Worcestershire Acute Hospitals NHS Trust

GUIDELINE FOR THE MANAGEMENT OF IMMUNE-RELATED ADVERSE REACTIONS FOLLOWING IMMUNOTHERAPY TREATMENT

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

This guideline refers to the management of immunotherapy induced adverse reactions. encompasses the pathway of care to follow, when a patient over the age of 16 who has received immunotherapy in adult services, presents to Worcestershire Acute Hospitals NHS Trust.

This policy refers to patients who may present to the trust via Accident & Emergency who are receiving Immunotherapy elsewhere but who live locally.

This guideline is for use by the following staff groups:

This guideline is for utilization by trained medical and nursing staff. Educational updates will be provided for medical and nursing staff.

Guideline approved by:

Oncology Governance meeting	31st January 2025
Medicines Safety Committee	11th June 2025
Review Date	31st January 2028

This is the most current document and is to be used until a revised version is available:

Lead Personnel (s)

Dr N Murukesh	Clinical Lead
Mrs H Grist	Immunotherapy Nurse Practitioner
Dr J Mahil	Medical Oncology Registrar
Mrs S Cook	Lead Pharmacist
Mrs A Jones	Acute Oncology Nurse Practitioner

Guideline approved by Accountable Director on: This is the most current document and is to be used until a revised version is available:

Key Amendments made to this document:

Date	Amendment	By
	Guideline approved by Clinical Effectiveness Committee	
9th October 2019	09/10/2019- Document extended for 6 months whilst document is taken through consultants meeting and reviewed	Helen Grist/Lisa Rowberry
May 2020	Document extended for 6 months during COVID-19	
October 2020	Guideline updated and derived from the Clatterbridge ones.	Helen Grist/MSC
20th December 2021	Pneumonitis Guideline added	Helen Grist
13th March 2024	Document extended for 6 months whilst under review.	Helen Grist
January 2025	Document reviewed and approved	Helen Grist

Sections:

Appendices:

Please note these guidelines have been adapted using UKONS Immunotherapy toxicity guidelines 2023
https://www.ukons.org/site/assets/files/1067/ukons_ao_initial_management_guidelines_final_version_2023.pdf

Guideline for The Management of Immune-Related Adverse Reactions Following Immunotherapy Checkpoint Inhibitor Treatment

1. INTRODUCTION

This policy refers to the management of immunotherapy induced adverse reactions. It encompasses the pathway of care to follow when a patient over the age of 16 who has received immunotherapy checkpoint inhibitors in adult services presents to Worcestershire Acute Hospitals NHS Trust.

2. DEFINITIONS

Immunotherapy checkpoint inhibitors are a relatively new class of anti-cancer drugs which reactivate the Immune system to destroy cancer cells. The side effect profile for these agents is different from that of standard cytotoxic drugs. They can cause severe immune-related adverse reactions (IrAE) including serious immune-related endocrinopathies, which can be fatal. Thus, it is important to recognise and address symptoms early.

The majority of IrAE occur over the course of treatment. However, they can occur weeks to months after discontinuation of treatment.

3. PRE TREATMENT INVESTIGATIONS AND PATIENT EDUCATION

Prior to commencing treatment all patients must be informed of the potential side effects (Risk of adverse reactions) and what action to take should they experience these side effects. All patients must be given drug specific information and an immunotherapy checkpoint inhibitor alert card containing contact details for the acute oncology service. Patients should be advised to contact the hospital straight away if they have any of the following symptoms:

- Lung : breathing difficulties, dry cough or haemoptysis
- Gastrointestinal: watery or loose stools, mucous or blood in stool, stomach pains, cramps or gastritis
- Liver: eye or skin yellowing, pain on right side of stomach
- Kidney: changes in volume of urine/frequency of urine or haematuria
- Endocrine: extreme tiredness, weight change, headache, visual disturbances, cognitive impairment or postural hypotension

- Diabetes symptoms: excessive thirst, large volumes of urine, increased appetite with weight loss, feeling tired, drowsy, weak, depressed, irritable and generally unwell
- Rheumatological : dry mouth, dry eyes, painful joints, erythema or joint swelling
- Skin : itching, rash, blisters, ulcers, peeling skin
- Eye : redness, pain, blurred vision
- Neurological : peripheral neuropathy, guillian barre (ascending paralysis/weakness), numbness or un-coordinated movements
- Heart problems: Chest pain, breathlessness, tiredness, leg swelling

Prior to initiation of treatment the following bloods should be taken as a baseline:

a. FBC, LFT's, Renal profile, Glucose, Cortisol, TFTs, LDH,
b. In the case of Nivolumab, a baseline ECG, CK and pro BNP should be considered as it can cause due to cardiotoxicity.
c. These bloods should be repeated before each cycle.

If the patient is stable on treatment the frequency of the blood test may be reduced.

Ideally, patients should have a clinic review prior to each treatment cycle. If the patient is stable on treatment, frequency of reviews could be reduced documented through letters/MOSAIQ/outcome forms. If the patient contacts the acute oncology service out of hours, the AOS nurse should complete the Immunotherapy 'Triage tool' (Appendix 1) and follow the instructions on the checklist.

If the patient contacts the acute oncology service during normal working hours or presents at the accident and emergency department they should be assessed and managed as detailed in the 'Initial Management of Immune-related Adverse reactions' flow chart below.

If the contacts the acute oncology service out of hours, the AOS nurse should complete the Immunotherapy 'Triage tool' (Appendix 1) and follow the instructions on the checklist.

INITIAL MANAGEMENT of IMMUNE – RELATED ADVERSE REACTIONS

WORKING HOURS: INFORM THE ACUTE ONCOLOGY TEAM OF ADMISSION.
OUT OF HOURS: INFORM THE CONSULTANT ONCOLOGIST ON CALL

On presentation, if no obvious infectious and / or disease-related etiologies

DO NOT WAIT, TREAT AS:

Immune –Related Adverse Reaction as tables below.

Follow link for CTCAE grading criteria:

Common Terminology Criteria for Adverse Events (CTCAE) | Protocol Development | CTEP (cancer.gov)

WORKING HOURS: Inform the Acute Oncology Team, for pathway of management of patient from Nurse led clinic, consultant clinic or pre proceed triage see Appendix 1

OUT OF HOURS: Inform the Acute Oncology Service, if patient requires assessment for admission to be directed to ED to be assessed by medics.

Having assessed the patient as per the guideline in the symptom management for adverse events it may be that referral to a specialist is required. The table below is a list of leads who are able to advise on symptom management as a specialist in their field.

Endocrinology	Dr. Babar Dr. Bhaskar
Cardiology	Dr. Wilson
Dermatology	Dr. Chalasani
Respiratory	Dr. Cusworth Dr. Johnstone
Rheumatology	Dr. Cardy
Renal	Dr. Ferring
Gastroenterology/Hepatology	Dr. Baker
Oncology	Dr. Murukesh
Neurology	TBC

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Immune-Related Adverse Event: Endocrinopathies - Adrenal Crisis

Immunotherapy has been causatively associated with a number of endocrinopathies that may present with nonspecific symptoms, which may resemble other causes such as brain metastasis or underlying disease.

Endocrine function panel:

U&E, LFT, TSH, Free T4, free T3, ACTH, LH, FSH & cortisol (between 9-11am if possible), prolactin, blood glucose +/- testosterone

Asymptomatic
Identified on routine blood tests.
Biochemical alteration in cortisol with serum level < 200nmol/L

Hypoadrenalism is likely if cortisol is <100nmol/L

Cortisol 100-200nmol/L
Investigations
- Repeat cortisol at 9am ≤ 48 hours - if <200 arrange short synacthen test
- If <100 see "Cortisol <100" green strand
- Complete endocrine function panel if outstanding.

Actions
- Monitor regularly (before each cycle as a minimum) and act as per algorithm if serum levels fall
- Continue immunotherapy.

Cortisol <100nmol/L
Investigations
- Repeat cortisol at 9am ≤ 24 hours – if <100 arrange short synacthen test
- Complete endocrine panel if outstanding.

Treatment
- Replace with hydrocortisone 10mg/5mg/5mg.

Actions
- Refer to Endocrine team
- Give emergency steroid advice and alert card.

Symptomatic
Mild/Non-life threatening.
Suspect endocrinopathy based on symptoms.
Tiredness/fatigue, headache, weight loss, susceptibility to infection, normal BP with no postural drop

Investigations:
- 9am Cortisol and ACTH
- If headache present, consider MRI brain with pituitary cuts.

Cortisol (9am) >400 nmol/L
Adrenal insufficiency unlikely
Actions
- Considerothercauses of symptoms.
- Continue immuno-therapy.

