NEW YORK STATE OF OPPORTUNITY. Department of Health

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RETRODUR INTERVENTION NOTICE: Kalydeco® and Orkambi®

Dear Prescriber, June 8, 2016

The New York State (NYS) Medicaid Drug Utilization Review (DUR) Program retrospectively reviews the prescribing and dispensing of outpatient prescription medications in order to ensure that prescriptions are appropriate, medically necessary, and are not likely to result in adverse medical outcomes. The NYS Medicaid DUR Board has reviewed ivacaftor (Kalydeco®) and lumacaftor/ivacaftor (Orkambi®) utilization within the NYS Medicaid program. NYS Medicaid pharmacy claims data indicate that you have written prescription(s) for Kalydeco® and/or Orkambi®.

The NYS DUR Board recommended an educational intervention at the prescriber level highlighting safety issues regarding the utilization of ivacaftor and lumacaftor/ivacaftor that are provided below.[1,2] The manufacturer's recommendations for addressing and monitoring for these issues are found in the prescribing information.

Liver function abnormalities*:

Ivacaftor (Kalydeco®)	Lumacaftor/ivacaftor (Orkambi®)
• Transaminase (AST or ALT) elevations have been reported. • Interrupt treatment in patients with AST or ALT >5 times ULN.	• Elevations in transaminases and, sometimes, bilirubin, have been reported. • Interrupt treatment in patients with AST or ALT >5 times ULN, or >3 times the ULN and bilirubin >2 times the ULN. • Worsening liver function, including encephalopathy, has been observed in some patients with advanced liver disease; use with caution (monitor closely and reduce dose) in these patients and only if benefits outweigh risks.

ALT=alanine transaminase; AST=aspartate transaminase; ULN=upper limit of normal

***Hepatic function should be assessed prior to initiation, every 3 months during the first year of treatment, and annually thereafter.**

Potential drug interactions:

- **Lumacaftor** is a strong inducer of CYP3A and may decrease the effects of CYP3A substrates. Co-administration with medications that are sensitive CYP3A substrates or CYP3A substrates with a narrow therapeutic index is not recommended.
- **Lumacaftor/ivacaftor** may decrease exposure to hormonal contraceptives, decreasing effectiveness and increasing the incidence of menstruation-associated adverse reactions. Hormonal contraceptives should not be relied upon as an effective method of contraception when co-administered with lumacaftor/ivacaftor.
- **Ivacaftor** is a substrate of CYP3A4 and CYP3A5 and may have reduced effectiveness when administered with strong CYP3A inducers (e.g., rifampin, St John's Wort). Co-administration with strong CYP3A inducers is not recommended.

Cataracts: Cases of non-congenital lens opacities/cataracts have been reported in pediatric patients treated with ivacaftor. Possible attribution to ivacaftor cannot be excluded. **Baseline and follow-up ophthalmological examinations are recommended in pediatric patients initiating treatment.**

Respiratory events: Respiratory events were seen more commonly during initiation of lumacaftor/ivacaftor compared to placebo. There is limited clinical experience with lumacaftor/ivacaftor in patients with percent predicted FEV_1 <40 and **additional monitoring of these patients is recommended during initiation of lumacaftor/ivacaftor.**

The DUR Program recognizes that safe and effective pharmacotherapy depends on the assessment of a patient's entire clinical profile. We ask that you consider the information provided regarding the prescribing of ivacaftor (Kalydeco®) and lumacaftor/ivacaftor (Orkambi®) therapy for your patients.

Thank you for your professional assistance in this matter.

Sincerely,

John F. Naioti, Jr., R.Ph.
Manager, Drug Utilization Review Program

References:
1. Kalydeco® [package insert]. 3/2015. Vertex Pharmaceuticals Inc. http://www.kalydeco.com. Accessed August 31, 2015.
2. Orkambi® [package insert]. 7/2015. Vertex Pharmaceuticals Inc. http://www.orkambi.com. Accessed August 31, 2015.