Cost of Adverse Event Management in Children, Adolescents, and Adults with Attention-Deficit/Hyperactivity Disorder in the United States

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Background

- Attention-deficit/hyperactivity disorder (ADHD) is a prevalent neurodevelopmental disorder, affecting approximately 12.4% of children and adolescents and 6% of adults in the United States, and is characterized by inattention, hyperactivity, and impulsivity, along with impairments in executive function, emotional regulation, and motivation[1-3]
- Adverse events (AEs) are common in the management of ADHD and have been associated with increased healthcare resource utilization and costs[4-8]
- Centanafadine, a novel investigational therapy, has demonstrated a favorable safety profile[9-15]
- As new treatment options emerge, it is important to understand how these therapies compare with commonly used options in terms of AE management costs to better inform stakeholder treatment decisions

Objective

To estimate the annual incremental AE management cost impact of shifting a proportion of treated patients from commonly used ADHD therapies to centanafadine from a US commercial payer perspective.

Methods

Model structure

- Two 1-year cost calculators were developed to estimate AE management costs for patients with ADHD (children/adolescents [6-17 years] and adults [≥18 years]) from a US commercial payer perspective
- Costs were reported in 2025 US Dollars (USD) for children/adolescents and in 2022 USD for adults, reflecting differences in the timing of the most recent available analyses
- A summary of key model attributes is provided in **Figure 1**

Model inputs

- Modeled populations were estimated using US census data and literature-derived epidemiologic inputs, including ADHD prevalence and treatment rates (**Figure 2**)[1,2,16-17]
- AE management costs were calculated on a pairwise basis for each comparator
- Each AE was assigned a cost, applied to the proportion of patients experiencing the AE and its estimated duration
- AE-related costs were estimated using two approaches derived from claims analyses: (1) AE-specific medical costs and (2) excess AE-related and other healthcare cost estimates (**Figure 3**)[4,5]
  - (1) AE-specific medical costs included inpatient, outpatient, and emergency room costs for medical claims for which there was a recorded diagnosis of the given AE
  - (2) Total excess healthcare costs comprised all-cause medical inpatient, outpatient, and emergency room visits and non-ADHD treatment-related pharmacy costs (reflecting the incremental all-cause cost difference between patients with versus without the AE diagnosis, after adjusting to make the cohorts comparable)
- AE frequencies were estimated using matching-adjusted indirect comparisons of phase 3 clinical trial data[12-15]
- AE duration was estimated based on a physician survey study[18]

Results

- Transitioning a hypothetical 20% of treated children and adolescents with ADHD (N = 2,063) from comparator therapy to centanafadine was associated with estimated annual plan-level cost reductions of $16,000–$316,000 from avoided AEs based on AE-specific medical costs and $126,000–$1,488,000 based on total excess healthcare costs (**Figure 4**)[a]
  - Cost reductions were greatest for centanafadine when compared to guanfacine extended-release (ER) and lowest when compared to viloxazine ER
- Transitioning a hypothetical 20% of treated adults with ADHD (N = 5,131) from a comparator therapy to centanafadine was associated with estimated annual plan-level cost reductions of $1,033,000–$2,126,000 from avoided AEs based on AE-specific medical costs and $2,347,000–$4,735,000 based on total excess healthcare costs (**Figure 4**)[a]
  - Cost reductions were greatest for centanafadine when compared to lisdexamfetamine dimesylate and lowest when compared to viloxazine ER

Footnote:
A. Proportion receiving centanafadine versus comparator in the current and future scenarios are hypothetical for illustrative purposes only

Figure 1: Model attributes

Model attributes	Details: Children & adolescents	Details: Adults
Population	Hypothetical 1,000,000-member health plan	
Perspective	US commercial payer perspective	
Intervention	Centanafadine	
Comparators	• Atomoxetine • Guanfacine ER • Lisdexamfetamine dimesylate • Methylphenidate hydrochloride ER tablet • Methylphenidate hydrochloride ER capsule • Viloxazine ER	• Atomoxetine • Methylphenidate hydrochloride ER tablet • Lisdexamfetamine dimesylate • Viloxazine ER
Time horizon	1-year	
Key model inputs	• Target population inputs • Hypothetical market shift assumptions for illustrative purposes • Frequency of AEs • Duration of AEs • Management cost of AEs	
Key model outputs	Annual incremental impact on AE management costs associated with shifting a proportion of treated patients from a comparator therapy to centanafadine	

Abbreviations: AE, adverse event; ER, extended-release; US, United States; USD, United States Dollar.

