

**Summary of Psychiatric and Neurological Adverse Events
from
June 2005 1-year Post Pediatric Exclusivity Reviews of Concerta and Other
Methylphenidate Products^{1,2}**

Table 1: Adverse event categories

AE category	Concerta	Immediate-release methylphenidate	Extended-release methylphenidate
Psychiatric	36	9	7
Neurological	16	7	11
Other	83	40	22
Total	135	56	40

Table 2: Brief case summaries of psychiatric adverse events for Concerta, immediate-release methylphenidate, and extended release methylphenidate (N=52)

ISR#	Age (yrs)	Gender	Summary
4601314-2	6	Male	Violent behavior, “psychotic” per mother, after 3 days methylphenidate. Methylphenidate discontinued and patient had severe headache all day. Events resolved.
4393027-X	9	Male	Acute psychosis (agitation, anxiety, social withdrawal, sweating, hyperventilation, confusion, quivering) same day methylphenidate was added to ongoing fluticasone propionate/salmeterol xinafoate inhaler treatment. Hospitalized, methylphenidate discontinued, events resolved.
4543940-5	7	Female	Psychotic behavior after first dose Concerta. Concerta discontinued, event resolved
4334819-2	14	Male	Psychosis and suicidal gesture during Concerta. Onset and outcome unknown
4357504-x	12	Male	Psychosis and aggression after 2 weeks Concerta. Concerta discontinued, events resolved
4295943-6	7	Male	Mania and psychosis during Concerta. Concerta discontinued, events resolved
4554624-1	8	Female	Psychotic episode during use of methylphenidate. Symptoms, onset, treatment, outcome unknown.
4343669-2	13	Male	Psychotic episode during methylphenidate use. Onset unknown. Methylphenidate discontinued, event resolved. Reporter’s nurse later said event not due to methylphenidate.

ISR#	Age (yrs)	Gender	Summary
4299018-1	13	Male	Psychotic episodes during methylphenidate, sertraline, and salmeterol concomitant use and during methylphenidate, sertraline, and atomoxetine concomitant use. One episode resolved with salmeterol discontinuation, before atomoxetine initiated. Psychiatric drugs continued, event outcome unknown.
4288789-6	13	Male	Manic symptoms during methylphenidate use. Hospitalized. Onset, treatment, outcome unknown.
4288742-2	16	Male	Mania with methylphenidate and Adderall. Onset, treatment, outcome unknown. Unknown whether these drugs were used concurrently.
4420654-3	13	Male	Hallucinations and mood swings during methylphenidate and paroxetine use. Onset, treatment, outcome unknown. Report source: consumer speaking on TV show.
4297425-4	6	Male	Hallucinations and headache after about 1 month Concerta. Concerta and events continue
4416161-4	6	Female	Visual hallucinations 4 days after dosage increase after 4 months interrupted Concerta. Concerta discontinued, event resolved
4370915-1	11	Male	Hallucinations and abnormal thinking after 6 weeks Concerta. Concerta discontinued, schizophrenic psychosis diagnosed, olanzapine started, events ongoing
4338458-9	8	Male	Hallucinations, insomnia, bad dreams after 1 day Concerta. Continue for 1 week during Concerta. Concerta discontinued, events resolved
4315723-2	7	Male	Hallucinations, anxiety, sleep disorder after about 1 ½ weeks Concerta. Concerta discontinued, events resolved
4332569-x	6	?	Hallucinations during Concerta. Onset and outcome unknown
4327846-2	10	Male	Hallucination, diplopia, headache with one dose Concerta. Concerta discontinued, events resolved. After rechallenge with 1 dose Concerta, chest pain and back pain. Concerta discontinued, events resolved
4383170-3	6	Male	Increased irritability, increased waking, possible hallucinations during Concerta. Concerta discontinued, events improved
4443828-4	12	Male	Hallucinations during methylphenidate. Methylphenidate discontinued, event resolved. Methylphenidate rechallenged and event returned. Methylphenidate discontinued, event resolved.

