RHEUMATOLOGY

GUIDE & HANDBOOK

RHEUMATOLOGY UNIT, HOSPITAL SELAYANG

Guide & Handbook

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Chapter

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Introduction

A very warm welcome to the Rheumatology Unit

This guide and handbook is to aid trainees and medical officers (MOs) that join the rheumatology unit. Similar to most rheumatology units in other states, the rheumatology unit at Hospital Selayang offers inpatient, outpatient and daycare Rheumatology services. Hence, the trainee and MOs will be rotated to these services, as well as to the 'periphery' rotation, which are to manage referrals and patients admitted to other wards. The unit is a very busy one and may seem rather daunting to the fresh trainee or uninitiated MO. We hope that this concise handbook and guide will equip you with the necessary knowledge needed for the day to day practice in the unit.

Although this guide and handbook will provide you with all the basic information you need, it is not meant to be a textbook of Rheumatology. Importantly, please do not hesitate to ask any of your fellow trainees or consultants if you have any doubts or if the information you need is not available here.

Teamwork is of utmost importance and we also work closely with other allied health professionals for the wellbeing of our patients. Whether you are joining us for your training programme, short attachment or as part of your rotation, we hope you will get to learn in a friendly and supportive environment.

Rheumatology Team

The team consists of senior consultants, consultants, fellows, specialist nurses, medical officers, house officers, specialist pharmacists, physiotherapists, occupational therapists, social workers and dietitians

Rotations during your attachment:

Clinic	Ward (10B)
Periphery & clinic	Daycare and clinic

Inpatient service

Patients may be admitted either for flare of disease, infections, rehabilitation or for investigations. They may be admitted directly from the clinic, or referred from the emergency department. We also accept direct transfers from other hospitals, but please ensure that a bed has been booked for the patient. When the ward is full, our priority is for our own inpatients. The following are several guidelines regarding ward patients:

- **Patients with active TB** should not be admitted to the rheumatology ward
- **Patients who are very immunocompromised** should be isolated (eg neutropaenic sepsis, on strong immunosuppression eg cyclophosphamide)

The trainee and MO who is in charge of the ward is expected to do ward rounds twice daily and whenever the need arises (eg. If a new case has been admitted or if an in-patient turns ill). Grand rounds are once a week, usually on a Friday and all trainees are expected to follow the rounds.

Outpatient service

There are clinics every day. The trainee and MO rotated to the clinic will have to start clinics at 8am whereas the trainee and MO in-charge of periphery patients will help to run the clinic after the rounds and other duties are done. The trainee rotated to the ward will also be expected to see outpatients once ward issues are settled. The unit receives many referrals daily and the on-call trainee will need to assign the time slots for the appointment as well as decide what investigations are needed prior to the first clinic visit.

CLINICS

- CTD *Mon am*
- RA *Tues &Thurs am*
- SpA/PsA/Metab *Thurs am*
- MSK US *Tues PM*
- Comb Resp *2nd Tues PM*
- Comb Obs *1st Wed AM*
- Biologic *3rd/4th Wed AM*
- MO rv *Wed&Thurs*
- Transition *3rd Wed AM*

The following is a brief guide regarding scheduling:

- In general, referred cases should be given an appointment within 1 month
- Patients referred from other rheumatology centres for continuation of care may be given an appointment within 2 to 3 months if there are no immediate issues
- Patients who require urgent review may be given appointments within 1 to 2 weeks but slots per day are limited
- Very urgent review (walk-in cases) may be allowed if urgently required (eg. Flare of disease, adverse reaction to medications etc)
- Teleconsultation (currently using phone consult) was initiated due to the COVID-19 pandemic. Patients will still need to be seen face to face at least once a year. Suitable patients are:

    1. Stable patients in remission who do not need medication adjustment
    2. Patients with osteoporosis who are otherwise stable
    3. Patients with many clinic appointments and who will be seen at other clinics periodically eg nephro/derm/medical

CONNECTIVE TISSUE DISEASE (CTD)

Types of diseases seen at the clinic:

- Systemic Lupus Erythematosus (SLE)
- Primary Vasculitis (Giant cell arteritis, Takayasu arteritis, Polyarteritis nodosa, Granulomatosis with Polyangiitis or GPA, Microscopic Polyangiitis, Behcet's disease)
- Systemic sclerosis (SSc)
- Mixed connective tissue disease (MCTD)
- Primary Anti-phospholipid Syndrome
- Primary Sjogren's syndrome

- Ensure all women of child-bearing age have contraceptive advice and pre-pregnancy counseling
- Appointments are generally 3 to 4 monthly unless patient has a flare or other issues
- All patients with interstitial lung disease need yearly influenza vaccination and 5 yearly pneumococcal vaccination

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

- Fever can be a manifestation of active lupus, infection, malignancy or drug reaction. Always rule out infection first in any patient presenting with fever
- Standard investigations include: - FBC, renal profile, ESR, CRP, complements, liver function tests, creatine kinase, ufeme, chest xray, please refer to ***Appendix 5 Investigations*** for guidance on immunological tests
- Send ufeme regularly and if protein is present, quantify the 24 hour urine protein; refer nephrologist if 24 hour urine protein is >0.5g and/or renal profile is abnormal
- Patients suspected to have neuropsychiatric lupus need a baseline Mini mental state examination (MMSE) – please refer ***Appendix 2 Disease Activity Assessments***
- All SLE patients have to be on Hydroxychloroquine unless contraindicated or intolerant – please refer ***Appendix 3 DMARDs***
- If a patient is admitted for serious infection, with-hold immunosuppressive therapy (if patient was prescribed the immmunosuppresive medication due to other reasons, please inform the treating team eg lupus nephritis on MMF, please inform nephrology team prior to stopping the medication)

- Do not stop steroids abruptly in patients who have been on long-term steroids (to avoid Addisonian crisis); if patient is admitted for serious infection or invasive procedures eg surgery, in general, the steroid dose is doubled (to cover for stress) unless the steroid dose needs to be higher to treat for concurrent flare (please discuss with Consultant)
- If patient is unable to take orally and oral steroid needs to be converted to IV, please refer to the steroid conversion table ***Appendix 4 Other Drugs***
- All patients who require moderate to high dose long-term steroids (>5mg >3months), require osteoporosis prophylaxis with calcium and vitamin D

SYSTEMIC SCLEROSIS/MIXED CONNECTIVE TISSUE DISEASE

- Patients with systemic sclerosis and Mixed connective tissue disease need to be seen at least once at the Combined Respiratory Clinic for cardiorespiratory screen preferably within 1 year of diagnosis
- Patients with pulmonary hypertension who require combined care with cardiologist, should be referred to the Combined PAH clinic at Hospital Serdang (runs every 1st Thursday of the month). Please provide a complete referral letter, refer to ***Appendix 8 Combined PAH Clinic Referral letter template***

Primary Antiphospholipid Syndrome

- Schedule INR monitoring at the medical INR clinic
- Clinic appointments may be given 4 to 6 monthly depending on patient's condition and other issues
- Guidance for procedures:
  - **patient at very high risk of thrombosis:** with-hold warfarin, once INR is below therapeutic range, start LMWH; with-hold LMWH 6 hours prior to procedure; reinstate LMWH and warfarin concurrently once procedure is completed and no excessive bleeding present; stop LMWH once INR is within therapeutic range
  - **usual patient:** with-hold warfarin 3 days prior to procedure, check INR, may proceed if INR is normal; reinstate warfarin once procedure is completed and no excessive bleeding present

RHEUMATOID ARTHRITIS CLINIC

- Baseline investigations include FBC, renal profile, liver function tests, ESR, CRP, rheumatoid factor, anti-CCP antibody; at subsequent visits, investigations will depend on the DMARDs patient is on; ESR and/or CRP will be required for disease activity measures

- Send Hepatitis Bs Ag and Hepatitis C Ab prior to starting MTX – if positive, refer to hepatology, KIV for initiation of anti-viral (please send viral screen too for patients already on MTX, referred from other centres, if the results are not provided in the referral letter)
- All patients require baseline CXR, hands and feet (minimum) and other joint xrays if involved then yearly (unless in remission)
- Please perform disease activity measures at each clinic visit – refer to ***Appendix 2 Disease activity measures***
- All newly diagnosed patients need to be started on DMARDs within 1 month of diagnosis. For guidance on starting DMARDs and monitoring, please refer to ***Appendix 3 DMARDs***
- Ensure all women of child-bearing age have contraceptive advice if started on Methotrexate or Leflunomide, please refer to ***Appendix 3 DMARDs***
- Patients with active disease need to be seen frequently (1 to 2 monthly) whereas those who are stable and with no other issues may be seen 5 to 6 monthly
- All patients need to be registered with the National Inflammatory Arthritis Registry (NIAR) at diagnosis

SPONDYLOARTHROPATHIES/ PSORIATIC ARTHRITIS/METABOLIC CLINIC

Types of diseases seen at this clinic

- Ankylosing Spondylitis and Spondyloarthropathies
- Psoriatic arthritis
- Gout
- Osteoarthritis
- Osteoporosis

Spondyloarthritides

- The spondyloarthritides are a family of conditions with multisystem problems including axial and peripheral arthritis, uveitis and inflammatory bowel disease
- Send baseline HLA-B27; other investigations as per RA clinic
- BASDAI and ASDAS should be performed at every visit and BASMI yearly – refer to ***Appendix 2 Disease activity measures***
- Long-standing patients are at risk of osteoporosis – screen for osteoporosis

Psoriatic arthritis

- Psoriatic arthritis patients may have peripheral arthritis (similar to RA), oligoarthritis, axial arthritis and dactylitis
- Baseline investigations include FBC, renal profile, liver function tests, ESR, CRP, rheumatoid factor (negative as per Caspar criteria)
- Patients often have metabolic syndrome, screen accordingly
- To measure disease activity, refer to ***Appendix 2 Disease activity measures***

Gout

- Gout patients newly started on treatment need to be seen frequently (1 to 2 monthly) for uptitration of medications. Once stable, they may be seen 5 to 6 monthly. For guidance on medications, refer ***Appendix 4 Other drugs***
- Target uric acid level for patients with gout is **<360 μmol/L and <300 μmol/L** for chronic tophaceous gout

Osteoarthritis & Osteoporosis

- Stable patients with osteoarthritis with no other issues may be discharged to health clinics for followup
- Patients at risk for osteoporosis may have a baseline DXA scan, then 2 yearly if abnormal; if normal, repeat in 5 years. Areas imaged are **spine and dual femur**. Patients on treatment may be seen 6 monthly if there are no other issues. For guidance on medications, refer ***Appendix 4 Other drugs***

Musculoskeletal Ultrasound Clinic

Indications :

- Diagnostic uncertainty – to look for subclinical synovitis for fulfillment of RA diagnostic criteria; To look for subclinical synovitis in determining true remission
- To determine pathology – differentiate causes of swelling eg tenosynovitis or synovitis
- To guide intra-articular injection

Combined Respiratory Clinic

- Main purpose is for cardiorespiratory screening for patients with SSc and MCTD
- Assessment includes: Echocardiogram, 6 minute walk test, spirometry, chest x-ray ± HRCT lungs; full lung function test if spirometry abnormal, NTproBNP
- If the assessment is normal, patients may be screened again yearly or 2 –yearly; ensure that patient has a CTD clinic appointment in the interim
- Other patients with ILD may be scheduled into this clinic for monitoring and respiratory review

Combined Obstetric Clinic

- Mainly for SLE patients who are pregnant, however pregnant patients with other rheumatic diseases may also be followed up at this clinic, especially if there is past history of pregnancy morbidity or patient needs to be followed up closely due to other reasons
- Follow-up visits are usually monthly, unless patient is very stable with no issues or not on any medications. In these cases, follow-up visits may be scheduled 2 to 3 monthly
- Baseline visit investigations should include: **uric acid, thyroid function test, anti-phospholipid screen (if not done previously), complement levels (SLE patients), antiRo (if not done previously)** please refer ***Appendix 5 Investigations***
- Check patient's medications and compatibility with pregnancy, ideally medications not allowed during pregnancy should have been stopped prior to conception. The following table lists common drugs used and guidance in pregnancy:

