The FDA's MedWatch program safety labeling changes for boxed warnings are compiled quarterly for drugs and therapeutic biologics where important changes have been made to the safety information. These and other label changes are searchable in the Drug Safety Labeling Changes (SLC) database, where data are available to the public in downloadable and searchable formats. Boxed warnings are ordinarily used to highlight either adverse reactions so serious in proportion to the potential benefit from the drug that it is essential that it be considered in assessing the risks and benefits of using the drug; or serious adverse reactions that can be prevented/reduced in frequency or severity by appropriate use of the drug; or FDA approved the drug with restrictions to ensure safe use because FDA concluded that the drug can be safely used only if distribution or use is restricted. For complete FDA Drug Safety Labeling changes, please visit http://www.accessdata.fda.gov/scripts/cder/safetylabelingchanges.

DESOGEN (DESOGESTREL AND ETHINYL ESTRADIOL TABLETS)

Edited boxed warning, June 2018

WARNING: CIGARETTE SMOKING AND SERIOUS CARDIOVASCULAR EVENTS

Cigarette smoking increases the risk of serious cardiovascular events from combination oral contraceptive (COC) use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked. For this reason, COCs are contraindicated in women who are over 35 years of age, and smoke.

TRIZIVIR (ABACAVIR, LAMIVUDINE, AND ZIDOVUDINE TABLETS)

Edited boxed warning, April 2018

Lactic Acidosis and Severe Hepatomegaly with Steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues, including abacavir, lamivudine, and zidovudine (components of TRIZIVIR). Discontinue TRIZIVIR if clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity occur [see Warnings and Precautions (5.4)].

AUSTEDO (DEUTETRABENAZINE)

Edited boxed warning, June 2018

WARNING: DEPRESSION AND SUICIDALITY IN PATIENTS WITH HUNTINGTON'S DISEASE

AUSTEDO can increase the risk of depression …

ERBITUX (CETUXIMAB)

Edited boxed warning, June 2018

WARNING: INFUSION REACTIONS and CARDIOPULMONARY ARREST

Infusion Reactions: ERBITUX can cause serious and fatal infusion reactions [see Warnings and Precautions (5.1), Adverse Reactions (6)]. Immediately interrupt and permanently discontinue ERBITUX for serious infusion reactions [see Dosage and Administration (2.4)].
Cardiopulmonary Arrest: Cardiopulmonary arrest or sudden death occurred in patients with squamous cell carcinoma of the head and neck receiving ERBITUX with radiation therapy or a cetuximab product with platinum-based therapy and fluorouracil. Monitor serum electrolytes, including serum magnesium, potassium, and calcium, during and after ERBITUX administration [see Warnings and Precautions (5.2, 5.6)].

EXJADE (DEFERASIROX)

Edited boxed warning, May 2018

Renal Failure: EXJADE can cause acute renal failure and death, particularly in patients with comorbidities and those who are in the advanced stages of their hematologic disorders. Evaluate baseline renal function prior to starting or increasing Exjade dosing in all patients. Exjade is contraindicated in adult and pediatric patients with eGFR less than 40 mL/min/1.73 m^2. Measure serum creatinine in duplicate prior to initiation of therapy. Monitor renal function at least monthly. For patients with baseline renal impairment or increased risk of acute renal failure, monitor renal function weekly for the first month, then at least monthly. Reduce the starting dose in patients with pre-existing renal disease. During therapy, increase the frequency of monitoring and modify the dose for patients with an increased risk of renal impairment, including use of concomitant nephrotoxic drugs, and pediatric patients with volume depletion or overchelation.

