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WHAT'S
NEW?

WHAT'S NEW IN DRUG THERAPY

THE FIRST HALF OF 2023

Kosar hospital library

July 2023





The following material represents a subset of new drugs, drug approvals, drug warnings, and drugs removed from the market from the past six months. This is not a complete list; it includes those topics considered by the authors and editors to be of particular interest or importance.



Updated Beers criteria for anticoagulants (July 2023)

The Beers criteria from the American Geriatric Society are used to determine appropriate drug prescribing in older adults. A 2023 update addressed anticoagulants and the relatively lower bleeding risk with direct oral anticoagulants (DOACs) over [warfarin](#), especially in older individuals [1]. The update recommends that patients ≥ 65 years of age not initiate warfarin for venous thromboembolism (VTE) or nonvalvular atrial fibrillation unless there are substantial barriers or contraindications to using a DOAC. Among DOACs, [apixaban](#) and [edoxaban](#) are considered safest. Individuals who have been using warfarin long term with good international normalized ratio (INR) control may reasonably continue warfarin. (See ["Warfarin and other VKAs: Dosing and adverse effects"](#), section on 'Older adults'.)



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Updated Beers criteria for drug prescribing in older adults (July 2023)

The Beers criteria, used to assess inappropriate drug prescribing for older adults, have been updated [2]. Changes in the 2023 criteria include avoidance of: 1) [rivaroxaban](#) for long-term treatment of nonvalvular atrial fibrillation or venous thromboembolism, as well as avoidance of [warfarin](#) as initial therapy for these conditions unless alternatives are contraindicated; 2) sulfonylureas as first- or second-line monotherapy or add on-therapy; and 3) initiation of oral or transdermal estrogen in older women. The use of [aspirin](#) for primary prevention of cardiovascular disease is also discouraged, and deprescribing of aspirin in older patients already taking it for primary prevention is recommended. (See ["Drug prescribing for older adults", section on 'Beers criteria'](#).)



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Apixaban not adequate for On-X valve (July 2023)

The only oral anticoagulants approved for patients with mechanical valves to prevent valve-related thromboembolism and valve thrombosis are vitamin K antagonists (VKA). The On-X valve requires less intense anticoagulation than other mechanical valves, but the safety of using a direct oral anticoagulant (DOAC) for this valve has not been determined. An open-label trial randomly assigned over 800 patients with an On-X aortic valve to the DOAC [apixaban](#) 5 mg daily or VKA (target international normalized ratio 2.0 to 3.0) [3]. Nearly all patients were also treated with low-dose [aspirin](#). The trial was stopped early due to excess valve-related thromboembolism/thrombosis in the apixaban group. Major bleeding rates were similar in the two groups. The findings indicate that apixaban is not an adequate anticoagulant for patients with an On-X valve. (See ["Antithrombotic therapy for mechanical heart valves", section on 'Apixaban not adequate for On-X valve'](#).)



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Shortages of antineoplastic agents in the United States

(June 2023)

In the United States, multiple antineoplastic agents are in short supply (eg, [cisplatin](#), [carboplatin](#)). Guidance in the setting of drug shortages has been provided by the American Society of Clinical Oncology (ASCO) [4] and is summarized in the table ([table 1](#)). Generally, use of the limited agent should be prioritized for settings in which there are proven benefits; dose and scheduling modifications may be necessary; and alternative agents should be chosen, when appropriate. Support services should be made available for both patients and treating clinicians impacted by drug shortages. (See ["Systemic therapy for advanced cholangiocarcinoma"](#), section on ["Drug Shortages"](#) and ["Multimodality approaches to potentially resectable esophagogastric junction and gastric cardia adenocarcinomas"](#), section on ["Drug Shortages"](#) and ["Choice of neoadjuvant chemotherapy for HER2-negative breast cancer"](#), section on ["Incorporation of carboplatin"](#).)



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Pharmacogenomic panels to guide drug dosing

(June 2023)

Adverse drug reactions (ADRs) remain a major cause of morbidity and mortality, but the role of pharmacogenomic testing to reduce ADRs remains unclear. A new trial randomly assigned nearly 7000 adults receiving a new drug prescription to undergo or not undergo testing with a pharmacogenomic genotyping panel consisting of 50 variants in 12 genes that regulate drug metabolism [5]. At least one actionable variant was identified in over 90 percent of participants; many had more than one actionable variant. During 12 weeks of follow-up, fewer clinically relevant ADRs occurred in the testing arm (22 versus 29 percent; odds ratio 0.70, 95% CI 0.61-0.79). Despite some methodologic concerns, this trial supports the use of pharmacogenomic testing to reduce ADRs. (See ["Overview of pharmacogenomics", section on 'Pharmacogenomics gene panels'](#).)



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Biosimilars for rheumatoid arthritis

(June 2023)

Most biosimilars used for rheumatologic diseases have received regulatory approval based on studies of diseases other than rheumatoid arthritis. A recent meta-analysis described the results of 25 clinical trials including over 10,000 patients with rheumatoid arthritis that compared biosimilar tumor necrosis factor (TNF)-alpha inhibitors with their reference biologic products, including [infliximab](#), [etanercept](#), and [adalimumab](#) [6]. Biosimilars were equivalent to reference biologics in terms of disease activity (as measured by the American College of Rheumatology 20 response) and patient function (as measured by the Health Assessment Questionnaire Disability Index scores). Rheumatoid arthritis patients managed with TNF inhibitors can be reassured that biosimilars are as effective as bio-originators for the management of their disease. (See "[Overview of biologic agents in the rheumatic diseases](#)", section on '[Biosimilars for biologic agents](#)'.)



