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AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases

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CONTRACEPTION

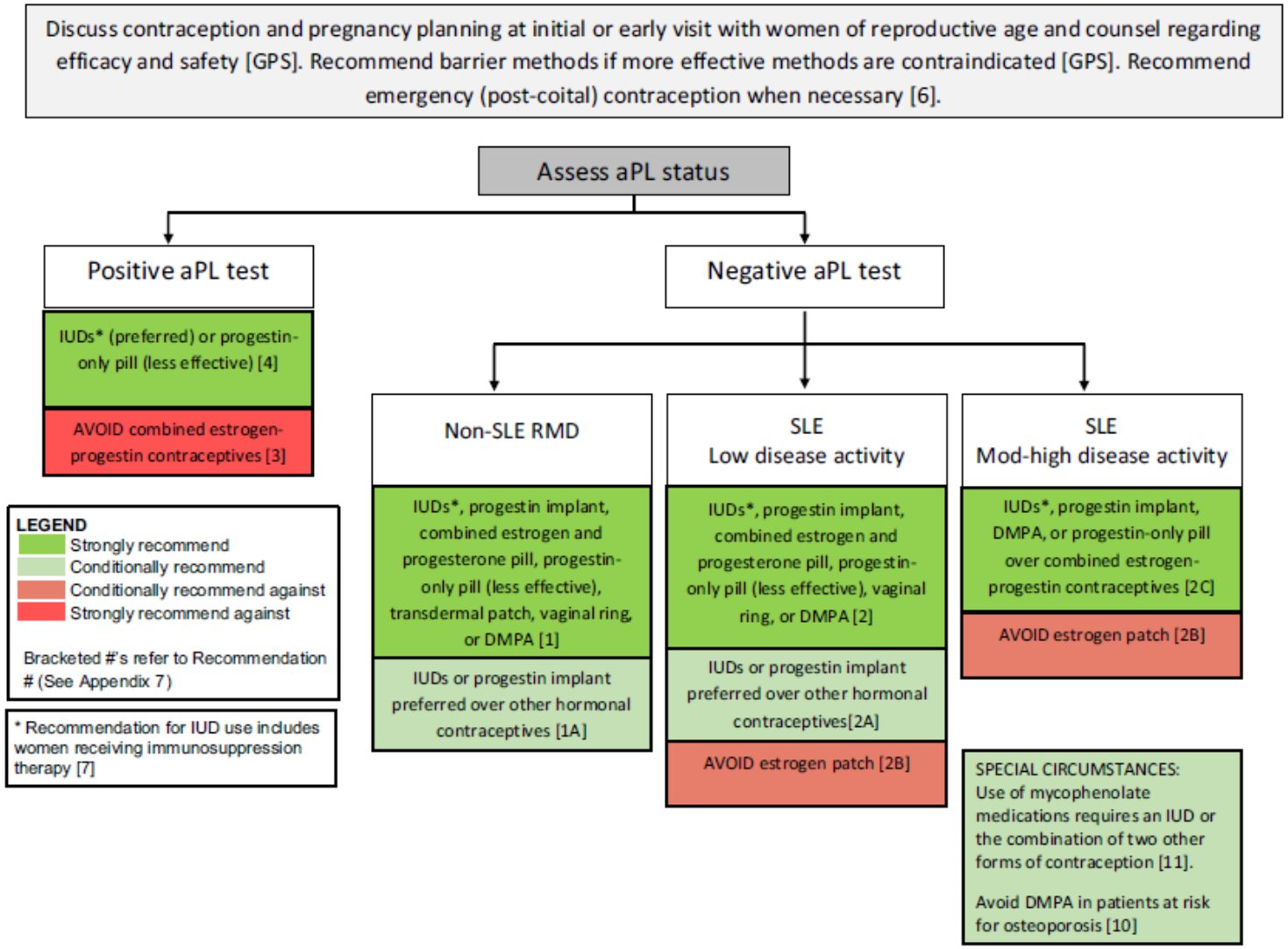


Figure 1. Recommendations and good practice statements (GPS) for use of contraception in women with rheumatic and musculoskeletal disease (RMD). aPL = antiphospholipid antibody (persistent moderate [Mod]–to-high–titer anticardiolipin or anti–β_2-glycoprotein I antibody or persistent positive lupus anticoagulant); IUDs = intrauterine devices (copper or progestin); SLE = systemic lupus erythematosus; DMPA = depot medroxyprogesterone acetate.

