX, atomoxetine; GXR, guanfacine extended release; LDX, lisdexamfetamine dimesylate; MPH, methylphenidate; OROS-MPH, osmotic release oral system-methylphenidate

Figure created by Shire

Treatment recommendations in guidelines may not necessarily reflect approval statuses in different countries.
GUIDELINES SUMMARY

Children and adolescents – recommendations for the pharmacological treatment of ADHD

<table>
<thead>
<tr>
<th>NICE¹</th>
<th>CADDRA²</th>
<th>German guideline³</th>
<th>Spanish guideline⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1st line 2nd line</td>
<td>3rd line 1st line* 2nd line</td>
</tr>
<tr>
<td>LDX</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>MPH</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>ATX</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>DEX</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>GXR</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td>AMF mixed salts</td>
<td>✓</td>
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*Non-stimulants may also be used in combination with 1st-line agents as a potential augmentation for 1st-line treatment suboptimal responders. Only GXR has been approved by Health Canada for the adjunctive treatment of ADHD in combination with psychostimulants.

†LDX is recommended if there is a clinically inadequate response to MPH.

‡GXR is only recommended if stimulants are not suitable, not tolerated or ineffective.

Adults – recommendations for pharmacological treatment of ADHD

<table>
<thead>
<tr>
<th>NICE¹</th>
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<td></td>
<td></td>
<td>1st line 2nd line</td>
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</tr>
<tr>
<td>LDX</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>MPH</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>ATX</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>DEX</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>GXR</td>
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*In Spain, only ATX is approved for treatment of ADHD in adults.

†Use of OROS-MPH and LDX can only be continued in patients who had ADHD in childhood and need to continue this treatment when they reach adulthood.

‡Use of OROS-MPH (extended release) is possible as continuation of a therapy initiated in childhood and adolescence.

§Use of ATX is approved in adults in the context of a differentiated treatment plan.

Figures created by Shire.

Treatment recommendations in guidelines may not necessarily reflect approval statuses in different countries.

AMF, amphetamine; ATX, atomoxetine; CADDRA, Canadian ADHD Resource Alliance; DEX, dexamfetamine; GXR, guanfacine extended release; LDX, lisdexamfetamine dimesylate; MPH, methylphenidate; NICE, National Institute for Health and Care Excellence; OROS-MPH, osmotic release oral system-methylphenidate.
REFERENCES