Cortisol (9am) 100-400 nmol/L
Adrenal insufficiency unlikely
Actions
- Arrange short synacthen test.
- Consider endocrine referral
- Complete endocrine bloods including prolactin, testosterone, and ACTH
- Continue immuno-therapy.

Cortisol (9am) <100nmol/L
Adrenal insufficiency likely
Treatment
- Commence hydrocortisone 10mg/5mg/5mg.

Actions
- Arrange short synachten test
- Refer to Endocrine team
- Complete endocrine bloods including prolactin, testosterone, and ACTH
- Give emergency steroid advice and alert card
- Continue immunotherapy.

Symptomatic
Severe or Life-threatening
Suspect adrenal crisis
Hypotension (SBP <90mm Hg)
Postural hypotension (>20mm Hg drop)
Dizziness/Collapse, Hypovolemic shock
Nausea/ Vomiting, Abdominal pain/ tenderness/guarding, Fever, Confusion/delirium, Coma

Admit patient
Immediate Intervention
- Send endocrine panel including and ACTH prior to giving steroids
- Immediate management with an ABCDE approach
- Commence IV hydrocortisone 100mg QDS immediately without awaiting blood tests
- Urgent Endocrinology referral
- Rule out superadded infections.

Society for Endocrinology [SfE] guidelines for adrenal crisis:
Next Steps are dependent on blood results.
- Introduce steroid replacement hydrocortisone PO 20mg, 10mg, 10mg
- Reduce hydrocortisone to 10mg, 5mg, 5mg after 2 weeks
- Once stable on hydrocortisone replacement for 3-5 days if thyroid deplete then commence levothyroxine
- Arrange short synacthen test
- Recheck testosterone after 3 weeks and replace if remains suppressed.
- Give emergency steroid advice and alert card.

All patients with hypoadrenalism should be assessed for postural hypotension and fludrocortisone (50mcg OD) considered if persistent.

If thyroid function is also compromised within a hypopituitary picture, ensure cortisol is replaced prior to commencement of thyroid replacement

A referral to a specialist may be required after assessment.
DR BHASKAR (Endocrinology)

Interrupt SACT immunotherapy until discussed with Acute Oncology Team.
Please contact on-call oncology/haematology team for advice.
Ensure that the patient has monitoring/follow up planned with their oncology/ immuno-oncology team.

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Immune-Related Adverse Event: Endocrinopathies – Hypophysitis

Immunotherapy has been causatively associated with a number of endocrinopathies that may present with nonspecific symptoms, which may resemble other causes such as brain metastasis or underlying disease. This includes inflammation of the pituitary gland. The pituitary gland is responsible for secreting hormones that govern the activity of the thyroid, adrenal and gonadal glands. Where pituitary inflammation occurs this often leads to deficiency in the hormones governing these glands and insufficiency of one, two or all end organs can occur.

CAUTION If the patient is on steroids (prednisolone/dexamethasone) then serum cortisol will likely be suppressed – please discuss with endocrinology team before commencing replacement.

***Endocrine function panel:**
U&E, LFT, TSH, Free T4, free T3, ACTH, LH, FSH & cortisol (between 9-11am if possible), prolactin, blood glucose +/- testosterone/oestrogen.

Asymptomatic
Identified on routine blood tests.
Biochemical alteration in cortisol with serum level <200nmol/L

Cortisol insufficiency is likely if cortisol is <100nmol/L

Cortisol 100-200nmol/L
Investigations
- Repeat cortisol at 9am ≤ 48 hours – if <200 and no other endocrine function abnormality arrange short synacthen test
- *Completeendocrinefunctionpanel.

Actions
- Monitor regularly (before each cycle minimum) and act as per algorithm if serum levels fall
- Ifcortisolreplaced,thenevaluateTFTs 1weeklater andreplace asrequired.
- If low testosterone/ oestrogen (in premenopausal women) consider replacement and seek endocrine.

Cortisol <100nmol/L
Investigations
- Repeat cortisol at 9am ≤ 24 hours – if <100 replace as below
- Complete endocrine panel Treatment
- Replace with hydrocortisone 10mg/5mg/5mg.

Actions
- Refer to Endocrine team
- If cortisol replaced, then evaluate TFTs 1 week later and replace as required
- If low testosterone/ oestrogen (in premenopausal women) consider replacement and seek endocrine advice if unsure
- Give emergency steroid advice and alert card
- Continue immunotherapy.

Symptomatic
Mild/Non-life threatening.
Suspect endocrinopathy based on symptoms
Tiredness/fatigue, headache, weight loss, susceptibility to infection, normal BP with no postural drop

Investigations:
- 9am Cortisol and ACTH
- MRI brain with pituitary cuts.

Cortisol (9am) >400 nmol/L
Adrenal insufficiency unlikely
Actions
- Considerothercauses of symptoms
- Continue immuno-therapy.

Cortisol (9am) 100-400 nmol/L
Adrenal insufficiency unlikely
Actions
- Consider endocrine referral
- Complete endocrine panel
- Ifcortisolreplaced,thenevaluateTFTs 1 weeklaterandreplace as required
- If low testosterone/ oestrogen (in premenopausal women) consider replacement and seek endocrine advice if unsure
- Continue immuno-therapy.

Cortisol (9am) <100nmol/L
Adrenal insufficiency likely
Treatment
- Commence Hydrocortisone 10mg/5mg/5mg.

Actions
- Refer to Endocrine team
- Complete endocrine panel
- Ifcortisolreplaced,thenevaluateTFTs 1 weeklaterandreplace as required
- If low testosterone/ oestrogen (in premenopausal women) consider replacement and seek endocrine advice if unsure
- Give emergency steroid advice and alert card
- Continue immunotherapy.

Symptomatic
Severe headache, visual disturbance, evidence of focal neurology
Combination of mild/moderate symptoms and pituitary inflammation on MRI
If severe symptoms/signs of hormonal insufficiency with no headache/visual disturbance/pituitary inflammation, then follow adrenal crisis algorithm

Admit patient
Immediate Intervention
- Commence IV Methylprednisolone 2mg/kg/ day for a minimum of 3 days without awaiting blood tests
- If clinically improved with mild/resolved symptomsswitch to prednisolonestarting at 60mg OD and reducing every 3 days
- Once at 10mg prednisolone introduce steroid replacement hydrocortisone 20mg, 10mg, 10mg
- Reduce hydrocortisone to 10mg, 5mg, 5mg after 2 weeks
- Continue weaning prednisolone till stop but continue hydrocortisone replacement
- Once stable on hydrocortisone replacement for 5-7 days commence thyroxine
- Recheck testosterone/oestrogen (in premenopausal women) after 3 weeks, if low consider replacement and seek endocrine advice if unsure
- Consider urgent Endocrinology referral
- Give emergencysteroidadvice and card.

If thyroid function is also compromised within a hypopituitary picture ensure cortisol is replaced prior to commencement of thyroid replacement

A referral to a specialist may be required after assessment.
DR BHASKAR (Endocrinology)

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Immune-Related Adverse Event: Endocrinopathies-Thyroid Dysfunction

Immunotherapy has been causatively associated with a number of endocrinopathies, including hypo/hyperthyroidism. Observational studies have shown that there is a typical pattern of thyroid specific biochemical disturbance presenting with asymptomatic hyperthyroidism before return to normal levels for a brief period. This is nearly always followed by the development of, in some cases profound, hypothyroidism which is frequently persistent and requires long term thyroid replacement. Smaller subsets of patients develop isolated hypothyroidism over a period of weeks. Both groups appear to require long term replacement in a majority of cases. These guidelines are in the basis of a clinically well patient and not experiencing thyroid disturbance due to being clinically unwell, if this is a concern Endocrinology advice should be sought.

Mild (Grade 1)

Asymptomatic with biochemical changes

Investigations

TSH, Free T4, free T3, ACTH, LH, FSH & cortisol, prolactin, blood glucose +/- testosterone

Hyperthroidism

TSH <0.38 mU/L and
Free T4 > 14.4pmol/L
(If TSH low and T4 normal or low, need to exclude pituitary dysfunction)

Treatment

- Steroids are not needed in this setting unless expressly advised by endocrinology.

Actions

- Recheck TFT's and cortisol within 3 weeks and then 3 weekly thereafter. N.B. the majority of cases become hypothyroid within a matter of weeks.

Once hypothyroid-managed as per hypothyroidism algorithm.

Hypothyroidism

TSH of >5.33mU/L
Free T4 < 7.9 pmol/L

Treatment

- Levothyroxine 50mcg/day.

