Northumbria Healthcare NHS
NHS Foundation Trust

NHS
North of England
Cancer Network

Systemic Anticancer Therapy
Drug Interactions Table

This guide is intended to cover the most common interactions involving Systemic Anticancer therapies, e.g. cytotoxic agents, monoclonal antibodies and targeted therapies.

Whilst every effort has been made to ensure it is a comprehensive resource, there may be some interactions which have been unintentionally omitted. Please interpret the information contained in this guide in addition to clinical information and performance status.

Version 4.1
October 2012
(Date of Review October 2014)

Any comments on this document to steve.williamson@necn.nhs.uk

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Bleomycin	Cisplatin	Increased risk of pulmonary toxicity when used in combination	1
	Clozapine	Increased risk of agranulocytosis	
	Digoxin	Possibility of reduced absorption of digoxin tablets-switch to liquid	
	Oxygen	Patients receiving bleomycin pre-operatively are at greater risk of developing pulmonary toxicity when oxygen is administered at surgery. A reduction in inspired oxygen concentration during operation and post-operatively is recommended	2
Bortezomib	Oral anti diabetic drugs	Monitor blood glucose levels, hyperglycaemia in is common	3
	Clozapine	Increased risk of agranulocytosis	1
	Potent CYP3A4 inhibitors and inducers (particularly ketoconazole, rifampicin, carbamazepine, phenytoin and St Johns Wart)	Closely monitor as may affect plasma concentration of bortezomib	1, 3
Busulfan	Clozapine	Increased risk of agranulocytosis	1
	Cyclophosphamide	Cyclophosphamide serum levels may be increased (& active metabolite decreased) if given within 24 hours of busulfan	4
	Itraconazole and Metronidazole	Increase in busulfan toxicity	1,3
	Ketobemidone	Increase in busulfan plasma concentration	4
	Paracetamol	May decrease intravenous busulfan plasma levels	
	Phenytoin	Increases busulfan clearance	
	Tioguanine	Increased risk of hepatotoxicity	1

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Capecitabine	Allopurinol	Possible decreased efficacy of capecitabine	5,6
	Aluminium and aluminium containing antacids	Small increase in capecitabine toxicity	5
	Cimetidine	Increased plasma concentration	1
	Clozapine	Increased risk of agranulocytosis	1
	Coumarins	Enhanced anticoagulant effect, monitor INR regularly	1,5
	Erlotinib	Could increase plasma concentration of erlotinib	
	Folinic acid	Increased toxicity of capecitabine, maximum tolerated dose is reduced.	
	Food	Decreased rate of capecitabine absorption if administered with food. Manufacturers recommend administration within 30 minutes of a meal.	
	Interferon Alpha	Maximum tolerated dose of capecitabine is decreased by interferon alpha	6
	Metronidazole	Increased toxicity	1
	Phenytoin	May lead to increased phenytoin levels	5
	Sorivudine and analogues	Potentially fatal combination – leads to increased fluoropyrimidine activity	
	Temoporfin	Increased photosensitivity risk when topical fluorouracil and temoporfin used concomitantly	1, 5

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Cyclophosphamide	Allopurinol	Potential for increased risk of toxicity when used in combination	6
	Amiodarone	Concomitant use may lead to early onset pulmonary toxicity	
	Azole antifungals	Fluconazole and itraconazole inhibit the metabolism of cyclophosphamide, leading to increased toxicity	
	Busulfan	Cyclophosphamide serum levels may be increased (and active metabolite decreased) if given within 24 hours of busulfan	5
	Cisplatin	Increased renal toxicity when used in combination or in patients who have had prior treatment with cisplatin	6
	Clozapine	Increased risk of agranulocytosis	1
	Digoxin	Reduces absorption of digoxin tablets	1
	Oral antidiabetic drugs	Potentiated by cyclophosphamide -monitor blood glucose levels	7
	Pentostatin	Increased risk of toxicity when pentostatin is given with high dose cyclophosphamide	
	Rifampicin	Increased metabolism of cyclophosphamide	6
	Suxamethonium	Enhances effect of suxamethonium	1
Dacarbazine	Aldesleukin	Avoid concomitant use	8
	Clozapine	Increased risk of agranulocytosis	1
	Cytochrome P450 (CYP1A1, CYP1A2, and CYP2E1)	Darcarbazine is metabolised by cytochrome P450, therefore levels may be altered if co-administered with other substrates	8

