

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) ADVERSE DRUG REACTION



1 What are Non-steroidal anti-inflammatory drugs (NSAIDs)?

- drugs widely used for their antipyretic, pain relief and anti-inflammatory properties.¹
- group of chemically diverse substances belonging to several classes²
- inhibit the enzyme cyclooxygenase-1 (COX) and, to a lesser extent, the COX-2 enzyme³

2 How common is the adverse drug reaction (ADR) to NSAIDs?

- with varying prevalence ranging from 1.6% - 68% of all NSAID users.³⁻⁵
- primary trigger for >40% of all drug-induced anaphylactic reactions in all ages⁶⁻⁷

3 How are NSAID ADRs categorized?

- Type A (80%) - pharmacologic and predictable (gastrointestinal bleeding and NSAID-induced nephrotoxicity)⁸
- Type B (20%) - unpredictable with five subgroup reaction patterns^{5,9}

Class	Typical Example
Salicylic acid derivatives	Acetylsalicylic acid* Sulfasalazine
Acetic acid derivatives	Diclofenac* Acemetacin Indomethacin
Propionic acid derivatives	Dexibuprofen Ibuprofen* Naproxen Ketoprofen Flurbiprofen
Enolic acid derivatives	Oxicams Meloxicam Lornoxicam* Piroxicam Pyrazolones Phenylbutazone Metamizole
Fenamates	Mefenamic acid
Selective COX-2 inhibitors	Celecoxib

*With chemical and structural similarities between the NSAID groups and paracetamol. The cross-reactivity is mediated via the common blockage of the COX enzyme.

Subgroup	Mechanism	Entities	Time of onset	Cross-reactivity	Drugs Involved
NECD	Unknown	CSU aggravated or reactivated by NSAIDs	~ 30 min	Cross-reactive	NSAIDs
NIUA	Unknown	Urticaria and/or angioedema, anaphylaxis, mixed reactions	~ 30 min	Cross-reactive	NSAIDs
NERD	Inhibition PG-LEK	Rhinitis, asthma, rhinosinusitis, nasal polyposis	15 min - 8h	Cross-reactive	NSAIDs
SNIDHR	T-cells	CD	Within days	Non cross-reactive	Diclofenac
		Photosensitive CD			Naproxen, Piroxicam
		Isolated mucosal involvement			Etoricoxib
		Bullous/desquamative exanthema			Diclofenac
		DRESS			Ibuprofen, Phenylbutazone
		TEN			Ibuprofen, Paracetamol, Celecoxib
		AGEP			Ibuprofen, Flurbiprofen, Piroxicam
		FDE			Diclofenac, Ibuprofen
SNIUAA	IgE-Ab/others	Anaphylaxis (urticaria, angioedema, asthma, hypotension, shock)	~ 10 min	Non cross-reactive	Aril-propionics



4 How are NSAID ADRs managed?

- diagnosis must be confirmed with a good history, possible skin testing and/or drug provocation test
- once confirmed, there should be avoidance of the culprit drugs, use of safe and non-cross-reactive alternatives, symptomatic treatment and desensitization as needed.³

If unsure of your diagnosis, consult with a Board-certified Allergist at psaii.org

References:

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- 8 Nagai J, Uesawa Y, Shimamura R, Kagaya H. Characterization of the adverse effects induced by acetaminophen and non-steroidal anti-inflammatory drugs based on the analysis of the Japanese adverse drug event report database. Clin J Pain. 2017;33:667-75.
- 9 Wichler WJ, Hausmann O. Classification of drug hypersensitivity into allergic, p-i, and pseudo-allergic forms. Int Arch Allergy Immunol. 2016;171:166-79.