

FACT SHEET FOR HEALTH CARE PROFESSIONALS

Interactions of St John's Wort (*Hypericum perforatum*) preparations

St John's Wort (SJW) preparations are unlicensed herbal remedies. Their levels of active ingredients can vary from one preparation to another. They are widely used in the UK, being available from pharmacies, health food shops and herbal practitioners.

Why do SJW preparations interact with other medicines?

New evidence suggests that SJW preparations may interact with medicines, either by affecting drug metabolism or levels of neurotransmitters. Drug metabolism may be affected by SJW preparations inducing certain cytochrome P450 isoenzymes in the liver (CYP 3A4, 1A2 and 2C9), as well as, P-glycoprotein. Pharmacodynamic (additive or potentiating) interactions may occur through the effects of SJW preparations on neurotransmitters in the brain (SJW may increase serotonin levels through weak monoamine oxidase inhibiting (MAOI) activity and serotonin re-uptake inhibition).

What is the clinical significance of these interactions?

Induction of drug metabolism increases the breakdown of drugs so reducing their blood levels and therapeutic effects. Because the levels of active ingredients can vary between preparations of SJW and patients may switch between preparations, the degree of induction is likely to change over time. **When patients stop taking SJW preparations, blood levels of interacting medicines may rise, leading to toxicity.**

Pharmacodynamic (additive or potentiating) interactions may occur with psychoactive medicines including Selective Serotonin Reuptake Inhibitors (SSRIs). St John's Wort preparations may also have pharmacodynamic interactions with triptans used to treat migraine. These interactions may result in serious adverse reactions.

Which medicines interact with SJW?

Table 1 lists medicines where in-vitro studies, pharmacokinetic studies or spontaneously reported suspected adverse reactions demonstrate clinically important interactions. In addition, other drugs are included where evidence is lacking but clinically important interactions are likely. Please note that the action of many other drugs depends on their rate of metabolism and thus other drugs may also interact with SJW preparations. In general, the following medicines are *not* likely to interact with SJW preparations:

- topical medicines with limited systemic absorption (inhalers, creams, ointments, eye and ear drops, enemas etc).
- Non-psychotropic medicines which are renally excreted.

For further information

Check the Medicines Control Agency (MCA) website at www.open.gov.uk-mca/mcahome.htm

Or phone the MCA on 0171 273 0000.

Reporting suspected adverse reactions including interactions

If you suspect your patient has had an adverse reaction associated with any licensed or unlicensed herbal remedy, including a SJW preparation, then please report this to the MCA/CSM using the Yellow Card Scheme in the normal way. Yellow Cards can be found in the back of the British National Formulary (BNF).

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TABLE 1 CLINICALLY IMPORTANT INTERACTIONS OF SJW

Drug	Effect of interaction on drug	Suggested management of patients already taking SJW preparations
HIV protease inhibitors (indinavir, nelfinavir, ritonavir, saquinavir)	Reduced blood levels with possible loss of HIV suppression.	Measure HIV RNA viral load and stop SJW.
HIV non-nucleoside reverse transcriptase inhibitors (efavirenz, nevirapine)	Reduced blood levels with possible loss of HIV suppression.	Measure HIV RNA viral load and stop SJW.
Warfarin	Reduced anticoagulant effect and need for increased warfarin dose.	Check INR and stop SJW. Monitor INR closely as this may rise on stopping SJW. The dose of warfarin may need adjusting.
Cyclosporin	Reduced blood levels with risk of transplant rejection.	Check cyclosporin blood levels and stop SJW. Cyclosporin levels may increase on stopping SJW. The dose of cyclosporin may need adjusting.
Oral contraceptives	Reduced blood levels with risk of unintended pregnancy and breakthrough bleeding.	Stop SJW.
Anticonvulsants (carbamazepine, phenobarbitone, phenytoin)	Reduced blood levels with risk of seizures.	Check anticonvulsant levels and stop SJW. Anticonvulsant levels may increase on stopping SJW. The dose of anticonvulsant may need adjusting.
Digoxin	Reduced blood levels and loss of control of heart rhythm or heart failure.	Check digoxin levels and stop SJW. Digoxin levels may increase on stopping SJW. The dose of digoxin may need adjusting.
Theophylline	Reduced blood levels and loss of control of asthma or chronic airflow limitation.	Check theophylline levels and stop SJW. Theophylline levels may increase on stopping SJW. The dose of theophylline may need adjusting.
Triptans (sumatriptan, naratriptan, rizatriptan, zolmitriptan)	Increased serotonergic effects with increased incidence of adverse reactions.	Stop SJW.
SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline)	Increased serotonergic effects with increased incidence of adverse reactions.	Stop SJW.

Patients taking drugs listed in Table 1 should not start taking SJW preparations

Notes:

1. The action of many other drugs depends on their rate of metabolism and thus other drugs may also interact with St John's Wort preparations.
2. St John's Wort preparations are unlikely to interact with topical medicines with limited systemic absorption and non-psychotropic medicines which are excreted renally.