<table>
<thead>
<tr>
<th>Immune-related adverse events systems review</th>
<th>Name:</th>
<th>DOB:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tick all of the boxes for symptoms you have at the moment; a family member can help you complete the form too.</td>
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</tbody>
</table>

### General:
- [ ] Fever
- [ ] Change in weight?
  - Current weight ........kg
- [ ] Extreme tiredness or weakness

### Musculoskeletal:
- [ ] Joint pain
  - Better or worse with exercise?
- [ ] Joint swelling
- [ ] Morning stiffness:
  - Lasts how long?
  - Minutes....... Hours......
- [ ] Muscle weakness
- [ ] Muscle pain
- [ ] Very dry eyes or mouth
- [ ] Tick all painful/swollen joint on stick man on reverse

### Skin:
- [ ] Rash
- [ ] Blistering
- [ ] Peeling off

### Abdomen:
- [ ] Pain
- [ ] Severe nausea/vomiting
- [ ] Constipated
- [ ] Dark urine (tea coloured)
- [ ] Yellowing of skin or eyes
- [ ] Severe diarrhoea?
- [ ] Blood in stools?

### Lungs:
- [ ] Short of breath walking
- [ ] Short of breath sitting
- [ ] Cough
- [ ] Cough up phlegm or blood

### Glands & hormones:
- [ ] Increased sweating

### Nervous system:
- [ ] Feeling more hungry or thirsty than usual
- [ ] Hair loss
- [ ] Urinating more than usual

### Circulation:
- [ ] Fits or seizures
- [ ] Look very pale
- [ ] Bleeding anywhere
- [ ] Easy bruising

### Heart:
- [ ] Chest pain
- [ ] Palpitations
- [ ] Ankle swelling
- [ ] Wake up short of breath

### Eyes:
- [ ] Red painful eye
- [ ] Eyelid swelling
- [ ] Blurred vision
- [ ] Change in colour vision
- [ ] Double vision
- [ ] Lost part of vision
Appendix 1 continued.

**Musculoskeletal symptoms:** These symptoms will occur in up to 40% of patients receiving immune checkpoint inhibitors [4].

**Two distinct phenotypes exist:** Inflammatory arthritis (3.8%), mainly rheumatoid arthritis, polymyalgia rheumatica or psoriatic arthritis, and non-inflammatory musculoskeletal conditions (2.8%). Myalgia is also common [4].

**Features suggestive of inflammatory arthritis:** Joint pain, swelling, tenderness and erythema. Early morning stiffness persisting for >30 minutes, arthralgia worsens with inactivity and improves with exercise, NSAIDs and corticosteroids. Symptoms for >six weeks.

**Examination:** All peripheral joints and spine for boggy swelling, tenderness and range of movement.

**Investigations:** Consider autoimmune bloods ANA, ENA, dsDNA (lupus), RF, anti-CCP (RA), CRP, ESR ± HLA B27 (spine involved or suspect reactive arthritis).

Consider joint aspirate if suspect septic arthritis, gout or pseudogout.

Consider XRAYs to exclude metastases and looks for joint erosions ± ultrasound or MRI to detect subtle synovitis.

Non-inflammatory musculoskeletal arthralgia can be managed with paracetamol NSAIDs ± physiotherapy.

**Management of inflammatory arthritis [8]:**

Grade 1: paracetamol, NSAIDs. Continue ICI.
Grade 2*: Increase NSAID dose or add oral prednisone 10-20 mg/d for four to six weeks. May offer intra-articular corticosteroid injections if one to two joints involved. Withhold ICI until on prednisone ≤ 10 mg/d. If no improvement after four to six, treat as grade 3. If can't wean to <10 mg/d after three months, may require DMARD.

Grade 3* and 4*: Prednisolone 0.5-1mg/kg/d. If no improvement of worsening after four weeks of prednisolone, consider synthetic (methotrexate, leflunomide) or biologic (anti-TNF or IL-6) DMARD.

*Rheumatology referral recommended if there is joint swelling AND tenderness (synovitis), arthralgia persists>four weeks or Grade 2-4 toxicity. Repeat joint exam and inflammatory markers every four to six weeks after treatment is initiated.