PROCRÉATION ASSISTÉE

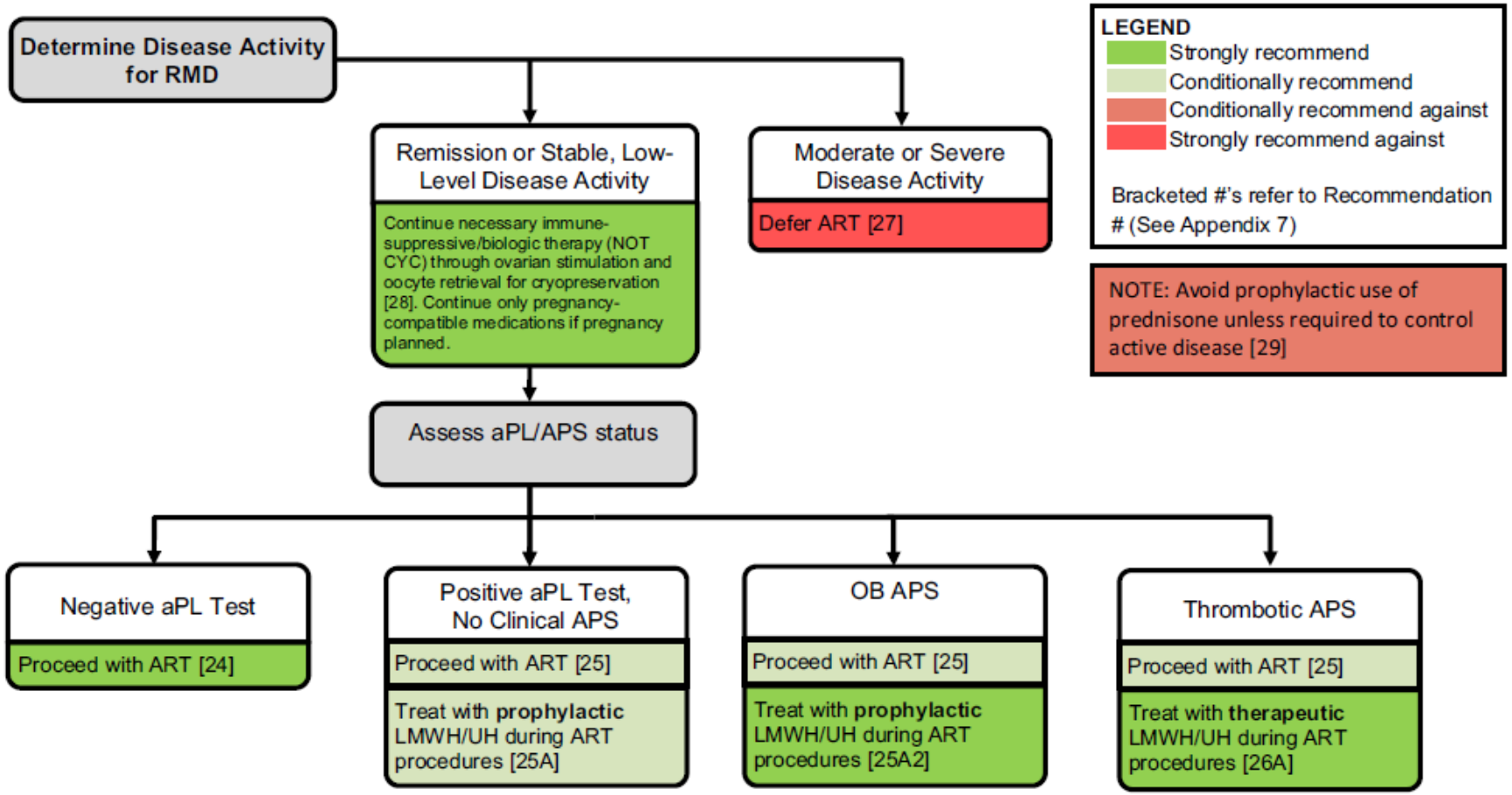


Figure 2. Recommendations for use of assisted reproductive technology (ART) in women with rheumatic and musculoskeletal disease (RMD). CYC = cyclophosphamide; aPL = antiphospholipid antibody (persistent moderate-to-high–titer anticardiolipin or anti–β_2-glycoprotein I antibody or persistent positive lupus anticoagulant); APS = antiphospholipid syndrome (obstetric and/or thrombotic); obstetric APS (OB APS) = patients meeting laboratory criteria for APS and having prior consistent pregnancy complications (≥3 consecutive losses prior to 10 weeks' gestation, fetal loss at or after 10 weeks' gestation, or delivery at <34 weeks due to preeclampsia, intrauterine growth restriction, or fetal distress) and with no history of thrombosis; thrombotic APS = patients meeting laboratory criteria for APS and having a prior thrombotic event (arterial or venous), regardless of whether they have had obstetric complications; LMWH = low molecular weight heparin; UH = unfractionated heparin.

