No. 11 April 2020

COVID-19

Questions, Answers and Actions

Extension of monitoring intervals for medicines in primary care (adults)

Question: "Can monitoring intervals be extended for adults prescribed shared care drugs and other drugs that require monitoring during the COVID-19 pandemic?"

Answer:

Extending monitoring intervals for medicines in primary care may be a pragmatic approach to minimising non-essential contact with the healthcare setting- e.g. in patients who are subject to CMO shielding recommendations. This document aims to provide pragmatic guidance to prescribers who are considering whether extended monitoring might be a suitable consideration for their patient. **Any decision to extend the duration of monitoring intervals should be made on a case-by-case basis. Specialist advice should be sought where necessary. We recommend reading the following guidance from the Specialist Pharmacy Service (SPS) Drug monitoring: factors to consider during Covid-19 prior to undertaking deviations from standard monitoring schedules.**

Version 4 update 30/04:

In light of the recently issued Second phase of NHS response to COVID-19: Letter from Sir Simon Stevens and Amanda Pritchard" letter which advocates a return to delivering 'as much routine and preventative work as can be provided safely', this QAA had been revised. Recommendations for DMARDS, lithium and antipsychotics are now more closely aligned with standard practice (as per GMMMG SCPs) with some flexibility maintained to allow for decisions to be made on a case-by-case basis.

It is recognised that this continues to be a rapidly changing situation, with guidance requiring updates in response to changing recommendations nationally. Decisions around extension of monitoring intervals made in the past few weeks may no longer be required, prescribers may wish to revisit these on an individual basis.

This guidance may be subject to further updates in response to shifts in COVID prevalence, national recommendations and local pressures within primary care.

With collaboration from the Greater Manchester Medicines Management Group and specialist clinical teams in Greater Manchester, recommendations on DMARDs monitoring in indications for which GMMMG shared care protocols apply have been developed; see **Table 1**. (Correspondence with respiratory and GI/hepatology is ongoing- recommendations for these patient groups will follow).

Guidance on extended monitoring of antipsychotics has been developed with support from Greater Manchester Health Teams, see **Table 2**.

Recommendations from the British Society of Haematology and NHSE have similarly been circulated around Greater Manchester clinician teams to produce the guidance for Sickle cell disease and myeloproliferative disorders in adults in **Table 3**.

Action:

- For **lithium**- consider delaying routine monitoring (as per GMMMG SCP) by a maximum of 4 weeks. **Electrolytes- including calcium-** should be checked as part of the monitoring schedule (along with thyroid function, renal function and BMI). 6 monthly serum lithium level monitoring may be appropriate in stable patients (>12 months on lithium) who are low risk as per NICE Guidance (CG185). Lithium levels should continue to be checked every 3 months for:
    - older people
    - people taking drugs that interact with lithium
    - people who are at risk of impaired renal or thyroid function, raised calcium levels or other complications
    - people who have poor symptom control
    - people with poor adherence
    - people whose last plasma lithium level was 0.8 mmol per litre or higher.

  If prescribers are considering extending the monitoring interval for serum lithium levels, this should be done in line with the NICE guidance. Seek specialist advice where necessary.

- For **warfarin** see RDTC COVID-19 QAA: Practical warfarin monitoring during the COVID pandemic response, available here.

- For **DMARDs**; see Table 1. (Correspondence with respiratory and GI/hepatology is ongoing- the recommendations that follow do not currently apply to these indications).

- For advice on **management of patients in the above groups who are suspected to have COVID-19**; follow drug specific advice issued by SPS available here).

- For **antipsychotics**; see Table 2.

- For **hydroxycarbamide** for haematology indications; see Table 3.

Any decision to extend the duration of monitoring intervals should be made on a case-by-case basis in stable patients only.

Seek specialist advice where necessary.

Ensure patients are aware of 'red flag' symptoms that would prompt urgent review.

Whilst Tables 1-3 aim to be as comprehensive and pragmatic as possible, readers are advised to check the BNF/ SPCs and relevant shared care protocols for full information where necessary.