ISR#	Age (yrs)	Gender	Summary
4443829-6	7	Male	Hallucinations during methylphenidate. Methylphenidate discontinued, event resolved.
4443812-0	7	Male	Hallucinations after about 1 year methylphenidate. Placebo substituted for methylphenidate and event resolved.
4358726-4	12	Male	Violent behavior during concurrent immediate-release methylphenidate and Concerta use. Drugs discontinued, event resolved.
4516223-7	12	Male	Anxiety, violent behavior, aggression after about 1 month Concerta. Concerta discontinued, events resolved
4516221-3	6	Female	Violent behavior and aggression soon after increase dosage after about 2 years Concerta. Concerta and events ongoing
4516214-6	8	Male	Anorexia, insomnia, and physical aggressiveness after more than 2 years Concerta. Concerta and events continue
4482604-3	8	Male	Disinhibition, physical aggression, abnormal behavior after 1 day Concerta. Concerta discontinued, events resolved
4337854-3	14	Male	Aggression, urticaria, decreased appetite after 2 days Concerta. Concerta discontinued, events resolved
4500602-8	6	Male	Increased activity and increased violent behavior soon after start Concerta. Concerta discontinued, other treatments given, events improved
4530562-5	9	Male	Threaten suicide and described as “danger to himself and others” after 2 years Concerta and fluoxetine. Both drugs discontinued, events ongoing 2 days later
4509680-3	5	Male	Aggression and suicide attempt after 1 day Concerta. Concerta discontinued, events ongoing
4377851-5	14	Male	Intentional self-injury and suicidal ideation after about 6 months Concerta. Concerta ongoing, event outcome unknown
4290062-7	12	Female	Depression, suicidal ideation after 1 month Concerta. Concerta discontinued, events resolved
4334699-5	12	Female	Trichillomania, self-injurious behavior, suicidal ideation soon after Concerta added to paroxetine. Both drugs discontinued, events resolved
4395831-0	10	Male	Suicide attempt and suicidal ideation 2-3 weeks after starting Concerta. Concerta discontinued, events resolved
4297427-8	9	Female	Suicidal ideation during Concerta. Time to onset and outcome unknown.

ISR#	Age (yrs)	Gender	Summary
4343732-5	9	Male	Suicidal ideation, sadness, anxiety, fearfulness, crying with first dose Concerta. Concerta discontinued, events resolved
4526725-5	15	Male	Suicidal ideation, anorexia, abdominal pain less than 8 months after starting Concerta. Concerta dosage increased and patient become "high" and aggressive. Concerta discontinued. After 5 months, Concerta restarted and "symptoms" (unspecified) recurred.
4385130-5	9	Male	Depression and suicide attempt after 1 week Concerta. Changed to Ritalin and events improved
4459444-4	4	Male	Depression, crying, headache, stomach pain after 4 months methylphenidate. Hospitalized for meningitis during methylphenidate use. Methylphenidate continued, headache and stomach pain continue. Outcome of depression and crying unknown.
4498015-0	4	Female	Increased "whiney" behavior, no improvement in ADHD behavior during about 6 months methylphenidate treatment. Outcome unknown.
4276318-2	6	Male	Increased school problems, refusal to do any work after switch to generic methylphenidate. Outcome unknown.
4305792-8	10	Male	Irritability, stomach burning, and nausea during 1 month use of methylphenidate. Methylphenidate discontinued, events resolved.
4414939-4	9	Male	Choreoathetoid movements, euphoria, insomnia after 4 days Concerta. Concerta discontinued, events ongoing 2 ½ weeks later
4290188-8	6	Male	Increased anxiety and pica less than 1 month after start Concerta. Concerta discontinued, events improved
4270799-6	6	Male	Abnormal behavior (licking table) after 1 day Concerta. Concerta ongoing, event resolved
4315477-x	6	Male	Unspecified change in behavior after 4 months Concerta. Outcome unknown
4437824-0	15	Female	Phobia after about 3 months Concerta. Concerta dosage decreased, event resolved
4404757-5	8	Male	Anxiety, social withdrawal, listlessness, fearfulness, excessive rumination after 1 ½ months Concerta. Concerta discontinued, events resolved
4258940-2	11	Male	Panic attack after 2 days Concerta. Concerta discontinued, event resolved

ISR#	Age (yrs)	Gender	Summary
4471609-4	8	Female	Paralyzing anxiety, anorexia, trembling, severe headache, psychomotor slowdown, nightmares, insomnia, abdominal and chest pain after 3 days Concerta. Changed to Ritalin and events resolved except for slight trembling

Table 3: Brief case summaries of neurological adverse events with Concerta, immediate-release methylphenidate, and extended-release methylphenidate (N=34)

