CONCERTA® (methylphenidate HCl ER)
Use of CONCERTA in Patients with Tic Disorders

SUMMARY

- According to the prescribing information, the use of CONCERTA in patients with motor tics or with a family history or diagnosis of Tourette's syndrome is contraindicated.[1]
- Studies have been conducted to assess the hypothesis that stimulants can cause, provoke or exacerbate tics and Tourette's syndrome with no confirmation.[2-7]
- **Palumbo et al (2004)**[7] analyzed the incidence of tics in children and adults with ADHD treated with CONCERTA across 5 studies:
  - In placebo-controlled studies (Studies 1-3), tics were reported in 4% for patients (9/224) treated with CONCERTA; all 9 patients had a history of tics.
  - In a long-term (2-years), open-label study (Study 4), tics as adverse events were reported in 9.8% of patients (40/407) over the 2-year treatment period.
    - The risk of tics was higher in patient with a history of tics than in those without (33% vs 7%, respectively; $P<0.0001$).
    - No correlation was found between the dose of CONCERTA and the frequency of tic episodes.
  - In a long-term (9-months), open-label study (Study 5), tics as adverse events were reported in 1.2% of patients (13/1082; safety population).
    - Three of these 13 patients had a history of tics.
- The use of CONCERTA in patients with ADHD and Tourette's syndrome has been documented in 2 case reports.[8,9]

PRODUCT LABELING

Please refer to the following section of the enclosed Full Prescribing Information that is relevant to your inquiry[1]: CONTRAINDICATIONS, Tics; and ADVERSE REACTIONS, Tics.

BACKGROUND

Stimulants have been hypothesized to cause, provoke or exacerbate tics and Tourette's Syndrome. Many authors have investigated this hypothesis with no confirmation from clinical observation and controlled trials.[2-7]

CLINICAL DATA

Incidence of Tics in Children and Adults with ADHD

Palumbo et al (2004)[7] analyzed the incidence of tics in children and adults with ADHD treated with CONCERTA across 5 studies.

Study Design/Methods

Analyses on the incidence of tics were conducted using pooled data from 3 short-term, placebo-controlled studies (Study 1, 2, and 3); separate analyses were conducted for each of the 2 long-term, open-label studies (Study 4: 2-years, and Study 5: 9-months). Patients with mild or moderate tics (without a diagnosis of Tourette's syndrome) were eligible to enroll in any of the 5 studies. In Studies 1-4, the parents were asked if their child had experienced tics during the time since the last study visit; new onset and change in severity were also assessed. In Studies 4 and 5, tics were reported as adverse events.

Results

Studies 1-3

- In the placebo-controlled studies, 224 children aged 6-13 years were treated with CONCERTA and 13% of these patients (29/224) had a history of tics.
- Tics were reported in 4% for patients (9/224) treated with CONCERTA. The difference between treatment groups was not statistically significant (CONCERTA, 4%; MPH IR, 2.3%; placebo, 3.7%).
    - In the CONCERTA group, all 9 patients who reported tics during the study had a history of tics.

Study 4

- Of the 407 children aged 6-13 years who participated in the first year of this open-label study, 11.8% (48/407) had a history of tics.
- Tics were experienced by approximately 5% of patients each month (most were not new onsets), and the severity remained unchanged or improved over the 12-month period.
- During the 2-year treatment period, tics as adverse events were reported in 9.8% of patients (40/407).
    - Of these 40 patients, 16 had a prior history of tics.
    - The majority of these events were mild or moderate in severity.
    - The risk of tics was 33% in patients with a history of tics and 7% in those without a history of tics ($P<0.0001$).
        - A statistically significant difference was observed in the mean duration of tics between patients with or without a history of tics (165 vs 79 days, respectively; $P=0.0318$).
        - No significant differences were observed between those with or without a history of tics in the mean number of tic episodes per patient (1.56 vs 1.58, respectively), and the mean time to first tic episode (204 vs 191 days, respectively).
    - No correlation was found between the dose of CONCERTA and the frequency of tic episodes.
    - Throughout the 2-year treatment period, 2% of patients (8/407) discontinued CONCERTA because of tics (history of tics, n=3; no history of tics, n=5).

Study 5

- Tics as adverse events were reported in 1.2% of patients (13/1082; safety population). See table Frequency of Tics During the Study.
- The majority of tic events were mild or moderate in severity; 2 patients experienced severe tics.
- Approximately 0.6% of patients (7/1082) discontinued treatment because of tics.

Frequency of Tics During the Study[7]

	Age Group: 6-12 years	Age Group: 13-17 years	Age Group: ≥ 18 years	TOTAL
Adverse event of tic, n	11	1	1	13
History of tics, n	2	1	-	3

Use of CONCERTA in Children with ADHD and Tourette's Syndrome

Jaworowski et al (2006)[8] described a case report in which atomoxetine and CONCERTA were successfully used concomitantly in a child with ADHD, comorbid bipolar disorder, and Tourette's syndrome.

- The boy was diagnosed with ADHD, obsessive-compulsive disorder (OCD), and oppositional-defiant disorder (ODD) at 5 years old.
- He experienced motor and vocal tics after treatment with methylphenidate and was diagnosed with Tourette's syndrome for which he was successfully treated with haloperidol, methylphenidate, and risperidone.
- He was referred for psychopharmacological review at the age of 10 years after being hospitalized for 6 months due to major mood disturbances and threats of harming himself and his baby brother. He was discharged on valproic acid, clonidine, and ziprasidone.
- Due to significant difficulties with concentration, distractibility, and multiple motor tics, the child was given atomoxetine 0.5 mg/kg/day, which was gradually increased to 1.2 mg/kg/day (50 mg/day) over a 2-week period.
- Although the child experienced some improvement in concentration, he continued to exhibit impulsive and disruptive behavior, so CONCERTA 18 mg/day was added in order to augment the effect of atomoxetine.
- The dose of CONCERTA was increased from 18 mg/day to 36 mg/day which resulted in a dramatic improvement in behavior both at school and at home.
- Despite improvement in behavior, the child demonstrated some increase in motor tics, which was then managed by increasing the clonidine dose from 75 µg/day to 150 µg/day in 3 divided doses. Positive behavior changes and improved concentration were maintained for up to a year.

Lan et al (2015)[9] described a case report of a 15-year-old boy with severe Tourette's syndrome and ADHD who was temporarily treated with CONCERTA.

- The child was diagnosed with Tourette's syndrome and ADHD at the age of 9 years and was initially treated with clonidine 37.5 µg/day and CONCERTA 36 mg/day.
- Risperidone 1.5 mg/day was added to his treatment regimen, and the dose was gradually increased to 3 mg/day as his tic symptoms progressed.
- At age 12, he experienced significant worsening of tics and was started on atomoxetine 50 mg/day. CONCERTA was discontinued.
- He was unable to tolerate atomoxetine and was restarted on CONCERTA 18 mg/day plus clonazepam 0.5 mg/day.
- The patient continued to experience severe motor tics and CONCERTA was discontinued due to unsatisfactory response. Further adjustments were made to his antipsychotic treatment.
- His tic disorder was eventually controlled with a combination of clozapine 50 mg/day and quetiapine 200 mg/day. Improvements were maintained for more than 1 year and up to the time of this publication.

LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 13 February 2025.

REFERENCES

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