Table 1: Guidance on extended monitoring of DMARDs in primary care						
Drug	Applicable indication(s)	Normal monitoring in **stable patients who have been on current treatment for >12months and at a stable dose for >6 weeks** (as per GMMMG SCPs and BSR/BHPR guidance (2017))	Proposed maximum extension during COVID -19 pandemic	**Avoid** extending if any: • Renal impairment (CKD 3 or greater) • Severe liver disturbance or abnormal liver results due to DMARDs within previous 3 months* or alcohol excess • Severe abnormal WBC results due to DMARDs within previous 3 months** • Dose change or additional DMARD started in preceding 6 weeks • High dose corticosteroids (equal to prednisolone 5mg or more daily)	Advise patient to report any of the following signs or symptoms to GP without delay: (For advice on **management of patients on DMARDS who are suspected to have COVID-19**; follow drug specific advice issued by SPS available here.)	Date issued
Azathioprine/ Mercaptopurine	Rheumatology, Dermatology, Neurology,	3 monthly: -FBC -U and E (plus calculated creatinine clearance) -LFTs (plus albumin)	Consider extending monitoring interval by 4 weeks (maximum)	**Caution** extending if co-prescribed: - More than one immunosuppressant (especially sulfasalazine) - Clozapine (increased risk myelosuppression) - ACE inhibitor (increased risk anaemia) - Allopurinol (increased risk azathioprine toxicity)	Signs or symptoms indicating blood dyscrasias or bone marrow suppression (e.g. sore throat, infection, unexplained or abnormal bruising or bleeding, fever). Jaundice. New onset abdominal pain; may be a sign of pancreatitis. Chicken pox or shingles (or contact with an infected person) if the patient has not had it before.	V1.0 15/04/20
Ciclosporin	Rheumatology, Dermatology	Usual max interval = 3 monthly: -FBC -U and E (plus calculated creatinine clearance) -LFTs (plus albumin) -BP -fasting lipids -fasting blood glucose	If agreed by specialist team, extend monitoring interval by additional 4 weeks (maximum)	**Caution** extending if co-prescribed: - More than one immunosuppressant (especially methotrexate) - Clozapine (increased risk myelosuppression) - NSAIDs (increased risk nephrotoxicity) - ACE inhibitor/ANG2 receptor antagonist/ aldosterone antagonists/ potassium sparing diuretics (increased risk hyperkalaemia) - Digoxin (increased risk of digoxin toxicity) - Amiodarone, dronedarone, calcium channel blockers, antivirals, allopurinol (increased risk ciclosporin toxicity)	Signs or symptoms indicating blood dyscrasias or bone marrow suppression (e.g. sore throat, infection, unexplained or abnormal bruising or bleeding, fever). Jaundice. New onset abdominal pain; may be a sign of pancreatitis. Chicken pox or shingles (or contact with an infected person) if the patient has not had it before.	V1.0 15/04/20

Hydroxychloroquine	Rheumatology, Dermatology	12 monthly eye assessment if continued for ≥5 years	Consider delaying eye assessment. Seek ophthalmologist advice for patients at highest risk of toxicity- i.e renal impairment, on maximum dose (>5 mg/kg per day), concurrent tamoxifen	**Caution** extending if co-prescribed: - More than one immunosuppressant - Clozapine (increased risk myelosuppression) - Tamoxifen (increased risk retinal toxicity)	**Myopathy** Signs or symptoms indicating blood dyscrasias or bone marrow suppression (e.g. sore throat, infection, unexplained or abnormal bruising or bleeding, fever). Jaundice. New onset abdominal pain; may be a sign of pancreatitis. Chicken pox or shingles (or contact with an infected person) if the patient has not had it before.	V1.0 15/04/20
Leflunomide	Rheumatology	3 monthly: -FBC -U and E (plus calculated creatinine clearance) -LFTs (plus albumin) -BP -weight	Consider extending monitoring interval by 4 weeks (maximum)	**Caution** extending if co-prescribed: - More than one immunosuppressant (especially methotrexate) - Clozapine (increased risk myelosuppression)	Signs or symptoms indicating blood dyscrasias or bone marrow suppression (e.g. sore throat, infection, unexplained or abnormal bruising or bleeding, fever). Jaundice. New onset abdominal pain; may be a sign of pancreatitis. Chicken pox or shingles (or contact with an infected person) if the patient has not had it before.	V1.0 15/04/20
Methotrexate	Rheumatology, Dermatology,	3 monthly: -FBC -U and E (plus calculated creatinine clearance) -LFTs (plus albumin)	Consider extending monitoring interval by 4 weeks (maximum)	**Caution** extending if co-prescribed: - More than one immunosuppressant (especially ciclosporin or leflunomide) - Clozapine (increased risk myelosuppression) - Acitretin/ retinoids (increased risk of hepatitis) - Levetiracetam (increased risk of methotrexate toxicity) - Phenytoin (increased antifolate effect) - NSAIDs (increased risk nephrotoxicity)	Signs or symptoms indicating blood dyscrasias or bone marrow suppression (e.g. sore throat, infection, unexplained or abnormal bruising or bleeding, fever). Jaundice. New onset abdominal pain; may be a sign of pancreatitis. Chicken pox or shingles (or contact with an infected person) if the patient has not had it before.	V1.0 15/04/20

