

# Methylphenidate Hydrochloride Extended Release Tablets (generic Concerta) made by Mallinckrodt and Kudco

**UPDATE [10-17-2016] FDA proposes to withdraw approval of two generic versions of Concerta (methylphenidate hydrochloride)**

The FDA is proposing to withdraw approval of two generic versions of Concerta (methylphenidate hydrochloride) extended-release (ER) capsules, used to treat attention-deficit hyperactivity disorder. Mallinckrodt Pharmaceuticals and UCB/Kremers Urban (formerly Kudco) the companies that make the generic products, have failed to demonstrate that their products provide the same therapeutic effect as (are bioequivalent to) the brand-name drug they reference.

This action is related to steps the FDA took in November 2014. At that time, the **FDA announced** (<http://www.fda.gov/drugs/drugsafety/ucm422568.htm>) that, based on an analysis of data, it had concerns that the Mallinckrodt and Kudco (now UCB/Kremers Urban) products may not produce the same therapeutic effects as Concerta. At that time, the FDA requested that Mallinckrodt and Kudco either (1) voluntarily withdraw their products from the market and request that FDA withdraw approval of their product's Abbreviated New Drug Applications (ANDAs) or (2) within six months, provide data to confirm that their products are bioequivalent to Concerta consistent with the revised **draft guidance for industry** (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM320007.pdf>) for bioequivalence testing for these products.

At that time, the FDA changed the Orange Book therapeutic equivalence code for these two products from AB (indicating therapeutic equivalence) to BX (data are insufficient to determine therapeutic equivalence).

Neither Mallinckrodt nor UCB/Kremers Urban has voluntarily withdrawn its product from the market, and neither has provided data confirming its product's bioequivalence consistent with the revised recommendations. Accordingly, the FDA is proposing to withdraw approval of the products' ANDAs and is announcing an opportunity for the firms to request a hearing on the proposal. As part of this process, the FDA is publishing Notices of Opportunity for Hearing (NOOHs) on its Proposals to Withdraw Marketing Approval in the Federal Register. If approval of these ANDAs is withdrawn by the FDA, the products will no longer be able to be marketed in the U.S.

Each NOOH explains that the firm may request a hearing to show why approval of their ANDA should not be withdrawn and has the opportunity to raise, for administrative determination, all issues relating to the legal status of the drug products covered by these applications. Each firm must respond in writing, within 30 days, to request a hearing. If the firm fails to do so, the opportunity for a hearing will be waived.

During the course of this process, the FDA will update the related **Mallinckrodt** (<https://www.federalregister.gov/d/2016-25093>) and **UCB/Kremers Urban** (<https://www.federalregister.gov/d/2016-25092>) dockets as new information becomes available.

The Mallinckrodt UCB/Kremers Urban products are still approved and can be prescribed, but they are not recommended as automatically substitutable for Concerta. Janssen manufactures an **authorized generic** ([http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm126389.htm#WHAT\\_IS\\_AG](http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm126389.htm#WHAT_IS_AG)) of Concerta, which is marketed by Actavis under a licensing agreement. The Actavis product is not impacted by this announcement.

If you or your health care professional are concerned that a methylphenidate hydrochloride ER product you are taking is not providing the desired effect, and you do not know the manufacturer, contact the pharmacy where the prescription was filled to verify the product's manufacturer. If you, or those under your care, are taking the Mallinckrodt or Kudco products and have concerns about lack of desired effect during the dosing period, contact the prescribing health care provider to discuss whether a different drug product would be more appropriate.

### **[11-13-2014] FDA concerns about therapeutic equivalence with two generic versions of Concerta tablets (methylphenidate hydrochloride extended-release)**

Based on an analysis of data, FDA has concerns about whether or not two approved generic versions of Concerta tablets (methylphenidate hydrochloride extended-release tablets), used to treat attention-deficit hyperactivity disorder in adults and children, are therapeutically equivalent to the brand-name drug. The two approved generic versions of **Concerta** (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.SetCurrentDrug&ApplNo=021121&DrugName=CONCERTA&ActiveIngred=METHYLPHENIDATE%20HYDROCHLORIDE&SponsorApplicant=JANSSEN>) are manufactured by Mallinckrodt Pharmaceuticals and Kudco Ireland Ltd.