HORMONOTHÉRAPIE DE REMPLACEMENT

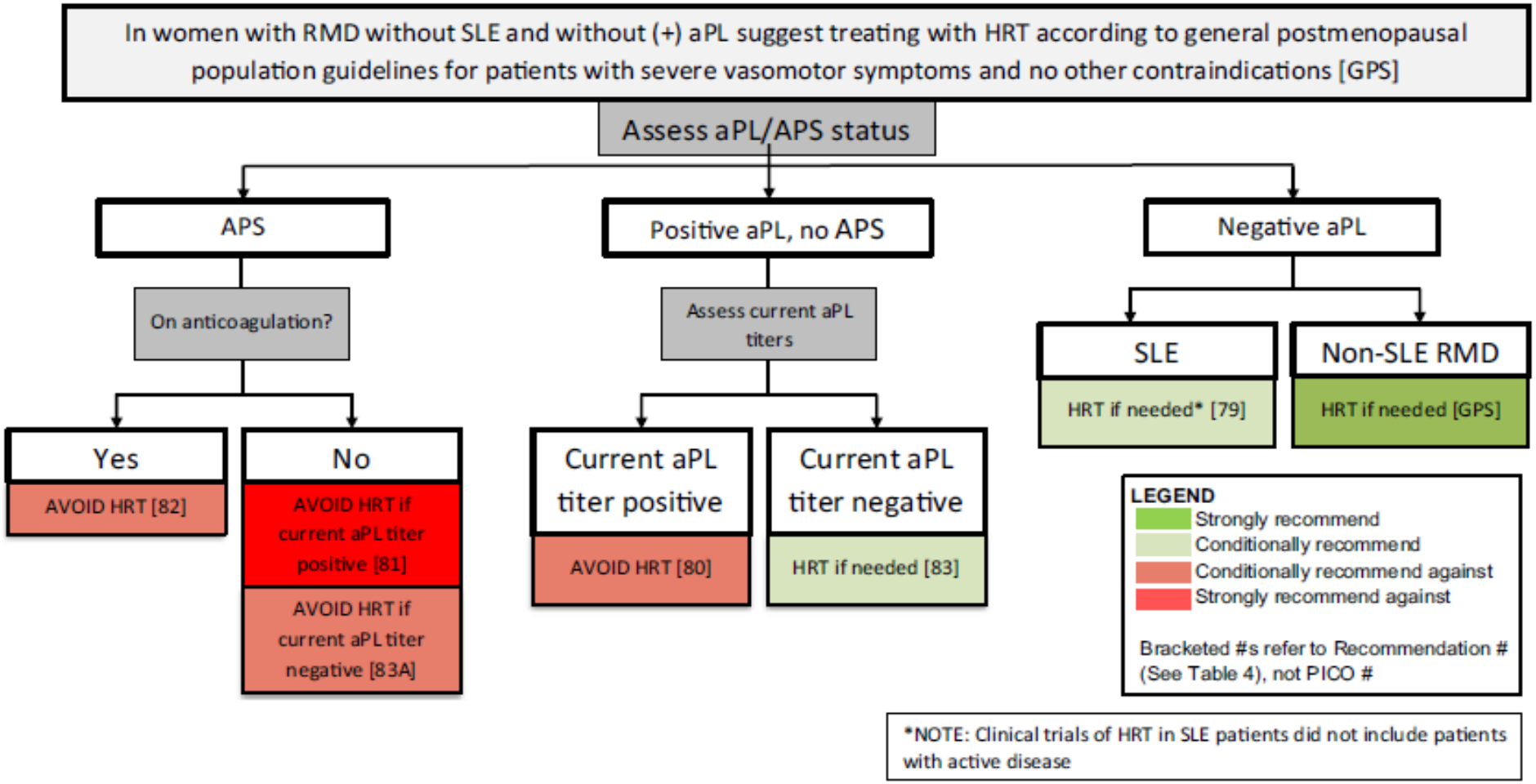


Figure 3. Recommendations and good practice statements (GPS) for hormone replacement therapy (HRT) use in postmenopausal women with rheumatic and musculoskeletal disease (RMD). SLE = systemic lupus erythematosus; aPL = antiphospholipid antibody (persistent moderate-to-high–titer anticardiolipin or anti–β_2-glycoprotein I antibody or persistent positive lupus anticoagulant); APS = antiphospholipid syndrome (obstetric and/or thrombotic); PICO = population, intervention, comparator, outcomes.