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Docetaxel	Clozapine	Increased risk of agranulocytosis	1
	CYP3A inducers and inhibitors	Metabolism of docetaxel clearance altered, may lead to increased toxicity or reduced efficacy of docetaxel.	9
	Lapatinib	Increased risk of neutropenia	9
	Ritonavir	Plasma concentration of docetaxel increased	1
	Sorafenib	Increases the plasma concentration of docetaxel	1
Doxorubicin	Amphotericin B	Marked increase in nephrotoxicity	10
	Anticonvulsants	Reduced absorption of anticonvulsants when administered in combination with doxorubicin	
	Anthracyclines and Cardiotoxic medication	Monitor cardiac function as increased risk of cardiotoxicity	
	Calcium Channel Blockers (verapramil)	Plasma concentration of doxorubicin is increased	1
	Ciclosporin	Increased risk of neurotoxicity	1
	Clozapine	Increased risk of agranulocytosis	1
	Cytarabine	Potential for severe infections and necrosis of intestine	10
	CYP3A4 inhibitors	Reduction in plasma concentration	
	Cytochrome P450 inducers and inhibitors	May affect doxorubicin metabolism, leading to increased toxicity or decreased efficacy	
	Digoxin	Possibility of reduced absorption of oral bioavailability of digoxin	
	Epirubicin	May increase concentration of epirubicin metabolites when docetaxel administered immediately after epirubicin	11
	Hepatotoxic medication (e.g. 6 – mercaptopurine)	Increased risk of hepatoxicity when used in combination	10

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Doxorubicin (continued)	Paclitaxel	Manufacturer advises to leave at least 24 hours between infusing both drugs as elimination of doxorubicin may be reduced if given within 24 hours of paclitaxel.	10
	Ritonavir	Elevated serum doxorubicin concentration	10
	Uric acid lowering agents	Doxorubin therapy may lead to an increase in serum uric acid	1
	Vaccines	Doxorubicin patients should not be actively vaccinated and also avoid contact with recently polio vaccinated patients	1, 10
Epirubicin	Cardiotoxic medication	Monitor cardiac function as increased risk of cardiotoxicity	11
	Ciclosporin	Plasma concentration of epirubicin increased by ciclosporin	1
	Cimetidine	Increases plasma concentration of epirubicin, not explained by CYP activity	
	Clozapine	Increased risk of agranulocytosis	
	Dexverapamil	Possible increased bone marrow suppression	11, 1
	Docetaxel	May increase concentration of epirubicin metabolites when docetaxel administered immediately after epirubicin	
	Interferon alpha 2b	May reduce total clearance of epirubicin	
	Hepatotoxic medication	May affect epirubicin efficacy and toxicity	
	Live vaccines	Live vaccines should be avoided	
	Paclitaxel	Increased risk of toxicity, manufacturers advise at least 24 hours between infusions if used in combination	
	Quinine	Can accelerate distribution of epirubicin into the tissues	

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Eribulin	Clozapine	Increased risk of agranulocytosis	12
	Enzyme inducers	Increased eribulin plasma concentration	
	Inhibitors of hepatic transport proteins	May reduce elimination of eribulin and result in up to three fold increase in plasma concentration	
	Substrates of CYP3A4	Eribulin may inhibit CYP3A4, resulting in increased plasma concentration of the substrate. Avoid concomitant use if substrate has narrow therapeutic range.	
Erlotinib	Antacids	Plasma concentration of erlotinib potentially reduced by antacids. Give antacids at least 4 hours before or 2 hours after	1
	Antivirals (bocepravir)	Avoid co-administration	
	Clozapine	Increased risk of agranulocytosis	
	Coumarins	Enhanced anticoagulant effect, monitor INR regularly as increased risk of bleeding	
	CYP1A2 inhibitors/inducers	May alter erlotinib levels	13
	CYP3A4 inhibitors/inducers	May alter erlotinib levels	
	H2 receptor antagonists	Avoid concomitant use with cimetidine. Give erlotinib at least 2 hours before or 10 hours after ranitidine.	1
	Nicotine	May reduce plasma concentration-smoking cessation advice should be given.	13
	NSAIDS	Increased risk of bleeding	1
	P-glycoprotein inhibitors	May alter erlotinib levels	13
	PPIs	May alter erlotinib levels- manufacturers recommend avoid concomitant use	1
	Statins	May increase risk of rhabdomyolysis	13