TUXARIN ER (CODEINE PHOSPHATE AND CHLORPHENIRAMINE MALEATE)

Edited boxed warning, June 2018

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; ULTRA-RAPID METABOLISM OF CODEINE AND OTHER RISK FACTORS FOR LIFE-THREATENING RESPIRATORY DEPRESSION IN CHILDREN; MEDICATION ERRORS; INTERACTIONS WITH DRUGS AFFECTING CYTOCHROME P450 ISOENZYMES; CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS; NEONATAL OPIOID WITHDRAWAL SYNDROME

Addiction, Abuse, and Misuse: TUXARIN ER exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Reserve TUXARIN ER for use in adult patients for whom the benefits of cough suppression are expected to outweigh the risks, and in whom an adequate assessment of the etiology of the cough has been made. Assess each patient's risk prior to prescribing TUXARIN ER, prescribe TUXARIN ER for the shortest duration that is consistent with individual patient treatment goals, monitor all patients regularly for the development of addition or abuse, and refill only after reevaluation of the need for continued treatment. [see Warnings and Precautions (5.1)]

Life-Threatening Respiratory Depression: Serious, life-threatening, or fatal respiratory depression may occur with use of TUXARIN ER. Monitor for respiratory depression, especially during initiation of TUXARIN ER therapy or when used in patients at higher risk [see Warnings and Precautions (5.2)].

Accidental Ingestion: Accidental ingestion of even one dose of TUXARIN ER, especially by children, can result in a fatal overdose of codeine [see Warnings and Precautions (5.2)].

Ultra-Rapid Metabolism of Codeine and Other Risk Factors for Life-Threatening Respiratory Depression in Children: Life threatening respiratory depression and death have occurred in children who received codeine. Most of the reported cases occurred following tonsillectomy and/or adenoidectomy, and many of the children had evidence of being an ultra-rapid metabolizer of codeine due to a CYP2D6 polymorphism. [see Warnings and Precautions (5.3)]. TUXARIN ER is contraindicated in children younger than 12 years of age and in children younger than 18 years of age following tonsillectomy and/or adenoidectomy [see Contraindications (4)]. Avoid the use of TUXARIN ER in adolescents 12 to 18 years of age who have other risk factors that may increase their sensitivity to the respiratory depressant effects of codeine. [see Warnings and Precautions (5.1)].

Interactions with Drugs Affecting Cytochrome P450 Isoenzymes: The effects of concomitant use or discontinuation of cytochrome P450 3A4 inducers, 3A4 inhibitors, or 2D6 inhibitors with codeine are complex, requiring careful consideration of the effects on the parent drug, codeine, and the active metabolite, morphine. Avoid the use of TUXARIN ER in patients who are taking a CYP3A4 inhibitor, CYP3A4 inducer, or 2D6 inhibitor [see Warnings and Precautions (5.8), Drug Interactions (7.1, 7.2, 7.4)].

Risks from Concomitant Use with Benzodiazepines, CNS Depressants: Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Avoid use of TUXARIN ER in patients taking benzodiazepines, other CNS depressants, or alcohol. [see Warning and Precautions (5.9) Drug Interactions (7.5)].

Neonatal Opioid Withdrawal Syndrome: TUXARIN ER is not recommended for use in pregnant women [see Use in Specific Populations (8.1)]. Prolonged use of TUXARIN ER during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If TUXARIN ER is used for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available [see Warnings and Precautions (5.15)].

PROGRAF (TACROLIMUS)

Edited boxed warning, May 2018
Increased risk for developing serious infections and malignancies with PROGRAF or other immunosuppressants that may lead to hospitalization or death [(see Warnings and Precautions 5.1, 5.2)].

SAMSCA (TOLVAPTAN)

Edited boxed warning, April 2018
Addition of the following:

WARNING: NOT FOR USE FOR AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD)

Because of the risk of hepatoxicity, tolvaptan should not be used for ADPKD outside of the FDA-approved REMS

GLUCOPHAGE/ GLUCOPHAGE XR (METFORMIN HYDROCHLORIDE)

Edited boxed warning, May 2018
PLR conversion; Lactic Acidosis warning is highlighted as boxed warning.