ISR#	Age (yrs)	Gender	Summary
4516224-9	12	Male	Seizures (per consumer) after 5 months Concerta. Concerta discontinued, events resolved
4516219-5	14	Male	Seizure-like activity and stress symptoms. Onset and outcome unknown
4443825-9	15	Male	Epilepsy. Onset unknown. Concerta and risperidone discontinued, events ongoing
4290182-7	10	Male	Seizures 2 weeks after increased Concerta dosage. Concerta discontinued, treated with Trileptal, events resolved
4415346-0	10	Male	Seizure with Concerta and sertraline. Onset and outcome unknown
4516211-0	6	Male	Seizure after 5 months Concerta. Concerta discontinued, event resolved
4254304-6	11	Male	Focal epilepsy, confusion, restlessness, retrograde amnesia, trembling, sleep walking, eye pain with Concerta. Concerta discontinued, eye pain, focal epilepsy, amnesia ongoing. Onset unknown
4280661-0	14	Male	Absence and tonic-clonic convulsions after 9 months Concerta. Concerta discontinued, events resolved
4601412-3	13	Male	Seizure during methylphenidate use. Treatment and outcome unknown.
4359306-7	12	Male	Seizure after 2 years extended-release methylphenidate and concomitant immediate-release methylphenidate of unknown duration. All methylphenidate discontinued, event resolved.
4508976-9	7	Male	Seizures, agitation, altered mental status same day methylphenidate dosage increased. Hospitalized. Treatment and outcome unknown.
4404706-X	8	Male	Seizure after 1 year methylphenidate and 1 month after dosage increase. Dosage decreased, event resolved.

ISR#	Age (yrs)	Gender	Summary
4554629-0	11	Male	Increased seizure frequency after less than 1 month methylphenidate. Methylphenidate discontinued, event ongoing. Seizure history.
4336843-2	8	Female	Tics with methylphenidate. Onset and outcome unknown.
4347965-4	6	Male	Tic after 2 months methylphenidate. Methylphenidate discontinued, tic treated with clonidine and risperidone. Tic subsided.
4394099-9	7	Male	Tic after 2 months methylphenidate. Methylphenidate discontinued, event ongoing.
4352177-4	14	Male	Tic exacerbated, “paradoxical effect”, and insomnia after 1 month extended-release methylphenidate (Metadate CD). Switched to immediate-release methylphenidate (Ritalin), events resolved.
4531859-5	13	Male	Leg numbness, abdominal pain, asthenia, sleep disorder, tic with Concerta. Concerta dosage decreased, leg numbness resolved. Other events ongoing. Onset unknown
4356824-2	11	Male	Dyskinesia aggravated after 4-6 weeks Concerta. Concerta discontinued, event outcome unknown
4288796-3	2	?	Dyskinesia, psychomotor hyperactivity, tachycardia, vomiting after accidental ingestion of 40 mg methylphenidate. Treated in ER with lorazepam. Outcome unknown.
4496410-7	11	Male	Dystonia, increased heart rate, tremor hours after dosage increased. Treated with Benadryl and Diastat rectal, events resolved.
4366761-5	7	Male	Paresis of left leg after 15 days methylphenidate. Methylphenidate discontinued, event ongoing.
4331504-8	11	Male	Facial paresis during use of methylphenidate. Onset, treatment, outcome unknown.
4300540-X	5	Male	Difficulty controlling eye movement, confusion, anxiety 1 day after starting methylphenidate. Events continued with dosage adjustments, resolved with methylphenidate discontinuation.
4458045-1	9	Male	Headache, fever after 2 days Concerta. Concerta discontinued, events resolved
4451998-7	13	Female	Headache and vomiting during methylphenidate use. Methylphenidate discontinued, event resolved.
4280109-6	7	Male	Decreased consciousness, increased heart rate after 2 nd dose Concerta. Concerta discontinued, events resolved
4436699-3	4	Female	Generic methylphenidate causes drowsiness.
4362495-1	10	Female	Syncope and bilateral delta waves on EEG after 1 year methylphenidate. Treatment and outcome unknown.

ISR#	Age (yrs)	Gender	Summary
4510046-0	8	Male	Loss of consciousness and hypertonia of limbs after about 2 months methylphenidate. Methylphenidate ongoing.
4486839-5	10	Male	Brain tumor and cyst after 2 years, 4 months Concerta. Concerta discontinued, surgery performed, events resolved. Concerta restarted
4252008-7	9	Male	Coma lasting 4 days and generalized slowed rhythm on EEG after 2-3 years methylphenidate. Hospitalized, methylphenidate discontinued, event slowly resolved. Previous similar incident while taking methylphenidate.
4554626-5	7	Male	“Sleep problem” after 1 year methylphenidate. Withdrawal syndrome after “all ADHD medications” discontinued. Symptoms, outcome unknown.
4258081-4	10	Female	Disorientation, visual disturbance, shaking, aching extremities day of dosage increase after 6 months Concerta. Concerta discontinued, events resolved

Reference:

1. K. Phelan. One year post-pediatric exclusivity postmarketing adverse event review, Concerta (OROS methylphenidate). June 14, 2005. PID #D040058
2. K. Phelan. Adverse events with methylphenidate products other than Concerta in pediatric patients during the first year after granting of pediatric exclusivity for Concerta (December 4, 2003 – January 4, 2005). June 14, 2005. PID#050249