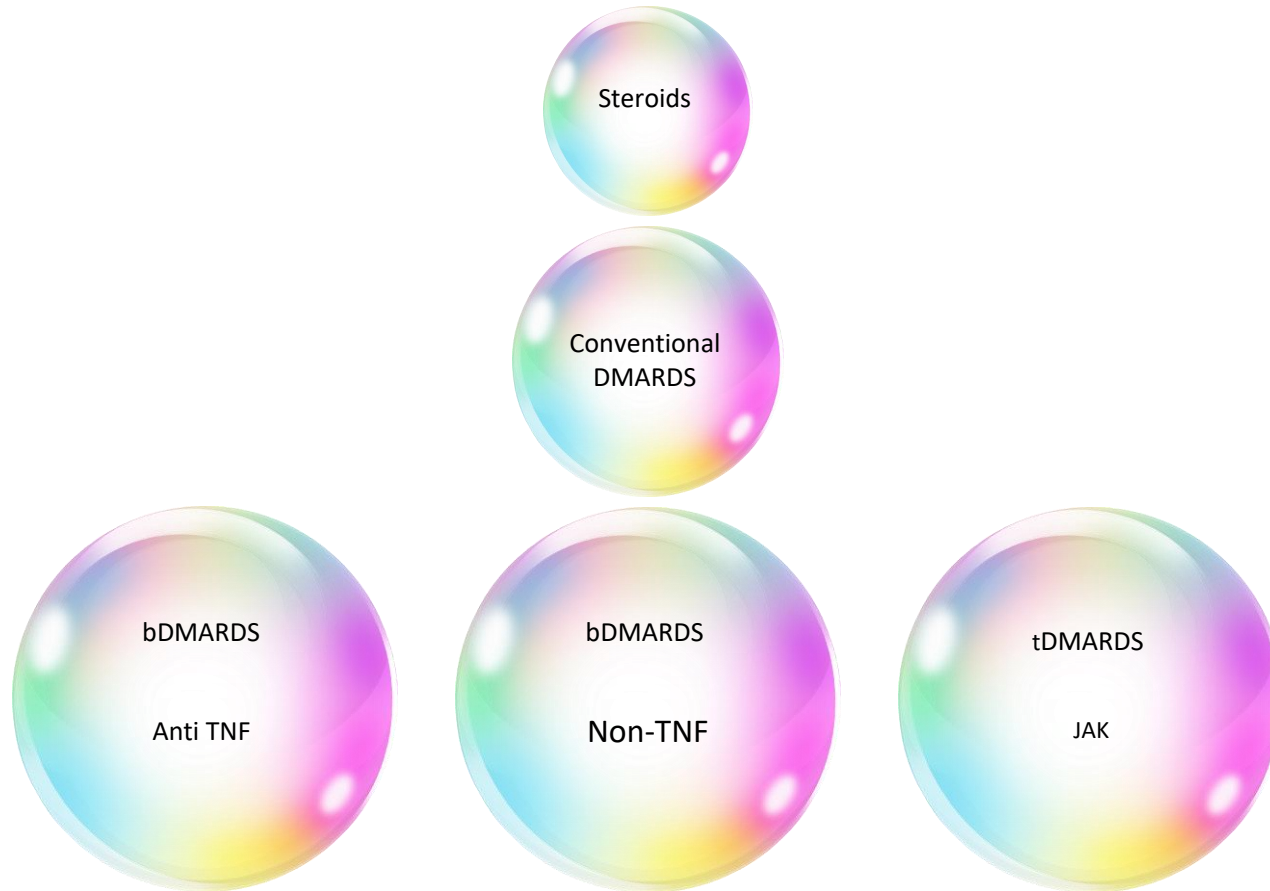


Biologic Treatments for Inflammatory Arthritis

Dr Orla Ni Mhuircheartaigh
Consultant Rheumatologist

Treatment options for Inflammatory Arthritis



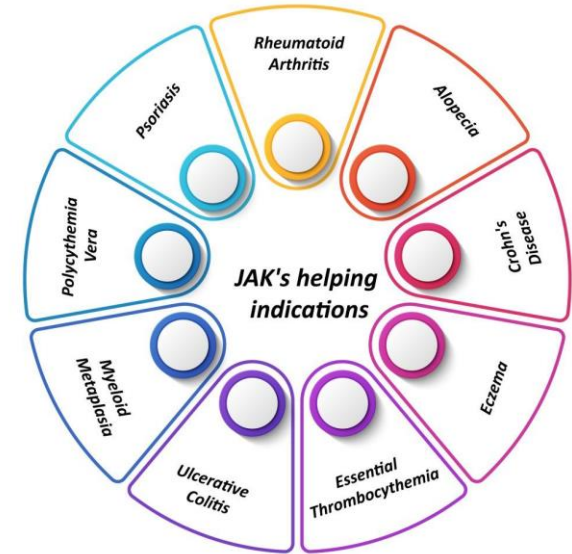
Anti TNF Agents

- Infliximab (IV)4, Etanercept (SC)2, Adalimumab (SC) (7), Certolizumab (SC)(0)and Golimumab (SC) (0)
- Indications: RA, PsA, Sero -ve , SpA
- Infection - TB, Bacterial, Opportunistic, viral reactivation
- Cancer- Lymphoma , NMSC
- CCF
- Antibody formation
- Autoimmune - DIL, MS



JAK Inhibitors

- Tofacitinib (2017)
- Baricitinib (2020)
- Upadacitinib (2020)
- Filgotanib (2024)
- Indications: RA, PSA, Sero -ve IA, SpA
- Shingles Risk
- Cardiovascular and Thrombotic risk
- Malignancies (Lymphoma , lung cancer)
- Dyslipidaemia



IL- 6 Inhibitors

- Tocilizimab (1)(2009)
- Indications RA, Sero -ve,
- Useful if High CRP competent
- Autoinflammatory Disease, CV-19, Stills, GCA, MAS, Cytokine storm, Serositis (SLE)
- Blunting of CRP
- Dyslipidaemia
- Neutropenia , Thrombocytopenia, Anaemia
- GI perforation (Diverticulitis)
- HTN/ CCF



- Block T cell Co-Stimulation
- Indications: RA /Sero -ve IA
- Infection Risk
- Malignancy risk ?
- Autoimmune risk DIL
- Benefit
- Slightly improved data on Infection risk