PLAN GÉNÉRAL

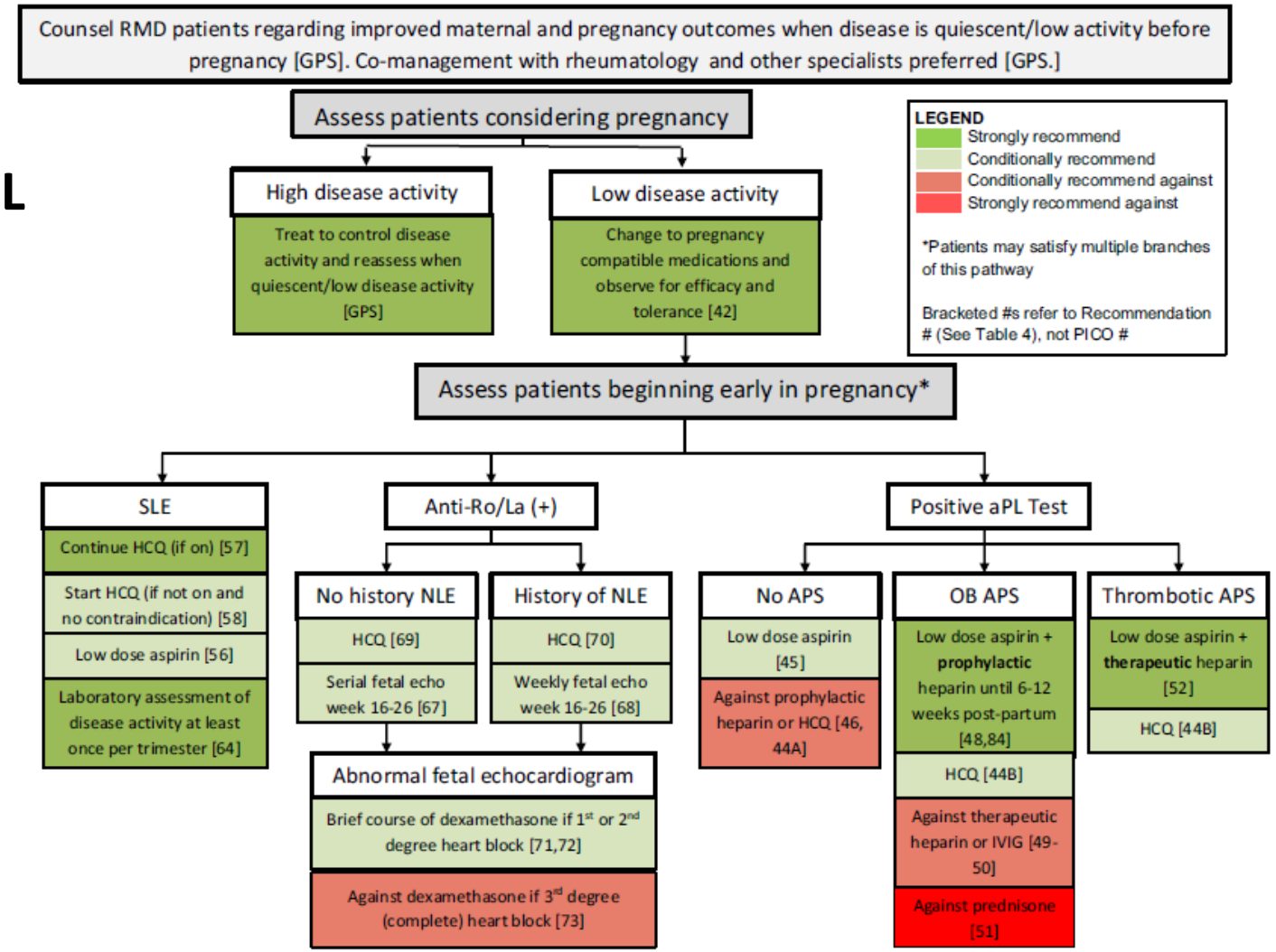


Figure 4. Recommendations and good practice statements (GPS) for pregnancy counseling, assessment, and management in women with rheumatic and musculoskeletal disease (RMD). SLE = systemic lupus erythematosus; HCQ = hydroxychloroquine; NLE = neonatal lupus erythematosus; aPL = antiphospholipid antibody (persistent moderate-to-high–titer anticardiolipin or anti–β_2-glycoprotein I antibody or persistent positive lupus anticoagulant); APS = antiphospholipid syndrome (obstetric and/or thrombotic); obstetric APS (OB APS) = patients meeting laboratory criteria for APS and having prior consistent pregnancy complications (≥3 consecutive losses prior to 10 weeks' gestation, fetal loss at or after 10 weeks' gestation, or delivery at <34 weeks due to preeclampsia, intrauterine growth restriction, or fetal distress) and with no history of thrombosis; thrombotic APS = patients meeting laboratory criteria for APS and having a prior thrombotic event (arterial or venous), regardless of whether they have had obstetric complications; IVIG = intravenous immunoglobulin; PICO = population, intervention, comparator, outcomes.

Inflammatory Arthritis	**Assessment**	• **In patients with RA or JIA check anti-Ro/SSA and/or anti-La/SSB antibodies once pre- or early pregnancy** • Evaluate joint range of motion that may affect ability to delivery vaginally (hips) or to undergo emergency intubation (cervical spine)