Mycophenolate mofetil/ mycophenolic acid	Rheumatology, Dermatology,	3 monthly: -FBC -U and E (plus calculated creatinine clearance) -LFTs (plus albumin)	Consider extending monitoring interval by 4 weeks (maximum)	**Caution** extending if co-prescribed: - More than one immunosuppressant - Clozapine (increased risk myelosuppression) - Aciclovir/ valganciclovir/ valaciclovir/ (increased risk myelosuppression)	Signs or symptoms indicating blood dyscrasias or bone marrow suppression (e.g. sore throat, infection, unexplained or abnormal bruising or bleeding, fever). Jaundice. New onset abdominal pain; may be a sign of pancreatitis. Chicken pox or shingles (or contact with an infected person) if the patient has not had it before.	V1.0 15/04/20
Penicillamine	Rheumatology, Endocrinology (Wilson's Disease)	3 monthly: -FBC -U and E (plus calculated creatinine clearance) -LFTs (plus albumin) -urinalysis	Consider extending monitoring interval by 4 weeks (maximum)	**Caution** extending if co-prescribed: - More than one immunosuppressant - Clozapine (increased risk myelosuppression) - NSAIDs (increased risk nephrotoxicity)	Signs or symptoms indicating blood dyscrasias or bone marrow suppression (e.g. sore throat, infection, unexplained or abnormal bruising or bleeding, fever). Jaundice. New onset abdominal pain; may be a sign of pancreatitis. Chicken pox or shingles (or contact with an infected person) if the patient has not had it before.	V1.0 15/04/20
Sulfasalazine	Rheumatology	If dose and monitoring is stable after 12 months, no routine monitoring required	No changes to the existing regimen is recommended	N/A	N/A	V1.0 15/04/20

* Severe liver disturbance or abnormal liver results due to DMARDs within previous 3 months is defined as:
- ALT and/ or AST >100units/L, or
- any sudden increase (e.g. a doubling of baseline ALT)

** Severe abnormal WBC results due to DMARDs within previous 3 months is defined as any of:
WCC <3.5 $x10^9$/L
Neutrophils <1.6 $x10^9$/L
Platelets <140 $x10^9$/L
Lymphocytes <0.5 $x10^9$/L
Unexplained eosinophilia >0.5 $x10^9$/L
Unexplained fall in serum albumin <30g/L

NB in addition to the above risk factors for toxicity, extremes of BMI (<18 or>30), pre-existing renal impairment, pre-existing liver disease (also history of alcohol excess), age >80 years, previous history of DMARD toxicity, and significant co-morbidities should also be borne in mind as increasing the risk of toxicity.