Actions

- Recheck TFT's and cortisol with next cycle of treatment.
- Increase Levothyroxine in 25mcg increments
- Discuss with endocrinologist to identify best pathway for long-term management and monitoring (primary/ secondary care)
- Consider referral to endocrinologist if unable to stabilise thyroid function.

Continue Immunotherapy.

Moderate (Grade 2)

Symptomatic or severe biochemical disturbance

Investigations

TSH, Free T4, free T3, ACTH, LH, FSH & cortisol, prolactin, blood glucose +/- testosterone

Hyperthroidism

TSH <0.38 mU/L and
Free T4 > 14.4pmol/L
(if TSH low and T4 normal or low, need to exclude pituitary dysfunction)

Treatment

- Consider Propanolol 10-40mg 3-4 times a day for symptoms
- Carbimazole-rarely indicated due to the transient nature of hyperthyroidism. If persistent or associated with anti-TSH antibodies consider in collaboration with an endocrinologist.

Actions

- Recheck TFT's and cortisol within 2 weeks and fortnightly thereafter. N.B. the majority of cases become hypothyroid within a matter of weeks.

Continue Immunotherapy as long as symptomatically stable.

Hypothyroidism

TSH of >5.33mU/L
Free T4 < 7.9pmol/L

Treatment

- Levothyroxine 50mcg/day.

Actions

- Recheck TFT's and cortisol with next cycle of treatment
- Increase Levothyroxine in 25mcg increments
- Consider referral to endocrinologist if unable to stabilise thyroid function.

Continue Immunotherapy following commencement of levothyroxine.

Having assessed the patient as per the guidelines in the symptom management for adverse events it may be referral to a specialist is required

DR BHASKAR (Endocrinology)

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Immune-Related Adverse Event: Diarrhoea & Colitis

Gastrointestinal (GI) irAEs are among the most common and although they are typically mild to moderate in severity, if they are left unrecognised or untreated, they can become life-threatening. These toxicities can be managed effectively in almost all patients by using established guidelines that stress vigilance and the use of corticosteroids and other immunosuppressive agents when necessary.

Mild (Grade 1)
- < 4 stools/day over baseline
- *or* mild increase in ostomy output in the absence of abdominal pain, mucous/blood in stools.

Investigations
- Baseline bloods (FBC, U&E, LFTs, TFTs, cortisol & CRP)
- Stool microscopy and culture
- C. difficile toxin
- Faecal calprotectin.

Treatment
- Encourage fluids
- Avoid high fibre and lactose.

Actions
- Regular monitoring
- Consider holding immunotherapy (if on combination anti-PD1/CTLA4 withhold immunotherapy).

Symptoms: PERSIST (≥5 days) or WORSEN or are associated with deranged U & E's

Moderate (Grade 2)
If any of the following symptoms are present:
- 4-6 stools/day over baseline or moderate increase in ostomy output
- Moderate abdominal pain/cramps/ discomfort (may represent enteritis/ gastritis in addition to colitis)
- Mucous in stool.

Clinical Assessment
As per mild (grade 1) +

Investigations
- CMV viral load + PCR (red top blood sample)
- Faeces CMV
- Faecal calprotectin
- Abdominal X-Ray (consider CT abdo/pelvis if AXR abnormal or in presence of abdominal pain)
- Consider Infliximab screen per Grade 3&4
- If recurrent, send for faecal elastase.

Treatment
- Prednisolone 60mg/day + gastric protection
- Fluid balance and replacement as appropriate (inc. diarolyte sachets).

Actions
- Omit next dose of immunotherapy
- Taper per steroid weaning guidance
- Telephone monitoring
- Endoscopy
- Gastroenterology advice/ review if not improving within 72hrs

Assess response to treatment within 72 hours

Symptoms: Resolve or Improve to Mild. See steroid tapering guidance

PERSIST or WORSEN or RELAPSE

Severe or Life-Threatening (Grade 3 + 4)
If any of the following symptoms are present:
- ≥7 stools/day over baseline or significant increase in osotomy output
- Severe abdominal pain
- Fever
- Dehydration
- Blood in stool
- Incontinence
- Limiting ADL's.

As per moderate (grade2) +
Consider Admission of patient

Investigations on day 1
- Screen for Infliximab administration suitability on admission (to include- TB Quantiferon test, hepatitis screen, HIV, varicella zoster anti-bodies (IGG antibody), chest X-Ray (if chest CT not already performed)
- Refer for Upper and lower GI endoscopy with biopsies on day 1 of admission (at least 4 biopsies)
- Daily bloods (FBC, U&E, LFTs & CRP)
- CT Abdomen/pelvis.

Treatment
- IV hydration and fluid balance
- IV Methylprednisolone 2 mg/kg/ day + gastric protection cover and continue for a minimum of 3 days
- Antibiotics are not required as standard
- **Use analgesia with CAUTION.**

Actions
- Daily stool chart
- Consider referral & potential transfer to gastroenterology
- Dietician review
- Consider discontinuation of immunotherapy
- Taper per steroid weaning guidance.

Interrupt SACT immunotherapy until discussed with AOS.

Please contact on-call oncology team for advice.

Having assessed the patient as per this guideline a referral to a specialist may be required.

DR BAKER (Gastroenterology)

Review patient daily, if no improvement within 72 hours, consider infliximab treatment Complete Blueteq

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Immune-Related Adverse Event Guideline: Hepatotoxicity

Hepatic transaminases (ALT/AST) and bilirubin must be evaluated before each dose of immunotherapy, as early laboratory changes may indicate emerging immune-related hepatitis. Elevations in LFTs may develop in the absence of clinical symptoms. This guidance should be used in context of baseline LFTs and presence of known liver metastases. No dose adjustment is required for mild hepatic impairment, but data is limited for use of these drugs in moderate/severe hepatic impairment and patients should be closely monitored for elevation in LFTs from baseline.

Prior to commencement of immunotherapy all patients should have LFTs checked.

Mild (Grade 1)
AST or ALT < 3 x ULN but increasing from baseline

Investigations
- Weekly LFT / AST check between cycles of immunotherapy and ensure remain stable prior to next cycle. Inform oncology team
- Consider culprit concomitant medications.

Actions
- Continue immunotherapy.

Biochemical Abnormality WORSENS or RELAPSE see moderate/ severe strand (LFT dependant)

Symptoms: Resolve or Improve to Mild. See steroid tapering guidance

Abbreviations
LFTs = liver function tests
INR = international normalised ratio
ULN = upper limit of normal
PD = progressive disease

Moderate (Grade 2)
AST or ALT >3 to ≤5 x ULN

Clinical Assessment
As per mild (grade 1) +

Investigations
- Regular LFTs, direct and indirect bilirubin and clotting profile
- MRI/USS of liver to exclude PD & thromboembolism and evaluate if evidence of inflammation
- Hepatitis viral panel (hepatitis A, B, C, E)
- CMV, EBV and HIV and auto-antibodies.

Treatment
- Commence prednisolone 60mg/ day+ gastric protection.

Actions
- Withhold dose until the adverse reaction resolves to Grade 0-1 (or returns to baseline)
- Review medications (e.g. statins, antibiotics)
- **Re-check LFTs every 3 days and review patient by phone twice weekly. If improving check LFTs weekly.**

Biochemical Abnormality PERSISTS (≥3 days), WORSEN or RELAPSE see severe strand

Symptoms: Resolve or Improve to Mild. See steroid tapering guidance

Severe or Life-Threatening (Grade 3 + 4)
AST or ALT >5 x ULN
(Grade 4 >20 x ULN)

As per moderate (grade2) +
Consider Admission of patient

Investigations
- Daily LFTs, clotting profile and lactate. If deteriorating, consider venous gas
- MRI of liver to exclude PD & thromboembolism and evaluate if evidence of inflammation or sclerosing cholangitis
- Exclude other causes (e.g. Heart failure/ PD).

Treatment
- IV methylprednisolone 2mg/kg/day
- *Increasing* to 4mg/kg/day could be considered if clinical improvement is unsatisfactory
- IV hydration (patients need to be well hydrated to promote hepatic perfusion with fluid balance)
- Vitamin K 10mg IV daily x 3 days if INR deranged
- **Grade 4 (loss of synthetic function or hyperbilirubinemia) consider commencing.** N-acetylcystine (NAC as per paracetamol overdose protocol in BNF). If albumin low, discuss with hepatologist and consider administration of human albumin solution (HAS).

Actions
- Referral to hepatologists for further advice
- Consider antibiotic prophylaxis with patients on high dose, prolonged steroids
- Establish escalation plan and ceiling of care.

Hepatology review and also confirm that this is after 72 hours IV steroids or 24 hours at 4mg/kg IV methylprednisolone. Consider additional immunosuppression.