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Etoposide	Atovaquone	Increases plasma concentration of etoposide	1
	Antiepileptics	Etoposide clearance may be increased by phenytoin and phenobarbital	1, 6
	Ciclosporin	Increased risk of etoposide toxicity with high dose ciclosporin	1
	Clozapine	Increased risk of agranulocytosis	
	Coumarins	Enhanced anticoagulant effect, monitor INR	
	CYP3A4 enzyme inhibitors	CYP3A4 Inhibitors may increase side effects and toxicity of etoposide	1, 6
	Myelosuppressive drugs (e.g. 5 – Fluouracil, vinblastine etc)	Increases the effect of etoposide and/ or co-administered drug on bone marrow	
	St John's Wort	May induce the metabolism of etoposide and also antagonise it's effects	
Fludarabine	Clozapine	Increased risk of agranulocytosis	1
	Dipyridamole	May reduce the efficacy of fludarabine	6
	Pentostatin	Increased risk of pulmonary toxicity when these drugs are used in combination, leading to fatalities.	1
Fluorouracil	Allopurinol	Manufacturer advises avoid, can affect bioavailability of active drug	1
	Cimetidine	Significant use of cimetidine (4 weeks or more) can increase fluorouracil levels	14
	Cisplatin	Possible increase in toxicity (particularly cardiotoxicity) if used in combination	6
	Coumarins	Enhanced anticoagulant effect, monitor INR	1

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Fluorouracil (continued)	Folic Acid	Increase in fluorouracil toxicity	6
	Leucovorin	Can affect availability of active drug	6,14
	Methotrexate	Increase in fluorouracil toxicity	
	Metronidazole	Increase in fluorouracil toxicity	
	Sorivudine and analogues	Potentially fatal combination – leads to increased fluoropyrimidine activity	
Gefitinib	Antiepileptics	Manufacturer advises avoid concomitant use with phenytoin and carbamazepine	1
	Boceprevir	Manufacturer advises to avoid concomitant use	
	Clozapine	Increased risk of agranulocytosis	
	Coumarins	Enhanced anticoagulant effect, monitor INR regularly	1, 15
	CYP2D6 inhibitors	May increase gefitinib levels, monitor for increased toxicity	15
	CYP2D6 substrates	Concomitant administration may alter levels of substrate, monitor if substrate with narrow therapeutic index	
	CYP3A4 inducers	May decrease gefitinib levels and therefore efficacy	
	CYP3A4 inhibitors	May increase gefitinib levels, monitor for increased toxicity	
	High dose short acting antacids	May reduce gefitinib levels and therefore efficacy	
	Ranitidine	May reduce gefitinib levels and therefore efficacy	15
	Rifampicin	Plasma concentration reduced-avoid concomitant use	
	St Johns Wort	Manufacturer advises to avoid concomitant use	1

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Gemcitabine	Clozapine	Increased risk of agranulocytosis	1
	Coumarins	Enhances anticoagulant effect. Monitor INR closely	1
	Yellow fever and other Live attenuated vaccines	Increased risk of systemic disease	16
	Platinum based chemotherapy	Carboplatin administered immediately after gemcitabine may cause increased severity of thrombocytopenia	6
	Radiotherapy	Gemcitabine may cause radiosensitisation when given concurrently with (or within 7 days of) radiotherapy	16
Imatinib	Antivirals (Boceprevir)	Avoid concomitant use with imatinib	1
	Clozapine	Increased risk of agranulocytosis	
	Coumarins	Monitor INR, SPC states patients should be treated with low molecular weight heparin or standard heparin	17
	CYP3A4 inducers	Lower plasma concentration of imatinib, reducing efficacy	
	CYP3A4 inhibitors	Increase plasma concentration of imatinib, monitor for toxicity	
	CYP3A4 substrates	Imatinib may alter the plasma concentration of substrates so caution should be used if they have a narrow therapeutic window, such as ciclosporin.	
	Enzyme inducing antiepileptics	May reduce plasma concentration of imatinib	
	L-asparaginase	Increased risk of hepatotoxicity	
	Levothyroxine	Plasma exposure to levothyroxine may be decreased when used in conjunction with imatinib. Monitor thyroid function tests.	
	Paracetamol	Caution should be used if co-administering high dose imatinib and paracetamol	
	Rifampicin	Plasma concentration of imatinib reduced, avoid concomitant use	1
	Statins	Plasma concentration is increased	
	St Johns Wort	Plasma concentration of imatinib reduced, avoid concomitant use	

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Irinotecan	Antiepileptics	Clearance of irinotecan increased by phenytoin and phenobarbital. Sodium valproate may decrease clearance of irinotecan active metabolite.	6
	Antivirals (Atazanavir)	Metabolism of irinotecan inhibited by atazanavir. Increased risk of toxicity	1
	Bevacizumab	May possibly reduce tolerated dose of irinotecan and result in increased incidence of side effects	18
	Clozapine	Increased risk of agranulocytosis	
	CYP3A4 inducing antiepileptics	May reduce irinotecan plasma levels	
	CYP3A4 inducers/inhibitors	May affect irinotecan levels by altering metabolism	
	Ketoconazole	Increases concentration of irinotecan active metabolite	1
	Lapatinib	Plasma concentration of irinotecan active metabolite increased by lapatinib	1
	Neuromuscular blocking agents	Irinotecan has anticholinesterase activity and may prolong neuromuscular blocking effects of suxamethonium, and may also antagonise neuromuscular blockade of non-depolarising drugs e.g. pancuronium, rocuronium	18
	Physotigmine	May inhibit irinotecan activation	6
	Sorafenib	Plasma concentration of irinotecan is increased	1
	St John's Wort	Increases metabolism of irinotecan, reducing plasma levels	1,18
	Vinorelbine	Affects metabolism of irinotecan	6

