U.S. Food and Drug Administration
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Drug Safety Communications

FDA Drug Safety Communication: FDA warns of rare risk of long-lasting erections in males taking methylphenidate ADHD medications and has approved label changes

Safety Announcement

[12-17-2013] The U.S. Food and Drug Administration (FDA) is warning that methylphenidate products, one type of stimulant drug used to treat attention deficit hyperactivity disorder (ADHD), may in rare instances cause prolonged and sometimes painful erections known as priapism. FDA continues to monitor the safety of drugs after they are approved, and, based on a recent review of methylphenidate products, we have updated the drug labels and patient Medication Guides to include information about the rare but serious risk of priapism. Patients who take methylphenidate and develop erections lasting longer than four hours should seek immediate medical treatment to prevent long-term problems with the penis. If not treated right away, priapism can lead to permanent damage to the penis.

Priapism can occur in males of any age and happens when blood in the penis becomes trapped, leading to an abnormally long-lasting and sometimes painful erection. Younger males, especially those who have not yet reached puberty, may not recognize the problem or may be embarrassed to tell anyone if it occurs. All male patients and their caregivers should be taught the signs and symptoms of priapism and the importance of seeking immediate medical treatment if it occurs.

Methylphenidate products are among the medicines that can be used to treat ADHD. One of the most common childhood brain disorders, ADHD can continue through adolescence and adulthood and causes symptoms such as difficulty staying focused and paying attention, difficulty controlling behavior, and hyperactivity. Medications such as methylphenidate used to treat ADHD benefit patients with the disorder by increasing focus, reducing impulsivity, and improving overall social functioning. Therefore, patients who have been prescribed a methylphenidate product should not stop taking it without first talking to their health care professionals. Table 1 lists methylphenidate products marketed in the United States.

In our review, the median age of patients taking a methylphenidate product who experienced priapism was 12.5 years (range 8 to 33 years). In a few patients, priapism occurred after an increase in the dosage of methylphenidate, but priapism has also occurred under other conditions, such as during short periods of time when the drug was stopped temporarily, when there was a longer than typical time between doses, or after stopping the drug permanently. Two patients required surgical intervention; one required shunt placement, and the other had to have needle aspiration of the corpus cavernosum.

The risk of priapism may cause some health care professionals toconsider switching patients to the non-stimulant drug Strattera (atomoxetine), another drug used to treat ADHD; however, atomoxetine has also been associated with priapism in young children, teenagers, and adults. Priapism appears to be more common in patients taking atomoxetine than in patients taking methylphenidate products. Health care professionals should be cautious when considering changing patients from methylphenidate to atomoxetine.

Amphetamine products are also used to treat ADHD, and we have received reports of priapism in four patients taking an amphetamine product. However, whether the amphetamine products caused the priapism is uncertain, because all of these patients had been taking other medications that are thought to cause priapism. Therefore, we cannot conclude that the use of amphetamine products can result in priapism.

Facts about Methylphenidate

- Central nervous system (CNS) stimulant used to treat attention deficit hyperactivity disorder (ADHD), a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate-to-severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity.
- During the year 2012, approximately 20 million prescriptions were dispensed and 3.9 million patients received a dispensed prescription for methylphenidate or dexmethylphenidate products through U.S. outpatient retail pharmacies. Of the total patients, approximately 61% (about 2.4 million patients) were male.[1]

Additional Information for Patients

- **Methylphenidate products may rarely cause priapism – long-lasting and sometimes painful erections in males of any age.** If not treated right away, priapism can lead to permanent damage to the penis.
- **Seek immediate medical care if priapism or any erection lasting longer than four hours occurs with or without sexual stimulation.**
- Do not stop taking your methylphenidate product without first discussing it with your health care professional.
- Carefully read the patient Medication Guide that comes with your filled prescription.
- Discuss any questions or concerns about methylphenidate products with your health care professional.
- Report any side effects you experience to your health care professional and the FDA MedWatch program, using the information in the Contact FDA box at the bottom of the page.

Additional Information for Health Care Professionals

- Talk to your male patients and their caregivers to make sure they know the signs and symptoms of priapism and stress the need for immediate medical treatment should it occur.
- Encourage your patients to read the Medication Guide they receive with every filled prescription.
- Another ADHD drug, Strattera (atomoxetine), has also been associated with priapism in children, teens, and adults. Priapism appears to be more common in patients taking atomoxetine than in those taking methylphenidate products; however, because of limitations in available information, we do not know how often priapism occurs in patients taking either type of product. Use caution when considering switching patients from methylphenidate to atomoxetine.
- FDA also identified four cases of patients developing priapism with amphetamine products that were taken for ADHD. However, all of these cases also reported use of concomitant medications thought to cause priapism; therefore, we cannot conclude that the use of amphetamine products alone can result in priapism, as we have observed with atomoxetine and methylphenidate products.
- Report adverse events involving methylphenidate products to the FDA MedWatch program, using the information in the Contact FDA box at the bottom of the page.

Data Summary

The FDA Adverse Event Reporting System (FAERS) and published literature were reviewed to identify male patients who reported one or more problems with sexual function in association with the use of a methylphenidate product. Such problems included ejaculation disorder, erectile dysfunction, more frequent erections, painful erections, penile pain, other disorders of the penis, priapism, and spontaneous penile erections. The data reviewed supported an association between the use of methylphenidate products and priapism. However, because FAERS is a spontaneous reporting system for adverse events, an incidence of priapism cannot be calculated.

There were 15 cases meeting the definition of priapism reported from 1997 through 2012 in association with a methylphenidate product. Of the 14 cases reporting an age, 12 cases were in patients less than 18 years of age. The median age of patients reporting priapism symptoms was 12.5 years (range 8 to 33 years). Some patients were hospitalized for treatment, including two who required surgical intervention: one with shunt placement and another with needle aspiration of the corpus cavernosum.

Four cases reported priapism following the withdrawal of methylphenidate use, including withdrawal because of drug discontinuation, drug-free holidays, and non-adherence. In some patients, priapism resolved after the drug was restarted. It is possible that priapism may be more likely to occur with the use of immediate-release methylphenidate, which has a shorter half-life.

In conclusion, priapism associated with the use of methylphenidate products appears to be rare. However, given the potential for serious outcomes, it is important that patients, caregivers, and health care professionals be aware of the need to seek immediate medical attention for priapism to avoid

permanent harm. In an effort to increase awareness of this rare but serious risk of priapism, FDA has updated the drug labels and patient Medication Guides for all methylphenidate products**.**

Table 1. Methylphenidate products marketed in the U.S.

Brand name	**Established name**
Concerta	Methylphenidate hydrochloride
Daytrana	Methylphenidate
Focalin, Focalin XR	Dexmethylphenidate hydrochloride
Metadate CD, Metadate ER	Methylphenidate hydrochloride
Methylin, Methylin ER	Methylphenidate hydrochloride
Quillivant XR	Methylphenidate hydrochloride
Ritalin, Ritalin LA, Ritalin SR	Methylphenidate hydrochloride

References

1. IMS Health, National Prescription Audit (NPATM) and Total Patient Tracker (TPT). Year 2012. Data Extracted September, 2013.