Interrupt SACT immunotherapy until discussed with AOS. Please contact 24-Hour on-call oncology for advice.

Having assessed the patient using this guidance a referral to a specialist may be required.
DR BAKER (Gastroenterologist)

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Immune-Related Adverse Event: Neurological Toxicities

Immunotherapy administration is associated with immune-related adverse events (irAEs). Neurologic irAEs can manifest as central abnormalities (e.g. aseptic meningitis, encephalitis) or peripheral sensory/motor neuropathies (e.g. Guillain-Barre Syndrome). Early recognition and treatment of neurologic AEs is critical to its management. As neurologic symptoms can be common in patients with cancer, it is important that an evaluation/work-up distinguish between non-drug-related causes (e.g. progression of disease, concomitant medications, infection) and a possible drug-related AE as the management can be quite different.

Mild (Grade 1)
- Asymptomatic
- Not interfering with normal function.

Investigations
- Neurological examination
- Diabetic screen
- B12 and folate
- Thyroid function tests
- Alcohol history and medications.

Actions
- Monitor
- Continue immunotherapy.

Symptoms: WORSEN

Symptoms: Resolve or Improve to Mild. See steroid tapering guidance

Moderate (Grade 2)

Any:
- Sensory alteration
- Paresthesia (including tingling)
- Cranial nerve problem
- Confusion/delirium.

Interfering with function, but not interfering with ADLs.

Clinical Assessment

As per mild (grade 1) +

Investigations
- Neurological examination
- FBC, biochemical profile, ALT, cortisol, TFT's, glucose, B12 and folate
- Alcohol history and medications
- Consider lumbar puncture.

Treatment
- Commence 1mg/kg/day oral prednisolone (max. 60mg/day prednisolone) + gastric protection.

Actions
- Regular monitoring
- Delay immunotherapy.

Symptoms: PERSIST (≥3 days) or WORSEN or RELAPSE

Symptoms: Resolve or Improve to Mild. See steroid tapering guidance

Severe or Life-Threatening (Grade 3 + 4)

Any:
- Severe
- Disabling
- Life threatening symptoms

that are **limiting self-care**.

As per moderate (grade2) +
Admit patient

Investigations
- Daily neurological examination
- Regular NEWS and GCS score
- MRI brain and/or spine
- Lumbar puncture if aetiology is unclear
- Nerve conduction studies for peripheral neuropathy
- Electromyography/EEG on discussion with neurology.

Treatment
- Commence IV methylprednisolone 2 mg/kg/day (consider gastric protection)
- If unsatisfactory improvement on day 3, consider increasing to 4mg/kg
- If rapid deterioration consider 1g per day for 3 days, prior to weaning
- If Myesthenia Gravis discuss with neurology prior/alongside introduction of steroids to discuss the use of simultaneous IVIG/ plasmapheresis and follow ESMO subsequent management guidelines
- If Guillain-Barre type syndrome suspected refer to ESMO subsequent management guidelines.

Review patient daily, if no improvement within 72 hours, seek neurologist advice for further advice and management. Consider further immunosuppression. Consider local or national Subsequent Management Guidelines

Interrupt SACT immunotherapy until discussed with Acute Oncology Team. Please contact 24-Hour on-call oncology for advice.

A referral to a specialist may be warranted.

Contact details for a neurology physician are TBC.

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Immune-Related Adverse Event: Pneumonitis

Pulmonary irAEs have been observed following treatment with immunotherapy and have occurred after a single dose and after as many as 48 treatments. The frequency of pulmonary AEs may be greater with immunotherapy combination therapies than with monotherapy. The majority of cases reported were Grade 1 or Grade 2 and subjects presented with either asymptomatic radiographic changes (eg, focal ground glass opacities, patchy infiltrates) or with symptoms of dyspnoea, cough, or fever. Subjects with reported Grade 3 or Grade 4 pulmonary AEs were noted to have more severe symptoms, more extensive radiographic findings, and hypoxia.

Mild (Grade 1)
Clinically asymptomatic with Radiographic changes only (e.g. focal ground glass opacities, patchy infiltrates)

Clinical Assessment & O2 SATS

Investigations
- Sputum sample for MC&S
- Baseline bloods (FBC, U & E's, LFT's, CRP, calcium)
- Procalcitonin
- CT Imaging and baseline X-Ray.

To exclude a-typical infections
- Beta-D-Glucan/Galactomanan
- A-typical Viral Screen
- Covid Swab
- Urine legionella and pneumococcal antigen
- Mycoplasma Serology.

Actions
- Monitor symptoms weekly and re-image if worsening
- Consider delay of Immunotherapy
- Consider 30mg daily Prednisolone with a weaning course
- Ensure patient referred to local monitoring provision e.g. Immunotherapy Team/Primary oncology team.

Symptoms: WORSEN

Symptoms: Resolve or Improve to Mild. See steroid tapering guidance

Moderate (Grade 2)
Mild to moderate new onset of symptoms limiting instrumental ADL (e.g dyspnoea, cough, fever, chest pain)

Clinical Assessment & O2 SATS
As per mild (grade 1) +

Investigations
- CT imaging as symptomatic for CTPA to exclude PE as a differential (if CTPA –ve for pathology but suspicion of Pneumonitis remains complete HRCT.

To exclude a-typical infections
- Beta-D-Glucan/Galactomanan
- A-typical Viral Screen
- Covid Swab
- Urine legionella and pneumococcal antigen
- Mycoplasma Serology
- Sputum for PJP.

Treatment
- Prednisolone 1mg/kg/day (max. 60mg/day prednisolone) + gastric protection
- If evidence of infection, consider ABX as per local protocol
- Optimise underlying respiratory condition e.g. COPD.

Actions
- Hold immunotherapy
- Monitor symptoms
- Clinical examination if symptoms worsening (with repeat imaging)
- Ensure patient referred to local monitoring provision e.g. Immunotherapy Team/Primary oncology team.

Assess response to treatment within 72 hours

PERSIST or WORSEN or RELAPSE

Severe or Life-Threatening (Grade 3 + 4)
Severe new onset of symptoms limiting self-care ADL;
or Hypoxia (new or worsening);
or ARDS

Consider Admission
As per moderate (grade2) +
Clinical Assessment & O2 SATS

Investigations
- Pulmonary function test.

Treatment
- IV Methylprednisolone 2mg/kg/day + gastric protection
- Oxygen therapy
- Consider increasing to 4mg/kg/day if clinical improvement is unsatisfactory
- If evidence of infection, consider ABX as per local protocol.
- Optimise underlying respiratory condition e.g. COPD.

Actions
- Consider discontinuing Immunotherapy
- Refer to a chest physician
- Monitor symptoms daily with clinical examination and repeat imaging as indicated, if symptoms worsening, repeat imaging is required
- Consider Second line Immunosuppression with Tacrolimus (MMF and Infliximab can be considered as alternative)
- Referral to Interstitial Lung MDT
- Consider referral to Chest Physician and Bronchial Alveolar Lavage
- Ensure patient referred to local monitoring provision e.g. Immunotherapy Team/Primary oncology team.

Review patient daily, if no improvement within 72 hours, seek chest physician advice for further advice and management. Conisder local/national subsequent management guidelines

