



## Mental health

# Psychopharmacology in children and adolescents: unmet needs and opportunities

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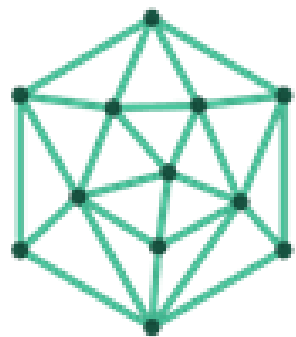
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# Child & Adolescent Neuropsychopharmacology

ECNP Network

## ECNP: European College of Neuropsychopharmacology

Concerned with setting the ground for development,  
implementation and education on  
neuropsychopharmacology in children and adolescents



For the first time, a major group of international experts and patients have cooperated defining new parameters for the development of medicines to treat children and young people.

They make a series of recommendations on how the processes should be improved.

## Position Paper

# Psychopharmacology in children and adolescents: unmet needs and opportunities



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Psychopharmacological treatment is an important component of the multimodal intervention approach to treating mental health conditions in children and adolescents. Currently, there are many unmet needs but also opportunities, alongside possible risks to consider, regarding the pharmacological treatment of mental health conditions in children and adolescents. In this Position Paper, we highlight and address these unmet needs and opportunities, including the perspectives of clinicians and researchers from the European College of Neuropsychopharmacology–Child and Adolescent Network, alongside those of experts by lived experience from national and international associations, via a survey involving 644 participants from 13 countries, and of regulators, through representation from the European Medicines Agency. We present and discuss the evidence base for medications currently used for mental disorders in children and adolescents, medications in the pipeline, opportunities in the development of novel medications, crucial priorities for the conduct of future clinical studies, challenges and opportunities in terms of the regulatory and legislative framework, and innovations in the way research is conducted, reported, and promoted.

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# Psychopharmacological treatment in CAP

Highlight and address the **unmet needs** and **opportunities**, including the perspectives of:

1. **clinicians and researchers** from the European College of Neuropsychopharmacology–Child and Adolescent Network
2. **experts by lived experience** from national and international associations, via a survey involving 644 participants from 13 countries
3. **regulators**, through representation from the European Medicines Agency (EMA)

# Current status...

Compound	Approved by EMA (note: national approvals are not included)	Age (years)	Approved by the FDA	Age (years)
<b>ADHD</b>				
Amphetamines/dextroamphetamine mixed salts			✓	3-17
Amphetamines/dextroamphetamines mixed salts			✓	6-17
Atomoxetine			✓	6-17
Clonidine, extended release			✓	6-17
Dexmethylphenidate			✓	6-17
Dextroamphetamine			✓	3-17
Dextroamphetamine SR			✓	6-16
Guanfacine, extended release	✓	6-17	✓	6-17
Lisdexamfetamine			✓	6-17
Methamphetamine			✓	6-17
Methylphenidate	(✓)	> 6 years	✓ (Immediate release tablet, Immediate solution, Extended-release (tablet, chewable), Controlled delivery, Multilayer extended-release, extended-release orally disintegrating tablets, transdermal system)	6-17
Viloxazine			✓	6-17

Anxiety disorders				
Duloxetine			✓ (generalised anxiety disorder)	7-17
Escitalopram			✓ (generalised anxiety disorder)	≥7
Autism spectrum disorder (irritability)				
Aripiprazole			✓	6-17
Risperidone			✓	5-17
Bipolar disorder (depressive episodes)				
Lurasidone			✓	10-17
Olanzapine/fluoxetine combination			✓	10-17
Bipolar disorder (manic or mixed episodes)				
Aripiprazole	✓ (manic episodes)	≥ 13 years	✓	10-17
Asenapine			✓	10-17
Olanzapine			✓	13-17
Quetiapine XR			✓	10-17
Risperidone			✓	10-17
Lithium			✓	12-17
Conduct disorder				
Risperidone	✓	5-18		
Depressive disorder				
Fluoxetine	✓ (major depressive episode unresponsive to psychotherapy)*		✓	8-18