Medications In Pregnancy

Medications	Action	Notes
NSAIDS	May continue if required	Stop 8 weeks prior to delivery to prevent premature closure of patent ductus arteriosus
COX-inhibitors	Stop	Avoid during pregnancy and lactation
Prednisolone	Continue	Avoid high doses during 1st trimester and lactation unless necessary
HCQ	Continue	Safe in pregnancy and lactation
Azathioprine	Continue	Safe in pregnancy and lactation
Cyclosporin	May continue	Use only if no other alternative
Sulphasalazine	Continue	Safe in pregnancy and lactation
Methotrexate	Stop	Teratogenic
Leflunomide	Stop	Teratogenic – for washout procedure, refer Appendix 3 csDMARDs
Mycophenolate mofetil	Stop	Teratogenic
Cyclophosphamide	Stop	Teratogenic
Anti-TNF	May continue	Etanercept and Certolizumab (currently not available) preferred; no data yet for other biologics
Sildenafil	Continue	Safe in pregnancy and lactation
Warfarin	Stop	Switch to low molecular weight heparin; use clexane if history of arterial thrombosis, otherwise may use tinzaparin
Bisphosphonates	Stop	
Calcitriol	Stop	Switch to cholecalciferol (if available)

- All patients started on biologics and targeted synthetic dmards are reviewed at this clinic
- Patients who are planned for biologics and awaiting funding and/or screening results can also be transferred to this clinic
- Choice of biologics to be discussed with consultant and also based on patient's preference

Indications for starting biologic DMARDs:

RA & PsA

persistently moderate or high disease activity despite 2 csDMARDs or intolerance

AS/SpA

as above and/or BASDAI>4 or ASDAS high disease activity despite trial of 2 different type of NSAIDS or COX-2 inhibitors

- ensure counselling is given regarding indication, risk of infection and mode of therapy
- Patients receiving biologics under the pensioner's JPA fund, do not require any special application, normal prescription will do; government servants requiring JPA funding will need a supporting letter, completed JPA form and manual prescription; for patients applying under Tabung Bantuan Perubatan,

fill up Borang C and refer patient to the social worker – please refer to ***Appendix 6 Biologic application*** for more details.

Contraindications for starting biologic DMARDs:

- Active infection including active TB
- HIV
- Acute hepatitis B&C
- Untreated chronic Hepatitis B or treated chronic Hepatitis B with Child-Pugh Class B and higher
- Septic arthritis of a native joint within the last 12 months
- Prosthetic joint sepsis within the last 12 months or indefinitely if the joints remain in situ
- Congestive cardiac failure with NYHA grade III or IV
- Multiple sclerosis or other demyelinating disorders
- Malignancy – treated solid malignancy ≤ 5 years ago; skin melanoma
- Lymphoproliferative disorders

Caution in:

High risk of infection

- Chronic leg ulcers
- Previous TB, unless completed a full course of anti-TB and measures taken to prevent reactivation
- Persitent or recurrent chest infections
- Indwelling catheter
- Treated chronic hepatitis B (Child-Pugh Class A)
- Hepatitis C

High risk of malignancy

- Pre-malignant conditions (eg Barret's oesophagus, cervical dysplasia and large bowel polyps)
- Previous history of malignancy with no recurrence for the past 5 years
- Possible history or strong family history of demyelination
- Patients with active psoriasis who have received >1000 joules cumulative PUVA dosage; especially those who have subsequently been treated with cyclosporine for at least a year (at risk for non melanoma skin cancer)
- Mild CCF
- Lung fibrosis
- History of uveitis

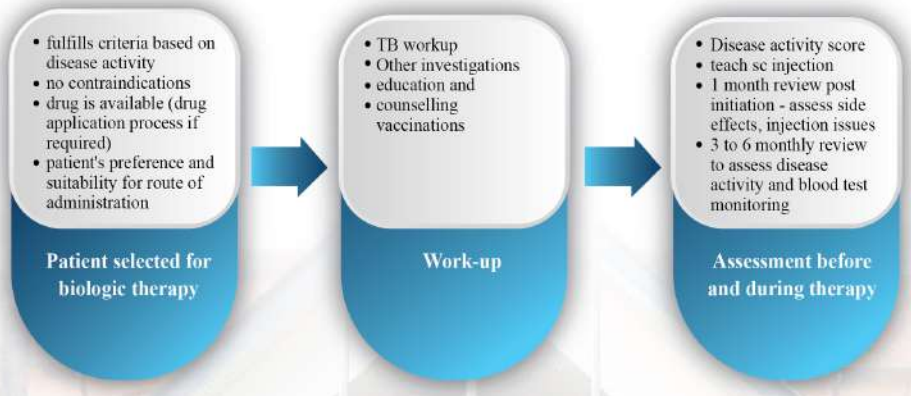
Source: Inflammatory arthritis and biologic therapy – Malaysian consensus

Pre-biologic TB Screening

Mandatory for all patients starting on biologics

- TB Gold Quantiferon-plus test – fill up green pathol lab form, bloods taken by rheumatology nurse, sent to the lab before 12noon
- Mantoux test – to be done AFTER Quantiferon test, may omit if Quantiferon test done; Two-Step Mantoux test – if the 1st Mantoux reading is 0mm, perform a 2nd Mantoux test at 2 weeks after the 1st Mantoux test
- HIV, HepBsAg, HepBcAb, HepCAb (unless done within last year)
- CXR(unless done within last year)

- Ideally, patients should receive vaccinations before starting biologics; **live vaccines are contraindicated during biologic therapy**
- Patients newly started on biologics should be seen 1 month after initiation of therapy to monitor for side effects, and 3 months after initiation to measure response to therapy; subsequent visits should be 3 monthly



Positive Mantoux: ≥5mm in patients on immunosuppressant (including MTX, Leflunomide, Pred>15mg/day for ≥1 month, biologics); other patients ≥10 mm

Latent TB Treatment:

- Start isoniazid 300mg od with pyridoxine 10mg od for 9 months
- Commence biologic 4 weeks after initiation of isoniazid (preferred duration); however if indicated, biologic may be commenced earlier

Daycare service

The daycare service was established to facilitate delivery of intravenous drug infusions in a safe and controlled environment for fit patients who do not require inpatient care. This is to minimize inpatient bed occupancy and ensure that patients receive medications in an efficient and timely manner.

For guidance on infusion protocols, refer to *Appendix 4 Other Drugs*

MEDICATIONS

- Infliximab
- Golimumab
- Tocilizumab
- Rituximab
- Belimumab
- Cyclophosphamide
- Cosmofer

General guidance

Ensure patients that are scheduled to receive infusions have been informed to the nurse in charge. Patients on biologics and receiving regular infusions at the daycare, also require an appointment at the clinic.

Note

Ensure that all patients receiving infusions have a rheumatology clinic appointment as well.

Inpatient service

- During a serious infection, all DMARDs and immunosuppressives (except prednisolone, see below) should be temporarily discontinued until patient has recovered from the infection, generally 1 week after completion of antibiotics
- Patients on chronic prednisolone may have the dose doubled during a serious illness to prevent adrenal insufficiency
- Elective perioperative procedures:
  - csDMARDs – usually not stopped, please discuss for high-risk procedures
  - Steroids – minimize exposure prior to surgical procedures, increase in dose usually not required
  - tsDMARDs and bDMARDs – refer to table below

Drugs	Schedule surgery (relative to last dose administered) during
Adalimumab	Week 2 or 3
Etanercept	Week 2
SC Golimumab	Week 5
IV Golimumab	Week 9
Infliximab	Week 5, 7 or 9 (depending on dosing interval of every 4, 6 or 8 weekly)
Rituximab	Month 7
SC Tocilizumab	Week 2
IV Tocilizumab	Week 5
Tofacitinib	7 days after last dose
Baricitinib	1 day after dose (ie with -hold on day of surgery)

Source: 2017 ACR/ American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee

Appendix 1

Classification Criteria

Rheumatoid Arthritis

ACR/EULAR 2010 CLASSIFICATION CRITERIA

SYMPTOM DURATION (AS REPORTED BY PATIENT)	POINTS
< 6 Weeks	0
> 6 Weeks	1

JOINT DISTRIBUTION	POINTS
1 large joint	0
2-10 large joints	1
1-3 small joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
> 10 joints (at least 1 small joint)	5

SEROLOGY	POINTS
RF- and CCP-	0
Low RF+ or CCP+	2
High RF+ or CCP+	3

ACUTE PHASE REACTANTS	POINTS
Normal ESRor CRP	0
Abnormal ESR or CRP	1

RF: rheumatoid factor. CCP: anti-citrullinated citric peptide. ESR: erythrocyte sedimentation rate. CRP: C-reactive protein. Low: < 3 x upper limit of normal (ULN). High: > 3 x ULN

Patients who have at least 1 swollen joint, and not better explained by another disease to be applied. A score ≥ 6 points is required for classification as definite RA.

Systemic Lupus Erythematosus

2012 SLICC CRITERIA

Requirements: ≥4 criteria (at least 1 clinical and 1 laboratory criteria) OR biopsy proven lupus nephritis with positive ANA or anti-DsDNA

	CLINICAL CRITERIA	NOTES
1	Acute cutaneous lupus or Subacute cutaneous lupus	Malar rash, bullous lupus, toxic epidermal necrolysis variant, maculopapular lupus rash, photosensitivity Noninudrated posirasiform and/or annular polycyclic lesions (resolve without scarring but may have postinflammatory dyspigmentation or telangiectasiae)
2	Chronic cutaneous lupus	Discoid rash localized (above neck) or generalized (above and below neck), hypertrophic (verrucous) lupus, lupus panniculitis (profundus), mucosal lupus, lupus erythematous tumidus, chilblains lupus, discoid/lichen planus overlap

3	Oral or nasal ulcers	Oral - palate, buccal, tongue Exclude other causes such as vasculitis, Behcet's disease, infection (herpesvirus), inflammatory bowel disease, reactive arthritis and acidic food)
4	Non-scarring alopecia	Diffuse thinning of hair fragility with visibly broken hairs in the absence of other causes such as alopecia areata, drugs, iron deficiency and androgenic
5	Arthritis	Synovitis involving 2 or more joints – ie tender and swollen OR Tender in 2 or more joints with at least 30 mins of morning stiffness
6	Serositis	Typical pleurisy for more than 1 day OR pleural effusions OR pleural rub Typical pericardial pain (pain with recumbency improved by sitting forward) for more than 1 day) OR pericardial effusion OR pericardial rub OR pericarditis by ECG
7	Renal	Urine protein-to-creatinine ratio (or 24-hour urine protein) ≥500mg OR red blood cell casts
8	Neurologic	Seizures, psychosis, mononeuritis multiplex (in the absence of other causes eg primary vasculitis), myelitis, peripheral or cranial neuropathy (in the absence of other known causes eg primary vasculitis, infection, DM), acute confusional state (exclude other causes eg toxic/metabolic, uraemia, drugs)
9	Haemolytic anaemia	
10	Leucopaenia OR lymphopenia	<4000/mm^3 at least once in the absence of other known causes eg Felty's syndrome, drugs, portal hypertension <1000/mm^3 at least once in the absence of other known causes eg corticosteroids, drugs and infection
11	Thrombocytopaenia	<100000/mm3 at least once in the absence of other known causes eg drugs, portal hypertension and TTP

	IMMUNOLOGIC CRITERIA	NOTES
1	ANA	
2	antiDsDNA	
3	Anti-Sm	
4	Antiphospholipid Ab	Positive lupus anti-coagulant; false-positive RPR; medium or high-titre anticardiolipin Ab (IgG, IgA, IgM); positive anti-2-glycoprotein (IgG, IgA or IgM)
5	Low complement	
6	Direct Coomb's test	Not counted in the presence haemolytic anaemia

Psoriatic arthritis

CASPAR (CLASSIFICATION CRITERIA FOR PSORIATIC ARTHRITIS)

A patient must have inflammatory articular disease (joint, spine or entheseal) and ≥3 points from the following categories:

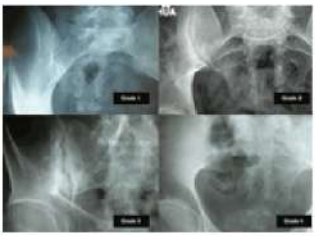
CATEGORY	DESCRIPTION	POINTS
Current psoriasis or personal or family history of psoriasis	Current psoriasis: skin or plaque disease confirmed by rheumatologist or dermatologist Personal history: obtained from patient or HCP Family history: 1stor 2 nddegree relative as reported by patient	2 (current) OR 1 (history)
Psoriatic nail dystrophy on current examination	Onycholysis, pitting, hyperkeratosis	1
Negative rheumatoid factor		1
Dactylitis (current or history)	Swelling of entire digit	1
Radiographic evidence of juxta - articular new bone formation	Ill-defined ossification near joint margins but excluding osteophyte formation on plain x-ray of hand or foot	1

Ankylosing Spondylitiis

1984 MODIFIED NEW YORK CRITERIA

CLINICAL CRITERIA
Low back pain ≥3 months, improved by exercise, not relieved by rest
Limitation of lumbar spine in sagittal and frontal planes
Limitation of chest expansion (relative to normal values corrected for age and sex
RADIOLOGIC CRITERIA
Bilateral grade 2-4 sacroiliitis OR
Unilateral grade 3-4 sacroiliitis

Requirement: bilateral grade 2-4 or unilateral grade 3-4 sacroiliitis AND any clinical criteria



XRAY GRADING OF SACROILIAC JOINTS	
Grade 0	Normal
Grade 1	Suspicious changes
Grade 2	Minimal definite changes: circumscribed areas with erosions or sclerosis with no changes of SIJ space
Grade 3	Distinctive changes: sclerosis, change of joint space (decrease or widened), partial ankylosis
Grade 4	Ankylosis

Spondyloarthropathy

ASAS CRITERIA FOR AXIAL SPA

In patients with ≥3 months back pain and age of onset <45 years

Sacroilitis on imaging AND ≥1 SpA feature

OR

HLA-B27 positive AND ≥2 other SpA features

Sacroilitis in imaging

- Active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
- Definite radiographic sacroiliitis according to modified New York criteria

SpA features

- Inflammatory back pain
- Arthritis
- Enthesitis (heel)
- Uveitis
- Dactylitis
- Psoriasis
- Crohn's/colitis
- Good response to NSAIDs
- Family history of SpA
- HLA-B27
- Elevated CRP

ASAS CRITERIA FOR PERIPHERAL SPA

Peripheral arthritis and/or enthesitis and/or dactylitis
PLUS

≥1 SpA feature

- Uveitis
- Psoriasis
- Crohn's/colitis
- Preceding infection
- HLA-B27
- Sacroiliitis on imaging

OR

≥2 other SpA features

- Arthritis
- Enthesitis
- Dactylitis
- Inflammatory back pain (ever)
- Family history of SpA

Systemic Sclerosis

2013 ACR/EULAR CLASSIFICATION CRITERIA

Item	Subitem	Score
Skin thickening of fingers of both hands extending proximal to MCPJs (sufficient criterion)		9
Skin thickening of fingers (only count the higher score)	Puffy fingers Sclerodactaly of fingers (distal to MCPJs but proximal to PIPJs)	2 4
Fingertip lesions (only count higher score)	Digital ulcers Fingertip pitting scars	2 3
Telangiectasia		2
Abnormal nailfold capillaries		2
Pulmonary arterial hypertension and/or interstitial lung disease (maximum score 2)	Pulmonary arterial hypertension Interstitial lung disease	2 2
Raynaud's phenomenon		3
SSc-related autoantibodies (anticentromere, anti-topoisomerase I/antiScl-70, anti-RNA polymerase III) (maximum score 3)	Anticentromere Anti-topoisomerase I Anti-RNA polymerase III	3

Exclude scleroderma-like disorder that better explains manifestations eg nephrogenic sclerosing fibrosis, generalized morphoea, eosinophilic fasciitis, scleredema diabeticorum, scoeromyxedema, erythromyalgia, porphyria, lichen sclerosis, GVHD, diabetic cheiroarthropathy)
Patients with a total score ≥9 are classified as having definite scleroderma

Fibromyalgia

2016 REVISION TO THE 2010/2011 FIBROMYALGIA DIAGNOSTIC CRITERIA

1. Widespread pain index (WPI) ≥7 and symptom severity score (SSS) score ≥5 or WPI 4-6 and SSS score ≥9
2. Generalised pain, defined as pain in at least 4 of 5 regions is present
3. Symptoms have been persistent for at least 3 months
4. Diagnosis is valid irrespective of other diagnoses.

Part 1

Over the last 7 days indicate the areas where you have had pain or tenderness:
Neck, upper back, chest/breast, abdomen, lower back, left jaw, right jaw, left shoulder, right shoulder, left upper arm, right upper arm, left lower arm, right lower arm, left hip, right hip, left upper leg, right upper leg, left lower leg, right lower leg

Part 2

Over the last 7 days, rate your symptoms based on the following scale:

1. Rating scale 0 no problem
   1 slight or mild
   2 moderate
   3 severe (life threatening problems)

2. Questions Fatigue
   Trouble thinking or remembering
   Waking up tired or unrefreshed

Part 3

Over the last 6 months, have you had any of the following symptoms
Score 1 for 1-10 positive; 2 for 11-24 positive; 3 for 25 or more
Fever, depressed mood, insomnia, nervousness, hair loss, headache, seizures, thinking or memory problem, numbness or tingling, dizziness, fatigue, hearing problems, tinnitus, blurred vision, dry eyes, dry mouth, oral ulcers, shortness of breath, chest pain, heartburn, pain in upper abdomen, pain or cramps in lower abdomen, nausea, vomiting, diarrhea, constipation, loss of appetite, loss or change in taste, irritable bowel syndrome, bladder spasms, frequent urination, painful urination, easy bruising, hives, itching, rash, sun sensitivity, Raynaud's phenomenon, muscle pain, muscle weakness

Osteoporosis

CLASSIFICATION	T-SCORE
Normal	-1.0 or greater
Low bone mass (osteopaenia)	Between -1.0 and below
Osteoporosis	-2.5 and below
Severe osteoporosis	-2.5 and below +fragility fracture

Appendix 2

Disease Activity Measures

Rheumatoid arthritis

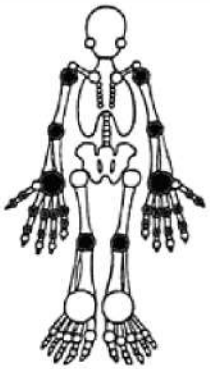


Figure 1: 28 joint count in RA

DAS28 ESR/CRP – use an online calculator
(SJC (28); TJC (28); ESR/CRP(mg/L); PGA 1-100)
Remission <2.6
Low disease activity ≥2.6 ≤3.2
Moderate disease activity >3.2 ≤5.1
High disease activity >5.1

CDAI = SJC (28) + TJC (28) + PaGH(0-10) + PrGH(0-10)
Remission ≤2.8
Low disease activity >2.8 and ≤10
Moderate disease activity >10 and ≤22
High disease activity ≥22
PGA 1-10 EGA 1-10

SDAI = SJC (28) + TJC (28) + PaGH + PrGH + CRP(mg/dl)
Remission ≤3.3
Low disease activity >3.3 and ≤11
Moderate disease activity >11 and ≤26
High disease activity >26

FUNCTIONAL CLASS	DESCRIPTION
Class I	Completely able to perform usual activities of daily living
Class II	Able to perform usual self-care and vocational activities but limited in avocational activities
Class III	Able to perform usual self-care activities but limited in vocational and avocational activities
Class IV	Limited in ability to perform usual self-care, vocational and avocational activities

Psoriatic arthritis

The same disease activity measures as RA are utilised if patient has peripheral arthritis.
If patient has axial involvement, the same measures for ankylosing spondylitis are utilized.

DAPSA = TJC (68) + SJC (66) + CRP (mg/dl) + VAS (activity) + VAS (pain) VAS 0-10
Remission 0-4
Low disease activity 5-14
Moderate disease activity 15-28
High disease activity >28

ASDAS ESR/CRP – use an online calculator (Back pain 0-10; Peripheral pain/Swelling 0-10; Duration morning stiffness 0-10; Patient global 0-10; CRP/ESR)

Inactive disease <1.3
Low disease activity 1.3 and <2.1
High disease activity 2.1 and <3.5
Very high disease activity >3.5
Difference ≥1.1 clinically important improvement; ≥2.0 major improvement

BASDAI

Please place a mark on each line below to indicate your answer to each question relating to the past week

1. How would you describe the overall level of fatigue/tiredness you have experienced?

NONE _____ VERY SEVERE

2. How would you describe the overall level of AS neck, back or hip pain you have had?

NONE _____ VERY SEVERE

3, How would you describe the overall level of pain/swelling in joints other than neck, back, hips you have had?

NONE _____ VERY SEVERE

4. How would you describe the overall level of discomfort you have from any areas tender to touch or pressure?

NONE _____ VERY SEVERE

5. How would you describe the overall level of morning stiffness you have had from the time you wake up?

NONE _____ VERY SEVERE

6. How long does your morning stiffness last from the time you wake up?

_____

0 hrs ½ 1 1 ½ 2 or more hours

BASDAI Score = Total divided by 5
>4 indicates active disease

BASFI

Please indicate your level of ability with each of the following activities during the past week (1 is easy and 10 is impossible)

1.Putting on your socks or tights without help or aids(eg sock aid).

2.Bending from the waist to pick up a pen from the floor without aid.

3.Reaching up to a high shelf without help or aids (eg helping hand)

4.Getting up from an armless chair without your hands or any other help.

5.Getting up off the floor without help from lying on your back.

6.Standing unsupervised for 10 minutes without discomfort.

7.Climbing 12-15 steps without using a handrail or walking aid.

8.Looking over your shoulder without turning your body.

9.Doing physically demanding activities (eg physiotherapy exercises, gardening or sports).

10.Doing a full days activities whether it be at home or at work.

BASFI Score = Total divided by 10

BASMI

Guide to obtaining the BASMI measurements:

Measure	Starting position	Method	Notes
Tragus to wall	Stand bare feet, back to wall. Knees straight; scapulae, buttocks, heels against wall. Shoulders level. Outer edges of feet 30cm apart and feet parallel. Ensure head in as neutral position as possible (anatomical alignment).	Patient draws chin in as far as possible (retraction). The examiner has side of face against wall and measure the distance between tragus of the ear and wall, using a rigid ruler.	Ensure no cervical extension, rotation, flexion or side flexion occurs.
Lumbar side flexion	Stand bare feet, back to wall. Knees straight; scapulae, buttocks, heels against wall. Shoulders level. Outer edges of feet 30cm apart and feet parallel.	First measure from tip of middle finger to floor. With arms relaxed by the sides, patient reaches towards floor by side flexing and maintaining shoulder depression. Re-measure from tip of middle finger to floor. Difference between 2 measurements represents amount of side flexion. Repeat on other side.	Ensure patient keeps arms, fingers and knees straight and heels on floor. May need to accommodate leg length discrepancy with block under foot.

Lumbar flexion (modified Schober's)	Stand with outer edges of bare feet 30cm apart and feet in line. Examiner marks a first point midway between the Dimples of Venus, a second point is marked 10cm above this and 5cm below the first line to give a 15cm line.	Patient flexes forward from the waist with knees fully extended. The distance between the upper and lower 2 marks is measured. Any increase beyond 15cm represents the amount of movement achieved.	
Cervical rotation	Patient supine on couch. Forehead horizontal and head in neutral position. May need to use pillow etc to achieve this.	Use goniometer/inclinometer. Patient rotates his/her head as far as possible, keeping shoulders still. Measure both sides.	Document aids used to achieve neutral position (for future assessments). If good ROM, may need to lie near edge of bed to allow movement to occur.
Intermalleolar distance	Patient lies supine on the floor or wide couch. Knees in extension.	Keep knees straight and legs in contact with resting surface. Patient is asked to move legs as far apart as possible. Distance between the medial malleoli is measured.	Measure quickly as movement may be painful.

