Drug Utilization Review (DUR) Newsletter

COLORADO
Department of Health Care Policy & Financing

Select HCPF Medication Use Policy Updates

WINTER 2024

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Anticoagulation and Non-valvular Atrial Fibrillation

A Refresher for Providers

Robert L Page II, PharmD, MSPH

The Problem

Atrial fibrillation (AF) is the most sustained common arrhythmia, and its incidence and prevalence are increasing in the United States and globally. The increasing burden is multifactorial; causes include the aging of the population, the rising tide of obesity, increasing detection, and increasing survival with AF and other forms of cardiovascular disease (CVD). The estimated global prevalence was 50 million in 2020. Although the prevalence of undiagnosed AF in the community is unknown, using back-calculation methodology, investigators have estimated that in 2015 about 11% (591,000) cases) of the >5.6 million AF cases in the United States were undiagnosed.[1,2]

The 2023 AHA/ACC/HRS Guidelines on the Management of AF emphasize the importance of optimal management strategies for AF to mitigate its associated risks, particularly the increased risk of stroke.[1] Stroke treatment and prevention have undergone significant strides in the last 10 years. Anticoagulation therapy with either warfarin, a direct oral-acting anticoagulant (DOAC), or a low molecular weight heparin (LMWH) is one of the most effective treatments for preventing strokes in people. In the case of non-valvular AF (NVAF), anticoagulation is determined based on the validated CHA2DS2-VASc Score. When the CHA2DS2-VASc is used, the AHA/ACC/HRS guidelines recommend oral anticoagulation for men whose score is ≥2 and for women whose score is ≥3, which is equivalent to an estimated thromboembolic risk of ≥2% per year. For men with a score of 1 and women with a score of 2, whose estimated thromboembolic risk is ≥1% but <2% per year, the AHA/ACC/HRS guidelines consider anticoagulation reasonable. Unfortunately, not all patients who are high risk for a stroke with AF who do not receive appropriate anticoagulation. According to the American College of Cardiology's Practice Innovation and Clinical Excellence (PINNACLE) Registry, about 40% of members with nonvalvular AF are not receiving anticoagulants.[3] These findings are consistent with a post-hoc analysis of the GARFIELD Registry, which found that 25–35% of members with AF who are at high risk of stroke are not receiving guideline-recommended anticoagulation.[4] Overall, it has been estimated that between 1 and 3 patients who should be receiving anticoagulation and are actually not.[5] Potential reasons for this may be due to clinician's choice, member refusal, bleeding predisposition, or sinus rhythm status.[5]

Evaluation of Stroke Risk

The first step following the diagnosis of AF is appropriately evaluating stroke and bleeding risk. There have been many attempts over the years to identify better ways to define or identify high-risk patients who could be targeted for oral anticoagulant therapy. Currently, the recommended scoring scheme for stroke risk assessment has shifted from the CHADS2 to CHA2DS2-VASc score (Table 1, Figure 1), with the aim to facilitate decision-making for stroke prevention. The default setting for stroke prevention is to provide OACs (preferred DOACs) for every AF patient unless they are low risk for stroke (a CHA2DS2-VASc score of 0 for men or 1 for women).Based on this concept, the international guidelines recommend no antithrombotic therapy for AF

Anticoagulation and Non-valvular Atrial Fibrillation, continued from Page 1

patients with a CHA2DS2-VASc score of 0 (men) or 1 (women), and OACs should be prescribed for those with a CHA2DS2-VASc score ≥2 (men) or ≥3 (women). However, whether OACs should be prescribed for AF patients with a single stroke risk factor beyond gender, that is score 1 for men or 2 for women, is less clear as such patients only represented a small subgroup of the randomized control trials and other evidence comes from observational cohorts suggesting that the net clinical benefit remains in favor of DOACs.[6-10]

