County Durham & Tees Valley
Area Prescribing Committee

County Durham & Tees Valley Primary Care Suggested Drug Monitoring Recommendations

This guide is intended as a quick reference for primary care clinicians and is not exhaustive. It is based on common recommendations. The frequency of testing may need to be tailored to individual patients, their condition and concurrent treatment. Users are advised to consult the following additional sources for more complete information. The NHS Specialist Pharmacy Service directory of monitoring recommendations [*up-to-date, comprehensive and searchable*]; BNF, NICE, CKS, local guidance & shared care documents and individual SPCs available at: www.medicines.org.uk.

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Drug	Baseline	Routine	Comments	Notes
Gastrointestinal system				
Mesalazine and Balsalazide	U&E, LFTs, Serum Creatinine, FBC and Urine Dipstick	U&E, serum Creatinine LFTs	Renal Function: every 3 months for the first year; every 6 months for the next 4 years; then annually Liver Function: every 6 months or annually based on the person's risk factors Haematological investigations should be performed if the patient develops unexplained bleeding, bruising, purpura, anaemia, fever, or sore throat. Treatment should be stopped if there is suspicion or evidence of blood dyscrasia.	Monitor renal function if pre-existing renal impairment, comorbid diseases, or nephrotoxic drugs. Use with caution in the elderly AST, ALT > twice upper limit of reference range, withhold treatment until discussed with the specialist.

Drug	Baseline	Routine	Comments	Notes
Cardiovascular System				
ACEi / A2RA See BNF for more detail regarding initiation in patients with hyponatremia, hypovolaemia, severe or unstable heart failure, known renovascular disease, is hypotensive or taking multiple or high-dose diuretics or high-dose vasodilators	U&E, creatinine, eGFR, (esp. if CKD), BP. **Hypertension**: Seek further advice if serum Cr >200micromol/L or eGFR < 30ml/min or confirmed renovascular disease before initiating treatment. **CKD**: ACEI or ARB therapy should not normally be started if the pre-treatment serum potassium is >5.0mmol/L	BP, U&E, Creatinine:	7-14 days after initiation and dose changes and then no less than every 12 months, especially after dose increments. Also, for use in - **Heart Failure**: Every 3 months and more frequently in patients taking combined loop and thiazide diuretic therapy and in those taking aldosterone antagonists. Monitor BP routinely. **Hypertension**: NICE guidance for resistant hypertension (step 4) suggests monitor blood sodium and potassium and renal function within 1 month and repeat as required thereafter. CKS advice: check electrolytes and renal function at least annually in stable patients (non- diabetic). **CKD**: In patients with CKD not due to diabetes, check BP every 3–6 months; urea and electrolytes, and eGFR, at least every 12 months **Post-MI:** Serum creatinine, electrolytes, and BP at least annually.	Combined use of ACEIs and ARBs not routinely recommended. Monitor potassium levels if used with an aldosterone antagonist / potassium-sparing diuretic. Stop ACEI/ARB therapy and other drugs known to promote hyperkalaemia and seek urgent clinical advice if serum potassium rises above 6.0mmol/L See also Think Kidneys Guidelines regarding medicines optimisation during Acute Kidney Injury (AKI).