	Management	• Continue pregnancy-compatible medications. • Stop methotrexate 1-3 months prior to attempting conception; stop leflunomide, test serum levels and treat with cholestyramine washout if necessary** • Use prednisone sparingly • Continue or restart breastfeeding compatible medication promptly after delivery to prevent a post-partum flare

- **In women with SLE who are currently pregnant:**
  - **We strongly suggest monitoring laboratory tests for disease activity at least once per trimester during pregnancy (GS64)**

- **In women with SLE who are considering pregnancy (or are pregnant):**
  - **If taking hydroxychloroquine, we strongly recommend continuing HCQ during pregnancy (GS57).**
  - **If not taking HCQ, we conditionally recommend starting HCQ if there is no contraindication (GS58)**
  - **We conditionally recommend treating with low dose aspirin (GS56)**

Scleroderma	**Assessment**	• **Evaluate for underlying scleroderma-related organ damage that may affect pregnancy risk**
	Management	• Continue pregnancy-compatible medications to control disease

In women who are pregnant with scleroderma renal crisis,

we strongly recommend **treating with an ACE-inhibitor**

or angiotensin receptor blocker (ARB) (GS55)

Vasculitis, myositis and other RMD	**Assessment**	• **Evaluate for underlying vasculitis-related organ damage that may affect pregnancy risk**
	Management	• Continue pregnancy-compatible medications to control disease • Use prednisone sparingly

GROSSESSE: MÉDICATION

Table 3. Maternal medication use: overview of medication use before and during pregnancy, and during breastfeeding

Medication	Pre-conception	During pregnancy	Breastfeeding
Conventional medications			
Hydroxychloroquine	++	++	++
Sulfasalazine	++	++	++
Colchicine	++	++	++
Azathioprine, 6-mercaptopurine	++	++	+ Low transfer
Prednisone	+ Taper to <20 mg/day by adding pregnancy-compatible immunosuppressants	+ Taper to <20 mg/day by adding pregnancy-compatible immunosuppressants	+ After a dose of >20 mg, delay breastfeeding for 4 hours
Cyclosporine, tacrolimus	+ Monitor blood pressure	+ Monitor blood pressure	+ Low transfer

++ Strongly recommend

\+ Conditionally recommend

× Conditionally recommend against

×× Strongly recommend against

Tumor necrosis factor inhibitors (tumor necrosis factor inhibitors are considered compatible with pregnancy)			
Certolizumab	++	++	++
Infliximab, etanercept, adalimumab, golimumab	+ Continue through conception	+ Continue in first and second trimesters; discontinue in third trimester several half-lives prior to delivery	++
Rituximab	+ Discontinue at conception	+ Life-/organ-threatening disease	++
Other biologics (limited safety data; limited transfer in early pregnancy but high transfer in second half of pregnancy)			
Anakinra, belimumab, abatacept, tocilizumab, secukinumab, ustekinumab	+ Discontinue at conception	× Discontinue during pregnancy	+ Expect minimal transfer due to large molecular size, but no available data

++ Strongly recommend

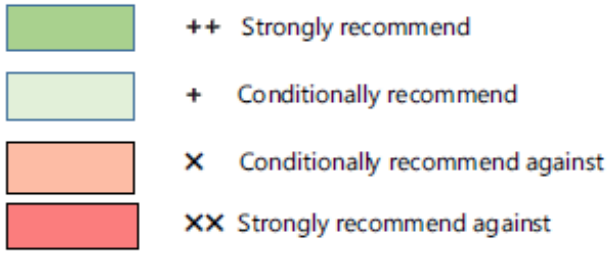
\+ Conditionally recommend

× Conditionally recommend against

×× Strongly recommend against

We conditionally recommend continuing tumor necrosis factor inhibitor therapy with infliximab, etanercept, adalimumab, or golimumab prior to and during pregnancy (164,165). The tumor necrosis factor inhibitor certolizumab does not contain an Fc chain and thus has minimal placental transfer (166). We strongly recommend continuation of certolizumab therapy prior to and during pregnancy.

Not compatible with pregnancy			
Methotrexate	XX Stop 1–3 months prior to conception	XX Stop and give folic acid 5 mg/day	X Limited data suggest low transfer
Leflunomide	XX Cholestyramine washout if detectable levels	XX Stop and give cholestyramine washout	XX
Mycophenolate mofetil and mycophenolic acid	XX Stop >6 weeks prior to conception to assess disease stability	XX	XX
Cyclophosphamide	XX Stop 3 months prior to conception	+ Life-/organ-threatening disease in second and third trimesters	XX
Thalidomide	XX Stop 1–3 months prior to conception	XX	XX
Tofacitinib, apremilast, baricitinib	Unable to determine due to lack of data; small molecular size suggests transfer across the placenta and into breast milk		



++ Strongly recommend

\+ Conditionally recommend

X Conditionally recommend against

XX Strongly recommend against

GROSSESSE : APL

Positive aPL only:

- **In pregnant women with positive aPL who do not meet obstetric or thrombotic APS criteria we conditionally recommend:**
  - **Treating with prophylactic low dose aspirin during pregnancy (GS45).**
  - **Against treating with prophylactic heparin or LMWH combined with low dose aspirin (GS46)**
  - **Against treating with prophylactic hydroxychloroquine during pregnancy, If the patient does not otherwise require hydroxychloroquine (GS44A).**

Obstetric APS:

In pregnant women with positive aPL who meet OB-APS criteria and have no history of thrombosis, we strongly recommend treating with *prophylactic* heparin or LMWH and low dose aspirin during pregnancy (GS48) and in the postpartum period (6-12 weeks, GS84)

- **In pregnant women with positive aPL who meet OB-APS criteria and have failed standard therapy with prophylactic heparin or LMWH and low dose aspirin:**
  - **We conditionally recommend against treating with therapeutic dose heparin or LMWH combined with low dose aspirin (GS49)**
  - **We conditionally recommend against treating with IVIG in addition to prophylactic heparin and low dose aspirin (GS50).**
  - **We strongly recommend against treating with prednisone in addition to heparin or LMWH combined with low dose aspirin (GS51)**

In pregnant women not otherwise requiring hydroxychloroquine and with obstetric and/or thrombotic APS, we conditionally recommend treating with hydroxychloroquine during pregnancy (GS44B)

We conditionally recommend the addition of HCQ to prophylactic-dose heparin or LMWH and low-dose aspirin therapy for patients with primary APS.

In pregnant women with positive aPL who do not meet criteria for APS and do not have another indication for the drug (such as SLE), we conditionally recommend *against* treating with prophylactic HCQ.

Thrombotic APS:

- **In pregnant women with thrombotic APS, we strongly recommend treating with therapeutic heparin and low dose aspirin rather than other non-heparin anticoagulation (GS52).**

GROSSESSE : SSA OU SSB+

Laboratory testing

- **In women with SLE or SLE-like disease, Sjogren's, systemic sclerosis, and RA who are considering pregnancy or are pregnant, we strongly recommend testing for anti-Ro/SSA and anti-La/SSB one time in early pregnancy, and against repeating the test during pregnancy (GS60, GS62).**

Positive anti-Ro/SSA and/or anti-La/SSB antibodies:

- **In pregnant women with anti-Ro/SSA and/or anti-La/SSB antibodies with no history of an infant with congenital heart block or neonatal lupus (risk of complete heart block ~2%) we conditionally recommend**

  - **Obtaining serial (less frequent than weekly, interval not determined) fetal echocardiography starting at weeks 16-18 through week 26. (GS67)**

- **In pregnant women with anti-Ro/SSA and/or anti-La/SSB antibodies with history of an infant with congenital heart block or neonatal lupus (risk of complete heart block is 13 -18%) we conditionally recommend:**

  - **Obtaining fetal echocardiography every week starting between weeks 16-18 through week 26. (GS68)**

Positive anti-Ro/SSA and/or anti-La/SSB antibodies:

We recommend treating with hydroxychloroquine during pregnancy (GS70)

Abnormal fetal echocardiogram:

- **In pregnant women with anti-Ro/SSA and/or anti-La/SSB antibodies with abnormal fetal echocardiograms, we conditionally recommend:**
  - **If 1st degree heart block or 2nd degree heart block, treating with dexamethasone 4 mg PO daily (GS71)**
  - **If isolated 3rd (complete) degree heart block (without other cardiac inflammation), against treating with dexamethasone (GS73)**

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ET SI C'EST L'HOMME QUI EST ATTEINT

Table 2. Recommendations regarding medication use for men with rheumatic and musculoskeletal disease who are planning to father a child

Strongly recommend continuing	Conditionally recommend continuing	Strongly recommend discontinuing	Conditionally recommend discontinuing	Unable to make a recommendation due to limited data
Azathioprine/ 6-mercaptopurine Colchicine Hydroxychloroquine Tumor necrosis factor inhibitors (all)	Anakinra Cyclooxygenase 2 inhibitors Cyclosporine Leflunomide Methotrexate Mycophenolate mofetil Mycophenolic acid Nonsteroidal anti-inflammatory drugs Rituximab Sulfasalazine *(semen analysis if delayed conception)* Tacrolimus	Cyclophosphamide *(discontinue 12 weeks prior to attempted conception)*	Thalidomide *(discontinue 4 weeks prior to attempted conception)*	Abatacept Apremilast Baricitinib Belimumab Secukinumab Tocilizumab Tofacitinib Ustekinumab