Adapted from The Bath Indices Royal National Hospital for Rheumatic Diseases, Irons K et al. 2016

Scores for each of the BASMI Measurements:

	0	1	2	3	4	5	6	7	8	9	10
Tragus to wall (cm)	<10	10-12.9	13-15.9	16-18.9	19-21.9	22-24.9	25-27.9	28-30.9	31-33.9	34-36.9	≥37
Lumbar side flexion (cm)	≥20	18-19.9	15.9-17.9	13.8-15.8	11.7-13.7	9.6-11.6	7.5-9.5	5.4-7.4	3.3-5.3	1.2-3.2	<1.2
Lumbar flexion (modified Schober's)(cm)	>7.0	6.4-7.0	5.7-6.3	5.0-5.6	4.3-4.9	3.6-4.2	2.9-3.5	2.2-2.8	1.5-2.1	0.8-1.4	≤0.7
Cervical rotation (degrees)	≥85	76.6-84.9	68.1-76.5	59.6-68	51.1-59.5	42.6-51	34.1-42.5	25.6-34	17.1-25.5	8.6-17	≤8.5
Intermalleolar distance (cm)	≥120	110-119.9	100-109.9	90-99.9	80-89.9	70-79.9	60-69.9	50-59.9	40-49.9	30-39.9	<30

Systemic lupus erythematosus

SELENA-SLEDAI

Physicians Global Assessment

0	1	2	3
None	Mild	Med	Severe

SLEDAI SCORE

Counted if descriptor is present at the time of visit or in the preceding 10 days

Wt	Descriptor	Definition
8	Seizure	Recent onset. Exclude metabolic, infectious or drug cause
8	Psychosis	Altered ability to function in normal activity due to severe disturbance in the perception of reality. Include hallucinations, incoherence, marked loose associations, impoverished thought content, marked illogical thinking, bizarre, disorganized, or catatonic behavior. Excluded uraemia and drug causes
8	Organic Brain Syndrome	Altered mental function with impaired orientation, memory or other intelligent function, with rapid onset fluctuating clinical features. Include clouding of consciousness with reduced capacity to focus, and inability to sustain attention to environment, plus at least two of the following: perceptual disturbance, incoherent speech, insomnia or daytime drowsiness, or increased or decreased psychomotor activity. Exclude metabolic, infectious or drug causes.
8	Visual Disturbance	Retinal changes of SLE. Include cytoid bodies, retinal haemorrhages, serious eudate or haemorrhages in the choroids, or optic neuritis. Exclude hypertension, infection or drug causes
8	Cranial nerve disorder	New onset of sensory or motor neuropathy involving cranial nerves
8	Lupus headache	Severe persistent headache: may be migrainous, but must be non-responsive to narcotic analgesia
8	CVA	New onset of CVS(s). Exclude arteriosclerosis
8	Vasculitis	Ulceration, gangrene, tender finger nodules, periungual, infarction, splinter haemorrhages, or biopsy or angiogram proof of vasculitis
4	Arthritis	More than 2 joints with pain and signs of inflammation (ie tenderness, swelling or effusion)
4	Myositis	Proximal muscle aching/weakness, associated with elevated CK/adolase or EMG changes or a biopsy showing myositis
4	Urinary casts	Heme-granular or red blood cell casts
4	Haematuria	>5 red blood cells/high power field. Exclude stone, infection or other cause
4	Proteinuria	>0.5gm/24 hours. New onset or recent increase of more than 0.5gm/24 hours
4	Pyuria	>5 white blood cells/high power field. Exclude infection
2	New rash	New onset or recurrence of inflammatory type rash
2	Alopecia	New onset or recurrence of abnormal, patchy or diffuse loss of hair
2	Mucosal ulcers	New onset or recurrence of oral or nasal ulcerations
2	Pleurisy	Pleuritic chest pain with pleural rub or effusion
2	Pericarditis	Pericardial pain with at least 1 of the following: rub, effusion, or ECG confirmation
2	Low complements	Decrease in CH50, C3 or C4 below the lower limit of normal for testing laboratory
2	Increased DNA binding	>25% binding by Farr assay or above normal range for testing laboratory
1	Fever	>38°C. Exclude infectious cause
1	Thrombocytopaenia	<100,000 platelets/mm3
1	Leucopaenia	<3,000 white blood cell/mm3. Exclude drug causes

_____ TOTAL SCORE (sum of weights)

Mild or Moderate Flare	Severe Flare
☐ Change in SLEDAI > 3 points	☐ Change in SLEDAI >12
☐ New/worse discoid, photosensitive, profundus, cutaneous vasculitis, bullous lupus, nasopharyngeal ulcers, pleuritis, pericarditis, arthritis, fever	☐ New/worse CNS-SLE, vasculitis, nephritis, myositis platelet <60,000, haemolytic anaemia Hb <7% or decrease in Hb >3%
☐ Increase in Prednisolone but not to >0.5mg/kg/day	☐ Double prednisolone or prednisolone>0.5mg/kg/day or hospitalization
☐ Added NSAID or Hydroxychloroquine	☐ New Cyclophosphamide, azathioprine, methotrexate, hospitalization
☐ ≥1.0 Increase in PGA, but not to more than 2.5	☐ Increase in PGA to >2.5

Mini mental state examination (MMSE)

Instructions: Ask the questions in the order listed. Score one point for each correct response.
Total score: ___/30

What is the year?	Where are we now: state?
What is the season?	Where are we now: country?
What is the date?	Where are we now: town/city?
What is the day of the week?	Where are we now: hospital?
What is the month?	Where are we now: floor?
(Maximum score 5)	(Maximum score 5)

The examiner names 3 unrelated objects clearly and slowly. Examiner may repeat the objects until patient learns all of the them. Then ask the patient to name all 3 of them. (maximum score 3)
Record number of trials.

"I would like you to count backward from 100 by sevens" (93,86,79,72,65….) Stop after 5 answers. (maximum score 5)
Alternative: "Spell WORLD backwards" (D-L-R-O-W).

"Earlier I told you the names of 3 things. Can you tell me what those were?" (Maximum score 3)

Show the patient 2 simple objects eg wristwatch and a pencil, and ask the patient to name them. (Maximum score 2)

"Repeat the phrase: 'No ifs, ands, or buts." (Maximum score 1)

"Take the paper in your right hand, fold it in half, and put it on the floor." (give the patient a piece of paper) (Maximum score 3)

"Please read this and do what it says." (Written instruction is "Close your eyes.") (Maximum score 1)

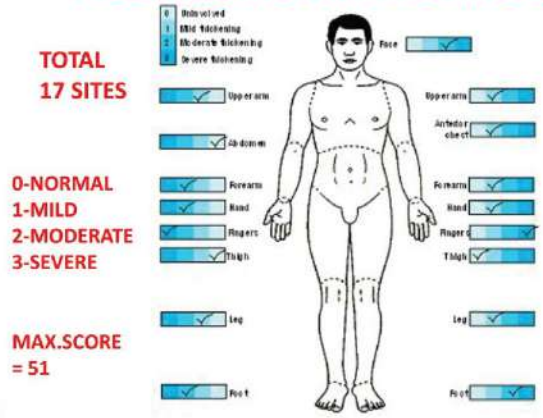
Write a sentence about anything. (the sentence must contain a noun and a verb). (Maximum score 1)

Please copy this picture. (Give the patient a piece of paper and ask him/her to draw the symbol below. All 10 angles must be present and the two must intersect.) (Maximum score 1)

Interpretation of the MMSE:
<24 abnormal
18-23 mild cognitive impairment
0-17 severe cognitive impairment

Systemic sclerosis

MODIFIED RODNAN SKIN SCORE



Polymyositis

MANUAL MUSCLE TESTING
Axial muscles (0-20) – neck flexors, neck extensors
Proximal muscles (0-160) – trapezius, deltoid middle, biceps brachii, gluteus maximus, gluteus medius, iliopsoas, hamstrings, quadriceps
Distal muscles (0-80) – wrist extensors, wrist flexors, ankle dorsiflexor, ankle plantar flexors
Total MMT26 score (0-260)

BIRMINGHAM VASCULITIS ACTIVITY SCORE (Version 3)

Manifestation	Definition	Persistent	New/Worse
1. General	**Maximum scores**	**2**	**3**
Myalgia	Pain in the muscles	1	1
Arthralgia/arthritis	Pain in the joints or joint inflammation	1	1
Fever ≥ 38°C	Oral/axillary temp. Rectal temp ≥38.5°C	2	2
Weight loss ≥2kg	Loss of weight without dieting	2	2
2. Cutaneous	**Maximum scores**	**3**	**6**
Infarct	Area of tissue necrosis or splinter haemorrhages	1	2
Purpura	Subcutaenous or submucosal haemorrhage in the absence of trauma	1	2
Ulcer	A disruption in the continuity of the skin	1	4
Gangrene	Extensive tissue necrosis	2	6
Other skin vasculitis	Livedo reticularis, subcutaneous nodules, erythema nodusum, etc	1	2
3. Mucous membranes/eyes	**Maximum scores**	**3**	**6**
Mouth ulcers/granulomata	Aphthous stomatitis, deep ulcers, strawberry gingival hyperplasia	1	2
Genital ulcers	Ulcers on the genitalia or perineum	1	1
Adnexal inflammation	Salivary or lacrimal gland inflammation	2	4
Significant proptosis	>2mm protrusion of the eyeball	2	4
Scleritis/episcleritis	Inflammation of the sclera	1	2
Conjunctivitis/Blepharitis/Keratitis	Inflammation of the conjunctiva, eyelids or cornea – but not due to sicca syndrome	1	1
Blurred vision	Deterioration of visual acuity from previous or baseline	2	3
Sudden visual loss*	Acute loss of vision	*	6
Uveitis	Inflammation of uvea (iris, ciliary body, choroid)	2	6
Retinal changes (vasculitis, thrombosis/exudate/haemorrhage)	Sheathing of retinal vessels or evidence of retinal vasculitis on fluorescein angiography, thrombotic retinal arterial or venous occlusion; soft retinal exudate (exclude hard exudates)/retinal haemorrhage	2	6
4. ENT	**Maximum scores**	**3**	**6**
Bloody nasal discharge/crusts/ulcers/granulomata	Bloody, mucopurulent, nasal secretion, light or dark brown crusts frequently obstructing the nose, nasal ulcers or granulomatous lesions observed on rhinoscopy	2	4

Paranasal sinus involvement	Tenderness or pain over paransal sinuses (usually confirmed by imaging)	1	2
Subglottic stenosis	Stridor or hoarseness due to inflammation and narrowing of the subglottic area observed by laryngoscopy	3	6
Conductive hearing loss	Hearing loss due to middle ear involvement (usually confirmed by audiometry)	1	3
Sensorineural hearing loss	Hearing loss due to auditory nerve or cochlear damage (usually confirmed by audiometry)	2	6
5. Chest	**Maximum scores**	**3**	**6**
Wheeze	Wheeze on clinical examination	1	2
Nodules or cavities*	New lesions detected on imaging	*	3
Pleural effusion/pleurisy	Pleural pain and/or friction rub on clinical assessment radiologically confirmed pleural effusion	2	4
Infiltrate	Detected on chest x-ray or CT-scan	2	4
Endobronchial involvement	Endobronchial pseudotumour or ulcerative lesions, NB: smooth stenotic lesions to be included in VDI; subglottic lesions to be recorded in the ENT section.	2	4
Massive haemoptysis/alveolar haemorrhage	Major pulmonary bleeding with shifting pulmonary infiltrates	4	6
Respiratory failure	The need for artifical ventilation	4	6
6. Cardiovascular	**Maximum scores**	**3**	**6**
Loss of pulses	Clinical absence of peripheral arterial pulsation in any limb	1	4
Valvular heart disease	Clinical or echo detection of aortic/mitral/pulmonary valve involvement	2	4
Pericarditis	Pericardial pain/friction rub on clinical assessment	1	3
Ischaemic cardiac pain	Typical clinicla history of cardiac pain leading to myocardial infarction or angina	2	4
Cardiomyopathy	Significant impairment of cardiac function due to poor ventricular wall motion confirmed on echocardiography	3	6
Congestive cardiac failure	Heart failure by history or clinical examination	3	6
7. Abdominal	**Maximum scores**	**4**	**9**
Peritonitis	Typical abdominal pain suggestive of peritoneal involvement	3	9
Bloody diarrhoea	Of recent onset	3	9
Ischaemic abdominal pain	Typicla abdominal pain suggestive of bowel ischaemia, confirmed by imaging or surgery	2	6
8. Renal	**Maximum scores**	**6**	**12**
Hypertension	Diastolic >95mmHg	1	4
Proteinuria	>1+ on urinalysis or >0.2g/24 hours	2	4
Haematuria	'Moderate' on urinalysis or ≥10 RBC per high power field, usually accompanied by red cell casts	3	6