Table 2: Guidance on extended monitoring of antipsychotics in primary care					
Drug	**Indication**	**Usual monitoring requirements in GM SCPs *(for patients who have been on treatment >12 months)***	**Summary/suggested action stable patients who have been on current treatment for ≥24 months and at a stable dose for >6 months**	**Avoid extending if:**	Date issued
First generation (typical) antipsychotic depots in adults • Flupentixol decanoate • Fluphenazine decanoate • Haloperidol decanoate • Zuclopenthixol decanoate (NOT zuclopenthixol acetate)	Maintenance of schizophrenia and other psychoses	Annually: U&Es*, renal function*, FBC*, lipids, weight, waist circumference & BMI, HbA1c or fasting glucose, ECG (if clinically indicated), blood pressure and pulse, prolactin, LFTs*, personal family history of diabetes & CVD risk, lifestyle review (smoking, diet, physical activity, drugs & alcohol), Side effect rating scale e.g GASS or LUNSRS Each administration: Injection site	Consider delaying monitoring for up to 4 weeks (Although does not address monitoring) RCPSYCH-Managing Long acting Antipsychotic Depots During COVID-19 provides some advice on extending administration intervals and how to manage administration in patients with suspected COVID.	- Abnormal blood results or dose change in preceding 6 months High risk for toxicity: - personal family history of diabetes & CVD risk, - lifestyle risks (smoking, diet, poor physical activity, drugs & alcohol abuse), - multiple co-morbidities (two or more of hypertension, diabetes, renal impairment, obesity) - co-prescribed immunosuppression (increased risk blood dyscrasias) Co-prescribed: - Medicines that prolong QT interval (e.g. methadone, TCAs)	V2.0 22/04/20
Antipsychotics Oral second generation (atypical) antipsychotics for adults • Amisulpride • Aripiprazole • Olanzapine • Quetiapine • Risperidone	Varies between drugs but includes schizophrenia, mania, bipolar disorder	Annually: U&Es*, renal function*, FBC*, lipids, weight, waist circumference & BMI, HbA1c or fasting glucose, ECG (if clinically indicated), blood pressure and pulse, prolactin (for amisulpride and risperidone), LFTs*, personal family history of diabetes & CVD risk, lifestyle review (smoking, diet, physical activity, drugs & alcohol),	Consider delaying monitoring for up to 4 weeks	- Abnormal blood results or dose change in preceding 6 months High risk for toxicity: - personal family history of diabetes & CVD risk, - lifestyle risks (smoking, diet, poor physical activity, drugs & alcohol abuse), - multiple co-morbidities (two or more of hypertension, diabetes, renal impairment, obesity) - co-prescribed immunosuppression (increased risk blood dyscrasias) Co-prescribed: - Medicines that prolong QT interval (e.g. methadone, TCAs)	V2.0 22/04/20

Long acting antipsychotic injections in adults: • aripiprazole, • paliperidone • risperidone	Maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole.	Annually: U&Es*, renal function*, FBC*, lipids, weight, waist circumference & BMI, HbA1c or fasting glucose, ECG (if clinically indicated), blood pressure and pulse, prolactin, LFTs*, personal family history of diabetes & CVD risk, lifestyle review (smoking, diet, physical activity, drugs & alcohol), Each administration: Injection site	Consider delaying monitoring for up to 4 weeks (Although does not address monitoring) RCPSYCH- Managing Long acting Antipsychotic Depots During COVID-19 provides some advice on extending administration intervals and how to manage administration in patients with suspected COVID.	Abnormal blood results or dose change in preceding 6 months High risk for toxicity: - personal family history of diabetes & CVD risk, - lifestyle risks (smoking, diet, poor physical activity, drugs & alcohol abuse), - multiple co-morbidities (two or more of hypertension, diabetes, renal impairment, obesity) - co-prescribed immunosuppression (increased risk blood dyscrasias) Co-prescribed: - Medicines that prolong QT interval (e.g. methadone, TCAs)	V2.0 22/04/20

Useful links:
RCPSYCH- COVID-19: Providing medication
RCPSYCH- Managing Long acting Antipsychotic Depots During COVID-19 (note current version states 'DRAFT' however confirmed with author that no changes are intended and 'DRAFT' watermark is due to be removed imminently.