Evaluation of Bleeding Risk

Like stroke risk, bleeding risk is also highly dynamic, and is an interaction between non-modifiable and modifiable bleeding risk factors. Importantly, bleeding risk assessment is to address and mitigate modifiable bleeding risk factors, and to identify high bleeding risk patients for early review and follow-up.[1,10]

There are various bleeding risk scores that have been published. The systematic review and evidence appraisal concluded that the HAS-BLED score (Table 2, Figure 2) provided the best prediction for bleeding risks.[1,10] Although some complex clinical scores and biomarker-based bleeding risk schemes were proposed, there is little evidence showing that they could confer added advantage in the real-world practice. Again, statistical significance is not the same as significant practical application. Nonetheless, a high score (>3) identifies patients who may be at high risk of bleeding, as well as potentially modifiable bleeding risk factors. More importantly, a high score does not necessarily indicate that anticoagulant medicines should be avoided; however, instead prompt a shared decision-making conversation regarding the risk and benefits of therapeutic anticoagulation.

The same as stroke risk, the HAS-BLED score would change over a patient's AF journey with hypertension being the most commonly incident bleeding risk factor. A frequently encountered clinical scenario is the increment of the HAS-BLED score of AF patients who were already under OACs. In a recent report, around 22.2% of anticoagulated AF patients who had a baseline HAS-BLED score of 0–2 would have an increasing HAS-BLED score to ≥3 at 1 year.[11] Patients who were kept on OACs even after their HAS-BLED scores increased to ≥3 were associated with a lower risk of ischemic stroke (hazard ratio [HR] 0.60; 95% CI: 0.53–0.69), major bleeding (HR 0.78; 95% CI: 0.67–0.91), all-cause mortality (HR 0.88; 95% CI: 0.79–0.97), and any adverse events (HR 0.75; 95% CI: 0.68–0.82). Therefore, for patients who were initially or become high bleeding risk, the evidence suggests that we should try to correct modifiable bleeding risk factors and schedule them for early review and follow-up, rather than withholding or discontinuing OACs.

Anticoagulation Treatment

In terms of achieving therapeutic anticoagulation, consideration should be given to the DOACs over warfarin (achieving an international normalized ratio of 2-3) except for mitral stenosis or mechanical heart valves. Table 3 summarizes the DOACs currently covered under the Health First Colorado Preferred Drug List and their dosing.[1] Of note, the 2023 AHA/ACC/HRS AF Management Guidelines, for patients with no risk factors for stroke, prophylactic aspirin to prevent thromboembolic events is not recommended. Additionally, aspirin either alone or with clopidogrel is not recommended to reduce stroke risk.[1]

Table 1. CHA2DS2-VASc score–Risk Factors and Definitions.[1,10]

Variable	Definition	Point Awarded
C	**Congestive heart failure** Clinical HF (irrespective of LVEF, thus including HFpEF, HFmrEF, and HFrEF), or objective evidence of moderate to severe LV dysfunction (LVEF ≤40%), or HCM	1
H	**Hypertension** or receiving antihypertensive therapy Resting blood pressure >140/90 mmHg on at least two occasions, or current antihypertensive treatment. The optimal BP target associated with lowest risk of major cardiovascular events is 120–129/70–79 mmHg (or keep as low as reasonably achievable).	1
A	**Age 75 years or older** Age is an independent determinant of ischemic stroke risk. Age-related risk is a continuum, but for reasons of practicality, two points are given for age ≥75 years.	2
D	**Diabetes mellitus** Diabetes mellitus (type 1 or type 2), as defined by currently accepted criteria, or treatment with glucose-lowering therapy.	1
S	**Stroke, Previous stroke, TIA, or thromboembolism** Previous thromboembolism is associated with highly elevated risk of recurrence and therefore weighted 2 points.	2
V	**Vascular disease** CAD, including prior myocardial infarction, angina, history of coronary revascularization (surgical or percutaneous), and significant CAD on angiography or cardiac imaging **OR** PVD, including intermittent claudication, previous revascularization for PVD, percutaneous or surgical intervention on the abdominal aorta, and complex aortic plaque on imaging (defined as features of mobility, ulceration, pedunculation, or thickness ≥4 mm)	1
A	**Age 65–74 years**	1
Sc	**Sex category (female)**	1
	Maximum Score	**9**

BP = blood pressure; CAD = coronary artery disease; EF = ejection fraction; HCM = hypertrophic cardiomyopathy; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; HFmrEF = heart failure with mid-ranged ejection fraction; HFpEF = heart failure with preserved ejection fraction; LV = left ventricle; PVD = peripheral vascular disease; TIA = transient ischemic attack.