Serum creatinine 124-249 µmol/L	At first assessment only	2	4
Serum creatinine 250-499 µmol/L		3	6
Serum creatinine ≥500 µmol/L		4	8
>30% rise in creatinine or >25% fall in cr clearance*	Progressive worsening of renal function. Can be used at each assessment if the renal function has deteriorated from prior value	*	6
9. Nervous system	**Maximum scores**	**6**	**9**
Headache	Unaccustomed & persistent headache	1	1
Meningitis	Clinical evidence of meningism	1	3
Organic confusion	Impaired orientation, memory or other intellectual funcitonin the absnece of metabolic, psychiatric, pharmcological or toxic causes	1	3
Seizures (not hypertensive)	Clinical or EEG evidence of aberrant electrical activity in the brain	3	9
Stroke	Focal neurological signs lasting >24 hours due to a CNS vascular event	3	9
Spinal cord lesion	Clinical or imaging evidence of spinal involvement	3	9
Cranial nerve palsy	Clinical evidence of cranial nerve palsy – score VIII nerve palsy as sensorineural hearing loss, do not score ocular palsies if they are secondary to pressure effects	3	6
Sensory peripheral neuropathy	Objective sensory deficit in a non-dermatomal distribution	3	6
Mononeuritis multiplex	Single or multiple specific motor nerve palsies	3	9

Revised 2011 five-factor score: each factor is given 1 point. Maximum score of 2

- Age >65 years
- Cardiac insufficiency
- Renal insufficiency (Creat 150micromol/L)
- Gastrointestinal involvement
- Absence of ENT manifestations (presence is a/w better prognosis)

Appendix 3

DMARDs

csDMARDs

Drug	Route	Dose	Adverse effects	Pregnancy & Lactation
MTX *ensure folic acid also prescribed - minimal dose 5mg weekly	Oral SC/IM	7.5mg - 20mg weekly Dose adjustment for renal impairment: CrCl %std dose ≥60 full 30-59 50 <30 CI	• GI intolerance • Alopecia • mucositis • photosensitivity, rash • abnormal FBC • elevated ALT/AST • interstitial pneumonia (acute/chronic)	Pregnancy • Contraindicated in pregnancy • Stop at least 3 months in women prior to conception Lactation • Avoid in lactation
Leflunomide	Oral	10-20mg OD	• Alopecia • Abnormal FBC • elevated ALT/AST • Elevated blood pressure	Avoid in pregnancy and lactation A washout procedure should be completed pre-conception (Cholestyramine 8g po TDS 11days test plasma levels by 2 separate tests at least 14 days apart; verify plasma level <0.02g/L; may rpt washout if needed)
SSZ	Oral	500-1500mg bd	• Pruritus • Rash • GI intolerance • Abnormal FBC • Elevated ALT/AST • Oligospermia	Pregnancy • Compatible in pregnancy with folate supplementation Lactation • Breastfeeding is safe in a healthy, full-term infant • Caution in premature infant, hyperbillirubinaemia and G6PD deficiency
HCQ	Oral	200-400mg OD (not to exceed 6.5mg/kg IBW)	• Retinal disorder	Compatible in pregnancy and lactation

csDMARDs

Drug	Baseline investigation	Subsequent investigations	Frequency of monitoring	Special monitoring	Action
MTX	Full blood count Liver function test Renal function test HepBsAg antiHCV Chest X-ray	Full blood count Creatinine ALT and/or AST Albumin	2 to 4 weekly for the first 3 months or at every dose increase then 3 monthly		Consider interruption in treatment if any of the following: 1. WBC <3.5 2. Neutrophils <1.6 3. Unexplained eosinophilia >0.5 x 10^9/L 4. MCV >105fL 5. Platelet <140 x10^9/L 6. Creatinine increase >30% 7. ALT +/- AST > 100/L 8. Unexplained reduction in albumin <30g/L
Lef				BP and weight at each visit	
SSZ					
HCQ		none	-	Baseline ophthalmic examination within 1 year of commencing antimalarial drug and annually after 5 years	-

tsDMARDs

Drug	Route	Dose	Adverse effects	Pregnancy & Lactation
Tofacitinib	Oral	5 mg BD 5 mg OD (CrCl 30-60mL/min)	• Increased low-density lipoprotein and high-density lipoprotein level • Herpes Zoster infection • Elevated ALT/AST • Gut perforation (especially in diverticulitis)	Pregnancy • Avoid in pregnancy • Should be stopped 2 months before conception Lactation • Insufficient data to support safety
Baricitinib	Oral	4 mg OD 2mg OD (CrCl 30-60mL/min)	• Elevated ALT/AST • GI intolerance • Herpes Zoster infection • Abnormal FBC • Increased low-density lipoprotein, high-density lipoprotein level and triglycerides	• Insufficient data to support safety in pregnancy and lactation

Biologic DMARDs				
Infliximab	IV	3 mg/kg every 8 weeks May increase to 5 mg/kg	• Rash • GI intolerance • Infusion related reaction • Infections (including TB)	Pregnancy • Can be continued up to gestational week 20; if indicated can be used throughout pregnancy Lactation • Compatible with lactation
Etanercept	SC	50 mg every week	• Injection site reaction • Infections (including TB)	**Pregnancy** • Can be continued up to gestational week 30-32; if indicated can be used throughout pregnancy **Lactation** • Compatible with lactation
Adalimumab	SC	40 mg every 2 weeks	• Injection site reaction • Rash • GI intolerance • Infections (including TB)	**Pregnancy** • Can be continued up to gestational week 20; if indicated can be used throughout pregnancy **Lactation** • Compatible with lactation
Golimumab	SC	50 mg every month	• Injection site reaction • Rash • Infections (including TB) • Elevated ALT/AST	**Pregnancy** • Limited evidence hence consider alternative treatments **Lactation** • Compatible with lactation
	IV	2 mg/kg every 8 weeks		
Tocilizumab	SC	162 mg every week	• Injection site reaction • Rash • GI intolerance • Elevated ALT/AST • Abnormal FBC • Infections (including TB) • Gut perforation (especially in diverticulitis) • Increased low-density lipoprotein level	• Contraindicated in pregnancy and lactation
	IV	4 - 8 mg/kg every 4 weeks		
Rituximab	IV	1000 mg on day 1 and day 15 May be repeated every 6 months	• Peripheral oedema • Pruritus • Rash • GI intolerance • Abnormal FBC • Infections • Infusion related reaction • Low IgG/IgA/IgM	**Pregnancy** • Can be used in exceptional cases in early gestation; if used at later stages of pregnancy, clinician should be aware of risk of B cell depletion and other cytopaenias in the neonate **Lactation** • Avoid in lactation

Appendix 4
Other drugs

Immunosuppressive (oral)

Drug	Route	Dose	Adverse effects	Pregnancy & Lactation
Azathioprine	Oral	2mg/kg start with 50mg daily, then gradually titrate up to required dose	• Leucopaenia • Thrombocytopaenia • transaminitis	Pregnancy • safe in pregnancy Lactation • safe in lactation
Mycophenolate	Oral	1-2g daily start with 500mg bd then titrate up to required dose	• Leucopaenia • Elevated blood pressure • Diarrhoea	Avoid in pregnancy and lactation
Cyclosporin	Oral	1.25mg/kg bd	• Tremor • Nephrotoxic • Hypertension • Hirsutism • Gum hyperplasia	Pregnancy • May be used in pregnancy Lactation • Avoid, excreted in breast milk

Drug	Laboratory monitoring	Other monitoring	Contraindication	Drug-drug interaction
Azathioprine	- FBC, Creatinine, ALT, AST every 2 weeks until on stable dose for 6 weeks - Once on stable dose, 12 weekly	GI side effect Infection	Hypersensitivity reaction	Allopurinol: Reduce Azathioprine dose to 1/3 or ¼ of usual dose
Mycophenolate	- FBC, Creatinine, ALT, AST every 2 weeks until on stable dose for 6 weeks - Once on stable dose, 12 weekly	GI side effect Infection	Hypersensitivity reaction Pregnancy	
Cyclosporin	- FBC, Creatinine, ALT, AST every 2 weeks until on stable dose for 6 weeks - Once on stable dose, 12 weekly	GI side effect Gum hypertrophy Hypertrichosis Tremors Infection BP each visit Fasting blood sugar / Fasting serum lipid 3-6 monthly	Hypersensitivity reaction	Allopurinol: May increase serum cyclosporine level

Gout Drugs

Drug	Route	Dose	Adverse effects	Pregnancy & Lactation
Allopurinol	Oral	100-800mg/day Dose adjustment (starting dose): CrCl Dose ≥20ml/min 100mg od 0-10ml/min 100mg every 2 days <10ml/min 100mg every 3 days	• Hypersensitivity syndrome (fever, rash, hepatitis, eosinophilia, renal impairment) • Rash • Bone marrow suppression • hepatitis	No clear recommendation
Febuxostat	Oral	40mg daily may increase to 80mg od if target uric acid not achieved Dose adjustment: CrCl<30ml/min – 40mg od only Hepatic impairment Child-Pugh Class C – use with caution	• liver function abnormalities • rash • arthralgia • nausea	Limited data
Probenecid	Oral	250mg bd 1 week 500mg bd to 1g bd maximum avoid if CrCl<30ml/min; renal stone present	• rash • GI upset	
Benzbromarone			•	

Drug	Laboratory monitoring	Other monitoring	Contraindication	Drug-drug interaction
Allopurinol	- FBC, Uric acid, Creatinine, ALT, AST 4 weekly during dose titration, then 6 monthly - 24 h urine uric acid level at baseline	Hypersensitivity reaction BMI, BP each visit Fasting blood sugar / Fasting serum lipid 3-6monthly	Hypersensitivity reaction	Vitamin K antagonist (ie warfarin): May enhance anticoagulant effect Azathioprine: Reduce Azathioprine dose to 1/3 or ¼ of usual dose
Febuxostat	- Uric acid, Creatinine, ALT, AST **? frequency** - 24 h urine uric acid level at baseline	Hypersensitivity reaction BMI, BP each visit Fasting blood sugar / Fasting serum lipid 3-6monthly Thromboembolic event-MI/stroke	Hypersensitivity reaction Concurrent use with azathioprine	

Probenecid	- FBC, Uric acid, Creatinine, ALT, AST **? frequency** - 24 h urine uric acid level at baseline	Hypersensitivity reaction GI side effect Uric acid stone	Hypersensitivity reaction G6PD deficiency Nephrolithiasis or urolithiasis Concurrent use of salicylates Severe renal impairment (CrCl < 30)	MTX and Mycophenalate: May increase serum concentration of MTX and Mycophenolate
Benzbromarone	- Uric acid, Creatinine, ALT, AST **? frequency** - 24 h urine uric acid level at baseline	Hypersensitivity reaction GI side effect Uric acid stone	Hypersensitivity reaction Nephrolithiasis or urolithiasis	Vitamin K antagonist (ie warfarin): May enhance anticoagulant effect

STEROID CONVERSION TABLE

EQUIVALENT DOSE	STEROID
1.9mg	Dexamethasone (long-acting)
10mg	Methylprednisolone (intermediate-acting)
10mg	Triamcinolone (intermediate-acting)
12.5mg	Prednisolone (intermediate-acting)
50mg	Hydrocortisone (short-acting)

IV Cyclophosphamide

Indications:

1. Severe SLE: both renal and non-renal disease
2. Vasculitis (Primary/Secondary)
3. Others: Connective tissue disease-associated interstitial lung disease

Dosing/Regime

- to be decided depending on indication
- CYC is available in 500mg/vial

1) National Institutes for Health (NIH)1

- Monthly i.v. CYC at 500-1000mg/m2 body surface area for 6months
- Plus Mesna 200mg monthly

2) Euro-Lupus protocol2

- 2-weekly 500mg fixed dose i.v. CYC for a total of 6 doses
- Plus Mesna 200mg every 2 weeks

3) Systemic vasculitis regime (CYCLOPS Trial)[3]

see next page for protocol

Potential adverse effects of CYC :

GIT: diarrhoea, mucositis, nausea and vomiting

Amenorrhoea/azoospermia: Permanent ovarian failure occurs in over 50% of women after one year's exposure and

is age-related; male infertility has been less well studied.