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Lapatinib	Antibacterials e.g. rifabutin, rifampicin, telithromycin	Manufacturer advises avoid concomitant use	1
	Antiepileptics	Avoid concomitant use with phenytoin and carbamazepine	
	Antifungals	Avoid concomitant use with ketoconazole, itraconazole, posaconazole and voriconazole	1
	Antivirals	Avoid concomitant use with boceprevir, ritonavir and saquinavir	
	Clozapine	Increased risk of agranulocytosis	
	CYP2C8 substrates e.g. repaglinide	Manufacturer advises avoid concomitant use with substrates that have a narrow therapeutic window	19
	CYP3A4 inducers	May decrease lapatinib levels and therefore efficacy	
	CYP3A4 inhibitors	May increase plasma laptanib levels. Co-administration with strong inhibitors should be avoided.	
	Docetaxel	Increased risk of neutropenia	
	Food	Bioavailability of lapatinib may be affected by food	
	Grapefruit Juice	Manufacturer advises avoid concomitant use	1
	Irinotecan	May increase levels of active metabolite of irinotecan	19
	Paclitaxel	Increase in diarrhoea and neutropenia observed due to increased plasma concentration of paclitaxel	
	P-glycoprotein substrates	Co-administration may increase plasma concentration of substrate drug. Manufacturer advices caution with substrates that have a narrow therapeutic window	
	Pimozide	Avoid concomitant use	1
	histamine and H2 Proton Pump Inhibitors	Co-administration may result in reduced laptanib levels	19
	Repaglinide (Substrates of CYP2C8)	Manufacturer advises to avoid concomitant use	1
	St Johns Wort		

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Lomustine	Cimetidine	May potentiate bone marrow toxicity	1, 20
	Clozapine	Increased risk of agraulocytosis	1
	Digoxin	Reduced absorption of digoxin tablets-switch to liquid	
	Pre- treatment of phenobarbital	May lead to increased elimination and reduced efficacy of lomustine	20
	Theophylline	May potentiate bone marrow toxicity	
Melphalan	Cardiac glycosides (digoxin)	Reduced absorption	1
	Ciclosporin	May increase risk of impaired renal function. Increased risk of nephrotoxicity	1, 21
	Cimetidine	Cimetidine may reduce bioavailability of melphalan	6
	Clozapine	Increased risk of agraulocytosis	1
	Food	Absorption of melphalan can be reduced by food	6
	Interferon Alfa	May increase cytotoxicity due to interferon induced fever	
	Live vaccines	Manufacturer advises to avoid concomitant use	21
	Nalidixic acid	May lead to haemorrhagic enterocolitis when used in combination with high dose intravenous melphalan	
	Phenytoin	Possibility of reduced absorption of phenytoin ?? (not listed in BNF or SPC?)	1

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Methotrexate	Acitretin	Increases methotrexate concentration and may increase risk hepatotoxicity	22
	Amphotericin B	May delay clearance of methotrexate	6
	Antibacterials e.g. co-trimoxazole, sulfamethoxazole, trimethoprim. Aminoglycosides Ciprofloxacin	Increased risk of haematological toxicity Aminoglycosides may reduce GI absorption Ciprofloxacin may increase methotrexate toxicity	1, 22
	Antibiotics	Reduced renal clearance of methotrexate, GI toxicity may occur	
	Antimalarials	Antifolate effect increased by pyrimethamine	
	Caffeine	Avoid as methotrexate efficacy may reduce due to interaction with methylxanthines at adenosine receptors	
	Ciclosporin	Increased risk of toxicity	
	Cisplatin	Increased risk of pulmonary toxicity	
	Chloramphenicol	May affect methotrexate transport function of renal tubules, increasing methotrexate concentration and toxicity	
	Clozapine	Increased risk of agranulocytosis	
	Colestyramine	Increases the non – renal elimination of methotrexate by interrupting the enterohepatic circulation	
	Folate antagonists e.g. trimethoprim, cotrimoxazole	Concomitant use should be avoided	
	Hepatotoxic medication	Concomitant use should be avoided. Increased hepatotoxicity	22
	Leflunomide	Increased risk of toxicity	
	Live vaccines	Manufacturer advises to avoid concomitant use	