FDA has not identified any serious safety concerns with these two generic products. Patients should not make changes to their treatment except in consultation with their health care professional.

If you or your health care professional are concerned the drug product is not providing the desired effect and you do not know the manufacturer, contact the pharmacy where the prescription was filled to verify the product's manufacturer. If you, or those under your care, are taking the Mallinckrodt or Kudco products and have concerns about lack of desired effect during the dosing period, contact the prescribing health care provider to discuss whether or not a different drug product would be more appropriate.

#### *FDA's Scientific Evaluation of Generic Concerta Products*

An analysis of adverse event reports, an internal FDA re-examination of previously submitted data, and FDA laboratory tests of products manufactured by Mallinckrodt and Kudco have raised concerns that the products may not produce the same therapeutic benefits for some patients as the brand-name product, Concerta, manufactured by Janssen Pharmaceuticals, Inc. Janssen also manufactures an authorized Concerta generic, which is marketed by Actavis under a licensing agreement and is identical to Janssen's Concerta. FDA included the **authorized generic** ([/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm126389.htm#WHAT\\_IS\\_AG](http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm126389.htm#WHAT_IS_AG)) in its analysis and found it to be bioequivalent to, and substitutable for, Concerta. Apart from the Mallinckrodt, Kudco, and Actavis products, there are no other generics for Concerta.

Methylphenidate hydrochloride extended-release products approved as generics for Concerta are intended to release the drug in the body over a period of 10 to 12 hours. This should allow for a single-dose product that is consistent with the effect of a three times per day dose of immediate-release methylphenidate hydrochloride.

In some individuals, the Mallinckrodt and Kudco products may deliver drug in the body at a slower rate during the 7- to 12-hour range. The diminished release rate may result in patients not having the desired effect.

As a result, the FDA has changed the therapeutic equivalence (TE) rating for the Mallinckrodt and Kudco products from AB to BX. This means the Mallinckrodt and Kudco products are still approved and can be prescribed, but are no longer recommended as automatically substitutable at the pharmacy (or by a pharmacist) for Concerta.

Consequently, FDA has revised its **[draft guidance for industry \(/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM320007.pdf\)](#)** for bioequivalence testing for methylphenidate hydrochloride extended-release tablets (Concerta). FDA has asked that within six months, Mallinckrodt and Kudco confirm the bioequivalence of their products using the revised bioequivalence standards, or voluntarily withdraw their products from the market.

FDA will continue to evaluate its testing and approval standards and bioequivalence guidances for other generic methylphenidate hydrochloride extended-release products and revise as needed.

#### Related Information

- **[Questions and Answers Regarding Methylphenidate Hydrochloride Extended Release Tablets \(generic Concerta\) made by Mallinckrodt and UCB/Kremers Urban \(formerly Kudco\) \(/Drugs/DrugSafety/ucm422569.htm\)](#)**
- **[FR Notice: Bioequivalence Recommendations for CONCERTA \(Methylphenidate Hydrochloride\) Extended-Release Tablets; Draft Guidance for Industry; Availability \(http://www.regulations.gov/#!documentDetail;D=FDA-2007-D-0369-0298\)](#)**

#### **[More in Drug Safety and Availability \(/Drugs/DrugSafety/default.htm\)](#)**

**[Drug Alerts and Statements \(/Drugs/DrugSafety/ucm215175.htm\)](#)**

**[Medication Guides \(/Drugs/DrugSafety/ucm085729.htm\)](#)**

**[Drug Safety Communications \(/Drugs/DrugSafety/ucm199082.htm\)](#)**

[Drug Shortages \(/Drugs/DrugSafety/DrugShortages/default.htm\)](#)



[Postmarket Drug Safety Information for Patients and Providers \(/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/default.htm\)](#)



**[Information by Drug Class \(/Drugs/DrugSafety/InformationbyDrugClass/default.htm\)](#)**

**[Medication Errors \(/Drugs/DrugSafety/MedicationErrors/default.htm\)](#)**

[Drug Safety Podcasts \(/Drugs/DrugSafety/DrugSafetyPodcasts/default.htm\)](#)



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**[Drug Recalls \(/Drugs/DrugSafety/DrugRecalls/default.htm\)](#)**