### Enuresis

Imipramine

✓

6-17

### Insomnia (in ASD or Smith Magenis syndrome)

Melatonin extended release

✓

2-18

### Narcolepsy

Amphetamines/dextroamphetamine mixed salts

✓

6-17

Dextroamphetamine

✓

6-17

Dextroamphetamine SR

✓

6-17

Sodium oxybate

✓

≥7

### Obsessive Compulsive Disorder

Clomipramine

✓

10-17

Fluoxetine

✓

7-17

Fluvoxamine

✓

8-17

Sertraline

✓\*

6-17

✓

6-17

### Schizophrenia

Aripiprazole

✓

≥ 15 years

✓

13-17

Brexpiprazole

✓

13-17

Lurasidone

✓

≥ 13 years

✓

13-17

Olanzapine

✓

13-17

Paliperidone

✓

≥ 15 years

✓

12-17

Quetiapine

✓

13-17

Risperidone

✓

13-17

### Tourette's disorder

Aripiprazole

✓

6-17

	Participants (N=644)	
	N	%
What do you think are the most important questions on medicines for children or teenagers with mental problems that researchers should try to answer in the future?		
<b>Rationale for using medications</b>		
When a non-pharmacological intervention is better	24	3.72%
Why a pharmacological treatment is needed	5	0.77%
What are the effects of taking versus not taking medications	1	0.16%
What are the goals of the pharmacological treatment	1	0.16%
<b>Efficacy-effectiveness</b>		
Finding curative rather than symptomatic treatments	15	2.33%
Efficacy versus tolerability	9	1.39%
Efficacy	6	0.93%
Improve adherence	4	0.62%
Tolerance	4	0.62%
Find medications with effectiveness	3	0.47%
Costs-benefits	3	0.47%
Effects on quality of life	3	0.47%
Understand factors that might increase the effects of medications (eg. diet or exercise)	3	0.47%
How to measure if a medication is working	1	0.16%
Improve duration of action	1	0.16%
Timely treatment	1	0.16%
Tackling prodromal symptoms	1	0.16%
Aiming at normalisation	1	0.16%
Risk of not taking medications	1	0.16%
<b>Disorders or conditions for which (additional) medications are needed</b>		
Cognitive issues or executive dysfunctions	2	0.31%
Disorders of early childhood	2	0.31%
Academic underperformance	1	0.16%
Agitation	1	0.16%
Conduct disorders	1	0.16%
Emotional dysregulation	1	0.16%
Inattention	1	0.16%
Sleep disturbance	1	0.16%
<b>Tolerability and safety</b>		
Understanding side effects (in general or in the long-term more specifically)	361	56.05%
Potential of medication of being addictive	83	12.88%
Effects on brain	9	1.39%
Contraindications	8	1.24%
Negative effects on personality	6	0.93%
Rebound effects	4	0.62%
Negative effects on weight	3	0.47%
Interactions among medications	2	0.31%
Negative effects on cognitive functions	2	0.31%
Finding medications with fewer side effects	1	0.16%
Link with neurodegenerative disorders	1	0.16%
<b>Practical issues related to prescribing</b>		
Individualise treatment	10	1.55%
Finding alternative formulations	10	1.55%

(Table 2 continues in next column)

	Participants (N=644)	
	N	%
(Continued from previous column)		
How to adjust the dose	6	0.93%
How long the medication should be taken for	6	0.93%
Assessing long-acting formulations	4	0.62%
How to taper down	3	0.47%
What are second-line medications	1	0.16%
<b>Other</b>		
Stigma	8	1.24%
How to train prescribers	2	0.31%
How to make medications more accessible	2	0.31%
Ethical aspects	1	0.16%
Involve parents in decision making	1	0.16%
Which professionals should prescribe	1	0.16%
Should we treat the child or the society	1	0.16%
<b>In your opinion, do people think that taking medicines for mental problems is bad?</b>		
Yes	518	80.43%
Often	103	15.99%
No	95	14.75%
It depends (on the type of problem, medication, person)	28	4.34%
Sometimes	8	1.24%
I don't know	12	1.86%
Maybe	2	0.37%
<b>What do you think we could do to help people understand that medicines may help children and teenagers with mental problems?</b>		
Education on mental health issues and their treatment	216	33.54%
Education lead by people with personal lived experience	91	14.13%
Finding medications with good efficacy or risk ratio	49	7.60%
Train mental health professionals	39	6.05%
Presenting the mechanism of action of medications in a clear way	32	5.06%
Train school personnel	27	4.96%
Make study results accessible to lay people	22	3.41%
Studies showing effects before and after medication	17	2.63%
Showing efficacy in the short and long term	16	2.48%
Associate the medication to non-pharmacological strategies	16	2.48%
Showing effects on quality of life	15	2.33%
I don't know	15	2.33%
Discussing the effects of not medicating	12	1.86%
Using the model of other medical conditions (we pharmacologically treat epilepsy...why not mental conditions?)	11	1.70%
Fight stigma	10	1.55%
Presenting medication as second-line choice after nonpharmacological options	7	1.08%
Education promoted by adults who used medication in childhood	4	0.62%
Educating via media	4	0.62%
Help accepting the disorder	3	0.47%
Showing medication does not change the personality	3	0.47%

