Management of Sulfonamide Allergies in Electronic Mediation Management (EMM) Systems

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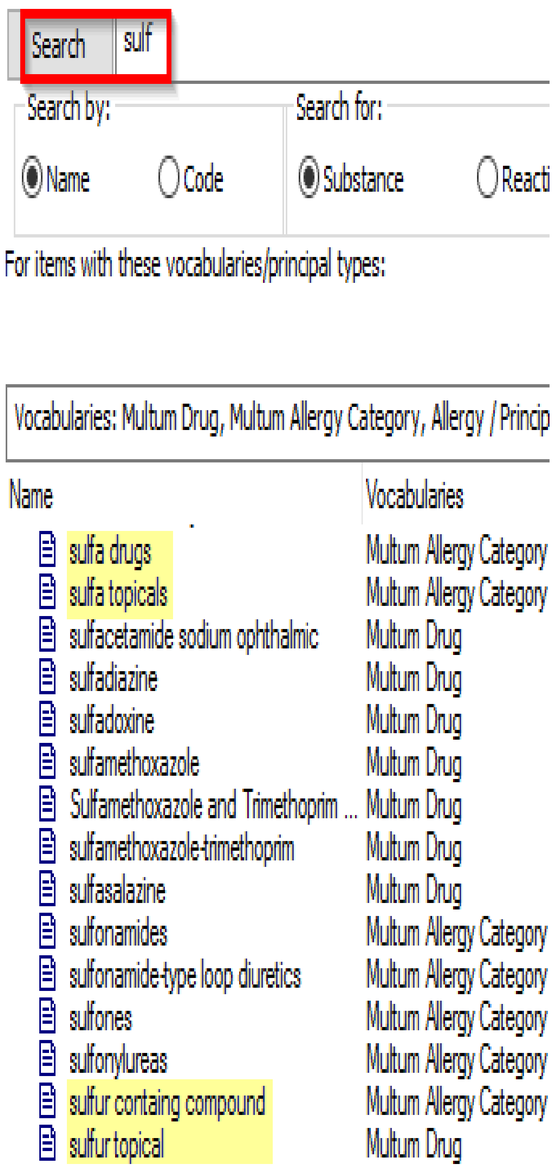
Background

Approximately 3% of the general population have adverse reactions when treated with sulfonamide antimicrobials.[1]

Unfortunately, documentation of sulfonamide allergies in digital systems has reportedly led to inappropriate prescribing. This is likely due to the following factors:

1. Digital drug-allergy medication clinical decision support (mCDS) alerts do not match clinical evidence surrounding sulfonamide allergies.
2. Available allergies for documentation in digital systems have not been adequately maintained. There are numerous allergies for selection that appear the same or similar but elicit very different alerts (Figure 1.); this promotes confusion and selection errors.
3. Clinicians' understanding of what constitutes a sulfur/sulfonamide allergy, and their ability to gather necessary allergy information from patients.

Figure 1. Allergies for selection in a digital system



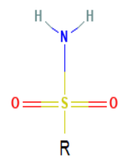
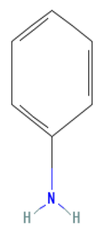
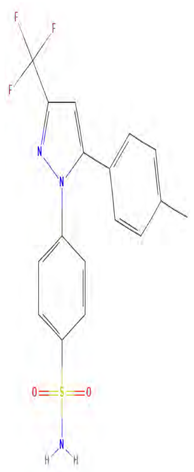
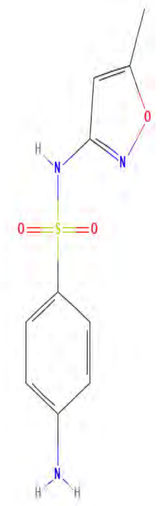
Assessment

Sulfonamide allergies are an immunological reaction to sulfonylarylamine (sulfonamide and arylamine) containing medications i.e., sulfonamide antibiotics (trimethoprim-sulfamethoxazole).

Many commonly used drugs such as glipizide, furosemide, and celecoxib, contain a sulfonamide structure however they do not contain an arylamine moiety (Figure 2).

