Safety and use of DMARDs in presence of renal and hepatic dysfunction

DMARD	General Safety recommendations	Dose modification in renal dysfunction.	Dose modification in liver dysfunction
Methotrexate	Monitor patients closely for bone marrow, liver, lung and kidney toxicities	CrCl 10-50 ml/min: 50% of dose at normal dosing interval CrCl<10 ml/min: avoid use	Bilirubin 3.1-5.0 mg/dl or AST> 3 times ULN: give 75% of dose Bilirubin >5.0 mg/dl: avoid use
Leflunomide	Can cause severe liver injury Recommend ALT monitoring monthly for 6 months after initiating, and q6-8weeks thereafter If ALT rises to >3x ULN, interrupt therapy while investigating probable cause; if likely leflunomide-induced, initiate cholestyramine washout to speed elimination and conduct follow-up LFTs at least weekly until ALT value within normal range; if not leflunomide-induced ALT elevation, may consider resuming leflunomide	There are no dosage adjustments provided in the manufacturer's labelling	Not recommended for use in patients with pre-existing liver disease or those with baseline ALT>2 times ULN; monitor liver function closely. Use is contraindicated in hepatic impairment.
Sulfasalazine	Can lead to hepatobiliary	Renal clearance: 37%	Data not available

DMARD	General Safety recommendations	Dose modification in renal dysfunction.	Dose modification in liver dysfunction
	disorders: reports of hepatotoxicity, including elevated liver function tests cholestatic jaundice, cirrhosis, hepatitis cholestatic, cholestasis and possible hepatocellular damage including liver necrosis and liver failure; Renal and urinary disorders: nephrolithiasis reported	There are no dosage adjustments provided in the manufacturer's labelling; use with extreme caution	
Hydroxychloroquine	Both chloroquine and HCQ can cause a 10 percent decrease in creatinine clearance by competitively inhibiting creatinine secretion; this does not represent a true change in renal function.	Excretion of these drugs is principally by direct renal clearance of the parent compound and hepatic metabolites. Manufacture does not provide instructions for use in renal failure. Expert recommendation is reduction of dose <250mg/day. antimalarials have been found in the urine five years after medication was stopped	Data not available. Dose should be reduced if continued.
Azathioprine	Increased risk of infection and hepatotoxicity; monitor	CrCl>50 ml/minute: no adjustment	There are no dosage adjustments provided in the manufacturer’s labelling.

DMARD	General Safety recommendations	Dose modification in renal dysfunction.	Dose modification in liver dysfunction
	liver function periodically; hepatic sinusoidal obstruction syndrome reported; discontinue therapy if suspected	recommended. CrCl 10 to 50 ml/minute: administer 75% of normal dose. CrCl<10 ml/minute: administer 50% of normal dose. Haemodialysis (partially dialyzable; ~45% removed in 8 hours): administer 50% of normal dose; supplement: 0.25 mg/kg. CRRT: administer 75% of normal dose.	However expert recommendation is that it may be used with caution.
Mycophenolate mofetil	Toxicity may increase in renal impairment; use caution	No specific dosage adjustments identified, Although use of lower doses may be required. Mycophenolic acid (MPA) exposure appears to be inversely related to renal function. With GFR less than 25mL/min/1.73m2 in renal transplant recipients doses more than 2g/d should be avoided.	It is not currently known whether dosage adjustments are necessary for hepatic disease with other aetiologies. Increased monitoring may be necessary in patients with hyperbilirubinemia and/or hypoalbuminemia
Apremilast	Renal/hepatic impairment	Severe renal impairment (CrCl<30 ml/min): reduce dose	Hepatic impairment: no dosage adjustment required

DMARD	General Safety recommendations	Dose modification in renal dysfunction.	Dose modification in liver dysfunction
		to 30 mg po qday Mild-to-moderate renal impairment: no dosage adjustment required	
Tacrolimus	Increased mortality in female liver transplant patients. Renal impairment does not affect the elimination or serum concentrations of tacrolimus; however, tacrolimus may cause nephrotoxicity requiring dose reduction. Post-transplant hepatic impairment may be associated with increased risk of developing renal insufficiency	Use lower end of dosing range Monitor renal function and adjust dose according to whole blood concentrations and tolerability	Mild: no dosage adjustment required Moderate: monitor whole blood concentrations and adjust dose accordingly Severe (mean child-pugh score >10): mean clearance of tacrolimus was substantially lower compared with normal hepatic function; dosage reduction recommended; administer 80% of preconversion daily dose of immediate release dosage form when converting from tacrolimus immediate release to extended release
Cyclophosphamide	Use with caution in patients with hepatic or renal impairment	Renal impairment: CrCl<10 ml/min, give 75% of normal dose; CrCl>10 ml/min, give full dose	Hepatic impairment: give 75% of normal dose if transaminase levels are >3 times upper limit of normal or bilirubin is 3.1-5 mg/dl
Rituximab	Increased risk of potentially fatal hepatitis b virus reactivation	There are no dosage adjustments provided in the manufacturer's labelling (has not been studied)	There are no dosage adjustments provided in the manufacturer's labelling (has not been studied)
Infliximab	There are no dosage adjustments provided in the manufacturer's labelling. There		

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DMARD	General Safety recommendations	Dose modification in renal dysfunction.	Dose modification in liver dysfunction
Adalimumab	are case reports of successful use in renal or hepatic failure.		
Etanercept			
Golimumab			
Secukinumab	Data not available	Data not available	Data not available
Tofacitinib	Associated with increased LFTs	Mild: no dosage adjustment required RA or PsA Moderate-to-severe: not to exceed 5 mg qday UC Moderate-to-severe: if taking 10 mg bid, reduce to 5 mg bid; if taking 5 mg bid, reduce to 5 mg qday	Mild: no dosage adjustment required Severe: not recommended Ra or PsA Moderate-to-severe : not to exceed 5 mg qday UC Moderate-to-severe: if taking 10 mg bid, reduce to 5 mg bid; if taking 5 mg bid, reduce to 5 mg qday
Baricitinib	Data not available	Renal impairment Egfr ≥60 ml/min/1.73 m^2: renal function significantly affects Baricitinib systemic exposure; monitor closely eGFR <60 ml/min/1.73 m^2: not recommended	Hepatic impairment Mild or moderate: no dose adjustment required Severe: not recommended