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Methotrexate (continued)	Nitrous Oxide	Antifolate effect of methotrexate increased by nitrous oxide. Avoid concomitant use.	1
	NSAIDs	May affect methotrexate transport function of renal tubules, increasing methotrexate concentration and toxicity	22
	Oral hypoglycaemics		
	Probenecid		
	Sulphonamides		
	Tetracyclines		
	Proton pump inhibitors (omeprazole)	Increased risk of toxicity	1
	Radiotherapy	Increased risk of soft tissue or bone necrosis	
	Theophylline	Methotrexate may possibly increase plasma level of theophylline	1
	Thiazide diuretics	May affect methotrexate transport function of renal tubules, increasing methotrexate concentration and toxicity	
	Vitamin preparations including folic acid	May alter response to methotrexate	22
Paclitaxel	Antivirals	Plasma concentration of paclitaxel increased by nelfinavir and ritonavir	1
	Cisplatin	Manufacturer recommends administration of paclitaxel before cisplatin, due to increased risk of toxicity and renal failure if administered post cisplatin	23
	Clozapine	Increased risk of agranulocytosis	1
	Digoxin	Reduced absorption of digoxin tablets-switch to liquid	
	Doxorubicin	Manufacturer advises to leave at least 24 hours between infusing both drugs as elimination of doxorubicin may be reduced if given within 24 hours of paclitaxel.	
	CYP2C8 inhibitors or inducers	Use with caution – may alter metabolism of paclitaxel	23
	CYP3A4 inhibitors/inducers		

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Paclitaxel (continued)	Lapatinib	Increased risk of neutropenia	1
	Nelfinavir and ritonavir (and other protease inhibitors)	May reduce paclitaxel clearance leading to increased toxicity	23
	Phenytoin	May reduce absorption of phenytoin when used concomitantly	1
Pemetrexed	Aspirin	May reduce clearance of pemetrexed when high doses of aspirin (>1.3g/day) administered concomitantly	24
	Clozapine	Increased risk of agranulocytosis	
	Digoxin	Reduced absorption of digoxin tablets-switch to liquid??	1
	Drugs secreted by renal tubules e.g. penicillin, probenecid	Possibly reduce clearance of pemetrexed, manufacturer advises use in combination with caution and with monitoring of creatinine clearance	24
	Nephrotoxic drugs	Possibly reduce clearance of pemetrexed, manufacturer advises use in combination with caution and with monitoring of creatinine clearance	
	NSAIDs	High doses (e.g ibuprofen > 1600mg daily or asprin > 1.3g daily) may decrease pemetrexed elimination. Manufacturer advises in patients with mild to moderate renal insufficiency treatment with longer acting NSAIDs such as piroxicam should be interrupted for at least 5 days prior to, on the day of, and at least 2 days following pemetrexed administration	6, 24
	Pyrimethamine	Antifolate effect of pemetrexed is increased by concomitant use with pyrimethamine	1
	Yellow fever and Live attenuated vaccines	Risk of fatal generalised vaccinale disease	

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Platinum compounds **Carboplatin** **Cisplatin** **Oxaliplatin**	Aldesleukin	Manufacturer advises to avoid concomitant use with cisplatin	1
	Allopurinol (and other drugs which affect serum uric acid levels e.g. colchicine, probenecid or sulfinpyrazone)	May require dosage adjustment as cisplatin can increase serum uric acid concentration	25
	Aluminium	Carboplatin may form a black precipitate in the presence of aluminium	26
	Antibacterials	Increased risk of nephro- and ototoxicity when platinum drugs given with aminoglycosides or polymixins	1
	Antiepileptics	May reduce therapeutic levels of phenytoin. Initiation of treatment with phenytoin when a patient is on cisplatin is contra-indicated. For patients who are already established on phenytoin, monitoring of levels is required.	25
	Antihistamines	May mask the symptoms of ototoxicity	
	Antihypertensives	May increase incidence of nephrotoxicity when given with cisplatin, (specifically furosemide, hydralazine, diazoxide, propanolol)	1, 25
	Bleomycin	Can lead to Raynaud phenomenon when given with cisplatin, and increase risk of pulmonary toxicity	1, 25
	Chelating agents (e.g. penicillamine)	Diminishes effectiveness of cisplatin	1, 25
	Ciclosporin	Excessive immunosuppression, with risk of lymphoproliferation	26
	Clozapine	Increased risk of agranulocytosis	1
	Diuretics	Increased risk of nephro- and ototoxicity when given with platinum compounds	
	Docetaxel	Greatly increased incidence of neurotoxic effects compared to each individual drug	25
	Ifosfamide	May increase risk of nephro- and ototoxicity when used in combination	