Drug	Baseline	Routine	Comments	Notes
Sacubitril/Valsartan https://medicines.necsu.nhs.uk/download/sacubitrilvalsartan-entresto-for-newly-diagnosed-or-existing-heart-failure-place-in-therapy/	U&Es, BP, LFTs	U&Es, BP	Sacubitril /valsartan should be started by a heart failure specialist with access to a multidisciplinary heart failure team. Do not initiate if SBP<100mmHg or K^+>5.4mmol/L. Use lower starting dose if SBP between 100-110mmHg or eGFR 30-60ml/min or AST/ALT >2xULN or if ACEi/A2RA naïve. Routine monitoring as for ACEi/A2RA - consider discontinuation if K^+ level>5.4	Sacubitril/valsartan must not be started until 36 hours after taking the last dose of ACE inhibitor therapy
Amiodarone Amiodarone has a long elimination t1/2 – it is only ever given once daily after the loading regimen is complete. NHS England (June 2019) advises that prescribers should not initiate amiodarone in primary care for any new patient	Thyroid Function Tests, Chest x-ray, LFTs, U&E, ECG Serum potassium concentration should be measured before treatment.	Thyroid function (T3, T4, TSH), LFTs, U&E: ECG:	Every 6 months (TFTs- for up to 12 months after stopping amiodarone) Periodically – suggested every 12 Months Ophthalmic examination may be needed if visual symptoms develop	If pulmonary toxicity suspected, chest x-ray & lung function tests required If added to maintenance digoxin, halve the digoxin dose. In warfarinised patients, more frequent monitoring of INR both during and after amiodarone treatment is recommended1; initially weekly for first 7 weeks
Dronedarone **Shared care** https://medicines.necsu.nhs.uk/download/dronedarone-cardiology-shared-care-guideline/	As appropriate to clinical application. Include ECG monitoring, BP, HR, U&Es, creatinine, eGFR, & LFTs before prescribing.	BP, HR, U&Es, creatinine, eGFR, and LFTs ECG and pulmonary monitoring	At month 4, 5, 6, 9 and 12 and annually thereafter — discontinue treatment if 2 consecutive ALT concentrations exceed 3 times upper limit of normal. Patients or their carers should be told how to recognize signs of liver disorders and new onset or worsening heart failure. ECG should be repeated every 6 months. Interstitial lung disease has been reported and onset of dyspnoea or non-productive cough may indicate pulmonary toxicity (MHRA)	Any potassium or magnesium deficiency should be corrected before initiation and during dronedarone therapy

Drug	Baseline	Routine	Comments	Notes
Digoxin	U&E, renal function Consider thyroid status: Initial and maintenance doses of digoxin should be reduced when thyroid function is subnormal. In hyperthyroidism there is relative digoxin resistance, and the dose may have to be increased.	U&E, creatinine: BP, Pulse: TFTs:	At least annually, especially for patients on diuretics; ACEIs/ARBs. Recheck 7 to 14 days after changes to co-medication. Hypokalaemia increases risk of toxicity. As appropriate at each appointment. If symptomatic of abnormal thyroid function or started on amiodarone. Adjust digoxin dose as appropriate. Samples for digoxin measurement should be taken at least 6 hours after the last dose ideally 8-12 hours	Routine serum level monitoring not recommended unless if poor adherence is suspected or if there are changes in • clinical state • concomitant use of drugs that may impact on toxicity e.g., amiodarone • recognition of situations predisposing to toxicity e.g., notable renal insufficiency.
Ivabradine (Specialist initiation)	HR	HR	Do not initiate if resting heart rate is less than 70bpm or less 75bpm if heart failure. Reduce dose or stop treatment if resting HR is persistently less than 50 bpm. If AF occurs, consider benefits and risks of continued treatment.	
Loop Diuretics	U&Es and BP	U&Es and BP	1-2 weeks after initiation and each dose increase Earlier monitoring (after 5–7 days) may be required for people with existing renal impairment or those taking a combination of a diuretic plus an ACEi/ARB, or an aldosterone antagonist. For people receiving a combination of a loop diuretic and a thiazide: check renal function within 5 days of starting combination treatment and recheck every 5–14 days until stable. Monitor weight and hydration status	See also Think Kidneys Guidelines regarding medicines optimisation during Acute Kidney Injury (AKI).
Thiazide and related Diuretics	U&E, glucose urinalysis eGFR, LFTs	**Heart failure** U&E, creatinine **Hypertension** U&E HbA1c (Thiazides)	Within 1 week after starting and 1-2 weeks after dose increases. Check every 3-6 months in stable high-risk patients & annually in low-risk patients. Check 4-6 weeks after initiation and annually thereafter. Check after at least 3 months then Annually NB. Thiazides and related diuretics are ineffective if eGFR is less than 30 mL/minute/1.73 m2 and should be avoided.	Thiazides may induce diabetes mellitus. Avoid co-use of potassium sparing diuretics / aldosterone antagonists with potassium supplements, and monitor potassium regularly if used with an ACEI or an ARB in heart failure. See also Think Kidneys Guidelines regarding Medicines optimisation during Acute Kidney Injury (AKI).