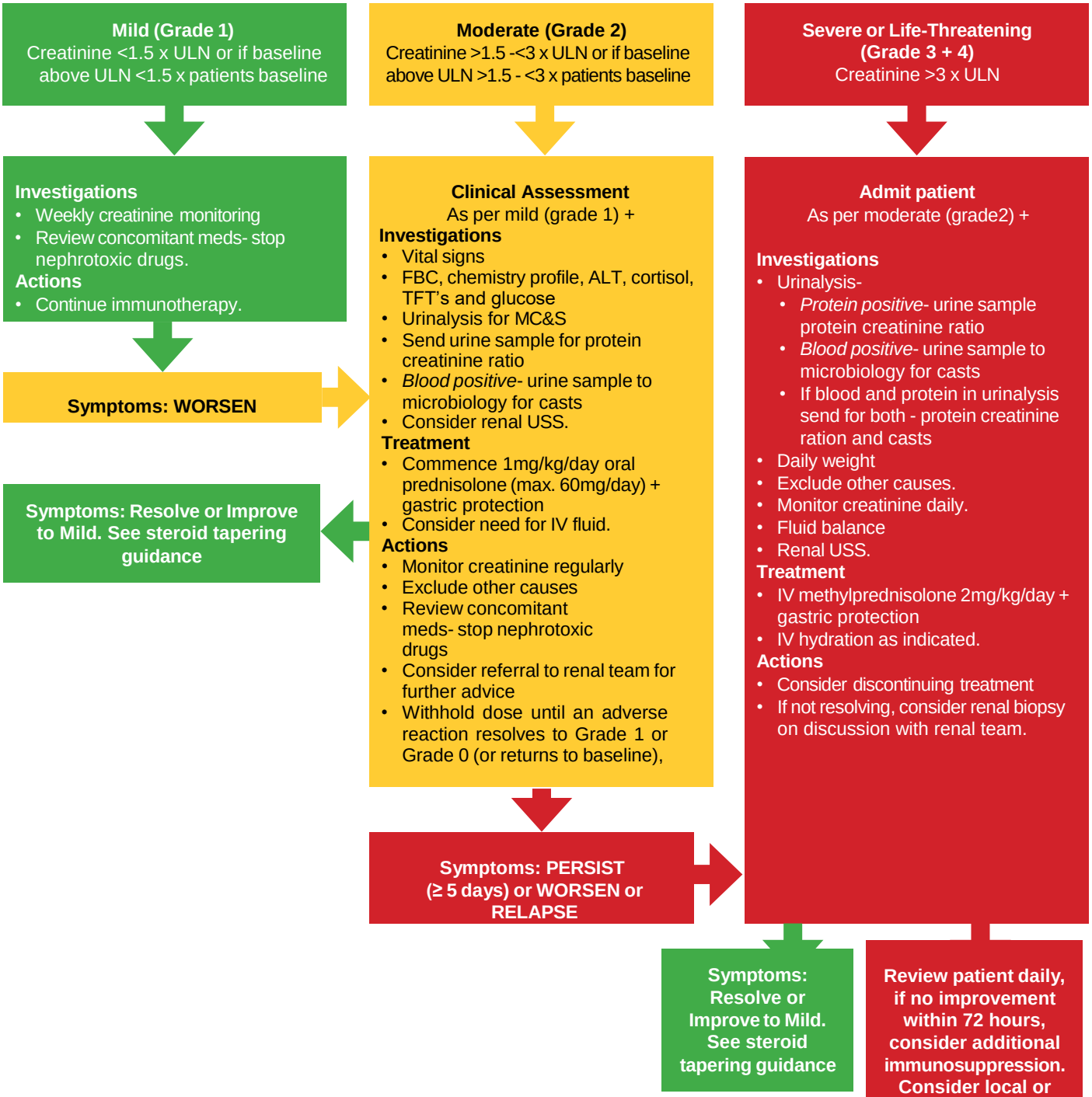
Interrupt SACT immunotherapy until discussed with Acute Oncology Team.
Please contact 24-Hour on-call oncology for advice.
A referral to a specialist may be required.

DR KATE CUSWORTH/DR JAMIE JOHNSTONE (Respiratory)

NHS Worcestershire Acute Hospitals NHS Trust

Immune-Related Adverse Event: Renal Toxicities

Renal function (urea and creatinine) must be evaluated before each dose of immunotherapy, as early laboratory changes may indicate emerging immune-related nephritis. Elevations in renal function may develop in the absence of clinical symptoms. This guidance should be used in context of baseline renal function and presence of known renal impairment. No dose adjustment is required for renal impairment but should be used in caution as per below in the presence of nephritis. Various histological nephritides have been identified in patients with IO induced nephritis. Patients should be closely monitored for elevation in U&Es from baseline. Patients with renal transplants receiving IO should be monitored closely for deterioration in renal function. Prior to commencement of immunotherapy all patients should have renal function checked.



Interrupt SACT immunotherapy until discussed with Acute Oncology Team.

Please contact 24-Hour on-call oncology team for advice.

Referral to a specialist may be required.
DR MARTIN FERRING (NEPHROLOGY)

NHS Worcestershire Acute Hospitals NHS Trust

Immune-Related Adverse Event: Skin Toxicities

Immunotherapy administration is associated with immune-related adverse events (irAEs). Dermatological irAEs common and although they are typically mild to moderate in severity, if they are left unrecognised or untreated, they can become life-threatening. These toxicities can be managed effectively in almost all patients by using established guidelines that stress vigilance and the use of corticosteroids and other immunosuppressive agents when necessary, consider the rule of nines.

Mild (Grade 1)
- Localised macular/Papular eruption
- Asymptomatic.

Treatment
- Emollient with paraffin content (eg Cetraben®)
- Consider anti-histamines- ideally non sedating

Actions
- Regular monitoring
- Continue immunotherapy.

Symptoms: WORSEN

Symptoms: Resolve or Improve to Mild. See steroid tapering guidance

Moderate (Grade 2)
- Rash affecting ≤ 50% skin surface
- Itchy
- Affecting ADL's/sleep.

Clinical Assessment

Investigations
- Vital signs
- FBC, chem profile, ALT, cortisol, TFT's and glucose
- Photograph rash (gain consent)
- Measure lesions.

Treatment
- Antihistamines- chlorpheniramine 4mg tablets qds
- Localised rash:
  - Betamethasone cream (eg Betnovate® cream bd)
  - Emollient with paraffin content (eg Cetraben®)
- Extensive rash:
  - Prednisolone - commence at 30mg OD and can be increased to 1mg/kg/day (max. 60mg/day) + gastric protection
  - Emollient with paraffin content (eg Cetraben®)
  - Betamethasone cream (eg Betnovate® cream bd).

Actions
- Withold treatment until ≤ grade 1
- Consider referral to local dermatology team
- Consider biopsy
- Monitor.

Symptoms: PERSIST (≥ 5 days) or WORSEN or RELAPSE

Severe or Life-Threatening (Grade 3 + 4)

Is defined as any of the following:
- >50% skin surface
- generalised
- exfoliative
- ulcerative
- bullous dermatitis.

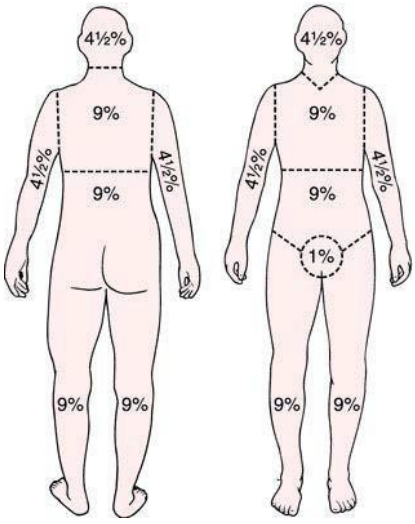
Admit patient

As per moderate (grade2) +

Investigations
- Antibiotics are not indicated unless there is a concern of recurrent infections and/or recommended by treating clinician.

Treatment
- Commence IV hydration
- IV methylprednisolone 2 mg/kg/day + gastric protection
- Regular vital signs and fluid balance
- Antihistamines- Chlorpheniramine 4mg QDS. Can add in fexofenadine Hydrochloride 120mg OD
- Emollient to 50:50 soft white paraffin (liquid paraffin).

Actions
- Consider discontinuing immunotherapy permanently.
- Urgent referral to local dermatology team for advice +/- biopsy
- Monitor daily.



The rule of Nines

Symptoms: Resolve or Improve to Mild. See steroid tapering guidance

Review patient daily, if no improvement within 72 hours, consider additional immunosuppression. Consider local or national subsequent management guidelines