Haematological: Bone marrow suppression, leucopenia (dose related, recovery :7-10 days after cessation)

Pulmonary Toxicity: pneumonitis, pulmonary fibrosis

Bladder toxicity is caused by renal excretion of the metabolite acrolein which can cause haemorraghic cystitis and a markedly increased risk of bladder cancer

Monitoring parameters:

- Sign and symptoms of infection (prior to and during therapy)-including tuberculosis
- FBC-D10 post infusion

CYCLOPS REGIME

Induction/consolidation regime for pulsed CYC

Time (week)	Pulse no	Route	Dosage
0	1	IV	15mg/kg
2	2	IV	15mg/kg
4	3	IV	15mg/kg
7	4	IV or oral	15mg/kg IV or 5mg/kg orally for 3 days
10	5	IV or oral	15mg/kg IV or 5mg/kg orally for 3 days
13	6	IV or oral	15mg/kg IV or 5mg/kg orally for 3 days
16	7	IV or oral	15mg/kg IV or 5mg/kg orally for 3 days
19	8	IV or oral	15mg/kg IV or 5mg/kg orally for 3 days
22	9	IV or oral	15mg/kg IV or 5mg/kg orally for 3 days
25	10	IV or oral	15mg/kg IV or 5mg/kg orally for 3 days

Note:

• The first 3 pulses are given at intervals of 2 weeks and must be given I.V.. If it is decided to give the subsequent pulses orally, which is recommended, the dose of CYC should be divided over 3 days giving 5 mg/kg each day. If it is decided to give the subsequent pulses I.V., the entire dose of CYC (15 mg/kg) can be given on one day.

• This regimen implies remission within 3 months and a further 3 months of pulse CYC after entry into remission (i.e. 6 months in total). Should remission not be achieved by 3 months, continue CYC pulses at 3 week intervals until remission is reached, then give another 3 months of CYC pulse therapy before you proceed to the remission maintenance regimen. Remission must be reached by 9 months and the total duration of CYC must not exceed 12 months as above

• CYC dose reduction for age > 60 and for creatinine 300-500umol/l as table below

• Maximum CYC pulse is 1.2g

Pulsed CYC dose reductions for renal function and age

age (years)	creatinine (umol/l)	
	150-300	300-500
>60	15mg/kg/pulse	12.5mg/kg/pulse
>60 and <70	12.5mg/kg/pulse	10mg/kg/pulse
>70	10mg/kg/pulse	7.5mg/kg/pulse

INTRAVENOUS CYCLOPHOSPHAMIDE

(PHYSICIAN ORDER SHEET)

[To be kept in Patient's Cylophosphamide File]

Based on NIH, EURO-LUPUS & Vasculitis Protocol
Adapted by Hospital Selayang

Date:

PRE-INFUSION CHECKLIST

Assess Signs & Symptoms of infection, fever, surgery, etc. (Contact physician if any issues)

NON-MEDICATION ORDERS

VITALS:

☐ Weight _____kg

☐ Vital Signs at Baseline

☐ Vital signs every ____ mins (Recommendation: q30min during & 30 mins after infusion. If prior history of an infusion reaction, monitor vitals q10mins for 30 mins then q30mins)

BLOOD WORKS

INFUSION DAY

☐Before Infusion

☐FBC, Platelets, Renal profile

☐(Creatinine), Urine.

☐ _____

☐ _____

Day-10 (After Cyclo)

☐ FBC, platelets, Renal profile (Creatinine), Urine

☐ _____

☐ _____

Physician Signature & Stamp:

PATIENT'S DATA

Name :

MRN :

Ward 10B Bed: _____ / Daycare

Drug Allergy:

_____

_____

MEDICATION ORDERS (Please tick (√) in appropriate ☒ boxes)

Cyclophosphamide Regimen *(Cyclophosphamide is available in 500mg/vial)*

Please tick (√) in appropriate ☒ boxes

Recommend: 3-6 doses depending on disease type, severity & response.

☐ **EURO-LUPUS Protocol**

IV Cyclophosphamide 500mg + Mesna 200mg every 2 weeks for ____ doses

☐ **NIH Protocol (Dose : 500 - 1000mg/m²)**

IV Cyclophosphamide _____mg + Mesna 200mg monthly for ____ doses

☐ **Vasculitis Protocol (Dose: 15mg/kg [Max: 1200mg])**

☐ IV Cyclophosphamide _____ mg + Mesna 200mg

☐ Every 2 weeks for 3 doses; then…

☐1st Dose ☐2nd Dose ☐3rd Dose

☐ Then, every 3 weeks. Once in remission, continue another 3 months

Others: IV Cyclophosphamide _____ mg _____

_____

Cyclophosphamide Preparation and Administration

☐ Cyclophosphamide Preparation is on **Monday & Wednesday**. Order form to arrive at pharmacy **before 10am on day of preparation**. Recommend to send order form for next Cyclophosphamide dose on patient's infusion day.

☐ Infuse IV Cyclophosphamide over _____(2) hours.

(**Rate: _____(250)mL/hr**)

☐ **Infusion Related Reaction: STOP infusion immediately. Notify Prescriber**

Hydration

☐ Normal Saline 0.9% _____ mL IV over _____ hour(s), start **1 hour before** IV Cyclophosphamide infusion

☐ Normal Saline 0.9% _____ mL IV over _____ hour(s), **after** IV infusion completed.

Pre/Post-Medication (ie. Metoclopramide, Dexamethasone)

☐ Pre / Post _____ ☐

Pre / Post _____

IV Golimumab

Human monoclonal antibody that binds to human tumor necrosis factor alpha (TNF)

Indications:

- Rheumatoid arthritis
- Psoriatic arthritis (please fill up "patient consent form")
- Ankylosing spondylitis (please fill up "patient consent form")

Dosage: (Appendix)

Golimumab is available in Intravenous (IV) or Subcutaneous (S/C)
*IV-Please apply for KPK approval

1) Rheumatoid arthritis:

IV: 2 mg/kg at weeks 0, 4, and then every 8 weeks thereafter (in combination with methotrexate or other nonbiologic DMARDs)
S/C: 50 mg once a month (in combination with methotrexate or other nonbiologic DMARDs)

2) Psoriatic arthritis/Ankylosing spondylitis:

IV: 2 mg/kg at weeks 0, 4, and then every 8 weeks thereafter (either alone or in combination with methotrexate or other nonbiologic DMARDs)
S/C: 50 mg once a month (either alone or in combination with methotrexate or other nonbiologic DMARDs)

Potential adverse effects:

- Infection – bacterial/viral/fungal
- TB
- SLE and autoimmunity: Positive ANA titre; lupus like syndrome
- Decreased neutrophils, leucopaenia
- Transaminitis

Monitoring parameters:

1) Signs and symptoms of infection
2) FBC, AST, ALT, Creatinine, CRP, ESR – prior to week 4 then 12 weekly during therapy

IV Infliximab

Infliximab is a chimeric monoclonal antibody that binds to human tumor necrosis factor alpha (TNF_α), thereby interfering with endogenous TNF_α activity

Use:

1) Rheumatoid arthritis
2) Psoriatic arthritis
3) Ankylosing spondylitis
4) JIA

Dosage:

1) Rheumatoid arthritis:

3 mg/kg at 0, 2, and 6 weeks, followed by 3 mg/kg every 8 weeks thereafter (in combination with methotrexate or other DMARDs)

2) Psoriatic arthritis /Ankylosing Spondylitis

5 mg/kg at 0, 2, and 6 weeks, followed by 5 mg/kg every 8 weeks thereafter (with or without methotrexate)

3) Potential adverse effects:

- Hepatic: Increased serum ALT (<3 x ULN: 17% to 51%; >3 x ULN: 2% to 10%; >5x ULN: 1% to 4%)
- Immunologic:
- Increased ANA titer (~50%), antibody development (double-stranded DNA, ~20%)
- antibody development (6% to 15%; more immunogenic when given as a single induction dose, episodic treatment, and monotherapy; Mayer 2006)
- Infection

Monitoring parameters:

Sign and symptoms of infection (prior to and during therapy)-including tuberculosis
FBC, LFT- prior to, week 4 then 8 weekly during therapy

Date:

INTRAVENOUS GOLIMUMAB

(PHYSICIAN ORDER SHEET)

[To be kept in Patient's Biologic File]

Based on Pack Insert of Simponi® for Malaysia
Adapted by Hospital Selayang

PRE-INFUSION CHECKLIST

Assess Signs & Symptoms of infection, fever, surgery, etc. (Contact physician if any issues)

NON-MEDICATION ORDERS

VITALS:

- ☐ Weight _____kg
- ☐ Vital Signs at Baseline
- ☐ Vital signs every ____ mins

(Recommendation: q30min during & 30 mins after infusion. If prior history of an infusion reaction, monitor vitals q15mins for 60 mins then q30mins)

BLOOD WORKS
(before next biologic clinic)

- ☐ FBC, ALT, AST, ALP, Creatinine, ESR, CRP
- ☐ _____
- ☐ _____

Physician Signature & Stamp:

PATIENTS DATA

Name :	Drug Allergy:
MRN :	_____
Ward 10B Bed: _____ / Daycare	_____

MEDICATION ORDERS (Please tick (√) in appropriate ☐ Boxes)

Dosing of Golimumab Infusion

- ☐ **Initial therapy:** Golimumab Loading Dose at:
  - ☐ Week 0 ☐ Week 4
- ☐ **Maintenance Therapy:** Golimumab every _____(8) weeks thereafter.

GOLIMUMAB INFUSION

(Golimumab is available in 50mg/4mL)

DOSE: Golimumab **2mg/kg**; **Total Dose**: _____ mg

- ☐ Withdraw required amount of Golimumab
- ☐ Dilute with 0.9% NS to a final volume of 100mL.
- ☐ Remember to attach infusion filter (pore size ≤1.2µm) to IV line
- ☐ Infuse Golimumab **over 30 minutes** (Rate: **200mL/h**)
- ☐ **Infusion related reaction: STOP infusion immediately. Notify Prescriber**

PRN Pre Med Medications *(if patient has previous infusion reaction before)*

Please tick (√) in appropriate ☐ boxes

- ☐ Chlorpheniramine (Piriton®) Tablet 4mg **OR** 10mg IV
- ☐ Paracetamol Tablet 1g
- ☐ Hydrocortisone 100mg IV **OR** ☐ Methylprednisolone 100mg IV

INTRAVENOUS INFLIXIMAB

(PHYSICIAN ORDER SHEET)

[To be kept in Patient's Biologic File]

Based on Pack Insert of Remicade® & Remsima® for Malaysia
Adapted by Hospital Selayang

Date:

PRE-INFUSION CHECKLIST

Assess Signs & Symptoms of infection, fever, surgery, etc. (Contact physician if any issues)

NON-MEDICATION ORDERS

VITALS:

- ☐ Weight _____kg
- ☐ Vital Signs at Baseline
- ☐ Vital signs every ____ mins

(Recommendation: q30min during & 30 mins after infusion. If prior history of an infusion reaction, monitor vitals q15mins for 60 mins then q30mins)

BLOOD WORKS
(before next biologic clinic)

- ☐ FBC, ALT, AST, ALP, Creatinine, ESR, CRP
- ☐ _____
- ☐ _____

Physician Signature & Stamp:

PATIENT'S DATA

Name :

MRN :

Ward 10B Bed: _____ / Daycare

Drug Allergy:

_____

_____

MEDICATION ORDERS (Please tick (√) in appropriate ☐ boxes)

INFLIXIMAB BRANDS

☐ Remicade® *(Innovator)* ☐

Remsima® *(Biosimilar)*

Dosing of Infliximab Infusion

☐ **Initial Therapy:** Infliximab Loading Dose at:

☐ Week 0 ☐ Week 2 ☐ Week 6

☐ **Maintenance Therapy:** Infliximab every _____ weeks thereafter.