Due to this structural difference, cross-reactivity between sulfonamide antibiotics and other sulfonamide drugs is unlikely.[2]

Figure 2. Key Structures Related to Sulfonamide Allergies

Sulfonamide	Arylamine
	
The sulfonamide structure is present in both sulfonylarylamine and non-sulfonylarylamine drugs, however, sulfonamide allergies are thought to only occur when an arylamine moiety is present in conjunction with sulfonamide structure (sulfonylarylamines).	
Celecoxib (non-sulfonylarylamine)	**Sulfamethoxazole (sulfonylarylamine)**
	

The co-existence of hypersensitivity reactions to several drugs does not prove cross-reactivity between them.[2]

Evidence suggests that non-antibiotic (non-arylamine) sulfonamide drugs are not contraindicated in those with a history of hypersensitivity to antibiotic(sulfonylarylamine) sulfonamides.[3]

These findings conflict with the product information of many drugs and current drug-allergy checking within EMM systems.

Figure 3. Allergy Documentation in Practice: Top 20 Documented 'Sulfur' Like Allergies Across All QLD Digital Hospital Sites'

Documented Allergy	Vocabulary	Grand Total
Sulphur	Allergy	33023
Sulfonamides	Multum Allergy Category	4049
Sulfur	Multum Drug	3508
sulfamethoxazole-trimethoprim	Multum Drug	3473
sulfa drugs	Multum Allergy Category	3067
sulfur containing compound	Multum Allergy Category	1989
sulfamethoxazole	Multum Drug	1769
Sulfadiazine	Multum Drug	1550
Sulfasalazine	Multum Drug	1083
Sulphites	Allergy	300
Sulphadiazine (Orion)	Multum Drug	197
Sulfamethoxazole and Trimethoprim (DBL)	Multum Drug	121
sulfonamide-type loop diuretics	Multum Allergy Category	119
sulfur topical	Multum Drug	112
Sulfamethoxazole-Trimethoprim DS	Multum Drug	76
Sulfonylureas	Multum Allergy Category	72
Sulfacetamide Sodium	Multum Drug	16
Sulfazine	Multum Drug	11
Sulfones	Multum Allergy Category	10
Sulphur and its derivatives	Free text	10

Figure 3. illustrates the top 20 documented allergies relevant to the term sulfur (and its various spellings) across QLD digital sites since 2014 (note: not all sites were live with digital allergy documentation for the duration of this period).

Of the top ten documented allergies across sites, six were recorded as general classes or groups of drugs. The allergy with the highest documentation rate across sites is 'Sulphur', which does not elicit mCDS drug-allergy alerts (see Figure 5.)

The second highest documented allergy is 'sulfonamides', which elicits an mCDS drug-allergy alert against many non-sulfonylarylamine drugs (Figure 5.) and conflicts with evidence-based practice.

Tickets logged by sites for system change requests illustrate documented allergies are promoting inappropriate prescribing due to system alerts; one such alert example is seen in Figure 4. Here, a clinician has attempted to prescribe furosemide to a patient with a documented sulfonamide allergy and was presented with an mCDS drug-allergy alert. This alert caused a delay in necessary therapy.

Figure 4. Example of mCDS Alert Delaying Therapy

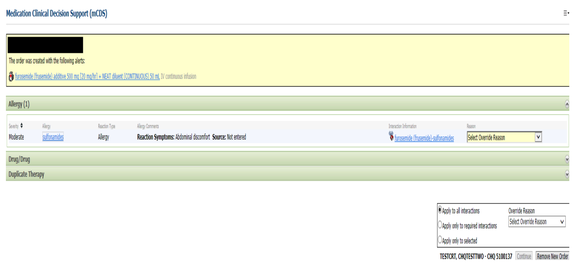


Figure 5. A Cross Match of Drug-Allergy mCDS Alerts

Legend	
x	mCDS alert fires
	Inappropriate alert flagged for suppression
	Naming update required
	Allergy to be obsoleted