Figure 2: Model population

Total individuals considered per cost calculator
N = 1,000,000

Children and adolescents 6-17 years (*15.1% of total population*)[16]	Adults ≥18 years (*77.6% of total population*)[17]
N = 151,000	**N = 776,000**

Children and adolescents with ADHD (*12.4% prevalence of ADHD*)[1,a]	Adults with ADHD (*6.0% prevalence of ADHD*)[2]
N = 18,724	**N = 46,560**

Children and adolescents with ADHD receiving treatment (*55.1% treated*)[1,b]	Adults with ADHD receiving treatment (*55.1% treated*)[c]
N = 10,317	**N = 25,655**

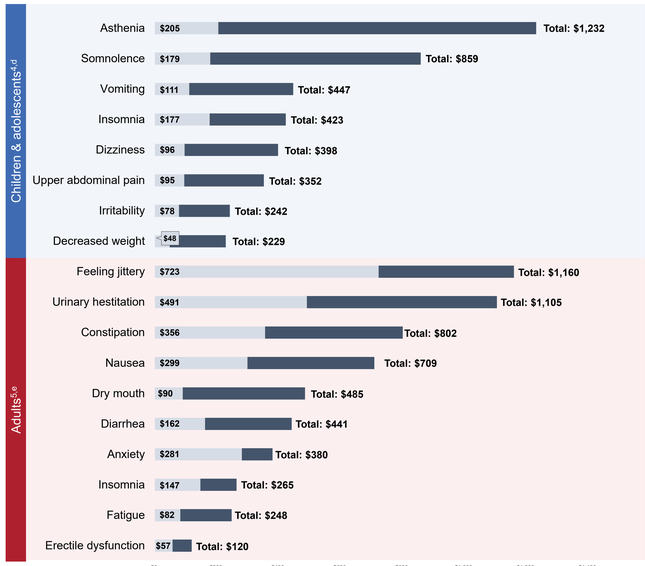
Total number of children, adolescents, and adults with ADHD receiving treatment
N = 35,972

Current scenario (*100% comparator*)[d]		**Future scenario** (*80% comparator; 20% centanafadine*)[d]	
Children and adolescents	Adults	Children and adolescents	Adults
Centanafadine: N = 0 Comparator: N = 10,317	**Centanafadine: N = 0 Comparator: N = 25,655**	**Centanafadine: N = 2,063 Comparator: N = 8,254**	**Centanafadine: N = 5,131 Comparator: N = 20,524**

Footnotes:
A. The prevalence of ADHD was estimated from a study utilizing the 2022 National Survey of Children's Health (NSCH) (N = 45,169), a population-based survey by the US Census Bureau. Prevalence of current ADHD diagnosis was reported among those 6-11 years and 12-17 years; overall prevalence among those 6-17 years of age was calculated using projected 2023 US Census data[16]
B. The proportion of individuals 6-17 years of age receiving medication for ADHD was estimated from a study utilizing the 2022 NSCH (N = 45,169). Proportion of individuals 6-11 years and 12-17 years currently receiving medication for ADHD were reported in the study; the overall proportion among those 6-17 years of age receiving medication for ADHD was calculated using projected 2023 US Census data[16]
C. In the absence of recent adult-specific treatment data, the proportion of adults with ADHD receiving medication for ADHD is assumed to be equivalent to the proportion of children and adolescents receiving medication for ADHD
D. Proportion receiving centanafadine versus comparator in the current and future scenarios are hypothetical for illustrative purposes only

Abbreviation: ADHD, attention-deficit/hyperactivity disorder.