(Usually every 8 weeks, ranged from 4-8 weeks)

Pre-Med Medications

Please tick (√) in appropriate ☐ boxes

- ☐ Chlorpheniramine (Piriton®) Tablet 4mg **OR** 10mg IV
- ☐ Paracetamol Tablet 1g
- ☐ Hydrocortisone 100mg IV **OR** ☐ Methylprednisolone 100mg IV

INFLIXIMAB INFUSION *(Complete infusion within 4hrs after reconstitution)*

(Infliximab is available in 100mg/vial)

DOSE: Infliximab ____ mg/kg; **Total Dose**: _____ mg

RA : 3mg/kg (ranged 3-10mg/kg); Others (ie. AS, PsA) : 5mg/kg

- ☐ Reconstitute each vial with 10mL WFI (10mg/mL)
- ☐ Withdraw required amount of Infliximab
- ☐ Dilute Infliximab with 0.9% NS to a final volume of 250mL.
- ☐ Remember to attach infusion filter (pore size ≤1.2µm) to IV line
- ☐ **Infuse Infliximab as below:**
  - ☐ **First Time / Whom have had an infusion reaction before**

    (Total infusion time approx: 3 hours)

    10mL/h for 15 mins, then

    ☐ 20mL/h for 15 mins, then ☒

    40mL/h for 30 mins, then ☒

    80mL/h for 30 mins, then ☒

    125mL/h until complete.

  REGULAR Patient

  Infuse over a minimum of 2 hours (Rate:≤125mL/h)

Infusion related reaction: STOP infusion immediately. Notify Prescriber

Tocilizumab

Tocilizumab is a recombinant humanised anti-human interleukin-6 receptor (anti-IL6) mono clonal antibody that binds both
soluble and membrane bound IL-6

Use:
Rheumatoid arthritis
Juvenile idiopathic arthritis
Giant Cell Arteritis

Dosage: (Appendix 4)
Tocilizumab is available in Intravenous (IV) or Subcutaneous (S/C)

1) Rheumatoid arthritis (with or without methotrexate)

IV: Initial: 4 mg/kg once every 4 weeks; may be increased to 8 mg/kg once every 4 weeks based on clinical response (maximum dose: 800 mg).

S/C:
A) <100 kg: 162 mg once every other week; increase to 162 mg once every week based on clinical response
B) >100 kg: 162 mg once every week

* Transitioning from IV therapy to S/C therapy: Administer the first S/C dose instead of the next scheduled IV dose

Potential adverse effect of tocilizumab:

1. Infection: Upper respiratory tract infections, herpes zoster
2. Metabolic: Hypercholesterolemia, increased LDL cholesterol
3. Hematologic: Neutropenia, thrombocytopenia, leukopenia
4. Hepatic: Increased serum alanine aminotransferase (<36%), increased serum aspartate aminotrans erase (<22%)

Monitoring parameters:

- Sign and symptoms of infection (prior to and during therapy)-including tuberculosis
- FBC, AST,ALT, Creatinine, CRP, ESR- prior to therapy, 4 to 8 weeks after start of therapy, and every 3 months thereafter
- Lipid profile-prior to, week 8 then every 6 months during therapy
- Signs and symptoms of CNS demyelinating disorders

Rituximab

Rituximab is a chimeric mouse/human monoclonal antibody directed against the CD20 antigen on the surface of B- lymphocytes.

Use:

1) Rheumatoid arthritis
2) Vasculitis

* off label use: Autoimmune hemolytic anemia, Immune thrombocytopenia (refractory), Lupus nephrtis (Please fill up consent form)

Dosage: (Appendix 5)

1) Rheumatoid arthritis: 1,000 mg on days 1 and 15 (in combination with methotrexate) subsequent courses may be administered every 24 weeks (based on clinical evaluation), if necessary may be repeated no sooner than every 16 weeks
2) Vasculitis: 375 mg/m2 once weekly for 4 doses (in combination with methylprednisolone IV for 1 to 3 days followed by daily prednisolone)

Potential adverse effect of Rituximab:

- Infusion reactions: usually occur within 30 to 120 minutes and may include hypotension, angioedema, bronchospasm, hypoxia, urticaria, and, in more severe cases, pulmonary infiltrates, acute respiratory distress syndrome, MI, ventricular fibrillation, cardiogenic shock, and/or anaphylactoid events
- Infection
- Hepatitis B virus reactivation

Monitoring parameters:

- Sign and symptoms of infection (prior to and during therapy)-including tuberculosis
- FBC, LFT- prior and at 2- to 4-month intervals
- Screen all patients for HBV infection prior to therapy initiation (eg, HBsAG and anti-HBc measurements), monitor patients for clinical and laboratory signs of hepatitis or HBV reacti vation during and up to 12 months after treatment

INTRAVENOUS TOCILIZUMAB

(PHYSICIAN ORDER SHEET)

[To be kept in Patient's Biologic File]

Based on Pack Insert of Actemra® for Malaysia
Adapted by Hospital Selayang

Date:

PRE-INFUSION CHECKLIST

Assess Signs & Symptoms of infection, fever, surgery, etc. (Contact physician if any issues)

NON-MEDICATION ORDERS

VITALS:

- ☐ Weight _____kg
- ☐ Vital Signs at Baseline
- ☐ Vital signs every ____ mins (Recommendation: q30min during & 30 mins after infusion.)

BLOOD WORKS
(before next biologic clinic)

- ☐ FBC, ALT, AST, ALP, Creatinine, ESR, CRP
- ☐ Fasting Lipids (6-12monthly)
- ☐ _____
- ☐ _____

Physician Signature & Stamp:

PATIENT'S DATA

Name :	Drug Allergy:
MRN :	_____
Ward 10B Bed: _____ / Daycare	_____

MEDICATION ORDERS (Please tick (√) in appropriate ☐ boxes)

Dosing of Infliximab Infusion

(Tocilizumab is available in 400mg/20mL and 80mg/4mL)

- ☐ **Frequency:** Tocilizumab given every ____(4) weeks
- ☐ **Dose:**
  - ☐ **Tocilizumab 8mg/kg:** Total Dose: _____ mg **(MAX : 800mg)**
  - ☐ **Tocilizumab 4mg/kg:** Total Dose: _____ mg
- ☐ Withdraw required amount of Tocilizumab
- ☐ Dilute with 0.9% NS to a final volume of 100mL.
- ☐ Infuse Tocilizumab over 60 minutes (**Rate: 100mL/h**)
- ☐ **Infusion related reaction: STOP infusion immediately. Notify Prescriber**

PRN Pre-Med Medications *(if patient has previous infusion reaction before)*

Please tick (√) in appropriate ☐ boxes

- ☐ Chlorpheniramine (Piriton®) Tablet 4mg **OR** 10mg IV
- ☐ Paracetamol Tablet 1g
- ☐ Hydrocortisone 100mg IV **OR** ☐ Methylprednisolone 100mg IV

INTRAVENOUS RITUXIMAB

(PHYSICIAN ORDER SHEET)

[To be kept in Patient's Biologic File]

Based on Pack Insert of MabThera® for Malaysia
Adapted by Hospital Selayang

Date:

PRE-INFUSION CHECKLIST

Assess Signs & Symptoms of infection, fever, surgery, etc. (Contact physician if any issues)

NON-MEDICATION ORDERS

VITALS:

☐ Weight _____kg

☐ Vital Signs at Baseline

☐ Vital signs every ____ mins (Recommendation: q30min during & 30 mins after infusion. If prior history of an infusion reaction, monitor vitals q10mins for 30 mins then q30mins)

BLOOD WORKS
(before next biologic clinic)

☐ FBC, ALT, AST, ALP, Creatinine, ESR, CRP

☐ _____

☐ _____

Physician Signature & Stamp:

PATIENT'S DATA

Name :	Drug Allergy:
MRN :	_____
Ward 10B Bed: _____ / Daycare	_____

MEDICATION ORDERS (Please tick (√) in appropriate☒ boxes)

Dosing of Rituximab Infusion

☐ **RA Protocol**

☐ 1st dose (1000mg) and repeat in 15 days

☐ 2nd dose (1000mg) and repeat cycle after 4-6 months.

☐ **Other Indications**

☐ 500mg weekly for 4 weeks and repeat cycle after 4-6 months.

☐ Week 1 ☐ Week 2 ☐ Week 3 ☐ Week 4

☐ **Other Dose:** _____

Pre-Med Medications (≥30 mins before infusion)

Please tick (√) in appropriate ☐ boxes

☐ Paracetamol Tablet 1g

☐ Chlorpheniramine (Piriton®) Tablet 4mg **OR** ☐ 10mg IV

☐ Methyprednisolone 100mg IV **OR** ☐ Hydrocortisone 100mg IV ☐

Others : _____

RITUXIMAB INFUSION

(Rituximab is available in 500mg/50mL)

☐ Withdraw required amount of Rituximab

☐ Dilute with 0.9% NS. (Recommended Concentration : 1-4mg/mL)

☐ 1000mg to final volume of 250mL

☐ 500mg to final volume of 125mL

☐ _____mg to final volume of _____mL

☐ **Infuse Rituximab as below:**

☐ **First Time / Whom have had an infusion reaction before**

Every 30 mins, titrate from **12.5mL/h** ☐ **25mL/h** ☐ **37.5mL/h** ☐ **50mL/h** ☐ **62.5mL/h** ☐ **75mL/h** ☐ **87.5mL/hr** ☐ **100mL/h** until complete

☐ **REGULAR Patient**

Every 30 mins, titrate from **25mL/h** ☐ **50mL/h** ☐ **75mL/h** ☐ **100mL/h** until complete

☐ **Other Infusion Rates (Max Rate: 100mL/h)**

Every 30 mins, titrate from _____**mL/h** ☐ _____**mL/h** ☐ _____**mL/h** _____**mL/h** ☐ _____**mL/h** ☐ _____**mL/h** ☐ _____**mL/h** ☐ _____**mL/h** ☐ _____**mL/h** ☐ _____**mL/h** until complete

☐ **Infusion related reaction: STOP infusion immediately. Notify Prescriber**

Belimumab

Belimumab is an IgG1-lambda monoclonal antibody that prevents the survival of B lympho cytes by blocking the binding of soluble human B lymphocyte stimulator protein (BLyS) to receptors on B lymphocytes

Use:

Systemic lupus erythematosus: Treatment of adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) who are receiving standard therapy

Dosage:

Initial: 10 mg/kg every 2 weeks for 3 doses; Maintenance: 10 mg/kg every 4 weeks

Potential adverse effect of Belimumab:

- Gastrointestinal: Nausea (15%), diarrhoea (12%)
- Hypersensitivity/infusion reaction: Hypersensitivity (13%), Infusion rela ted reaction (17%)
- Infection

Monitoring parameters:

- Latent TB screening prior to therapy initiation
- Sign and symptoms of infection (prior to and during therapy)-including tuberculosis
- FBC, LFT- prior to therapy, 4 to 8 weeks after start of therapy, and every 3 months thereafter
- Worsening of depression, mood changes, or suicidal thoughts

INTRAVENOUS BELIMUMAB
(PHYSICIAN ORDER SHEET)

[To be kept in Patient's Biologic File]

Based on Pack Insert of Benlysta® for Malaysia
Adapted by Hospital Selayang

Date:

PRE-INFUSION CHECKLIST

Assess Signs & Symptoms of infection, fever, surgery, etc. (Contact physician if any issues)

NON-MEDICATION ORDERS

VITALS:

Weight _____kg

Vital Signs at Baseline

Vital signs every ____ mins

(Recommendation: q30min during & 30 mins after infusion. If prior history of an infusion reaction, monitor vitals q15mins for 60 mins then q30mins)

BLOOD WORKS
(before next biologic clinic)

- FBC, ALT, AST, ALP, Creatinine, ESR, CRP
- _____
- _____

Physician Signature & Stamp:

PATIENT'S DATA

Name:	Drug Allergy:
MRN:	_____
Ward 10B Bed: _____ / Daycare	_____

MEDICATION ORDERS (Please tick (√) in appropriate boxes)

Dosing of Belimumab Infusion

Initial Therapy: Belimumab Loading Dose at:

Week 0 Week 2 Week 4

Maintenance Therapy: Belimumab every _____ weeks thereafter.