Table 2. HAS-BLED Score-Risk Factors and Definitions.[1,10]

Variable	Definition	Point Awarded
H	**Uncontrolled hypertension** SBP >160 mmHg	1
A	**Abnormal renal and/or hepatic function** Renal: dialysis, transplant, serum creatinine >200 mmol/L (≥2.3 mg/dL) Hepatic: cirrhosis, bilirubin >2x ULN, AST/ALT/ALP >3 x ULN	1 point for each
S	**Stroke** Previous ischemic or hemorrhagic stroke	1
B	**Bleeding history or predisposition** Previous major hemorrhage or anemia or severe thrombocytopenia	1
L	**Labile INR** TTR <60% in patient receiving VKA	1
E	**Elderly** Aged >65 years or extreme frailty	1
D	**Drugs that increase bleeding risk or excessive alcohol drinks per week** Concomitant use of antiplatelet or NSAID; excessive alcohol use	1 point for each
	Maximum Score	**9**

ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; INR = international normalized ratio; NSAID = non-steroidal anti-inflammatory drug; SBP = systolic blood pressure; TTR = time in therapeutic range; ULN = upper limit of normal; VKA = vitamin K antagonist.

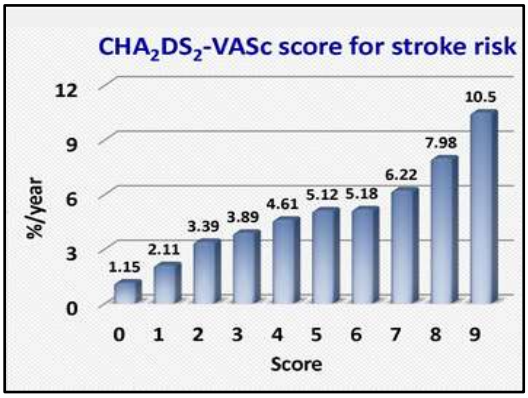
Table 3. Summary of Dosing Considerations for DOACs in NVAF.[1]

Class	Direct Thrombin Inhibitor	Factor Xa Inhibitor	
Drug	dabigatran	apixaban	rivaroxaban
Route	oral	oral	oral
Metabolism	minimal	CYP3A4	CYP3A4/5
Excretion	80% renal	27% renal 73% biliary and intestinal	66% renal 28% feces
Typical Dose	150 mg twice daily	5 mg twice daily	20 mg daily with largest meal*
Renal Dosing Adjustment	CrCL >30 mL/min: 150 mg twice daily CrCL 15-30 mL/min: 75 mg twice daily	If any two of the following, then 2.5 mg twice daily: • age ≥80 years • body weight ≤60 kg • SCr ≥1.5 mg/dL	CrCL >50 mL/min: 20 mg daily with largest meal* CrCL 15-50 mL/min: 15 mg daily with the largest meal*

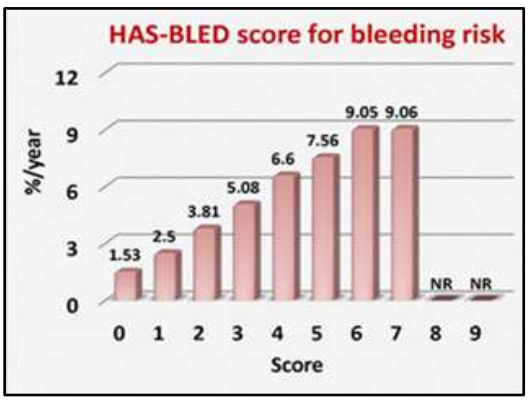
CrCL= creatine clearance; CYP = cytochrome P450 isoenzyme; SCr = serum creatinine

