Management of patients post liver transplantation– Full clinical guideline

The transplant clinic is held on the 2nd Friday of each month. Every third month Professor Mutimer from the liver transplant unit at the Queen Elizabeth Hospital, Birmingham attends and the clinic is then held on the first or second Tuesday of the month. These are a complex group of patients and trainees should have a low threshold for discussing patients with a consultant, **especially if altering the dose of immunosuppression medication**. The initial post-transplant care will all occur at the transplant centre. Once a patient is 3-12 months post-transplant then some or all of their care may move to the Derby transplant clinic.

Follow-up

Patients are initially seen weekly at the transplant centre. After 3 months and if the liver function is normal then they are seen:

- 4 weekly until 6 months
- Then 2 monthly for remainder of first year
- 3 monthly thereafter (if patients still attends a clinic at the transplant centre then appointments may alternate and they may only be seen in Derby every 6 months)

Immunosuppression

The usual initial drug combination following a liver transplant is triple therapy; a Calcineurin inhibitors (CNI) - usually Tacrolimus (but occasionally Ciclosporin), Azathioprine (or Mycophenolate Mofetil - MMF) and Prednisolone. Prednisolone is usually gradually reduced with the aim of stopping after 3 months if the liver is functioning well (patients grafted for autoimmune hepatitis should continue with Prednisolone 7.5mg od indefinitely). The transplanted liver becomes partially tolerant of immune mediated injury so the requirement for immunosuppression declines after 3 months. The aim is for patients to receive the minimum immunosuppression to maintain the graft function. Tacrolimus and Mycophenolate are supplied by RDH via PRIDE on-site pharmacy and must be prescribed by the proprietary name e.g. Prograf, Cellcept in order to avoid switching between brands and consequent fluctuating drug levels. It is usual to offer 3 months' supply at a time. Homecare delivery is also available for post transplant patients and this option can be selected on Lorenzo when prescribing. Patients must consent to their data being shared with the Homecare companies – the consent form 'UHDB homecare patient consent form' can be found on Net-I and on the shared drive in the Liver Transplant folder. Prescribing for homecare delivery should be done in discussion with the Hepatology CNS.

Azathioprine

1-2mg/kg taken once daily with food and rounded to the nearest 25mg (usually 50-150mg/d). The tablets should not be halved or crushed.

Adverse drug reactions

- Bone marrow suppression - half dose if WCC < 4 x 10^9/l, stop if < 3 x 10^9/l
- Malaise, dizziness, diarrhoea, rash, myalgia and arthralgia can occur
- Nausea can occur initially which can be reduced by taking the tablets after food
- Pancreatitis

Drug Interactions

- **Allopurinol** inhibits the clearance of azathioprine. The azathioprine dose would need to be one quarter of the original dose if used with allopurinol.
- **Warfarin** effect may be reduced requiring an increased warfarin dose.
- **Rifampicin** may reduce the efficacy of azathioprine and lead to transplant rejection.

Mycophenolate mofetil (Cellcept®) - MMF

MMF should be considered in those patients intolerant of azathioprine or in place of Azathioprine in re-grafts or patients who encounter problems with rejection. MMF can be used in conjunction with a low dose of tacrolimus in those with or at risk of renal impairment. 0.5-1g bd taken ideally on an empty stomach (gastrointestinal adverse effects may necessitate taking with food). Mycophenolate mofetil (Cellcept®) is available in 250mg capsules, 500mg tablets and oral suspension 1g/5ml.

Adverse drug reactions

- Bone marrow suppression **-** leucopenia – reduce or stop
- Gastrointestinal upset is the most common side effect - typically diarrhoea. Suggest to the patient they try taking with food and/or splitting the dose (e.g. 250mg four times daily).
- Teratogenecity - Both men and women require counselling on the risk of harm to the foetus. Patients must use effective contraception during and for 6 weeks (female)/ 12 weeks (male) after stopping treatment. Counselling on avoiding unplanned pregnancy should be documented in the notes.

Drug Interactions

- **Antacids & colestyramine:** should not be taken at the same time of day as they will impair the absorption of mycophenolate.

Tacrolimus

ALL TACROLIMUS SHOULD BE BRAND PRESCRIBED Advagraf Envarsus and Daliport -modified release, Prograf and Adoport - normal release - given BD). The vast majority of patients will be on Prograf.