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Platinum compounds (continued) **Carboplatin** **Cisplatin** **Oxaliplatin**	Lithium	Monitoring of lithium levels recommended when a combination of lithium and cisplatin are used.	
	Yellow fever vaccine	Risk of fatal systemic vaccinal disease	26
	Live vaccines	Manufacturer advises to avoid concomitant use??	25
	Methotrexate	Increased risk of pulmonary toxicity	1
	Nephrotoxic drugs	May increase risk of toxicity due to changes in renal clearance	1, 25
	Ototoxic drugs	May increase risk of toxicity due to changes in renal clearance	25
	Paclitaxel	May reduce clearance of cisplatin when cisplatin treatment given prior to paclitaxel, increasing neurotoxicity	
	Pyridoxine	May increase time to response when used in combination	25
	Topotecan	If either cisplatin or carboplatin is given on day 1 of the topotecan dosing, a lower dose of each agent must be given to improve tolerability compared to the dose of each agent which can be given if the platinum agent is given on day 5 of the topotecan dosing.	27
	Vinblastine	Can lead to Raynaud phenomenon and increased plasma levels of vinblastine when given with cisplatin	25
	Warfarin	Regular monitoring of INR recommended	
Topotecan	Ciclosporin A	May increase plasma topotecan levels	27
	Cisplatin/Carboplatin	If either cisplatin or carboplatin is given on day 1 of the topotecan dosing, a lower dose of each agent must be given to improve tolerability compared to the dose of each agent which can be given if the platinum agent is given on day 5 of the topotecan dosing.	
	Inhibitors of ABCB1 and ABCG2 (P-glycoprotein inhibitors)	May increase plasma topotecan levels	
	Phenytoin	May increase phenytoin clearance and reduce levels when used concomitantly	6

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
Vinca Alkaloids **Vinblastine** **Vincristine** **Vindesine** **Vinorelbine**	Antiepileptics	Levels, particularly of phenytoin, may be reduced by regimes including vinblastine and vincristine	28
	Antivrals (ritonavir)	Plasma concentration of vinblastine is increased	1
	Antifungals (Itraconazole, Posaconazole, Voriconazole)	Inhibits hepatic metabolism of vinblastine and vincristine, leading to increased neurotoxicity.	6, 28,30
	Allopurinol	May increase bone marrow depression with vincristine	29
	Asparaginase	May lead to increased neurotoxicity when given with vincristine. It is recommended that vincristine should be administered 12 to 24 hours before asparaginase	6
	Bleomycin	Can lead to raynaud phenomenon and gangrene when given concomitantly with vinblastine. May also lead to serious cardiovascular toxicity.	6, 28
	Ciclosporin	Increased risk of immunosuppression and lymphoproliferation when given in conjuction with vinorelbine	31
	Cisplatin	Can lead to Raynaud Phenomenon and increased plasma levels of vinca alkaloids when given concomitantly.	25
	Clarithromycin	Increased risk of neutropenia with vinorelbine	1
	Clozapine	Increased risk of agranulocytosis	1
	CYP3A4 inducers	May increase metabolism of vinca alkaloids, leading to reduced efficacy	29, 31
	CYP3A4 inhibitors	May inhibit metabolism of vinca alkaloids, leading to increased incidence of neuromuscular side effects	29
	Digoxin	Vincristine - possibility of reduced absorption of digoxin tablets- switch to liquid	1
	Drugs which act on the peripheral nervous system	May have an additive neurotoxic effect when given with vincristine	29
	Erythromycin	Can Increase vinblastine toxicity	6, 28
	Isoniazid	May increase bone marrow depression with vincristine	6, 29
	L-asparaginase	Vincristine should be given 12 to 24 hours before administration of L-asparaginase in order to minimise toxicity, since administering L-asparaginase first may reduce hepatic clearance of vincristine.	29
	Live attenuatedvaccines	Manufacturer of vinorelbine advises to avoid live vaccines	31

DRUG	INTERACTION WITH	INFORMATION	REFERENCE
	Methotrexate	Vincristine increases cellular uptake of methotrexate.	29
	Mitomycin	May result in respiratory distress and pulmonary infiltration when given with vinca alkaloids	6, 28, 29, 30
	Nifedipine	Reduces the clearance of vincristine	6
	P-glycoprotein inhibitors/inducers	May alter vinorelbine levels as it is a p-glycoprotein substrate. Manufacturer advises caution when used in combination.	31
	Pyridoxine	May increase bone marrow depression with vincristine	29, 30
	Radiotherapy	Vincristine and vindesine treatment should be delayed until radiotherapy is finished when using portals in the liver	
	Tacrolimus/ Ciclosporin	Increased risk of immunosuppression and lymphoproliferation when given in conjuction with vinorelbine	31

MONOCLONAL ANTIBODY	INTERACTION WITH	INFORMATION	REFERENCE
Alemtuzumab	Chemotherapy	Manufacturer advises that three weeks should be left between administration of chemotherapy and alemtuzumab	32
	Itraconazole	Increased neuro- toxicity due to decrease of hepatic metabolism	
	Live attenuated vaccines	Avoid concomitant use – risk of generalised vaccine disease – possibly fatal	
	Phenytoin	Risk of toxicity enhancement or loss of efficacy of cytotoxic drug	32
Bevacizumab	Anti-EGFR monoclonal antibodies (e.g. cetuximab/panitumumab)	Trial data suggests the combination of Anti-EGFR monoclonal antibody, plus bevacizumab and chemotherapy leads to decreased performance status and increased toxicity	33
	Platinum based chemotherapy	Increased risk of infection and neutropenia, including severe neutropenia, when used in combination	
	Sunitinib	Some trial data to suggest increased risk of microangiopathic haemolytic anaemia when used in combination. Reversible upon discontinuation of both drugs	
	Taxane based chemotherapy	Increased risk of infection and neutropenia, including severe neutropenia, when used in combination	
Cetuximab	Bevacizumab	Trial data suggests the combination of Anti-EGFR monoclonal antibody (cetuximab), plus bevacizumab and chemotherapy leads to decreased performance status and increased toxicity	34
	Fluoropyrimidines	Increased risk of cardiac ischaemia, myocardial infarction and palmar-plantar erythema	
	Platinum based chemotherapy	Increased risk of infection and neutropenia, including severe neutropenia, when used in combination	
	XELOX (capecitabine and oxaliplatin)	Increased frequency of severe diarrhoea	

MONOCLONAL ANTIBODY	INTERACTION WITH	INFORMATION	REFERENCE
Infliximab	Abatacept	Avoid concomitant use	1, 35
	Anakinra		
	Immunomodulators	Reduced formation of antibodies against infliximab and increased infliximab plasma concentration	35
	Live vaccines	Avoid concomitant use	1, 35
Panitumumab	Bevacizumab	Trial data suggests the combination of Anti-EGFR monoclonal antibody (panitumumab), plus bevacizumab and chemotherapy leads to decreased performance status and increased toxicity	34,36
	IFL chemotherapy (bolus 5-fluorouracil (500 mg/m^2), leucovorin (20 mg/m^2) and irinotecan (125 mg/m^2)	Increased risk of severe diarrhoea	36
	Oxaliplatin containing regimes	Contraindicated in patients with mutant *KRAS* expression or where *KRAS* status is unknown, due to decreased performance status and reduced overall survival	36
Rituximab	Immunomodulators	Increased risk of infection when used in combination	37
Tocilizumab	Live vaccines	Avoid concomitant use	1
	Substrates of CYP450 3A4, 1A2 or 2C9	Doses of medication metabolised by these isoenzymes may need to be increased to maintain the same therapeutic effect achieved prior to tocilizumab treatment	38
Trastuzumab	Cardiotoxic medication	Increased risk of cardiotoxicity	39
	No formal interaction studies performed	Manufacturer cannot rule out risk of interaction with other medication	

Examples of enzyme inducers/ inhibitors

	SUBSTRATES		INHIBITORS		INDUCERS
CYP1A2	acetaminophen amitriptyline caffeine chlordiazepoxide clomipramine clopidogrel clozapine cyclobenzaprine desipramine diazepam estradiol flutamide fluvoxamine haloperidol imipramine levobupivacaine	mexiletine mirtazapine naproxen nortriptyline olanzapine ondansetron propafenone propranolol riluzole ropinirole ropivacaine tacrine theophylline verapamil (R)-warfarin zileuton	amiodarone cimetidine ciprofloxacin citalopram clarithromycin diltiazem enoxacin erythromycin ethinyl estradiol fluvoxamine isoniazid ketoconazole	methoxsalen mexiletine nalidixic acid norethindrone norfloxacin omeprazole oral contraceptives paroxetine tacrine ticlopidine troleandomycin zileuton	carbamazepine charbroiled food lansoprazole omeprazole phenobarbital phenytoin primidone rifampin ritonavir smoking St John's wort
CYP2C9	amitriptyline carvedilol celecoxib clomipramine desogestrel diazepam diclofenac dronabinol fluoxetine flurbiprofen fluvastatin formoterol glimepiride glipizide glyburide ibuprofen imipramine indomethacin irbesartan & losartan	mefenamic acid meloxicam montelukast naproxen nateglinide omeprazole phenytoin piroxicam rosiglitazone sildenafil sulfamethoxazole tolbutamide torsemide valdecoxib valsartan voriconazole (S)-warfarin zafirlukast zileuton	amiodarone chloramphenicol cimetidine clopidogrel cotrimoxazole delavirdine disulfiram efavirenz fenofibrate fluconazole fluorouracil fluoxetine fluvastatin fluvoxamine gemfibrozil imatinib isoniazid itraconazole	ketoconazole leflunomide lovastatin metronidazole modafinil omeprazole paroxetine sertraline sulfonamides ticlopidine voriconazole zafirlukast	aprepitant carbamazepine phenobarbital phenytoin primidone rifampin rifapentine

	SUBSTRATES		INHIBITORS		INDUCERS
CYP2C19	amitriptyline carisoprodol cilostazol citalopram clomipramine cyclophosphamide desipramine diazepam esomeprazole formoterol hexobarbital imipramine indomethacin lansoprazole mephobarbital moclobemide	nelfinavir nilutamide omeprazole pantoprazole pentamidine phenytoin progesterone proguanil propranolol rabeprazole teniposide thioridazine tolbutamide voriconazole (R)-warfarin	citalopram delavirdine efavirenz felbamate fluconazole fluoxetine fluvastatin fluvoxamine indomethacin isoniazid ketoconazole	letrozole modafinil omeprazole oxcarbazepine paroxetine sertraline telmisartan ticlopidine topiramate voriconazole	carbamazepine norethindrone phenobarbital phenytoin prednisone rifampin
CYP2D6	amitriptyline amphetamine atomoxetine bisoprolol carvedilol cevimeline chlorpromazine clozapine codeine cyclobenzaprine desipramine dexfenfluramine donepezil doxepin encainide fenfluramine fentanyl flecainide fluphenazine	imipramine lidocaine maprotiline meperidine methoxyamphetamin e metoprolol mexiletine nortriptyline olanzapine ondansetron oxycodone propranolol quetiapine risperidone thioridazine timolol tolterodine tramadol venlafaxine	amiodarone bupropion celecoxib cimetidine citalopram clomipramine cocaine desipramine diphenhydramine fluoxetine fluphenazine halofantrine haloperidol imatinib levomepromazine methadone moclobemide norfluoxetine	paroxetine perphenazine propafenone propoxyphene quinacrine quinidine ranitidine ritonavir sertraline terbinafine thioridazine	carbamazepine ethanol phenobarbital phenytoin primidone rifampin ritonavir St John's wort

	SUBSTRATES		INHIBITORS		INDUCERS
CYP3A4	alfentanil almotriptan alprazolam amitriptyline amiodarone amlodipine amprenavir aprepitant atorvastatin bepridil bexarotene bromocriptine budesonide buprenorphine cilostazol cisapride delavirdine desogestrel dexamethasone dextromethorphan diazepam dihydroergotamine diltiazem disopyramide docetaxel dofetilide dolasetron donepezil doxorubicin dronabinol dutasteride efavirenz ergotamine etoposide exemestane felodipine fentanyl	mometasone montelukast nateglinide nefazodone nelfinavir nevirapine nicardipine nifedipine nimodipine nisoldipine nitrendipine norethindrone omeprazole ondansetron oral contraceptives sertraline sibutramine temazepam testosterone tiagabine tolterodine toremifene tramadol trazodone triazolam trimetrexate valdecoxib verapamil vinblastine vincristine vinorelbine voriconazole (R)-warfarin zaleplon zileuton ziprasidone zolpidem	acitretin amiodarone amprenavir aprepitant cimetidine ciprofloxacin clarithromycin cyclosporine danazol delavirdine diltiazem diethyldithiocarbamate efavirenz erythromycin ethinyl estradiol fluconazole fluoxetine fluvoxamine gestodene grapefruit indinavir imatinib isoniazid itraconazole ketoconazole	metronidazole methylprednisolone miconazole mifepristone nefazodone nelfinavir nicardipine nifedipine norethindrone norfloxacin norfluoxetine oxiconazole prednisone quinine ritonavir roxithromycin saquinavir sertraline Synercid troleandomycin verapamil voriconazole zafirlukast zileuton	aminoglutethimide aprepitant carbamazepine dexamethasone efavirenz ethosuximide garlic supplements glucocorticoids glutethimide griseofulvin modafinil nafcillin nevirapine oxcarbazepine phenobarbital phenytoin primidone rifabutin rifampin rifapentine St John's wort

	SUBSTRATES		INHIBITORS		INDUCERS
CYP2C8	amiodarone benzphetamine carbamazepine docetaxel fluvastatin isotretinoin paclitaxel phenytoin pioglitazone	repaglinide retinoic acid retinol rosiglitazone tolbutamide tretinoin verapamil warfarin zopiclone	anastrozole gemfibrozil nicardipine quercetin sulfaphenazole sulfinpyrazone trimethoprim		carbamazepine phenobarbital rifabutin rifampicin rifampin

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