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Levothyroxine dosing in young, healthy adults with primary hypothyroidism

(May 2023)

The initial dose of levothyroxine in young, healthy adults with primary hypothyroidism is typically the average full replacement dose, approximately 1.6 mcg/kg body weight per day. However, the range of required doses is broad, depending on the etiology of hypothyroidism and individual patient characteristics. In a retrospective study of post thyroidectomy patients, only 285 of 951 (30 percent) who received initial weight-based dosing of levothyroxine met their thyroid-stimulating hormone (TSH) goal at the first postoperative assessment [7]. A levothyroxine dose calculator based on weight, height, age, sex, and calcium supplementation was able to modestly increase the number of patients meeting their TSH goals (43 percent). Serum TSH should be reevaluated four to six weeks after initiation of levothyroxine and after any dose adjustment; most patients will need one or more dose adjustments before the optimal maintenance dose is identified. (See "Treatment of primary hypothyroidism in adults", section on 'Initial dose'.)



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Inaccurate melatonin labeling and unintentional ingestions in young children (May 2023)

- Melatonin is widely used for insomnia despite modest effects on sleep, and, as a dietary supplement, it is subject to less stringent regulatory oversight in the United States. Actual quantities of melatonin contained in marketed supplements may vary from what is listed on the label (ranging from 74 to 347 percent of the labeled quantity in one recent study) [8]. Products may also contain substances not listed on the label. As with prescription medications, melatonin should be stored safely in locked containers out of the reach of children. Unintentional pediatric ingestions of melatonin are rising in the United States despite declines in unsupervised medication exposures in young children more generally [9]. (See ["Pharmacotherapy for insomnia in adults", section on 'Melatonin'](#) and ["Pharmacotherapy for insomnia in children and adolescents: A rational approach", section on 'Melatonin'.](#))



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Contribution of inflammation to cardiovascular risk in patients receiving statin therapy (April 2023)

In patients with an indication for statin therapy, lipid lowering therapy has an anti-inflammatory effect but may not completely reduce inflammation, which may contribute to atherosclerotic cardiovascular disease. In an analysis of over 31,000 patients from three clinical trials of statin therapy, baseline levels of high-sensitivity C-reactive protein (CRP), a biomarker of residual inflammatory risk, were associated with incident major adverse cardiovascular events and cardiovascular mortality [10]. By contrast, baseline levels of low-density lipoprotein cholesterol (LDL-C), a biomarker of residual cholesterol risk, were not associated with major adverse cardiovascular events but were associated with cardiovascular mortality. These findings suggest that among patients receiving statin therapy, residual inflammation may be a stronger predictor for cardiovascular risk than LDL-C. (See "[C-reactive protein in cardiovascular disease](#)", section on '[CRP after statin treatment and cardiovascular disease](#)'.)



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Removal of X-waiver requirement to prescribe buprenorphine for opioid use disorder (February 2023)

Previously, in order to prescribe [buprenorphine](#) for opioid use disorder (OUD) in the United States, clinicians had to apply for a federally required DATA Waiver (X-Waiver). In January 2023, the Consolidated Appropriations Act of 2023 removed this requirement and allowed clinicians with schedule III authority on their Drug Enforcement Administration (DEA) registration to prescribe buprenorphine for OUD treatment if permitted by applicable state law [\[11\]](#). We believe this change will encourage buprenorphine prescribing and thus prevent opioid overdose. (See "[Acute opioid intoxication in adults](#)", section on '[Prevention of recurrent opioid overdose](#)'.)



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Changes to heart failure therapy in patients recently hospitalized for heart failure (February 2023)

Patients with heart failure (HF) benefit from optimal medical therapy, but it is unclear whether patients recently hospitalized with HF can safely undergo rapid changes to their pharmacologic regimen. In a trial in nearly 1100 patients hospitalized with HF who were randomly assigned to high-intensity care (drug adjustment to target within two weeks of discharge and clinical surveillance) or to usual care, patients assigned to high-intensity care were more likely to achieve target doses of primary therapies for HF with reduced ejection fraction (eg, [sacubitril-valsartan](#), beta blockers) and had a lower risk of hospital readmission by 180 days [12]. Although overall adverse effects were more frequent in the high-intensity care group, rates of serious adverse events were similar between the groups. In highly selected inpatients scheduled for discharge who can reliably undergo frequent observation in the outpatient setting, HF medications can be added or adjusted toward their target doses. (See ["Treatment of acute decompensated heart failure: Specific therapies"](#), section on 'Approach to long-term therapy in hospitalized patients'.)



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Torsemide or furosemide for diuresis after heart failure hospitalization

(January 2023)

Torsemide and furosemide have different pharmacologic properties, but it is unknown whether one agent is superior to the other in patients with heart failure (HF). In a trial in nearly 2900 patients hospitalized with HF who were randomly assigned to treatment with furosemide or torsemide prior to discharge, the rates of all-cause mortality and all-cause hospitalization at 12 months were similar between the groups [13]. However, immediate crossover between treatments and the open-label design may have obscured differences in diuretic efficacy. In patients recovering from acutely decompensated HF without known resistance to a specific diuretic, furosemide and torsemide are reasonable options for outpatient diuresis. (See "[Use of diuretics in patients with heart failure](#)", section on 'Choice of loop diuretic'.)



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