Providing renal function is normal, the starting dose of tacrolimus (Prograf) is 0.05mg/kg every 12 hours. Doses are titrated to the desired trough level. Tacrolimus should be prescribed at 10am and 10pm so that blood samples for trough levels can be taken by the phlebotomists in the morning.

In a stable patient aim for 12 hour post dose level of 10-12ng/ml in first month, 7-12ng/ml during months 2 & 3, and 3-8ng/ml after 3 months (provided stable graft function). Patients on Mycophenolate may run with lower levels (2-5ng/ml). Doses required to achieve this level vary between patients, though typically a range of 0.5mg to 5mg twice daily for the normal release preparation and 1mg to 10mg once daily for the modified release preparation is common in adults. Both the standard and modified release capsules should be taken on an empty stomach or 2-3 hours after a meal to achieve maximal absorption

Patients with renal impairment or malignancy may be run with levels less than 5ng/ml. These are general guidelines and it may be preferable to run higher or lower levels depending on sepsis/rejection/renal function.

Adverse effect monitoring

- **Hypertension** - see guidance below on management post-transplant.
- **Headache, tremor, insomnia and visual disorders** are frequently seen. If persistent or severe these effects may reflect toxic levels of tacrolimus.
- **Alopecia** occurs in around 10% of patients on tacrolimus and may necessitate alternative immunosuppression.
- **Hyperkalaemia** - usually managed with oral sodium bicarbonate.
- **Nephrotoxicity** Tacrolimus exhibits an acute blood level related nephrotoxicity, identified primarily by serum creatinine monitoring. Chronic nephrotoxicity does occur which may necessitate withdrawal of the drug.
- **Hyperglycaemia** and diabetes are more common with tacrolimus than ciclosporin.

Drug interactions: CONSULT APPENDIX 1 OF BNF

Common drug interactions	Effect on tacrolimus/ ciclosporin blood level
Erythromycin, clarithromycin, Doxycline	Increased
Diltiazem, nicardipine, verapamil, felodipine	Increased
Fluconazole, itraconazole, ketoconazole	Increased
Cimetidine	Increased
HIV protease inhibotprs	Increased
Thiazides, Danazol, Oral contraceptives	Increased
Rifampicin, Isoniazid	Decreased
Carbamazepine, Phenytoin, Phenobarbitone	Decreased
Co-Trimoxazole (iv)	Decreased
Corticosteroids	Decreased
Orlistat	Decreased
St Johns Wort	Decreased

- Patients should not consume grapefruit juice or grapefruit, because it can increase tacrolimus levels.
- Nephrotoxic drugs should be used with extreme caution.
- NSAIDs (except low dose Aspirin) should be avoided
- Potassium-sparing agents may exacerbate tacrolimus-induced hyperkalaemia and should only be initiated with regular monitoring of U&Es.

Ciclosporin (Neoral®)

ALL CICLOSPORIN SHOULD BE PRESCRIBED BY BRAND (Neoral®), since it has a narrow therapeutic index and different formulations can result in greatly altered blood levels

Monitoring

Broadly speaking, these are the levels of **trough** ciclosporin that will be aimed for:

Months 0 to 3 175 - 300ng/ml
Months 3 to 12: 125 - 250ng/ml
Months 9 onwards: 50 - 150ng/ml

Target levels will be lower in patients receiving mycophenolate mofetil. Patients beyond one year with renal impairment may be run with a trough level <100. Patients who are a long way out with stable liver function will often be run with levels <100.

Adverse drug reactions

Hypertension, Headache, tremor and paraesthesia, Hyperkalaemia and Nephrotoxicity - are seen with both calcineurin inhibitors. See Tacrolimus section for advice.
Benign gingival hyperplasia is relatively common with ciclosporin especially when nifedipine is co-prescribed. Transplant recipients are advised to brush their teeth twice daily.
Hirsutism may be a problem, particularly to dark-skinned females. Facial hair bleaches and depilatory creams are safe and often effective but electrolysis should be avoided because of the infection risks.

Drug interactions: CONSULT APPENDIX 1 OF BNF

See Tacrolimus section for advice

Sirolimus

Very few patients will be taking sirolimus, as it is reserved for special circumstances, such as late acute rejection resistant to 2 courses of pulsed steroids, chronic ductopenic rejection or in patients with calcineurin inhibitor induced renal dysfunction. The usual starting dose is 2mg OD. The laboratory reports a therapeutic range of 5-8ug/l. If used as monotherapy then aim for levels closer to 10ug/l than 5ug/l, whereas if used in combination with either MMF or low dose tacrolimus then aim for levels no higher than 5ug/l.

Sirolimus should not be given within 3 months of liver transplantation because of the uncertain risk of hepatic artery thrombosis and potential for poor wound healing. In the case of re-grafting (or other elective surgery), patients should stop sirolimus (where possible) at least 2 weeks before being activated on the liver transplant list to allow a "washout period".

It is a teratogen and other side effects include leucopenia, thrombocytopenia, hypertriglyceridaemia and hypercholesteraemia, oedema, interstitial lung disease, joint pains and acne. Intolerance is common and can be overcome in some patients by reducing the level to < 5ng/ml (this may require use of the liquid formulation).

IN ALL CASES DISCUSS WITH A TRANSPLANT HEPATOLOGIST AT QEHB PRIOR TO INITIATING SIROLIMUS

Prophylactic drugs post-transplant

- **Protection of the hepatic artery anastomosis** - The majority of patients will be on Aspirin 75mg or low dose warfarin.
- **Pneumocystis Carinii Pneumonia (PCP) Prophylaxis -** Co-trimoxazole (Septrin®) is started on day 5 post transplant at a dose of one tablet - 480mg and is taken on alternate days for the initial 3 months post-transplant.
- **Cytolomegalovirus (CMV) Prophylaxis -** Oral valganciclovir is started on day 5 post transplant in all CMV donor positive/recipient negative mismatches for 3 months.
- **Anti-TB prophylaxis -** Patients of Asian/African origin or a past history of TB will usually receive a 6 month course of isoniazid 100mg daily and pyridoxine 10mg
- **Peptic ulcer prophylaxis** - treatment dose oral PPI until prednisolone dose < 10mg/day
- **Lamivudine/hepatitis B prophylaxis -** in those with pre-existing HBsAg or recipients of HBcAb+ve donor

Immunisation post-transplant

- AVOID LIVE VACCINES (MMR, BCG, Varicella, Yellow fever, oral typhoid, Polio -Sabin)
- Recommend influenza (annual) and pneumococcal (3-5 years) vaccine
- Avoid contact with recently vaccinated children

Investigation of Abnormal LFTs post-transplant

All patients with abnormal LFTs should have a prompt clinical assessment and set of investigations to elicit the cause for abnormal graft function. **All such patients should be urgently discussed with a consultant** with a low threshold to discuss with the relevant transplant unit.

Common causes of graft dysfunction post-transplant

Parenchymal	Rejection
	Infection
	Disease recurrence
Drugs	Antibiotics or immunosuppression
Biliary	Strictures, leak (early) or stones
Malignancy	Primary or secondary
Vascular	Hepatic artery thrombosis

Initial assessment for abnormal LFTs post-transplant

- Check compliance and careful medication history including OTC/herbal drugs
- Urgent ultrasound for biliary anatomy and to exclude SOL as well as Doppler of the hepatic artery and portal vein (request specifically for Consultant Radiologist to do)
- Viral hepatitis screen to include hepatitis A, B, C and E; CMV and EBV
- Check levels of immunosuppression where appropriate (may help assess compliance)
- Consider liver graft biopsy if cause remains unclear

Management of Rejection - this will mainly take place in transplant centre

Wherever possible, all rejection episodes should be confirmed histologically before starting therapy. In the presence of improving LFT's, mild or moderate rejection does not usually need to be treated with high dose steroids.
Aim for Tacrolimus levels > 10ng/ml in all patients with rejection, provided renal function permits.

1st Episode of Rejection
Prednisolone 200 mg/day orally for three days (or methylprednisolone 1g IV for 3 days). The prednisolone is given as a single daily dose.
Subsequently, resume maintenance prednisolone at 20mg/day and taper by 5mg/day after 3 weeks etc
Check Tacrolimus trough blood level > 10 ng/ml

2nd Episode or Persistent Rejection
Repeat course of high dose steroids.
Switch from Azathioprine to Mycophenolate Mofetil 2gm/day
Consider increasing Tacrolimus trough levels to 15-20ng/ml.

Late Acute Rejection

Initial treatment as above Subsequently, re-start prednisolone 20mg/day and consider long term maintenance on 10mg/day.
Switch to MMF if previous rejection.
Maintain Tacrolimus levels > 10ng/ml long term (renal function permitting).
N.B. Consider non-compliance as a cause.

Management of infection risk post-transplant

The interval from 3-6/12 month post LT is a high risk period for opportunistic pathogens.

CMV
Laboratory surveillance for CMV infection is not currently recommended. Asymptomatic CMV infection is of unproven consequence, and should not be treated. Symptomatic CMV infection (often called CMV disease) classically develops in the second post-transplant month but may present at any time. Pyrexia is the principal sign of CMV disease. CMV disease is usually associated with leucopenia – bone marrow suppression or GI tract/ Liver involvement, usually where the donor is CMV positive (especially if recipient CMV negative) and/or augmented immunosuppression. The following patients are at greatest risk of developing CMV disease:

- Sero-negative recipients of seropositive livers (donor and recipient CMV IgG status should be known)
- Patients with septic biliary complications (including hepatic artery thrombosis)
- Patients transplanted for fulminant liver failure.

Diagnosis:

- Blood for quantitative CMV PCR assay – send weekly samples while infection is suspected. CMV infection is invariably associated with a positive PCR result although the specificity for CMV disease is about 50-60%.
- Biopsy specimens (usually liver, duodenal or rectal) and bronchoalveolar lavage (BAL) fluid can be tested by PCR to confirm the diagnosis of CMV disease. A positive biopsy or BAL result in association with a negative blood result should be interpreted with caution

Treatment:
Consider when there is a high index of suspicion. The institution of treatment does not require laboratory confirmation of CMV infection.

- **Reduction of immunosuppression (ALL patients) -** the degree of reduction depends on the severity of the illness. For most patients, azathioprine is stopped.
- **Intravenous Ganciclovir (MOST patients)** is indicated for all but the most trivial infections. Treatment duration should be at least 14 days, and further therapy depends on treatment response CMV PCR). The dose of Ganciclovir is 10 mg/kg/day iv in 2 doses for 14 days - adjust for renal dysfunction. Patients can be switched to oral valganciclovir 900mg bd (adjust dose for eGFR) until viraemia has resolved.
- **Intravenous immunoglobulin (SOME patients)** is indicated for all patients with suspected CMV pneumonitis, and for any symptomatic infection when response to Ganciclovir is poor (persisting symptoms after 7 days of Ganciclovir treatment). Polyclonal preparations are probably as efficacious as the CMV hyperimmune product. An appropriate course of therapy is Sandoglobulin 500 mg/kg on days 1 and 7. A further dose should be administered on day 14 when response to therapy in the first week is poor.

Chronic Hepatitis E infection
Under-recognised and an important cause of graft dysfunction. Check Hepatitis E PCR in any transplant patient presenting with abnormal LFTs. Ribavirin treatment may be indicated if virus fails to clear with reduction of immunosuppression.

Pneumocystitis jirovecii (carinii)
Rare due to prophylaxis - presents with respiratory symptoms, hypoxia and fever, with bilateral interstitial infiltrates on CXR. Treat with Co-trimoxazole 15-20mg/kg/day (adjusted for eGFR) for minimum 14/7 ± steroids if significant hypoxia.

Fungal Infections
These can be difficult to diagnose and may require tissue for diagnosis. Treatment is dependent on the pathogen and may require reduction in immunosuppression. In a liver transplant patient isolation of *Candida* species from a normally sterile site (e.g. blood), would be an indication for treatment with high-dose fluconazole 200-400 mg / day intravenously. Lack of clinical response or isolation of a non albicans Candida (with uncertainty over fluconazole susceptibility until speciation is available) would

be an indication for converting to a therapeutic dose of Ambisome (3mg/kg/day) intravenously until speciation is available.

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In any patient already receiving fluconazole prophylaxis, isolation of *Candida* species from a normally sterile site would also suggest fluconazole resistance and would be an indication for conversion to a therapeutic dose of Ambisome.

Liaise with clinical microbiology regarding treatment modification / cessation according to speciation /sensitivities of positive culture and remember the potential for drug interactions

Isolation of Aspergillus species:
Abelcet 5mg/kg/day can be used in all such patients BUT Liase with clinical microbiology regarding treatment modification/cessation according to speciation /sensitivities of positive cultures. Newer agents such as voriconazole or posocanoazole would be considered on an individual case basis. Voriconazole would usually be recommended for CNS infections.

Isolation of fungus from urine is an indication for removing the urinary catheter
Isolation of fungus from blood is an indication for removing all intravascular catheters and replacing with new ones as required.

TB
Donor derived TB rare. Treatment is with a 4-drug regimen - the doses of CNIs will need to be increased 2-5 fold where Rifampicin used.

Chicken-pox
If patient has had contact with chicken-pox check immune status (if not done pre-transplant). Offer treatment with acyclovir if negative. The risk of chickenpox is small if the patient is immune to the virus and is smaller following contact with shingles than to chickenpox. The decision to offer treatment is complex and will depend on many factors, including the closeness of the contact. If in doubt, seek the advice of the on-call virologist.

Other medical problems post-transplant

Management of Cardiovascular risk post liver transplant
Liver transplant recipients are at greater risk of cardiovascular and cerebrovascular disease. The cause of this increased risk is multi-factorial, but includes:

- **Hypertension - *BP should be assessed at each clinic visit - Target BP 130/80.***
  White collar hypertension common - ensure three consecutive elevated reading (usually in primary care) or evidence from a 24hr ambulatory BP study before treatment. Initial treatment should be to minimise CNI and steroid dose where possible and if appropriate to promote weight loss and restriction of dietary salt. First line treatment is Amlodipine (counteracts the vasoconstrictive effect of CNIs) with betablockers 2nd line. Diltiazem, nicardipine, felodipine and verapamil should not be used as they have the potential to increase plasma tacrolimus levels. ACE inhibitors or Angiotensin II blockers are preferred if the patient is diabetic or has an increased albumin creatinine ratio, but renal function and potassium levels must be monitored.
- **Diabetes mellitus – Check HbA1c annually.**
  Non-insulin dependent diabetes is seen in 5-26% of patients who are more than 1 year post transplant. Aim for HBA1C of < 7%. Metformin and sulphonylureas may both be used in LT recipients. Consider switching from Tacrolimus to ciclosporin.
- **Dyslipidaemia – Check fasting lipids annually.**
  70% of liver transplant recipients have dyslipidaemia. CNIs and steroids both increase the prevalence. It is suggested **that all adult liver transplant recipients aged over 30 years should be offered life-long treatment with a statin to reduce the risk of a cardiovascular or cerebrovascular event**. Pravastatin 40mg/day (those on ciclosporin should be given 20mg/day) should start 3-4 months post-transplant. Statins are contra-indicated in pregnancy and so should be stopped in those women who are or may become pregnant.
- **Obesity -** common after transplantation with > 30% of patients having a BMI>30kg/m^2 by 2 years
- **Renal dysfunction - UEs assessed at each clinic visit. Urine Albumin creatinine ratio checked annually**. 60-80% of patients have pre-dialysis CKD. 5-8% of patients will require dialysis in first 10 years post-transplant. Causes include CNIs, hypertension, diabetes, obesity,

dyslipidaemia, chronic HCV and pre-transplant renal dysfunction. CNI withdrawal and substitution with mycophenolate 2g/day and prednisolone 10mg/day should be considered when creatinine > 150 μmol/L despite a reduction in CNI.

- **Little exercise -** this may occur following a prolonged illness and protein malnutrition

Post-transplant lymphoproliferative disorder (PTLD)
Complicates solid organ transplant requiring long term immunosuppression. It is rare (affects 1-2% of adult liver transplant recipients, but more common in paediatric cohort) but serious. PTLD is heterogeneous and ranges from a polyclonal, often infectious mononucleosis-like syndrome to malignant neoplasia. The majority are EBV-associated.
Presentation is diverse but PTLD should be considered in patients presenting with:

- Fever, weight loss, sweats
- GI disturbance, diarrhoea
- Lymphadenopathy
- Tonsillitis
- Hepatosplenomegaly
- Anaemia, pancytopenia
- Haemophagocytosis
- Glandular fever-like illness

Investigations: Biopsy of lymph node or affected organ (FNA cytology will not suffice). Histology of biopsy for suspected PTLD **must be sent fresh (not in formalin) and portered as an urgent sample directly to Histopathology** (this is to ensure the sample is suitable for immunohistology, cytogenetics and molecular analysis).
If PTLD is detected, the patient needs to complete staging investigations with:

- Chemistry, serum LDH, FBC and film
- CT neck, chest, abdomen, pelvis
- BM aspirate, trephine, immunophenotype and cytogenetics
- Lumbar puncture +/- CT head if neurological symptoms
- EBV serology and quantitative EBV PCR is recommended at presentation

Treatment: Refer for treatment to Haem-Oncologists with an interest in lymphoma. Treatment planning depends on careful evaluation of patient condition, histological grade and prognostic factors. Cases should be discussed at the Lymphoma MDT.

Osteoporosis - ***Consider assessment of BMD annually in those with osteopenia and every 2-3 years in those with normal bone density (particularly in first 5 years)***
Accelerated bone loss is seen in the first few months post-transplant, after which steroids (if continued) and possibly CNIs contribute to further bone loss. Treat osteopenic patients with AdCal D3 2 tabs daily or a bisphosphonate if osteoporosis present.

Cancer risk – ***Refer to Dermatology for annual skin check. Advise referral to a smoking cessation service if available. Advise on sun protection. Advise to participate in national screening programmes (bowel, cervical, breast).***
The cumulative incidence of de-novo cancer post liver transplant is 3-5% at 1-3 years and 11-20% at 10years. As an example the relative risk of skin cancer (SCC and BCC) is 20-70%, Lymphoma 10-30% and oropharyngeal 3-14% (25% if prior diagnosis was ALD).

Reproductive health - ***Pregnancy should only be considered once the woman is more than 1 year post transplant, allograft function is stable, medical co-morbidities well controlled and on a low maintenance level of immunosuppression (that does not include Mycophenolate or Sirolimus)***
Pregnant women should have graft function and CNI levels every 4 weeks until 32/40 then weekly.
The risk of breast feeding while taking CNIs, Azathioprine and steroids (advise wait for 4hrs after administration) is small. Mycophenolate and Sirolimus are potentially hazardous.
Menstruation and fertility return by 10mths in 90% of women. Recovery of male gonadal function is often incomplete. Liver transplant has limited efficacy in curing sexual dysfunction in both men and women.

Recurrent disease post liver transplant

For some indications (e.g Wilson's disease) liver transplant is a cure. In the majority of cases, however, the underlying disease can recur, though often without clinical sequelae (e.g PBC, haemochromatosis).

HCV: recurrent disease is invariable, but with the advent of new directly active anti-viral drugs for HCV the majority of patients can be cured of their HCV pre or shortly after transplantation.

HBV: recurrent disease can be prevented in almost all (≥ 90%) patients using Hepatitis B immune globulin (HBIG) and a nucleos(t)ide analogue. Patients with low/ undetectable HBV DNA before LT and absence of risk factors for recurrence can usually discontinue HBIG. Combination therapy (NUC + with immunoglobulins) is recommenced after liver transplantation for the prevention of HBV recurrence (risk <5%) until Anti-HBs levels are >50-100 IU/L. Lifelong combination therapy should be administered to patients who at high risk of HBV recurrence (HBV DNA +ve at time of transplantation, HBeAg +ve, have HCC, or are co-infected with HDV/ HIV. HBsAg-ve patients who receive organs from anti-HBc +ve patients should receive lifelong prophylaxis with lamivudine

PSC: recurrent disease is seen in 50% of patients at 5 years with graft loss in 25% with recurrence. Patients with an intact colon continue to require annual colonoscopy as the cancer risk remains.

AIH: patients transplanted for AIH should remain on prednisolone 7.5mg od as part of their immunosuppression.

Further reading:

AASLD practice guideline: Adult Liver Transplant. 2013
Adult liver transplantation: UK clinical guideline – part 2: surgery and post-operation. BSG 2020

Documentation Controls (these go at the end of the document but before any appendices)

<table>
<tr><td>Reference Number

CG-T/2023/207</td><td colspan="2">Version:

4</td><td>Status

Draft or Final</td><td>Final</td></tr>
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<tr><td>4</td><td>2022</td><td>Liver Management Group</td><td colspan="2">Previous version of guideline expired</td></tr>
<tr><td></td><td></td><td></td><td colspan="2"></td></tr>
<tr><td colspan="5">Intended Recipients: All clinicians managing patients with liver disease</td></tr>
<tr><td colspan="5">Training and Dissemination: Forms part of liver handbook which is disseminated to all clinicians rotating through Hepatology</td></tr>
<tr><td colspan="5">Development of Guideline:
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<tr><td colspan="5">Consultation with: Liver management group -cross-site teams</td></tr>
<tr><td colspan="5">Linked Documents: State the name(s) of any other relevant documents</td></tr>
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