The Triple Whammy is defined as ‘three simultaneous deleterious blows with compounded effect’. The combination of medicines above can result in significant patient harm; used individually or combined, they are involved in more than half of reported iatrogenic (treatment-related) acute renal failure cases.

AVOID THIS COMBINATION IF POSSIBLE

The combination of all three of these medicines should be avoided in those with risk factors for renal failure. Older adults and patients with co-morbidities, such as heart failure or severe liver disease, have an increased risk of renal failure.

ACE inhibitors and NSAIDs adversely affect renal blood flow and diuretics have the potential to cause dehydration. Further, NSAIDs antagonise the control of hypertension by ACE inhibitors and diuretics and their beneficial effects in heart failure.

If NSAIDs are unavoidable, use at the lowest dose for the shortest duration possible in those with risk factors for renal failure. Check renal function at baseline and periodically during treatment.

**Monitoring Recommendations**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Interaction with NSAIDs</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors</td>
<td>↓Antihypertensive effect, ↑Risk of renal impairment, Hyperkalaemia</td>
<td>Monitor blood pressure, weight and renal function. Monitor serum potassium</td>
</tr>
<tr>
<td>Diuretics</td>
<td>↓Diuretic effect, ↑Risk of renal failure, Heart failure may be exacerbated</td>
<td>Monitor blood pressure, weight and renal function</td>
</tr>
<tr>
<td>ACE inhibitors + diuretics</td>
<td>↑Risk of renal failure</td>
<td>AVOID combination with NSAIDs if possible</td>
</tr>
</tbody>
</table>

**BE AWARE OF THE RISK FACTORS OF RENAL FAILURE**

Dehydration from vomiting, diarrhoea or sepsis can be a trigger for renal failure; minor illness can place susceptible patients at risk if they are taking Triple Whammy combinations. Advise patients to avoid hypovolaemia (drink plenty of water) and to seek medical advice if they become acutely unwell.

Vomiting → hypovolaemia → precipitation of renal failure

Prescribers may also wish to consider stopping NSAIDs in these circumstances and to monitor renal function and serum potassium levels.

**TAKE CARE WITH OLDER ADULTS**

Older patients are especially vulnerable to the Triple Whammy because they often have a degree of pre-existing renal impairment. They may also be prone to diuretic-induced dehydration and hypotension, and have an inadequate fluid intake.

**Prescribing NSAIDs in older adults**

Due to the increased susceptibility of adverse effects from NSAIDs, the New Zealand Formulary recommends the following:

**Osteoarthritis, soft-tissue lesions, or back pain:**

- Try weight reduction first if obese, warmth, exercise, and use of a walking stick

**Osteoarthritis, soft-tissue lesions, back pain or pain in rheumatoid arthritis:**

- Try paracetamol first OR low-dose NSAID (e.g. Ibuprofen up to 1.2 g daily)
- If inadequate try full dose paracetamol plus a low-dose NSAID
- If necessary, increase NSAID dose OR use an opioid analgesic* with paracetamol

* note constipation risk

**continued**
ADVISE PATIENTS WHO ARE PRESCRIBED ACE INHIBITORS AND DIURETICS NOT TO ‘SELF-MEDICATE’ WITH NSAIDs

Combination ACE inhibitor or angiotensin II receptor antagonists with diuretics (eg Inhibace Plus®) are useful products, however, always advise patients to avoid self-medicating with ‘over-the-counter’ NSAIDs if they are taking these products.

ACKNOWLEDGEMENTS

We wish to thank Sarah Roberts, Renal Pharmacist at Waitemata District Health Board, for her valuable contribution to this bulletin.

KEY REFERENCES


CLICK HERE FOR FURTHER INFORMATION ON THE TRIPLE WHAMMY AND A FULL REFERENCE LIST

For further information on other high-risk medicines visit our website at: www.saferx.co.nz

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DISCLAIMER: This information is provided to assist primary care health professionals with the use of prescribed medicines. Users of this information must always consider current best practice and use their clinical judgement with each patient. This information is not a substitute for the exercise of clinical judgement by individual clinicians. Issued by the Quality Use of Medicines Team at Waitemata District Health Board, email: feedback@saferx.co.nz