Medicine interactions: using the New Zealand Formulary

The New Zealand Formulary uses **Stockley's Drug Interactions** – one of the world's most comprehensive and authoritative international reference sources on drug interactions.

Medicine interactions usually result from potentiation or antagonism of one drug by another. Medicine selection should aim to minimise interactions. If it is necessary to prescribe a potentially serious combination of medicines, patients should be informed and monitored appropriately.

The New Zealand Formulary (NZF) presents two options for obtaining information about medicine interactions:

1. Stockley's Interaction Alerts
2. British National Formulary (BNF) interaction summaries (synonymous with Appendix 1 in the BNF)

Individual drug monographs in the NZF contain links to the relevant section of Stockley's Interaction Alerts, which rates information according to three categories, and the relevant BNF interaction summary. The alerts give additional information to assist in the management of an interaction. The BNF interaction summaries provide a more general interaction overview. The Stockley's Interaction Alerts database is also used for the NZF interaction checker.

The clinical notes section of the NZF contains links to BNF interaction summaries for the associated drug group or class. This provides an overview for general reference.

It is important that any adverse medicine interactions are reported to the New Zealand Pharmacovigilance Centre: **http://carm.otago.ac.nz**

How to interpret Stockley's Interaction Alerts

The alerts are rated using three separate categories:

- **Action:** this describes whether or not any action needs to be taken to accommodate the interaction. This category ranges from "avoid" to "no action needed".
- **Severity:** this describes the likely effect of an unmanaged interaction on the patient. This category ranges from "severe" to "nothing expected".
- **Evidence:** this describes the weight of evidence behind the interaction. This category ranges from "extensive" to "theoretical".

How to use the interactions checker

To launch the interactions checker, select the interactions tab at the top of the page. Start typing the name of the medicine in the search bar and select the appropriate medicine from the dropdown list. You can enter all of your patient's medicines plus any others you may want to check. Food and herbal products can also be checked (where available within the database). Compound preparations may also be entered.

Once two medicines have been entered, any potential interactions will automatically appear on the screen with an explanation of the interaction (Figure 1). The interactions are sorted by a simple "traffic light" colour-coding system (there is a key to the colours at the top right of the window). A short description of what action should be taken is also displayed. Hovering over the text in the severity or evidence columns gives a description of what these classifications are.