Documented Allergy		Medication order		
Allergy	**Multum Vocabulary**	**Sulfonylarylamines** (sulfadiazine, sulfadoxine, sulfamethoxazole, sulfasalazine, darunavir, fosamprenavir)	**Non-sulfonylarylamines** (acetazolamide, brinzolamide, bumetanide, celecoxib, chlortalidone, diazoxide, dorzolamide, furosemide, glibenclamide, gliclazide, glimepiride, glipizide, hydrochlorothiazide, indapamide, parecoxib, tamsulosin)	**Sulfonamide containing** (naratriptan, probenecid, sulthiame, sumatriptan, zonisamide)
Sulfonylarylamines (sulfadiazine, sulfadoxine, sulfamethoxazole, sulfasalazine, darunavir, fosamprenavir)	Multum drug	x	x	x
Non-sulfonylarylamines (acetazolamide, brinzolamide, bumetanide, celecoxib, chlortalidone, diazoxide, dorzolamide, furosemide, glibenclamide, gliclazide, glimepiride, glipizide, hydrochlorothiazide, indapamide, parecoxib, tamsulosin)	Multum drug	x	x	x
Sulfonamide containing (naratriptan, probenecid, sulthiame, sumatriptan, zonisamide)	Multum drug	x	x	x
Sulfur topical	Multum drug	Nil	Nil	Nil
sulfa topicals	Multum Allergy Category	x	x	x
Sulfa drugs	Multum Allergy Category	x	x	x
sulfur containing compound	Multum Allergy Category	Nil	Nil	Nil
Sulfur	Multum drug	Nil	Nil	Nil
Sulphur	Allergy	Nil	Nil	Nil
sulfonamides	Multum Allergy Category	x	x	x
Sulfonamide-type loop diuretics	Multum Allergy Category	x	x	x
Sulfone	Multum Allergy Category	x	x	x
sulfonylurea	Multum Allergy Category	x	x	x

Figure 5. illustrates where mCDS drug-allergy alerts populate in relation to sulfur-related documented allergies and prescribing. This table demonstrates many instances of inappropriate alerting based on current evidence.

Alert dismissal is becoming habitual across all levels of physician rank and experience.5

Maintenance of inappropriate alerts contributes to this pervasive tendency and overall alert fatigue

Recommendations

1. Customise sulfonamide drugs via the healthcare technology provider's new custom interactions tool so that only clinically significant cross-reactive agents will fire a drug-allergy mCDS alert e.g., antibiotic(sulfonylarylamine) sulfonamides will only cross-react with other antibiotic(sulfonylarylamine) sulfonamides see Figure 5. for alert suppression recommendations.
2. Obsolete allergies for documentation that do not provide benefit / add confusion to allergy selection and documentation (highlighted red in Figure 5.)
3. Update naming convention to comply with TGA-approved terminologies: 'sulfur (rather than sulphur) is used in names containing this word or its derivatives, e.g. sulfate, sulfonate.[4]

Current	Future
Sulfa topicals	Sulfur topicals
Sulfa drugs	Sulfur drugs
Sulfonamides	Sulfonamide antibiotics

4. Education — When documenting allergies, clinicians should use the specific name of the drug(s) and the nature of the reaction when recording allergic adverse reactions to medications. A claimed sulfonamide allergy should be confirmed to ensure that it is an allergy and not an adverse effect. The term 'sulfur (or sulphur, sulpha, sulfa) allergy' should not be used.[2]

Conclusion

EMM decision support should reflect evidence-based practice. Where backend tool preferences do not allow for this or have not been customised/maintained appropriately, this is to the detriment of prescribing habits and patient outcomes.

Clinical informaticians have an opportunity to close the gap between healthcare technology providers and clinicians, ensuring technological advancements and adoption meet clinical workflow requirements to better patient outcomes.

References

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2. Smith WB, Katelaris CH. 'Sulfur allergy'label is misleading.
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5. Wang L, Goh KH, Yeow A, Poh H, Li K, Yeow JJ, Tan G, Soh C. Habit and Automaticity in Medical Alert Override: Cohort Study. Journal of medical Internet research. 2022 Feb 16;24(2):e23355.