# Neurological Immune-Related Adverse Event Management Algorithm (1)

| Grading of neurological symptoms | Action | Follow up |
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| **Grade 1**[a]<br><br>For example:<br>*- Reduced motor or sensory function in limbs (e.g. peripheral neuropathy)*<br>*- Muscle or neuropathic pain (no or minimal effect on ADLs)* | **Investigations**<br>• Urgent neurology referral<br>• Measure creatine kinase<br>• Swallow and respiratory assessment<br><br>**Management**<br>• Hold I-O therapy until grade confirmed (continue I-O therapy only if confirmed G1)<br>• Close monitoring of symptoms | **If worsens:**<br>• Treat as G2 or above |
| **Grade 2**<br><br>For example:<br>*- Features of peripheral neuropathy which have some effect on ADLs or otherwise causes symptoms concerning to the patient such as pain*<br>*- Features of myasthenia or myopathy with ocular symptoms or mild generalised weakness only*<br>*- Autonomic neuropathy which has some effect on ADLs* | **Investigations**<br>• Urgent neurology referral<br>• Measure creatine kinase<br>• Swallow and respiratory assessment<br><br>**Management**<br>• Delay I-O therapy [b]<br>• Commence oral prednisolone (0.5 - 1mg/kg, max 60mg OD) with PPI cover<br>• If symptoms improve, wean steroids as per regime below (wean over at least 1 month) [c] | **If no improvement:**<br>• Commence methylprednisolone 1-2mg/kg/day IV or oral<br>• Rediscuss with neurology |
| **Grade 3 – 4**<br>Severe or life-threatening symptoms<br><br>*For example:*<br>*- Guillain-Barre type syndrome*<br>*- Myasthenia gravis or myositis with any dysphagia, facial weakness, respiratory muscle weakness or rapidly progressive symptoms*<br>*- Transverse myelitis*<br>*- Brainstem or brain syndromes* | **Investigations**<br>• As per G1/2<br>• Admit to hospital<br>• Autoantibody tests<br>Consider the following as appropriate:<br>• MRI head and spinal cord<br>• NCS and EMG<br>• MRI muscles<br><br>**Management**<br>• See specific algorithms overleaf<br>• Discontinue I-O therapy<br>• Commence methylprednisolone 1-2mg/kg/day IV or oral<br>• Daily neurological assessment | **If no improvement:**<br>• Consider IVIg or plasmapheresis following consultation with neurology [d]<br>• For life-threatening symptoms, consider methylprednisolone 1g IV for 3-5 days |

*[a]Note that suspected Myasthenia Gravis or Guillain-Barre like syndromes cannot be Grade 1. Please see specific algorithm overleaf.*
*[b]Only consider re-challenge with I-O therapy if:*
1. *Patient had confirmed G1 - 2 symptoms*
2. *Symptoms improved or stabilised on low dose or no steroids*
3. *Patient had a convincing response to I-O therapy prior to the development of G1 - 2 symptoms*

*[c]Consider bone protection (with AdCalD3 +/- bisphosphonates), BM monitoring and PCP prophylaxis in patients with prolonged high dose steroids.*
*[d]Consider IVIg (2g/kg cumulative dose split over 3-5 days) or plasmapheresis (PLEX, 5-7 sessions) if rapidly progressing symptoms*

# Neurological Immune-Related Adverse Event Management Algorithm (2)

| Suspected neurological syndrome | Investigations | Management |
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| **Myasthenia Gravis or myositis**<br><br>*Suspect in patients with symptoms such as new proximal muscle weakness, ptosis, diplopia, dysphagia, slurred speech, neck or facial muscle weakness, respiratory muscle weakness (sometimes muscle pain in myositis)* | • Urgent neurology advice<br>• Swallow and respiratory assessment (FVC)<br>• Measure AChR and MuSK antibodies, creatine kinase, myositis antibody screen<br>• Consider MRI head +/- cervical spine to exclude alternative diagnoses<br>• Consider troponin + ECG to exclude concurrent myositis<br>• Consider nerve conduction studies/ EMG following consultation with neurology | • Hold I-O therapy<br>• Admission to hospital as patients can deteriorate rapidly<br>• Commence pyridostigmine 30mg PO TDS following neurology review (can gradually increase to up to 120mg PO QDS max based on symptoms, response and tolerance)<br>• Commence oral prednisolone 0.5mg/kg/day. Wean based on neurology advice.<br>• If severe symptoms- IVIG or plasmapheresis with likely ITU admission. |
| **Guillain-Barre Syndrome**<br><br>*Suspect in patients with (usually ascending) symptoms such as new bilateral weakness, sensory changes, areflexia, dysphagia, respiratory muscle weakness, autonomic dysfunction* | • Urgent neurology advice<br>• Swallow and respiratory assessment (FVC)<br>• Consider MRI whole spine to exclude compressive lesion<br>• Consider lumbar puncture (inc. cell count and differential, protein, glucose, bacterial MCS +/- virology & cytology)<br>• Consider paraneoplastic workup, serum antiganglioside<br>• Consider nerve conduction studies following consultation with neurology | • Hold I-O therapy<br>• Regularly reassess neurology<br>• Admit to hospital capable of rapid transfer to ITU setting<br>• Commence IVIg (2g/kg ideal weight dose split over 5 days)<br>• Whilst steroids are not usually recommended for idiopathic GBS, trial of steroids can be considered for suspected immunotherapy induced GBS e.g. 2-4mg/kg/day IV methylprednisolone or 1g for G3/4 with IVIG or PLEX |
| **Demyelinating diseases including multiple sclerosis, transverse myelitis**<br><br>*Suspect if symptoms such as new weakness, sensory changes, impaired coordination, brainstem syndromes (oculomotor changes or facial/ trigeminal deficits), acute loss of vision.* | • Urgent neurology advice<br>• MRI brain / spine with contrast<br>• Consider lumbar puncture (inc. oligoclonal bands, autoimmune panel)<br>• Consider B12, copper, HIV, syphilis, CMV, ANA, TSH, AQP-4 IgG, MOG-IgG, neuronal antibodies (for paraneoplastic syndromes) | • Hold I-O therapy<br>• Commence methylprednisolone 2mg/kg (or consider 1g/ day)<br>• Consider IVIg or PLEX if no improvement or worsening of symptoms after 3 days following consultation with neurology |
| **Aseptic meningitis / encephalitis**<br><br>*Aseptic meningitis - suspect in patients with fever, headache, neck stiffness, nausea*<br><br>*Encephalitis - suspect in patients with fever, headache, new confusion, seizures, drowsiness, focal neurological deficits* | • Urgent neurology advice<br>• MRI head with contrast<br>• Consider lumbar puncture (inc. opening pressure, cell count and differential, protein, glucose, bacterial MCS +/- virology and cytology)<br>• Consider autoimmune and paraneoplastic panels<br>• Consider 9am cortisol and ACTH to exclude adrenal insufficiency | • Hold I-O therapy<br>• Empiric antibiotic and antiviral therapy pending PCR results<br>• Commence oral prednisolone 0.5-1mg/kg/day (max 60mg OD) or IV methylprednisolone 1-2mg/kg/day. Exclude bacterial and viral infections before starting high dose steroids<br>• For refractory encephalitis, consider methylprednisolone 1g/day for 3 days +/- IVIg or PLEX following neurology discussion |

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