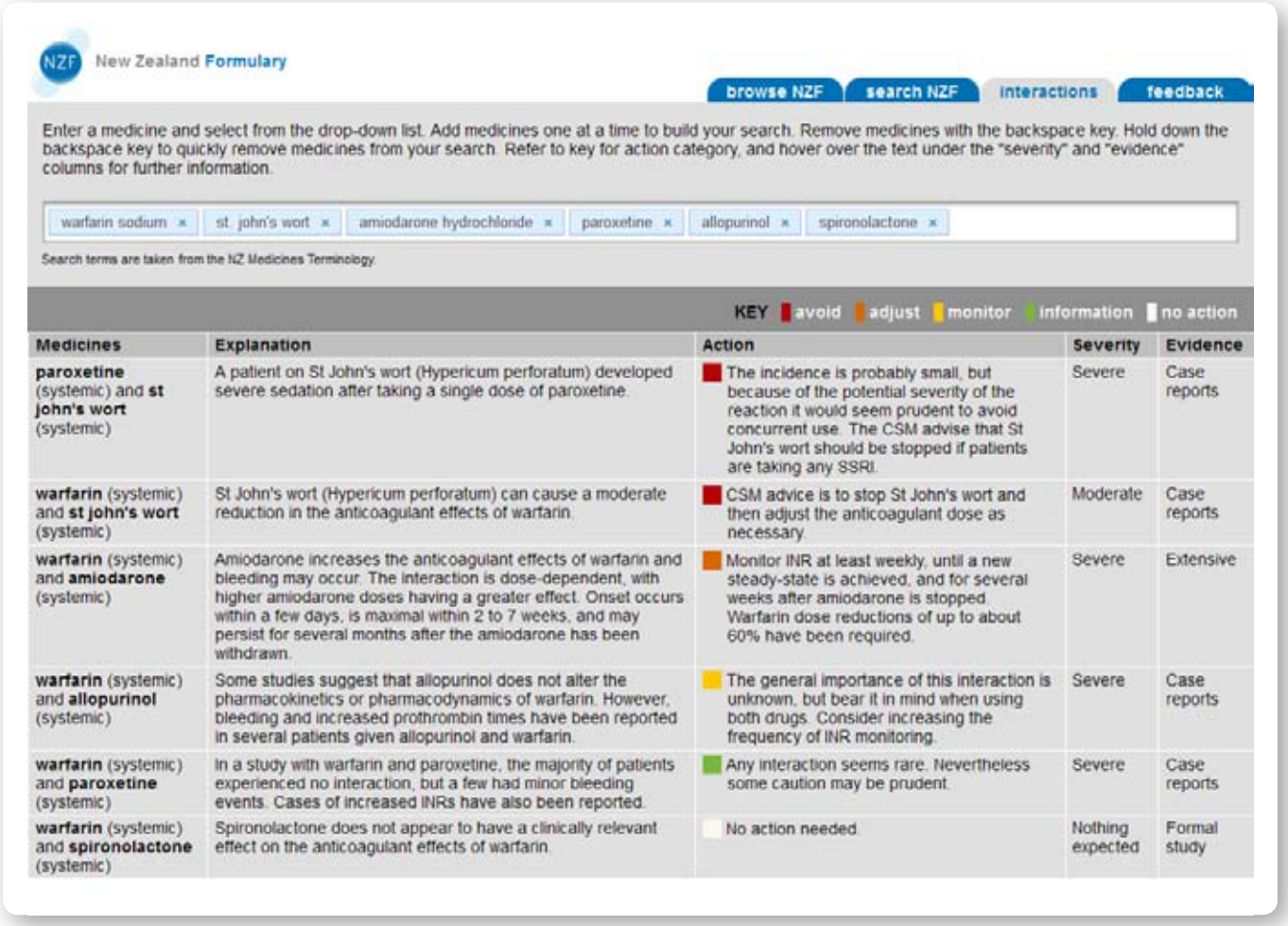

Figure 1: NZF interactions checker screen shot

Definitions of severity and evidence:

Severity	
Severe	Interactions that could totally incapacitate a patient or result in either a permanent detrimental effect or a life-threatening event.
Moderate	Interactions that could result in an effect that may either cause considerable distress or partially incapacitate a patient. These interactions are unlikely to be life-threatening or result in long-term effects.
Nothing expected	Interactions that are unlikely to result in an effect, or for drugs pairs where no interaction occurs.
Evidence	
Theoretical	Based on a theoretical interaction or lack of interaction. This information may have been derived either from in vitro studies involving the drug in question or based on the way other members of the same group act.
Case reports	Based either on a single case report or a limited number of case reports. No trials appear to have been conducted.
Formal study	Based on formal study. This may be one small or medium size study, or several small studies. The studies may or may not be supported by case reports.
Extensive studies	Based on numerous small or medium size studies or several large studies. The information is usually supported by case reports.

Types of interactions

Pharmacodynamic interactions

These are interactions between drugs which have similar or antagonistic pharmacological effects or adverse effects. They may be due to competition at receptor sites, or occur between drugs acting on the same physiological system. They are usually predictable from a knowledge of the pharmacology of the interacting drugs; in general, an interaction demonstrated with one drug is likely to occur with related drugs. N.B. Pharmacodynamic interactions can be compounded by two or more drugs with similar actions.

Pharmacokinetic interactions

These occur when one drug alters the absorption, distribution, metabolism or excretion of another, thus increasing or reducing the amount of drug available to produce its pharmacological effects. Individual variation in metabolic capacity, genotype, organ function and other factors result in a degree of unpredictability and many pharmacokinetic interactions do not affect all patients taking the same combination of drugs. Pharmacokinetic interactions occurring with one drug cannot be assumed to occur with related drugs unless their pharmacokinetic properties are known to be similar.

Relative importance of interactions

Many medicine interactions are harmless and many of those which are potentially harmful only occur in a small proportion of patients. The severity of an interaction varies from one patient to another. Drugs with a small therapeutic window (e.g. phenytoin) and those which require careful control of dosage (e.g. anticoagulants, antihypertensives and antidiabetics) are most often involved in interactions.

Elderly people and people with impaired renal or liver function are at increased risk of medicine interactions.

Additional interactions information from the BNF

BNF interaction summaries are also provided within the NZF. Interactions shown in **bold** and against a pink background are **potentially serious**; concomitant administration of the medicines involved should be **avoided** (or only undertaken with caution and appropriate monitoring). Interactions that are not in bold type do not usually have serious consequences.

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