*The effect of food (high-fat, high-calorie meal) on bioavailability for the 10 mg and 20 mg tablet was evaluated in 24 subjects under fed and fasting conditions. After a single oral 20 mg dose, area under the curve was increased by 39%, and Cmax was increased by 76% under fed condition, but area under the curve and Cmax were similar between fasting and fed conditions.

Figure 1. CHA2DS2-VASc score for stroke risk and HAS-BLED score for bleeding risk and potential considerations.[1,10]



- First reassessment of stroke risk should be made 4 to 6 months after index evaluation, then again at least annually and ideally every 4 months if possible.
- Consider OAC for initially "low-risk" patients who develop new stroke risk factors.
- Consider management of incident comorbidities.
- Confirm compliance of DOAC; keep a high TTR for warfarin (ideally >65%, optimal >70%).



- A high bleeding risk is not a reason to not to prescribe OACs.
- Correct modifiable risk bleeding risk factors.
- Schedule high bleeding risk patients (e.g., HAS-BLED >3) for early review and follow-up.
- Consider continuation of OACs for anticoagulation in patients even when they become high bleeding risk. This should prompt a risk vs benefit shared decision conversation.

OAC = oral anticoagulation therapy. TTR = time in therapeutic range

Take the quiz!

A member comes to your pharmacy and is out of medication. What options do you have as a pharmacist in Colorado?

Gina Moore, PharmD, MBA

A Health First Colorado member presents to your pharmacy on a Saturday stating they are out of Humalog® insulin. Their last prescription was written by a provider in Nebraska. The patient tells you they have an appointment scheduled with a Colorado provider, but not until next week.

The member shows you their insulin package and you are able to verify the medication, dose, and name of the prescriber.

What do you tell this patient?

- ☐ **A.** The patient should go to the nearest urgent care or hospital to obtain a new insulin prescription.
- ☐ **B.** Since the patient is seeing a Colorado provider in a week, they should hold their insulin for a few days and get a new prescription filled asap after their upcoming appointment.
- ☐ **C.** You attempt to call the Nebraska provider's office, but are unable to reach anyone since it's a weekend. Because you have proof of the recent prescription, you dispense the insulin to the patient in the last quantity dispensed and notify the practitioner of the emergency dispensing.
- ☐ **D.** You refer to the 72-hour rule, and since a vial of insulin exceeds a 72-hour supply of medication, you tell the member there's nothing you can do.

If you answered C you are right!

- ☑ **C.** *You attempt to call the Nebraska provider, but are unable to reach the provider as it is a weekend. Since you have proof of the recent prescription in the name of the prescription, you dispense the insulin to the patient in the last quantity dispensed and notify the practitioner of the emergency dispensing.*

Emergency Supplies of Chronic Maintenance Drugs

In January 2020, Colorado passed legislation authorizing pharmacists to dispense an emergency supply of a chronic maintenance drug to a patient if:

- The pharmacist makes every reasonable attempt but is unable to obtain authorization to refill the prescription from the prescribing healthcare provider or another provider responsible for the patient's care;
- The pharmacist either has record of a prescription at the pharmacy or has been presented proof of a recent prescription for a chronic maintenance drug in the name of the prescription who is requesting the drug; or
- In the pharmacist's professional judgment, the refusal to dispense an emergency supply of the chronic maintenance drug will endanger the patient's health or disrupt essential drug therapy for a chronic condition;
- The amount of the chronic maintenance drug dispensed does not exceed the amount of the most recent prescription or the standard quantity or unit of use package of the drug;
- The pharmacist has not dispensed an emergency supply of the chronic maintenance drug to the same patient in the previous twelve-month period; and
- The prescriber has not indicated that no emergency refills are authorized.