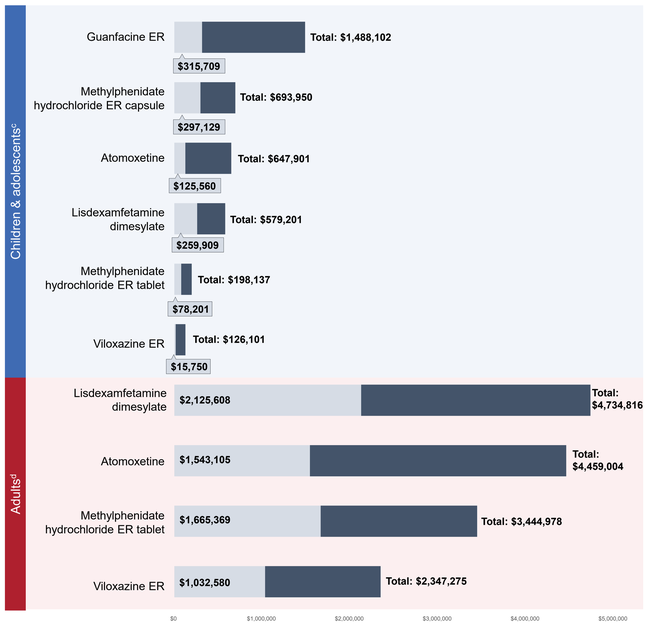
Figure 3: Monthly healthcare costs associated with AE management (PPPM)[a-c]



Footnotes:
A. Due to lack of data availability in claims, assumptions were made for the following AEs in children and adolescents: the cost for abdominal pain was assumed equal to upper abdominal pain; fatigue assumed equal to asthenia; lethargy assumed equal to asthenia; nausea assumed equal to vomiting; cost for decreased appetite, dry mouth, headache, pyrexia, rash, and sedation were assumed to be the cost of an outpatient visit (HCPCS code 99213)[19]
B. Due to lack of data availability in claims, assumptions were made for the following AEs in adults: the cost for initial insomnia was assumed equal to insomnia; cost for headache, lack of appetite, dizziness, irritability, and palpitations were assumed to be the cost of an outpatient visit (HCPCS code 99212)[19]
C. AE-specific medical costs included inpatient, outpatient, and emergency room costs for medical claims for which there was a recorded diagnosis of the given AE; total excess healthcare costs comprised all-cause medical inpatient, outpatient, and emergency room visits and non-ADHD treatment-related pharmacy costs (reflecting the incremental all-cause cost difference between patients with versus without the AE diagnosis, after adjusting to make the cohorts comparable)[4,5]
D. 2025 USD
E. 2022 USD

Abbreviations: AE, adverse event; PPPM, per patient per month; USD, United States Dollar.

Figure 4: Annual plan-level healthcare cost reductions related to AE management when switching from a comparator to centanafadine[a,b]



Footnotes:
A. When shifting a hypothetical 20% of patients from a comparator to centanafadine for illustrative purposes
B. AE-specific medical costs included inpatient, outpatient, and emergency room costs for medical claims for which there was a recorded diagnosis of the given AE; total excess healthcare costs comprised all-cause medical inpatient, outpatient, and emergency room visits and non-ADHD treatment-related pharmacy costs (reflecting the incremental all-cause cost difference between patients with versus without the AE diagnosis, after adjusting to make the cohorts comparable)[4,5]
C. 2025 USD
D. 2022 USD

Abbreviations: AE, adverse event; ER, extended-release; USD, United States Dollar.

Conclusions

Across all pairwise comparisons, centanafadine was associated with lower estimated AE management costs

Centanafadine has the potential to reduce AE-related healthcare costs compared with alternative ADHD therapies for children, adolescents, and adults

Limitations

- A key limitation of the cost calculators is that treatment efficacy was not explicitly modeled
- Efficacy was not included due to limited evidence demonstrating meaningful differences in efficacy across ADHD therapies and the lack of robust, validated framework linking changes in clinical trial rating scales to downstream real-world medical costs[20-22]
- As a result, it remains challenging to reliably translate small differences in trial-based efficacy measures into cost offsets within an economic model

Disclosures

- This work was supported by Otsuka Pharmaceutical Development & Commercialization, Inc. JS is an employee of Otsuka Pharmaceutical Development & Commercialization, Inc.
- TW, OR, AK, and MC are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Otsuka Pharmaceutical Development & Commercialization, Inc.
- AC is an employee of Center for Psychiatry and Behavioral Medicine

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