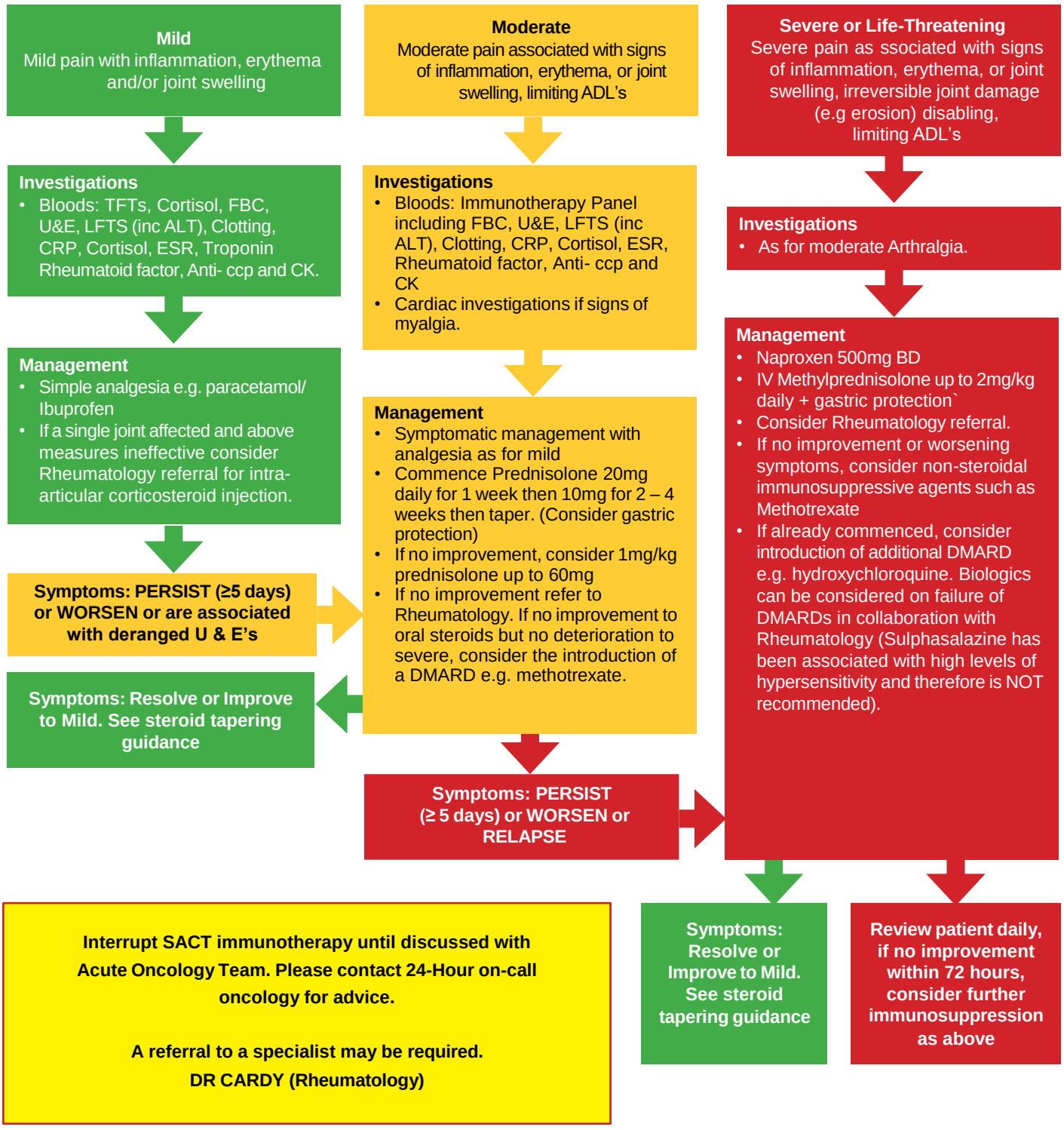
Interrupt SACT immunotherapy until discussed with Acute Oncology Team.
Please contact 24-Hour on-call oncology for advice.

A referral to a specialist may be required.
Contact for dermatology – DR SAILEESH CHALASANI.

Worcestershire Acute Hospitals NHS Trust

Immune-Related Adverse Event: Arthralgia/Myalgia

Arthralgia is an increasing recognised side effect of oncological immunotherapy. This may manifest with single joint involvement or multi-articular involvement with synovitis. Additionally, patients may develop myalgia which may go on to develop myositis. It is important to note that myositis can evolve into myocarditis and thus it is important to undertake the investigations recommended and monitor both symptomatic and biochemical responses to treatment. Patients often require non-steroid sparing agents so please implement the protocols for management of patients on these agents e.g. methotrexate and consider early referral to local rheumatology services.
NB Myalgia can be a sign of myositis, which can transform into Myocarditis therefore cardiac involvement should be excluded.



Worcestershire Acute Hospitals NHS Trust

Immune-Related Adverse Event: Myocarditis

Myocarditis is a recognised complication of immune checkpoint inhibitors. The majority of reported cases have occurred within the first month of therapy. Approximately 1% of patients treated with checkpoint inhibitors develop cardiotoxicity. Myocarditis is associated with a high mortality rate if not treated. It is common for patients to be asymptomatic/ have minimal symptoms and abnormal cardiac tests are significant.

Mild (Grade 1)

Clinically asymptomatic or presenting with fatigue/new pedal oedema

Cardiac enzymes

- **Trop T** is >14 and <30 ng/L **OR** elevated above baseline by <20 ng/L (if raised at baseline)
- **NT-Pro-BNP** is >500 <1000 ng/L.

Clinical Assessment

Investigations

- ECG
- Bloods (Troponin, NT-pro-BNP, Creatinine Kinase, FBC, U&Es
- Chest X-ray.

Actions

- Consider delay of immunotherapy
- Repeat ECG & bloods in 2 weeks
- Consider echocardiogram in the presence of pedal oedema.

Interrupt SACT immunotherapy until discussed with Acute Oncology Team. Please contact 24-Hour on-call oncology for advice.

A referral to a specialist may be required. DR WILSON (Cardiology)

Moderate (Grade 2)

New onset of symptoms with moderate exertion (e.g. Dyspnoea, chest pain, palpitations, peripheral oedema, pre-syncope, syncope) OR evidence of elevated cardiac enzymes/ECG changes even in the absence of symptoms

Cardiac Enzymes

- **Trop T** is >30 <100 ng/L **OR** elevated above baseline by >20 ng/L (if raised at baseline)
- **NT-Pro-BNP** is ≥1000 <3000 ng/L OR increased from baseline.

Clinical Assessment

As per mild (grade 1) plus

Investigations

- Echocardiogram
- Cardiac Magnetic Resonance Scan
- Infliximab screen
- TPMT Levels
- Whilst on IV steroids for Daily ECG and repeat cardiac markers.

Treatment

- IV Methylprednisolone 4mg/kg/day + gastric protection for 5/7. Taper to 2mg/kg/day for 3/7. Step down to Oral Prednisolone 1mg/kg. Review response and oral steroid taper (see tapering guidance)
- Consider ACEi +/- beta-blocker.
- If evidence of overload, consider diuretics
- If evidence of cardiac impairment refer for heart failure optimisation.

Actions

- Hold immunotherapy
- Consider hospital admission
- Consider referral to cardio-oncologist.

Severe or Life-Threatening (Grade 3 + 4)

New onset of severe symptoms at rest or with minimal exertion; intervention indicated

Cardiac Enzymes

- Trop T is ≥100 ng/L
- NT-Pro-BNP is ≥3000 ng/L.

Clinical Assessment

As per moderate (grade2) +

Treatment

- IV Methylprednisolone 1g + gastric protection for 3/7. Taper to 4mg/kg/day for 3/7. Taper to 2mg/kg/day for 3/7. Step down to Oral Prednisolone 1mg/kg. Review response and oral steroid taper (see tapering guidance)
- Supportive therapy (inotropes, anti-arrhythmics*) and as for grade 2.

Actions

- Stop immunotherapy
- Consider whether patient requires admission to CCU/HDU and their ceilings of care
- Refer to cardio-oncologist and IO Clinician
- Consider Mycophenolate or Tacrolimus, in patients not responding optimally to high dose steroids
- If limited response, consider biologic e.g. Infliximab, Tocilizumab or abatacept. A further DMARD e.g. azathioprine, could also be considered
- Consider local or national subsequent management guidelines

**If anti-arrhythmics are required amiodarone should be avoided if possible and only used on discussion with immunotherapy specialist due to the risk of pneumonitis.*

Steroid Tapering Guidance

Many patients will receive moderate- to high-dose steroid therapy for their immune-related toxicity for several weeks. Length of tapering is usually dictated by the severity of the irAE. Regular monitoring during tapering is strongly advised as there is an increased risk of irAE recurrence.

Oral steroid tapering
Initiate corticosteroid taper over 3-6 weeks

Tapering guidance
- Monitor patient during taper
- Reduce prednisolone dose by 10mg every 3 days (as toxicity allows) until dose is 10mg/day
- Once steroid dose is 10mg/day continue for 5 days then reduce to 5mg for 5 days then stop
- **Please provide full course of steroid tapering.**

ALL PATIENTS SHOULD HAVE A 9AM CORTISOL CHECKED WITHIN THE 5-7 DAYS FOLLOWING COMPLETION OF THEIR STEROID TAPER

Intravenous steroid tapering
Corticosteroid taper over at least 3-6 weeks

Tapering guidance
- Continue IV methylprednisolone 2mg/kg/day for a total of 5 days then switch to oral prednisolone 60mg/day
- If following a re-flare and reintroduction of IV steroids reduce to 1mg/kg/day of prednisolone PO for 3 days, then commence taper
- Upon discharge
  - Monitor patient during taper
  - Reduce prednisolone dose by 10mg every 5 days (as toxicity allows) until dose is 10mg/day
  - Once steroid dose is 10mg/day, reduce by 5mg for 5 days then stop
- **Please provide full course of steroid tapering.**

Supportive measures

Hyperglycaemia

A baseline HbA1c should be requested at steroid initiation and random blood sugar monitoring (BM) alongside biochemical monitoring should be undertaken whilst on treatment. If new hyperglycemia is detected, then the UK Chemotherapy Board and The Joint British Societies for Inpatient care joint guideline on the management of glycaemic control in patients with cancer should be followed including advice from local endocrinology teams. Patients may require oral anti-diabetic medication or insulin in the short term.