Emergency Supplies of Chronic Maintenance Drugs, continued from Page 4

When an emergency dispensing does occur, the dispensing pharmacist or their designee must notify the practitioner of record of the

1. Name, address, and telephone number of the pharmacy
2. Name, strength, dosage form, directions, and quantity of the drug dispensed
3. Name and date of birth of the patient
4. Date of the dispensing

Pharmacists, please don't direct patients to urgent care or to a costly emergency department setting for refills of chronic medications unless you are unable to verify proof of a prescription or if the patient is otherwise unstable and in need of a higher level of care.

This legislation was originally passed to allow for situations in which a unit-of-use container for medications such as insulin would exceed a 72-hour supply previously allowed in rule. However, there are numerous situations in which a patient might be taking a chronic medication for hypertension, neurologic disease, or other chronic condition in which an emergency dispensing of the medication in the last quantity prescribed may be appropriate. Pharmacists can still offer a 72-hour emergency supply pending practitioner authorization. However, if the prescriber has not yet responded or the patient is leaving town, the pharmacist may legally provide a full fill to a patient if appropriate and in the patient's best interest.

The Colorado Evidence-Based Drug Utilization Review (CO-DUR) Program

at the University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences

Photo credit: Amy Wright

The Colorado Evidence-Based DUR Program at the University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences in Aurora has provided research analytics and clinical pharmacy support to Health First Colorado, Colorado's Medicaid Program for over a decade.

Originally established in 2012, the CO-DUR team is responsible for supporting a diverse range of services in collaboration with the Pharmacy Office at the Department of Health Care Policy & Financing. This high level of professional collaboration with an academic institution is unique among Medicaid programs across the U.S.

CO-DUR$_x$ | Skaggs School of Pharmacy and Pharmaceutical Sciences

The University of Colorado Evidence-Based Drug Utilization Review Program

Left to right:

Julia Rawlings, PharmD
Director, HCPF Contracts and Partnerships
Associate Professor and DUR Clinical Lead
Department of Clinical Pharmacy

Garth Wright, MPH
Biostatistician II
Department of Clinical Pharmacy

Heather Anderson, PhD
Director of Assessment and Outcomes
Associate Professor
Department of Clinical Pharmacy

Robert L. Page II, PharmD, MSPH
Clinical Director, CO-DUR
Professor, Departments of Clinical Pharmacy and Physical Medicine

Mouna Dardouri, PharmD, MPH, PhD Student
Pharmaceutical Outcomes Research Program

Gina Moore, PharmD, MBA
Senior Associate Dean
Associate Professor

DUR Spotlight

by Andrew Rukavina
PharmD Candidate
DUR Intern

Marshal Ash, DO

In August we were fortunate to welcome Dr. Marshal Ash to the Health First Colorado DUR Board. Dr. Ash is a community psychiatrist based in Colorado Springs.

Dr. Ash was born and raised in Minnesota, growing up in a rural area about an hour north of the Twin Cities. With his small-town roots, Dr. Ash is deeply committed to rural medicine, and he sought a career where he could help expand healthcare resources to underserved populations.

Dr. Ash left Minnesota for Colorado, where he earned his medical degree before completing a psychiatry residency in Dayton, Ohio. During his residency, he also pursued a fellowship in child psychiatry, a program that prepared him to provide comprehensive psychiatric care to both pediatric and adult patients. Upon returning to Colorado, Dr. Ash was recruited to help pilot a new program at Peak Vista Community Health Center, focusing on Integrated Psychiatry. In this role, he collaborates with an interprofessional team of providers to best serve his patients and expand the range of services available to the health center's community.

In addition to his clinical work, Dr. Ash joined the DUR board to lend his expertise to healthcare decision making at the state level, advocating for changes that will directly impact his patients' outcomes. With a systems-based approach, he is committed to improving health outcomes across a broader network, striving to provide top-quality care for all Colorado residents. Outside of his professional work, Dr. Ash enjoys playing in a sand volleyball league and spends as much time as possible in the mountains.

November 2024

PDL Drug Classes reviewed by the DUR Board

- Human Immunodeficiency Virus (HIV) Treatments
- Immune Globulins
- Methotrexate Products
- Targeted Immune Modulators
- Respiratory Agents
  - Inhaled Beta-2 Agonists
  - Phosphodiesterase Inhibitors
  - Inhaled Anticholinergics
  - Inhaled Anticholinergic Combinations
  - Inhaled Corticosteroids
  - Inhaled Corticosteroid Combinations
- Inhaled Antibiotics
- Oral and Topical Antiherpetic Agents
- Oral Fluoroquinolones
- Hepatitis C Virus Treatments
  - Direct Acting Antivirals
  - Ribavirin
- Antihistamines
  - Newer Generation Products
  - Antihistamine/Decongestant Combinations
- Intranasal Rhinitis Agents
- Leukotriene Modifiers
- Epinephrine Products
- Newer Hereditary Angioedema Products

The January 1, 2025
Colorado Preferred Drug List (PDL)
is available at
https://www.colorado.gov/hcpf/pharmacy-resources

Announcement Column

Pharmacy Office updates

Effective 1/1/2025

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Humira® biosimilars

Three new Humira biosimilars will be preferred products on the Health First Colorado preferred drug list. The list of preferred adalimumab products will now include

- Adalimumab-aaty pen and syringe
- Adalimumab-adbm pen and syringe
- Cyltezo® (adalimumab-adbm) pen and syringe
- Hadlima™ (adalimumab-bwwd) Pushtouch and syringe
- Humira (adalimumab)

Cyltezo is the first preferred biosimilar product that is directly interchangeable with Humira, the originator biologic product.

Paxlovid™

(nirmatrelvir tablets, ritonavir tablets)

Pharmacy participants in the 340B program may submit claims for Paxlovid products through the Health First Colorado pharmacy benefit instead of through the Pfizer PAXCESS™ Patient Support Program.

DUR Spotlight

by Nina Gyasi
PharmD Candidate
DUR Intern

Greg Miller, PharmD

Dr. Greg Miller is the PDL and Clinical Strategy Pharmacist with the Colorado Department of Health Care Policy and Financing (HCPF). He received his Doctor of Pharmacy degree at Butler University in Indianapolis before coming to Colorado. His career began as a pharmacy intern at CVS. That experience led him to become a pharmacist and move into management roles at long-term care pharmacies such as Wellfount Corporation and MedScript LTC. Dr. Miller's journey pushed him to become a consultant pharmacist before accepting his current role with HCPF.

Dr. Miller's daily responsibilities include a large project to transition to a new pharmacy benefit manager (PBM), managing drug shortages, and integrating new medication indications into existing healthcare information systems.

With the rising costs involved in drug innovation, Dr. Miller works with his team to make decisions that save taxpayer dollars while strategically coming up with ways to maintain robust coverage for a wide range of medications. Dr. Miller's work directly influences patient health outcomes in Colorado. His role allows opportunities to make changes that affect over a million Medicaid beneficiaries, engage with advocacy groups, and interact with industry leaders regarding medications and their financial implications. By addressing product shortages and policy changes, he demonstrates a commitment to optimize care for a vulnerable population.

If Dr. Miller were given the opportunity to implement a major healthcare policy change, he would want to address the rising costs of medications and advocate for maintaining reasonable pricing to ensure access for patients. Dr. Miller will continue to keep up with the quickly changing landscape of drug policy and drug pricing. Whether by addressing shortages of antipsychotics or evaluating the implication of new generics, his expertise helps ensure that medication policies remain relevant and effective. His role is instrumental in ensuring seamless access to medication for all Health First Colorado members.
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Anticoagulation and Non-valvular Atrial Fibrillation: A REFRESHER FOR PROVIDERS

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