(Table 2 continues in next column)

	Participants (N=644)	
	N	%
(Continued from previous column)		
Saying that medication is only a temporary help	3	0.47%
Trial of medication with strict monitoring	21	3.26%
Education promoted by famous people with the disorder	21	3.26%
Publish more studies	21	3.26%
Education to children in school	21	3.26%
Improve ethical procedures of drug companies	1	0.16%
Urge caution vis-à-vis what is reported by lay press	1	0.16%
Promote empathy for people who need medication	1	0.16%
Studies not funded by drug companies	1	0.16%
Education especially for newer medications	1	0.16%
Doing studies on natural products	1	0.16%
Use simple examples (eg. like wearing glasses)	1	0.16%
Normalise the concept of mental condition	1	0.16%
Make service access easier	1	0.16%
Seeing medication as the last resort	1	0.16%
Trusting professionals rather than Internet	1	0.16%
Listening to parents' concerns and discuss with them	1	0.16%
Patience and persistence	1	0.16%
Consider faith or religion of parents	1	0.16%
Education independent from drug companies	1	0.16%



## Survey among n=644 experts by lived experiences – most common responses:

**1. What do you think are the most important questions on medicines for children or teenagers with mental problems that researchers should try to answer in the future?**

- *Understanding side effects (in general or in the long-term more specifically): 361 (56.05%)*
- *Potential of medication of being addictive: 83 (12.88%)*

**2. In your opinion, do people think that taking medicines for mental problems is bad?**

- *Yes: 518 (80.43%)*

**3. What do you think we could do to help people understand that medicines may help children and teenagers with mental problems?**

- *Education on mental health issues and their treatment 216 (33.54%)*
- *Education lead by people with personal lived experience 91 (14.13%)*



# Issues which need to be addressed

- A greater focus on disorders for which no evidence-based or no well-studied pharmacological interventions are available

*Top-3: autism spectrum disorder, emotional dysregulation/irritability, anorexia nervosa*

- Taking an overview of other important outcomes, not just the core symptoms tested in trials
- Adapting the approval process so that that effective medicines for children can be approved more efficiently
- A better understanding of long term-effect on the developing brain (both beneficial and harmful)

# Recommendations

## Key opportunities include

- learning from failed trials (e.g., insufficient recruitment) – involve people with lived experiences
- reducing the placebo effect in trials –e.g., improve understanding how to minimize placebo effects
- assessing outcomes beyond core symptoms - e.g., more PROMs (Patient-Reported Outcome Measures), functional level and QoL (quality of life) measures
- considering developmental stage – e.g., adapt the timing of interventions to the underlying developmental windows and consider pubertal maturation stages
- comparing pharmacological and non-pharmacological treatments
- using innovative designs beyond standard randomised controlled trials – e.g., pharmaco-epidemiological studies, self-control methods, emulated targeted trials

# Recommendations (cont'd)

- moving towards precision medicine and stratification approaches - well defined groups sharing similar clinical characteristics or profiles of biomarkers
- investigation and implementation of digital technologies - ranges from incorporating artificial intelligence in diagnostic devices to using real world data
- focusing on conditions that are non-responsive to initial treatment
- improving the regulatory and legislative framework – e.g., the EMA action plan
- innovation in the way research is conducted, reported, and promoted