(Usually every 4 weeks)

Pre-Med Medications

Please tick (√) in appropriate boxes

☐ Chlorpheniramine (Piriton®) Tablet 4mg **OR** 10mg IV

☐ Paracetamol Tablet 1g

Hydrocortisone 100mg IV **OR** Methylprednisolone 100mg IV

BELIMUMAB INFUSION

(Belimumab is available in 120mg/vial)

DOSE: Belimumab **10mg/kg**; **Total Dose**: _____ mg

- Reconstitute with 1.5mL WFI in each vial(s) [Final Concentration after recon: 80mg/ml/Vial]
- Withdraw required amount of Belimumab
- Dilute with 0.9% NS to a final volume of 250mL.
- Infuse Belimumab **over 60 minutes (Rate: 250mL/h)**

ø **Infusion related reaction: STOP infusion immediately. Notify Prescriber**

PRN Pre-Med Medications *(if patient has previous infusion reaction before)*

Please tick (√) in appropriate boxes

Chlorpheniramine (Piriton®) Tablet 4mg **OR** 10mg IV

Paracetamol Tablet 1g

Hydrocortisone 100mg IV **OR** Methylprednisolone 100mg IV

Appendix 5
Investigations

Immunological tests			
Test	Indication		Notes
Rheumatoid factor (RhF)	Send for all suspected RA cases at baseline Send for all suspected PsA cases at baseline	Local lab	Has prognostic value in RA May also be +ve in Sjogren's and cryoglobunaemic vasculitis -ve RhF is part of CASPAR criteria
Citrullinated cyclic peptide antibody (anti-CCP)	Send for all suspected RA cases at baseline	Local lab	Has prognostic value
Anti-nuclear antibody	Send for all suspected CTD cases at baseline	Local lab	
Extractable nuclear antigens (antiRo, antiLa, antiJo, antiScl70, antiSm, anti-histone)	Send for all suspected CTD cases at baseline	Local lab	
Antidouble-stranded DNA (anti-DsDNA)	Send for suspected SLE cases at baseline and when flare suspected; may repeat at yearly intervals once stable	Local lab	High titre may indicate disease flare esp lupus nephritis
Complement 3 & 4 (C3, C4)	Send for suspected SLE cases at baseline and when flare suspected; may repeat at 6 monthly intervals once stable	Local lab	Low level may indicate disease flare/impending flare esp in lupus nephritis
Anti-neutrophil cytoplasmic antibody (ANCA)	Send for suspected vasculitis cases at baseline and when flare suspected; may repeat at 6 monthly intervals once stable	Local lab	Cytoplasmic ANCA (cANCA) and proteinase 3 antigen (PR3) suggests granulomatous polyangiitis (GPA/Wegener's) Perinuclear ANCA (pANCA) and Myeloperoxidase antigen (MPO) suggests microscopic polyangiitis (MPA); with eosinophilia suggests Churg-Strauss pANCA also found in other CTDs
Serum IgA	Send in suspected Henoch-Schonlein-Purpura cases	Local lab	Increased in 50% of cases

Myositis specific antibodies	Send for all suspected polymyositis and dermatomyositis causes at baseline antiJo1, antiPL7, antiPL12 – antisynthetase syndrome antiEJ – DM and ILD anti-OJ- myositis and ILD antiKS – ILD with less myositis antiZo – myositis and ILD antiMi2 – DM, good resp to steroid anti-SRP – PM, treatment-resistent myopathy (necrotising myopathy) anti-MDA5;CADM140 – clincally amyopathic DM, rapidly progressive DM antiTIF1-y (anti155/150) – cancer associated myositis anti-SAE – clinically amyopathic DM antiHMGCR – a/w statin use antiNXP2 – JDM with calcinosis, contractures, increased risk of cancer in adults	IMR/PPUM	*other tests for suspected inflammatory myopathy: MRI of affected muscles; EMG; muscle biopsy (targeted using MRI) Use green lab form PPUM (Ext 2025)
Myositis associated Ab	antiPM/SCL, antiKu, antiU1RNP	IMR/PPUM	
anti-phospholipid antibody (anticardiolipin Ab; antiβ2gp1)	Send at baseline, then repeat 12 weeks apart (to meet antiphospholipid syndrome diagnostic criteria)	Local lab	Also part of SLICC criteria
Lupus anticoagulant	Send at baseline BEFORE starting anticoagulation	Pusat Darah Negara	Use thombophilia screening form
Genetic tests			
HLAB27	Send for all suspected spondyloarthropathy cases (AS, PsA with SpA, enteropathic arthritis) at baseline	IMR (orderable in system)	Inform nurse to get appointment from IMR Fill up 'HLA typing test' request form
HLAB51	Send for suspected Behcet's disease at baseline	IMR	As above
HLAB*5801	For patients suspected of risk of allopurinol hypersensitivity	IMR	As above
Misc tests			
TB Gold Quantiferon	Pre-biologic screening: Before starting any new biologic/tsDMARD	Local lab	Fill up green lab form; ELISA tubes are in the clinic (test taken by nurse)
Procalcitonin	To differentiate bacterial infection (>5mcg/L) and flare in SLE/other CTD	IKN	Inform IKN pathology MO oncall Fill up green lab form Blood in 1 plain tube with >2ml blood Test is run on Mon;Wed;Fri

Aquaporin4 serum or CSF	Send for suspected neuromyelitis optica spectrum disease (NMOSD)	IMR	Fill up green lab form
Electromyogram (EMG)	To distinguish between inflammatory myopathies and muscular dystrophies	HKL	Call Neurophysiology room (ext 1052) to set date If need urgent/early date, call Neurology specialist Fill up EMG/NCS form and fax to HKL Neurophysiology unit
Nerve conduction study	Assess peripheral nerve dysfunction in patients at baseline and to assess response to treatment	HKL	As above
Muscle biopsy	Distinguish DM, PM and other forms of myopathy	HKL	Refer orthopaedic team for muscle biopsy (sample size 1*1*1cm) Call Dr Suryati Yusoff (HKL Histopathologist ext 5619) Inform HKL histopathology lab ext 6651) – MLT Nadiah, call back 1 day before the procedure Use green lab form Specimen handling: Wrap sample with aluminium foil and palce inside specimen bottle. Transport in ice-packed bag and send within 4 hours after tissue sampling Sample to be sent to 'Pintu 6' Histopath Lab, Level 1, Main Block

Appendix 6

Biologic Application

Government/ATM pensioner

- Inform rheumatology pharmacist before prescribing biologics (only applicable at initiation of biologic and change of biologic)

Government employee

- Fill up Form: Jabatan Perkhidmatan Awam Borang Perubatan 1/09(T), to be signed by gazet ted rheumatologist
- Provide manual PS, apply for 6 months each time
- Provide supporting letter, address to 'Pegawai Berkenaan, Kementerian …' eg. For teachers, 'Kementerian Pendidikan'
- Inform the rheumatology pharmacist regarding the application (will arrange for invoice from supplier)
- Repeat the above steps every 6 months

TBP

- Only applicable for applicants who are applying for the first time and with 1 repeat (in a lifetime), each approval will be granted for 6 months
- Fill up Borang C (to be signed by gazetted rheumatologist and HOD) and Lampiran D (top section; bottom section to be filled up by Head of Rheumatology Service)
- Refer patient to Social worker for financial assessment and preparation of other forms required for submission
- Inform rheumatology pharmacist (will arrange for quotations)

Appendix 7

Drugs in renal patient

Prepared by Ms Ong Zee Yun, Pharmacist (Nephrology)
Hospital Melaka

Renal dose adjustments of drugs commonly used in rheumatology

NSAIDs and COX-2 inhibitors

Drugs	Dose	Renal adjustment		
		>60 ml/min	30-60 ml/min	<30 ml/min
Diclofenac sodium	50 mg tds/qid	No dose adjustment. Lowest effective dose for shortest possible duration		Avoid
Ibuprofen	400-800 mg tds/qid (max: 3.2 g/day)	No dose adjustment. Lowest effective dose for shortest possible duration		Avoid
Indomethacin	25 mg bd/tds, may increase at weekly intervals until satisfactory response (max: 200 mg/day)	No dose adjustment. Lowest effective dose for shortest possible duration		Avoid
Mefenamic acid	500 mg tds or 250mg qid	No dose adjustment. Lowest effective dose for shortest possible duration		Avoid
Naproxen sodium	550-1100 mg/day in 2 divided doses	No dose adjustment. Lowest effective dose for shortest possible duration		Avoid
Meloxicam	7.5-15 mg od	No dose adjustment. Lowest effective dose for shortest possible duration		Avoid ≤ 20ml/min
Celecoxib	200 mg bd	No dose adjustment. Lowest effective dose for shortest possible duration		Avoid
Etoricoxib	90 mg od Acute Gout: 120 mg od for max 8 days	No dose adjustment. Lowest effective dose for shortest possible duration		Avoid

Immunosuppressant Agents

Drugs	Dose	Renal adjustment		
		>60 ml/min	30-60 ml/min	<30 ml/min
Azathioprine	1 mg/kg/day (50-100 mg/day in 2 divided doses) (max 2.5 mg/kg/day)	>50 ml/min: no dose adjustment	10-50 ml/min: 75% of normal dose	<10 ml/min: 50% of normal dose; HD: 50% of normal dose, supplement: 0.25 mg/kg CRRT: 75% of normal renal dose
Cyclosporine	2.5 mg/kg/day in 2 divided doses; increase gradually after 6-8 weeks (max: 4 mg/kg/day)	Abnormal renal function during treatment - Se Cr level increase >30% from baseline: decrease cyclosporine dosage by 25-50% ; discontinue if dose reduction is ineffective in controlling Se Cr elevation or if Se Cr elevation is severe		
Leflunomide	10-20 mg od	No dosage adjustments provided in manufacturer's labelling; use with caution. Use is contraindicated in moderate to severe impairment		
Methotrexate	7.5-25 mg/weekly	(Aronoff 2007) 10-50 ml/miin: 50% of normal dose		<10 ml/min: Avoid Intermittent HD / CRRT: 50% of normal dose
		(Kintzel 1995) 46-60 ml/min: 65% of normal dose 31-45 ml/min: 50% of normal dose		<30 ml/min: Avoid

Antimalarial drugs

Drugs	Dose	Renal adjustment		
		>60 ml/min	30-60 ml/min	<30 ml/min
Hydroxychloroquine	200-400 mg/day : daily or in 2 divided doses (not to exceed 6.5 mg/kg/day based on IBW)	No dose adjustment provided in manufacturer's labelling; dose reduction may be needed. Use with caution.		

5-Aminosalicylic Acid Derivative

Drugs	Dose	Renal adjustment		
		>60 ml/min	30-60 ml/min	<30 ml/min
Sulfasalazine	500 mg od/bd, increase weekly to max of 2-3 g/day	No dose adjustment provided in manufacturer's labelling. Use with extreme caution.		

Appendix 8

Combined PAH Clinic Referral Letter Template

information to be provided in the referral letter

General

Patient's Name:

IC Number:

Contact details: HP

Email

Referred from: Name

Hospital

Indication for referral:

Rheum Diagnosis

Details of Rheum diagnosis:
Year diagnosed
Manifestations
Immunology

Other Diagnosis

Investigations done

HRCT
CTPA
Pulmonary function test
Echocardiogram
*if patient has HRCT or CTPA done, pls attach CD with images
Baseline FBC, renal profile, liver function test

Medications

Current medications:

Immunosuppressive history:

Vaccination status:
Pneumococcal
Influenza

Notes

Notes

Notes