Insomnia

This is the most common steroid-related side effect. Sleep hygiene counselling is important. Patients may require short-term use of zopiclone (benzodiazepines should only be considered in rare circumstances for a max 3-5 days). Patients should be counseled about the importance of early morning steroid administration.

Osteoporosis

Vitamin D and calcium levels should be taken at baseline and if low, replaced as appropriate. In patients on steroids for >3 months, or with pre-existing osteoporosis, a bone density scan and AdcalD3 and alendronate (or another bisphosphonate should be considered).

Infection

In patients receiving the equivalent of prednisolone 25mg for > 6 weeks or 2 or more immunosuppressant's, PCP prophylaxis with co-trimoxazole (800/160mg Mon/Wed/Fri) should be considered (incidence of PCP in this patient group is very low).

The oropharynx should be monitored for candidiasis and may require topical therapy such as Nystatin or oral antifungals. Azole antifungals commonly cause hepatitis and so should be used with caution in prophylactic setting.

If patients are on other immuno-modulatory agents e.g. Mycophenylate mofetil (MMF), consideration may be given to CMV prophylaxis with gancyclovir, especially if CMV IgG negative and lymphopenic. Acyclovir prophylaxis should be considered in patients who are immune-suppressed and have required treatment for oral viral infection.

General

Ensure all patients are given a national Steroid Alert Card when commencing on corticosteroids.

Ensure steroid sick day rules are implemented as required.

IF PATIENT CANNOT TAKE STEROIDS FOR ANY REASON, THEY SHOULD SEEK URGENT ADVICE VIA AOS/ IMMUNOTHERAPY TEAM/ ON CALL ONCOLOGY TEAM

5. ONGOING MANAGEMENT

Treatment should be withheld for patients suffering any grade 2 or above toxicity.

The ongoing management will be co-ordinated by the consultant oncologist in charge of the patients care.

6. CONTACT NUMBERS FOR ADVICE

Acute Oncology Service 24 hours a day, 7 days a week	01905 760158 / 30049
Acute Oncology Nurse Practitioners (Mon-Fri 0900-1700)	Ext 30058 WRH Bleep 398 or 491 Alex Bleep 0192
Oncology Consultant On-call (24 hours)	Via Switchboard

7. TRAINING

Oncology consultant presentation to acute medical staff and oncology medical team.

Training for nursing staff covering OOH acute oncology service by acute oncology nurses.

Training regarding administration and management of side effects is also included in the annual chemotherapy update for nurses and pharmacists (training for pharmacists through in house training program).

8. REFERENCES

https://www.medicines.org.uk/emc/medicine/30476

Home :: The Clatterbridge Cancer Centre (clatterbridgecc.nhs.uk)

Please note these guidelines have been adapted using UKONS Immunotherapy toxicity guidelines 2023
ukons_ao_initial_management_guidelines_final_version_2023.pdf

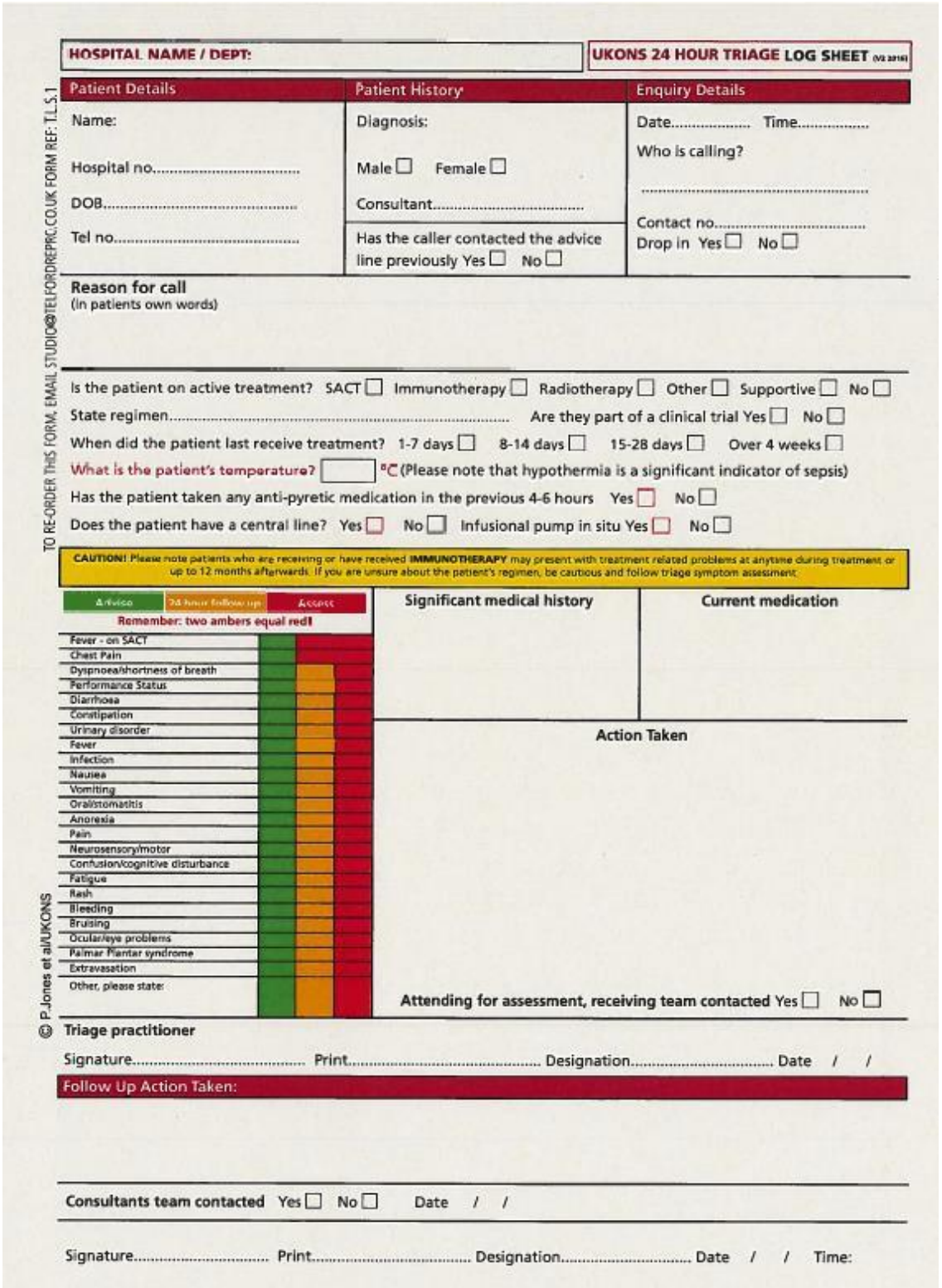
CT CAE grading criteria
Common Terminology Criteria for Adverse Events (CTCAE) | Protocol Development | CTEP (cancer.gov)

With Thanks for Nicola Jones UHB Chemotherapy lead for sharing Patient and GP letters

9. MONITORING TOOL

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
	All patients with immune-related reactions receive appropriate and timely management	Audit to monitor compliance with guidance after 6 months	After 6 months	Immunotherapy nurse / Lead Chemotherapy Nurse	Haematology/Oncology directorate	Annually by IO/AOS team

Appendix 1 – Triage Tool



HOSPITAL NAME / DEPT:

UKONS 24 HOUR TRIAGE LOG SHEET (V2 2016)

TO RE-ORDER THIS FORM, EMAIL STUDIO@TELFORDREPRO.CO.UK FORM REF: T.L.S.1

Patient Details	Patient History	Enquiry Details
Name: Hospital no..... DOB..... Tel no.....	Diagnosis: Male ☐ Female ☐ Consultant..... Has the caller contacted the advice line previously Yes ☐ No ☐	Date..... Time..... Who is calling? ..... Contact no..... Drop in Yes ☐ No ☐

Reason for call
(In patients own words)

Is the patient on active treatment? SACT ☐ Immunotherapy ☐ Radiotherapy ☐ Other ☐ Supportive ☐ No ☐

State regimen..... Are they part of a clinical trial Yes ☐ No ☐

When did the patient last receive treatment? 1-7 days ☐ 8-14 days ☐ 15-28 days ☐ Over 4 weeks ☐

What is the patient's temperature? ☐ °C (Please note that hypothermia is a significant indicator of sepsis)

Has the patient taken any anti-pyretic medication in the previous 4-6 hours Yes ☐ No ☐

Does the patient have a central line? Yes ☐ No ☐ Infusional pump in situ Yes ☐ No ☐

CAUTION! Please note patients who are receiving or have received **IMMUNOTHERAPY** may present with treatment related problems at anytime during treatment or up to 12 months afterwards. If you are unsure about the patient's regimen, be cautious and follow triage symptom assessment.