Table 3: Guidance on extended monitoring of hydroxycarbamide in primary care						
Drug	**Indication**	**Usual monitoring requirements in GM SCPs *(for patients who have been on treatment >12 months)***	**Summary/suggested action stable patients who have been on current treatment for >12months and at a stable dose for >6 months**	**Avoid extending if:**	**Advise patient to report any of the following signs or symptoms to GP without delay:**	Date issued
Hydroxycarbamide	Sickle cell disease in adults	Every 8-12 weeks: Serum creatinine Haemoglobin Neutrophils Reticulocytes Platelets LFTs (AST, ALT, GGT) U&Es Every 3 months: Haemoglobin F%	For patients being monitored every 12 weeks, consider extending monitoring interval to a maximum of 16 weeks. In patients being monitored more frequently than 12 weekly, consider extending monitoring interval to a maximum of every 12 weeks.	Higher risk of complications: - elderly (those aged over 50) - history of respiratory or cardiac disease - with multiple co-morbidities (including renal or hepatic impairment) - co-prescribed more than one immunosuppressant, including oral prednisolone 5mg or greater - co-prescribed clozapine - dose change or abnormal test results in previous 6 months - high dose (>20mg/kg)	Leg ulcers: review treatment if cutaneous vasculitic ulcerations develop)	V2.0 22/04/20
Hydroxycarbamide	Myeloproliferative disorders in adults (myelofibrosis, essential thrombocythaemia and polycythaemia)	Every 8-12 weeks: Serum creatinine Haemoglobin Neutrophils Reticulocytes Platelets LFTs (AST, ALT, GGT) U&Es	Extended monitoring may be an option in stable patients with previously normal monitoring results and are taking doses in the lower range (20mg/kg or less). **GPs should seek advice from specialists prior to any decisions to extend monitoring.**	Higher risk of complications: - elderly (those aged over 50) - history of respiratory or cardiac disease - with multiple co-morbidities (including renal or hepatic impairment) - co-prescribed more than one immunosuppressant, including oral prednisolone 5mg or greater - co-prescribed clozapine - dose change or abnormal test results in previous 6 months - high dose (>20mg/kg)	Leg ulcers: review treatment if cutaneous vasculitic ulcerations develop	V2.0 22/04/20

Useful links:
- NHSE: Clinical guide for the management of haemoglobinopathy patients (sickle cell disease and thalassaemia) during the coronavirus pandemic
- Haemoglobinopathy Co-ordinating Centres (HCCs) and Clinical Reference Group (CRG) for Haemoglobin Disorders: Advice on COVID-19 in patients with Sickle Cell Disease and Thalassaemia

References:

1. GMMMG Shared Care Protocols (various). Available via*:*
2. http://gmmmg.nhs.uk/html/gmmmg_app_scgs.php
3. Specialist Pharmacy Service (SPS)- Guidance on the management of drugs requiring monitoring during COVID-19. Available via: https://www.sps.nhs.uk/articles/drug-monitoring-in-primary-care-for-stable-patients-during-covid-19/
4. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, 2017. Available via: https://academic.oup.com/rheumatology/article/56/6/865/3053478#97289271
5. Royal College of Psychiatry/ North East London Foundation Trust- Managing Long acting Antipsychotic Depots During COVID-19, March 2020. Available via: https://www.rcpsych.ac.uk/docs/default-source/improving-care/better-mh-policy/managing-depots-during-covid.pdf?sfvrsn=fdaffc8b_2

GMMMG
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Version: 4.0

Changes to this version:

- In light of the Second phase of NHS response to COVID-19: Letter from Sir Simon Stevens and Amanda Pritchard" letter, this QAA had been revised; recommendations for DMARDs, lithium and antipsychotics are now more closely aligned with standard practice (as per GMMMG SCPs), with some flexibility maintained to allow for decisions to be made on a case-by-case basis.

Changes in version 3.0

- Clarification of routine 6 monthly lithium level monitoring in stable (>12 months) low risk patients is in line with NICE CG 185- Bipolar disorder: assessment and management (last updated Feb 2020). Available via*:* https://www.nice.org.uk/guidance/cg185

Changes in version 2.0

- Addition of guidance for antipsychotics, hydroxycarbamide. Alcohol excess added as a contra-indication to extending monitoring of DMARDs.

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