Drug	Baseline	Routine	Comments	Notes
Eplerenone **(Specialist initiation)**	U&E, Renal function, BP	U&E, Renal function, BP Please set up recall for potassium monitoring on initiation,	ONE week after any dose increase. Once the target, or maximum tolerated dose is reached, monitor monthly for 3 months and then at least every 6 months, and at any time the person becomes acutely unwell. NICE - If serum potassium rises to between 5.5 and 5.9 mmol/L, halve the eplerenone dose and monitor closely. If serum potassium rises to ≥ 6.0 mmol/L, stop eplerenone and seek specialist advice	NICE NG 106: Chronic heart failure in adults: diagnosis and Management See also Think Kidneys Guidelines regarding medicines optimisation during Acute Kidney Injury (AKI).
Spironolactone (Specialist initiation for Heart Failure) **adjunct in moderate to severe heart failure**	U&Es (including Cr) and eGFR	U&Es (including Cr)	As adjunct in moderate to severe heart failure: Weeks 1, 4, 8 & 12; then at 6, 9 and 12 months, then 6 monthly, or otherwise as clinically indicated. SIGN - If serum potassium rises above 5.5 mmol/L or creatinine rises to >220 micromol/L reduce the dose to 25mg on alternate days and monitor blood chemistry closely. If potassium rises to ≥ 6 mmol/L or creatinine to 310 micromol/L, stop spironolactone immediately and seek	NICE NG 106: Chronic heart failure in adults: diagnosis and Management See also Think Kidneys Guidelines regarding medicines optimisation during Acute Kidney Injury (AKI).
Statins	LFTs, U&Es, Lipids, CK – if risk factors present	Lipids	At 3 months, aim for 40% reduction in non HDL-C levels Consider annual assessment of non HDL-C levels to inform medication/chronic disease reviews	
		LFTs	Repeat after 3 months and 12 months. Do not measure again unless clinically indicated (e.g., signs or symptoms of hepatotoxicity)	
		CK	Before starting treatment: If CK levels are > 5 times the upper limit of normal, re-measure after 7 days. If CK levels are still 5 times the upper limit of normal, do not start statin treatment. If creatinine kinase levels are raised but < 5 times the upper limit of normal, start statin treatment at lower dose. Check CK as soon as possible if the person reports new muscular symptoms.	
Fibrates	LFTs, CK, Lipids, U&Es	LFTs U&Es	Every 3 months for first year then annually. Fenofibrate – during first 3 months then annually. Otherwise annually	
		Lipids	If response inadequate after 3 months stop. 12 monthly thereafter.	
		CK	Check only if myopathy suspected which is more common when used in combination with a statin	
		FBC	Gemfibrozil requires FBC 3 monthly for first year. Otherwise not required	

Drug	Baseline	Routine	Comments and Notes
Warfarin	Coagulation screen, FBC, U&Es, LFTs, BP	INR	BP should be used to calculate HAS-BLED score INR should be checked at least every 12 weeks (Max 6 weeks if prosthetic heart valve) once stable in individual therapeutic range. If changes in patient's general health or medication regimen check more regularly.
Direct Oral Anticoagulants (DOACs) **See also: Prescribing anticoagulants in NVAF – CD&TV APC**	U&Es & CrCl, LFTs, FBC, coag screen, Wt (to calculate CrCl), BP (for HAS- BLED)	U&Es, LFTs & FBC	**Use Creatinine Clearance (CrCl) calculated using the Cockcroft-Gault formula** to estimate renal function. Do not base dose decisions on eGFR • If under 75 years and CrCl>60ml/min ensure **annual** U&Es • If 75 years or over or CrCl 30-60ml/min ensure **6 monthly** U&Es • If CrCl 15-30mL/min ensure **3 monthly** U&Es • Recalculate CrCl if any significant changes or if intercurrent condition that may have impact on renal function Annual LFTs and FBC

Dosing in Renal Impairment (also refer to individual Summary of Product Characteristics):

Creatinine Clearance	Rivaroxaban	Dabigatran	Apixaban	Edoxaban
>50ml/min	AF and continued VTE treatment (Day 22 onwards): 20mg od NB. VTE prophylaxis: 10mg daily after 6 months (consider 20mg in those at high risk of recurrence, such as complicated co-morbidities or recurrence on Rivaroxaban 10mg)	AF and VTE: 150mg bd or 110mg bd if: • Age>80 yrs. • Use of verapamil Consider 110mg bd if patient at increased risk of bleeding, aged between 75-80 years or has GORD.	AF: 5mg bd or 2.5mg bd if 2 or more of the following are present: • >80yrs old, • • <60kg • Serum Cr >133µmol/L Maintenance of VTE treatment: 5mg bd (or 2.5mg bd after 6 months treatment)	AF and VTE: 60mg od *or* 30mg od if: • Wt ≤ 60kg • Use of Ciclosporin Dronedarone, erythromycin or ketoconazole
30 – 49 ml/min	AF:15mg od VTE: 20mg od; (unless bleeding risk outweighs risk of further VTE, then use 15mg od)	AF and VTE: Dose as in normal renal function. Consider 110mg bd for those at high risk of bleeding.	AF and VTE Dose as in normal renal function above	AF and VTE: 30mg od
15 – 29 ml/min	As above with caution	**Avoid**	AF: 2.5mg bd VTE: Use with caution	AF and VTE: 30mg od
<15ml/min	**Avoid**			

Drug	Baseline	Routine	Comments and Notes
Respiratory System			
Theophylline	U&Es, LFTs smoking status	Drug level, U&Es periodically	Check plasma drug levels 2- 6 weeks following dose changes to assess response and 12 monthly once maintenance dose reached, or if toxicity suspected. Check more regularly in older people and in those with heart failure or hepatic impairment Range 10-20mg/l. Sample 4-6 hours after last dose. Dose adjustments may be required if a patient starts or stops smoking during treatment.
Central Nervous System			
Section 4 has been removed and replaced with: TEWV Psychotropic Medication Monitoring Guide Other guidelines, including transfer of prescribing documents and shared care documents for antipsychotic, antidepressant and antiepileptic medications, lithium and drugs for ADHD can be found at: TEWV Pharmacy Publications			
Infections			
Nitrofurantoin	U&Es and Liver Function	LFTs	Nitrofurantoin is contraindicated in patients with an eGFR of less than 45 ml/min/1.73m ^{2}. Short courses of nitrofurantoin may be used with caution in patients with eGFR 30-44ml/min. For prophylactic therapy: Treatment should not normally exceed 6 months and patients should remain under the care of urology specialists during this period. Consideration should be given to pulmonary fibrosis if respiratory symptoms develop, especially in the elderly, and treatment should be discontinued if any evidence of deterioration in lung function. BNF recommends LFT monitoring for long term treatment – 6 monthly
Minocycline (not a preferred treatment option)	LFTs	FBC and LFTs	3 monthly. Check for signs/symptoms of hepatotoxicity or Systemic Lupus Erythematosus (SLE) pigmentation
Terbinafine	LFTs	LFTs	4-6 weeks after initiation; may need periodic monitoring if longer courses needed
Endocrine System			
Levothyroxine	TFTs (especially TSH & FT4), ECG	TSH: TFTs:	Check 6-8 weeks after initiation (sooner in elderly especially if have IHD) Annually once stabilised
Carbimazole	TFTs, WBC, LFTs	TFTs	Every 4-6 weeks after initiation, reduced to every 3 months once maintenance dose is achieved For adults who have stopped carbimazole, consider measuring TSH (with cascading) within 8 weeks of stopping, then every 3 months for a year, then once a year
		LFTs	If any signs and symptoms of hepatic disorder, stop carbimazole and perform liver function tests immediately
		WBC	Risk of neutropenia and agranulocytosis: Patients should be asked to report symptoms and signs suggestive of infection, especially sore throat. Check WBC if there is any clinical evidence of infection. Repeat WBC if patient develops fever, mouth ulcers, or if there are persistent symptoms of infection. If leucocyte count falls to <1.5x109/L or neutrophil count to <0.5x109/L - STOP carbimazole and immediate refer to specialist. Regular full blood count checks should be carried out in patients who may be confused or have a poor memory

Drug	Baseline	Routine	Comments and Notes
Propylthiouracil	TFTs, WBC, LFTs	TFTs	Monitor TSH, FT4 and FT3 every 6 weeks until TSH within reference range Monitor TSH (with cascading to check FT4 and FT3) every 3 months until propylthiouracil is stopped Repeat WBC if patient develops fever, mouth ulcers, sore throat, or other symptoms of infection. Stop drug and recommend immediate specialist referral if leucocyte count falls to $<1.5x10^9$/L or neutrophil count to $<0.5x10^9$/L Stopping propylthiouracil - consider measuring TSH (with cascading), within 8 weeks of stopping the drug, then, every 3 months for a year, then, once a year
		LFTs	At 3 and 6 months then annually Monitor for signs and symptoms of liver injury, especially during the first 6 months after initiation of therapy. Discontinue drug and repeat LFTs if patient develops pruritic rash, jaundice, light coloured stool or dark urine, joint pain, abdominal pain or bloating, anorexia, nausea, or fatigue. Provide supportive care.
Metformin	U&Es	U&Es	12 monthly (6 monthly for elderly patients or if worsening renal function – dose adjustment may be required)
Pioglitazone	LFT, FBC, U&E, bodyweight	LFT, body weight, HbA1c (3-6 monthly to determine treatment efficiency and discontinue if no effect	Periodically based on clinical judgement – at least annually or more frequently as necessary. Review the safety and efficacy of pioglitazone in individuals after 3–6 months of treatment to ensure that only patients who are deriving benefit continue to be treated. The risk of fractures should be considered in the long-term care of patients treated with pioglitazone. If pioglitazone is used in combination with insulin patients should be observed for signs and symptoms of heart failure, weight gain, and oedema
Gliptins	U&Es, LFTs and HbA1C	LFTs	Vildagliptin only - 3 monthly for first year, then 12 monthly
		HbA1c	2 to 6 monthly until person stable on treatment, then 6 monthly (or according to individual need). Discontinue if HbA1c has not reduced by at least 5.5 mmol/mol within 6 months of starting treatment.
		U&Es	6 monthly. Dose adjustments may be required if renal function declines – check for individual products
GLP1-agonists	Weight and HbA1c	Weight and HbA1c	3 monthly. Discontinue if HbA1c has not reduced by at least 11 mmol/mol and if a weight loss of at least 3% has not been achieved at 6 months.

Drug	Recommendations
Musculoskeletal System	
DMARDs	**see County Durham & Tees Valley APC approved CDDFT shared care guidelines for individual drugs.**
NSAIDs	Consider monitoring BP, renal function, and for features of heart failure 1–2 weeks after starting or increasing dose of NSAID, and then regularly thereafter, if any of the following apply: • Elderly • Heart failure • Ischaemic heart disease. • Cerebrovascular disease. • Peripheral vascular disease. • Risk factors for cardiovascular disease. BP: Periodically during treatment in elderly and people taking COX-2 inhibitors. Renal function should be monitored in patients with renal, cardiac, or hepatic impairment. In renal impairment, monitor regularly or at least annually. Also consider monitoring for patients prescribed additional drugs that can affect renal function (e.g., ACE inhibitors, angiotensin-II receptor antagonists, or diuretics). Liver function: In liver impairment and on long-term NSAID therapy

Abbreviations:			
A2RA	Angiotensin-II receptor antagonists	HbA1c	Glycosylated Haemoglobin (mmol/mol)
ACEi	Angiotensin converting enzyme inhibitors	HR	Heart rate/pulse
ALT	Alanine transaminase	LFTs	Liver function tests
AST/ALT	Aspartate transaminase	NECS	North of England Commissioning Support
BP	Blood pressure	SBP	Systolic blood pressure
CK	Creatine kinase (creatinine phosphokinase)	TFTs	Thyroid function tests
ECG	Electrocardiogram / electrocardiograph	TSH	Thyroid stimulating hormone
FBC	Full blood count	U&Es	Urea and electrolytes, creatinine and eGFR
fT3	Free T3	ULN	Upper limit of normal
fT4	Free T4	Wt	Weight

References

1. British National Formulary – https://bnf.nice.org.uk/
2. NHS Specialist Pharmacy Service – Summary of Recommendations and Guidance for medicines requiring monitoring – https://www.sps.nhs.uk/home/guidance/drug-monitoring/
3. Summaries of Product Characteristics – https://www.medicines.org.uk/emc
4. Arden and Greater East Midlands CSU - Suggested Guidance on Monitoring Drugs in Primary Care March 2019 – https://www.knowledgeanglia.nhs.uk/LinkClick.aspx?fileticket=yBMYpPZQu-c%3D&tabid=1672&portalid=1&mid=2074