	Advise	24 hour follow up	Assess
Remember: two ambers equal red!			
Fever - on SACT			
Chest Pain			
Dyspnoea/shortness of breath			
Performance Status			
Diarrhoea			
Constipation			
Urinary disorder			
Fever			
Infection			
Nausea			
Vomiting			
Oral/stomatitis			
Anorexia			
Pain			
Neurosensory/motor			
Confusion/cognitive disturbance			
Fatigue			
Rash			
Bleeding			
Bruising			
Ocular/eye problems			
Palmar Plantar syndrome			
Extravasation			
Other, please state:			

Significant medical history

Current medication

Action Taken

Attending for assessment, receiving team contacted Yes ☐ No ☐

© P Jones et al/UKONS

Triage practitioner

Signature..... Print..... Designation..... Date / /

Follow Up Action Taken:

Consultants team contacted Yes ☐ No ☐ Date / /

Signature..... Print..... Designation..... Date / / Time:

Appendix 2 – Patient letter for Immunotherapy

PATIENT LETTER

Please always carry this letter with you and show it to any Healthcare professional you are seen by.

Dear (Affix Sticker)

You are due to commence Immunotherapy under the care of.....(Consultant's name & place of work) on ……..

The Immunotherapy drug/s name is/are

Immunotherapy can cause serious side effects.

If you experience any of the following symptoms you should contact the Acute Oncology service from the alert card given to you.

- **Diarrhoea (more than 3 episodes of diarrhoea in a 24 hour period) or blood or mucus in stools, cramps or stomach pains**
- **Cough / Acute shortness of breath developed over a few days**
- **Extreme tiredness alongside dizziness**
- **Loss of limb movement**

There is a risk for developing Sepsis which could be life threatening. In case you develop any of the symptoms mentioned below, you should contact the Acute oncology service from the alert card.

- **Fever / temperature**
- **Any sign of infection**
- **Shivers, shakes or flu like symptoms**
- **Excessive bruising or bleeding from anywhere**
- **Generally feeling dreadful for no specific reason**
- **Severe vomiting, diarrhoea or exhaustion**

The acute oncology emergency number is 01905 760158.

Thank you

Signed ……. Name…….

Title…….

Appendix 3 – Alert card

Fold line -->

Outside of card

URGENT ADVICE FOR CLINICIANS

This patient is on immunotherapy and may be at risk of developing autoimmune side effects which require urgent treatment with corticosteroids.

These may include: diarrhoea and colitis, pituitary and thyroid dysfunction, hepatotoxicity, neuropathy, pneumonitis, renal toxicities and skin rashes.

Within Worcester Acute Hospitals Trust please refer to management of immune-related adverse events in immunotherapy guidelines on Intranet. For community or other Hospitals please contact the acute oncology service on the reverse of the card.

WAHT-CS-094 - Version 1

Patient

NHS
Worcestershire Acute Hospitals NHS Trust

I am currently receiving

IMMUNOTHERAPY
Alert card

I am or have received Immunotherapy for cancer and may be at risk of Immune-related-Adverse Events which require urgent treatment.

Please contact the Acute Oncology service **01905 760158** and ask for switchboard to **Bleep 398**

On Presentation to the hospital, please follow the Management Instructions inside this card.

Fold line -->

Inside of card

Patient

Contact Telephone Number

Acute Oncology Service

01905 760158

24hrs a day

URGENT

You must contact the acute oncology service immediately if you experience any of the following:

- Diarrhoea or blood or mucus in stools, cramps or stomach pains -more than 3 episodes in a 24 hour period
- Cough / Acute shortness of breath -developed over a few days
- Extreme tiredness alongside dizziness
- Muscle weakness, pins & needles

Clinician

IMMUNE RELATED ADVERSE REACTIONS MANAGEMENT

Contact the On-Call Oncologist Immediately

Immune related adverse reactions can occur at anytime during treatment and up to 12 months after treatment has completed.

Please attach ID label or write details.

Patient's Name .....

Address .....

.....

Telephone .....

Hospital Record Number .....

Name of Treatment .....

Supporting Document 1 – Equality Impact Assessment form

To be completed by the key document author and included as an appendix to key document when submitted to the appropriate committee for consideration and approval.

Please complete assessment form on next page;

Herefordshire & Worcestershire STP - Equality Impact Assessment (EIA) Form
Please read EIA guidelines when completing this form

Section 1 - Name of Organisation (please tick)

Herefordshire & Worcestershire STP		Herefordshire Council		Herefordshire CCG	
Worcestershire Acute Hospitals NHS Trust	x	Worcestershire County Council		Worcestershire CCGs	
Worcestershire Health and Care NHS Trust		Wye Valley NHS Trust		Other (please state)	

Name of Lead for Activity	**Helen Grist**

Details of individuals completing this assessment	**Name**	**Job title**	**e-mail contact**
	Helen Grist	**SACT ACP Immunotherapy lead**	**h.grist@nhs.net**
Date assessment completed			

Section 2

Activity being assessed (e.g. policy/procedure, document, service redesign, policy, strategy etc.)	**Title: Guideline for the management of immune related adverse reactions following immunotherapy treatment**
What is the aim, purpose and/or intended outcomes of this Activity?	This guideline refers to the management of immunotherapy induced adverse reactions. encompasses the pathway of care to follow, when a patient over the age of 16 who has received immunotherapy in adult services, presents to Worcestershire Acute Hospitals NHS Trus

Who will be affected by the development & implementation of this activity?	❑ x ❑ ❑	Service User Patient Carers Visitors	x ❑ ❑ ❑	Staff Communities Other _____
Is this:	x Review of an existing activity ❑ New activity ❑ Planning to withdraw or reduce a service, activity or presence?			
What information and evidence have you reviewed to help inform this assessment? (Please name sources, eg demographic information for patients / services / staff groups affected, complaints etc.				
Summary of engagement or consultation undertaken (e.g. who and how have you engaged with, or why do you believe this is not required)				
Summary of relevant findings				

Section 3

Please consider the potential impact of this activity (during development & implementation) on each of the equality groups outlined below. **Please tick one or more impact box below for each Equality Group and explain your rationale**. Please note it is possible for the potential impact to be both positive and negative within the same equality group and this should be recorded. Remember to consider the impact on e.g. staff, public, patients, carers etc. in these equality groups.

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Age		x		
Disability		x		
Gender Reassignment		x		
Marriage & Civil Partnerships		x		
Pregnancy & Maternity		x		
Race including Traveling Communities		x		
Religion & Belief		x		
Sex		x		

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Sexual Orientation		x		
Other Vulnerable and Disadvantaged Groups (e.g. carers; care leavers; homeless; Social/Economic deprivation, travelling communities etc.)		x		
Health Inequalities (any preventable, unfair & unjust differences in health status between groups, populations or individuals that arise from the unequal distribution of social, environmental & economic conditions within societies)		x		

Section 4

What actions will you take to mitigate any potential negative impacts?	Risk identified	Actions required to reduce / eliminate negative impact	Who will lead on the action?	Timeframe
		.		
How will you monitor these actions?				
When will you review this EIA? (e.g in a service redesign, this EIA should be revisited regularly throughout the design & implementation)				

Section 5 - Please read and agree to the following Equality Statement

1. Equality Statement

1.1. All public bodies have a statutory duty under the Equality Act 2010 to set out arrangements to assess and consult on how their policies and functions impact on the 9 protected characteristics: Age; Disability; Gender Reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual Orientation

1.2. Our Organisations will challenge discrimination, promote equality, respect human rights, and aims to design and implement services, policies and measures that meet the diverse needs of our service, and population, ensuring that none are placed at a disadvantage over others.

1.3. All staff are expected to deliver services and provide services and care in a manner which respects the individuality of service users, patients, carer's etc, and as such treat them and members of the workforce respectfully, paying due regard to the 9 protected characteristics.

Signature of person completing EIA	
Date signed	
Comments:	
Signature of person the Leader Person for this activity	
Date signed	
Comments:	

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue	No
3.	Does the implementation of this document require additional manpower	No
4.	Does the implementation of this document release any manpower costs through a change in practice	No
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	No
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval