Medications and Heat

For Providers

This tool is designed to help prescribers and pharmacists with the identification of medications that may increase the risk of patient harm during extreme heat. This document includes some commonly used medications which are associated with increased risk for patients who use them during hotter weather.

This list of medications is based on a combination of known pharmacological effects and mechanisms of heat sensitization across several classes of medication and larger epidemiologic studies showing increased risks of morbidity for those who take certain medications during extreme heat. In general, medications and hot weather interact in several ways which can increase the risk of patient harm during summer months. Some medications disrupt thermoregulatory response mechanisms and/or alter fluid and electrolyte status, increasing the risk of overheating, dehydration, or other harm in hot weather.[1–3] Heat exposure and dehydration can alter the pharmacokinetics of medications (i.e., absorption, distribution, or elimination), which can increase the risk of adverse effects.[4] Examples include insulin (increased absorption with heat exposure resulting in increased risk of hypoglycemia) and lithium (increased serum concentrations and acute toxicity with dehydration).[1,4,5]

Evidence to guide specific dosing or medication changes specifically to reduce risks during extreme heat is limited, but some suggestions for patient management have been included at the end of this document. Regular comprehensive medication reviews, including evaluation of OTCs and supplements, can help identify these medications, assess patient risk, and proactively address potential medication-related issues.

It should also be noted that hot temperatures can degrade or damage medications and medical devices, which may lead to loss of medication efficacy or device malfunction. Patients should be advised on proper storage methods to protect their medications and medical devices during high temperatures. This applies to medications like inhalers, EpiPens, and insulin and equipment like blood glucose meters and test strips.[6–8]

Although many products are labeled for storage under refrigeration only, some temperature excursions may be allowable based on the individual drug product.[9] For instance, while manufacturer recommend that unopened insulin vials and pens are maintained between 36-46°F, several recent studies have suggested that when refrigeration is not possible, insulin will maintain its stability for longer periods of time outside of this range when stored in environments that prevent it from becoming very hot (e.g., insulated container maintaining temperatures between 77-80°F).[10] Patients should be educated on appropriate medication storage and should have a backup plan for keeping refrigerated medications as cool as possible if transporting them during hot weather or in the case of a power outage which impacts refrigerator functioning.

Heat-sensitizing medications

The following broad medication categories and medication classes are associated with alterations in thermoregulatory response, increased risk of dehydration, and/or increased risk of electrolyte abnormalities during hot weather.

Psychotropic medications

Psychotropic medications can increase heat sensitivity and pose risks during hot weather. Additionally, individuals with substance use disorder or recreational drug use are at higher risk during heat waves[11–15]. Not all medications carry the same risk, and some evidence suggests that anticholinergic effects, anticholinergic burden, and overall number of psychotropic medications may have additive risk[16–19].

Medication class	Effect on thermoregulation and heat sensitivity[1–3]
SSRIs & SNRIs	Impaired central thermoregulation, increased sweating and increased risk of dehydration and electrolyte abnormalities[1]
Tricyclic antidepressants	Impaired central thermoregulation, decreased sweating; Sedation or altered cognition impacting behavioral response to heat[1,16]
Antipsychotics	Impaired central thermoregulation and impaired sweating; increased sedation, cognitive effects may lead to reduced alertness, judgement, and perception of hot weather which impact behavioral responses to heat. Antipsychotics with increased anticholinergic effects (e.g., clozapine, olanzapine, quetiapine) may have additive blunting of thermoregulation and increased risk[16,18]
Stimulants	Impaired central thermoregulation, increased metabolic rates leading to excess heat production and hyperthermia, and altered heat perception[20,21]
Benzodiazepines	Sedation, altered cognition impacting behavioral response to heat[1]
Mood stabilizers	Electrolyte imbalances; risk of toxicity in the setting of dehydration[1]
Opioids	Sedation, altered cognition impacting behavioral response to heat; potential for misdiagnosis of opioid overdose vs heat stroke delaying appropriate treatment[12]
Alcohol	Increased sweating combined diuretic effects leading to dehydration; Sedation, altered cognition, altered heat perception impacting behavioral response to heat[11,13,22]
Cocaine	Impaired central thermoregulation, delayed and reduced sweating, increased thermogenesis, impaired cutaneous vasodilation, and impaired heat perception[23]
MDMA	Increased core temperature and elevated metabolic rate, delayed sweating[24,25]

Cardiovascular medications

Commonly used cardiovascular medications can alter thermoregulation, fluid status, electrolyte balance, and/or blood pressure, increasing risks during heat exposure through multiple mechanisms. The combination of ACEi and diuretic therapy has been associated with particularly elevated risk in several studies, pointing to the need for careful assessment and monitoring of these patients during hot weather.[26,27] Prescribers should use caution and provide patient-specific recommendations for management of hydration and medication dosing for those with conditions requiring careful management of fluid balance (e.g., heart failure, renal disease). Diuretics may also cause electrolyte imbalances (e.g., hyponatremia, hypokalemia) which may be exacerbated by over-hydration with water alone.[28,29]

Limited studies have demonstrated reduced risks with the use of some medications during extreme heat. In one study, statin use was associated with lower all-cause mortality during extreme heat events, and a similar study demonstrated a reduction in risk during extreme heat for patients prescribed empiric potassium supplementation when using furosemide ≥40 mg per day.[30,31]

Medication class	Effect on thermoregulation and heat sensitivity[1–3,26]
Diuretics	Increased risk of dehydration and hypovolemia; risk of electrolyte abnormalities; risk of hypotension and fainting/falls[1,3,5]
ACEi & ARB	Suppressed thirst sensation impacting fluid intake behaviors and increasing risk of dehydration; increased risk of renal injury with dehydration; increased risk of hyperkalemia and other electrolyte abnormalities; risk of hypotension and fainting/falls[32]
Beta-blockers	Disrupted thermoregulatory response through inhibition of cutaneous vasodilation and decreased sweat response; risk of hypotension and fainting/ falls[3]
Calcium channel blockers	Increased risk of hypotension and fainting/falls; risk of electrolyte abnormalities[2]
Antiplatelets	Both aspirin and clopidogrel have been shown to impair thermoregulatory responses during passive and exertional heat stress by reducing skin blood flow and possibly suppressing sweat responses.[3]

Antidiabetic medications

Patients with diabetes often use multiple medications which increase the risk of heat-related harms. Patients taking insulin may be at an increased risk of hypoglycemia due to increased absorption of insulin with heat exposure and cutaneous vasodilation. One epidemiologic study found insulin users' risk of serious hypoglycemic events was approximately 40% higher on days with a heat index ≥99th percentile vs days with heat index in 25–74th percentile.[5] Patients who use insulin should be instructed to carefully monitor their blood glucose during extreme heat and should have a plan for management of hypoglycemia.

Medication class	Effect on thermoregulation and heat sensitivity[1–3]
Insulin	Altered thermoregulatory response; increased subcutaneous absorption of insulin leading to hypoglycemic emergencies[4,5]
SGLT2i	Increased osmotic diuresis and increases the risk of dehydration; dehydration may increase the risk of euglycemic DKA with SGLT2i use[3,33,34]
Metformin and GLP-1 RA medications	Increased GI disturbances and diarrhea upon drug initiation or dose increase, leading to increased risk of dehydration[3]

Anticholinergic medications

Anticholinergic medications influence thermoregulation and response to heat through several mechanisms, including alterations in central thermoregulation, decreased sweating, decreased peripheral vasodilation, and sedation or cognitive effects which may reduce heat awareness and inhibit behavioral responses to promote cooling.[4] Some evidence suggests that the increased relative anticholinergic effects of individual medications and increasing anticholinergic burden may be associated with greater risk of heat-related harm.[16,35] Anticholinergic medications should be evaluated, particularly in older adults, and deprescribing or other steps to reduce anticholinergic burden should be used wherever risk outweighs benefit. Anticholinergic medications that may be

associated with increased heat-related risks include:[1,3,36,37]

- Anti-histamines (e.g., diphenhydramine, chlorpheniramine)
- Drugs for urinary incontinence (e.g., oxybutynin, solifenacin)
- Antiemetics (e.g., meclizine, promethazine, scopolamine)
- Tricyclic antidepressants (e.g., amitriptyline, nortriptyline)
- Antipsychotics (e.g., clozapine, olanzapine, quetiapine)
- Muscle relaxants (e.g., carisoprodol, methocarbamol, tizanidine)
- Medications for insomnia (e.g., doxylamine, hydroxyzine, doxepin)
- Antispasmodics (e.g., hyoscyamine, dicyclomine)

Ambient temperature, altered fluid status and pharmacokinetics

The pharmacokinetics of some medications may be altered during periods of elevated ambient temperatures. The absorption and/or distribution of medications may be altered by thermoregulatory changes in vasodilation and circulation. Heat exposure, dehydration and hypovolemia can decrease visceral blood flow to the liver and kidneys, resulting in an increased risk of organ damage and decreased clearance of medications.[38] The resulting elevations in serum concentrations, particularly for drugs with a narrow therapeutic index, can lead to acute toxicity. Examples of some drugs which may have altered pharmacokinetics during periods of extreme heat include:

- Drugs with narrow therapeutic index: Lithium, digoxin39,40
- Direct-oral anticoagulants (apixaban, rivaroxaban, dabigatran)1
- Transdermal medications (e.g., fentanyl patches)4
- Subcutaneous medications (e.g., insulin)[4,5]

What you can do

Prescribers and pharmacists should review patient medication lists to assess heat-related medication risks and make patient-specific plans to manage medications during hot days. The list of medications above is not intended to be all-inclusive. Both prescription and over-the-counter medications, supplements, and herbals can affect fluid and electrolyte balance, hemodynamics, thermoregulatory set-point, and/or cognition and alertness. It is important to obtain a complete and accurate list of patient medications, including non-prescription medications, at every visit to fully assess medication-associated risks. Efforts to reduce drug burden and discontinue high-risk medications should be considered as a part of usual care, particularly in older adults where polypharmacy is a common concern. Evidence to provide broad guidance on medication management during heat is limited, but individualized patient plans may include:

- Educating patients on their medication-related risks and self-monitoring strategies, know the signs and symptoms that might indicate drug-related problems during hot weather, and have a plan in place outlining appropriate actions to take if patients experience these symptoms (i.e., self-management versus seeking care).
- Avoiding or delaying initiation or dose increases of heat-sensitizing medications if heat is forecasted in the near future.
- Considering adjustments to fluid restrictions and/or dose reductions for diuretics during hot weather, along with home monitoring of weight to assess fluid status.
- Considering dose adjustments for heat-sensitizing medications during periods of hot weather, especially if the patient is taking multiple medications that increase heat-related risks (e.g., ACEi/ARB and diuretic) or if they have other risk factors (e.g., older patients).
- Using shared decision-making and deprescribing where possible if risk outweighs benefit, particularly in the case of medications which are otherwise considered high-risk and high priority for deprescribing (e.g., anticholinergic medications in older adults, benzodiazepine receptor agonists, opioids, long-term antidepressant therapy).

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Notes:

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