- Smokers
- Anti CCP



Rituximab

- B cell inhibitor, Anti-CD 20-
- Blocks Antibody production
- Indications: Moderate to Severe RA
- Other Uses: ANCA Vasculitis NHL, CLL, MS
- Failed bDMARDS
- Seropositive Disease
- ILD
- Severe Nodular RA
- Long lasting effects, - 9-12 months
- Hypogammaglobulinaemia
- Blunted effect to vaccinations
- PML



IL - 17 Inhibitors

- Secukinumab (Cosentyx) IL-17A (2015)
 - Ixekizumab (Taltz) IL-17A (2016)
 - Bimekizumab IL17-A (2023)
-
- Indications: Psoriasis , PSA, SpA.
 - Taltz- slightly more likely to develop drug induced antibodies
 - Infection risk
 - Candida



IL 12/ 23 Inhibitors

- Ustekinumab (Stelara) IL 12/23 (2009) (4)
- Indications: Psoriasis, PSA, Crohns, UC
- Guselkumab (Tremfya) (IL23)
- Rosankizumab. (Skyrizi) (IL 23)
- Tildrakizumab (ilumetri) (IL 23)
- IL-23 - Less effective Axial spine disease, Severe Enthesitis
- Infection risk
- Candida
- Cancer Risk



**2022 American College of Rheumatology/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 Arthroplasty**

Guideline Summary

Revised July 18, 2022

MEDICATIONS TO CONTINUE THROUGH SURGERY

DMARDs: CONTINUE these medications through surgery. (All patients)	Dosing Interval	Recommended timing of surgery since last medication dose
Methotrexate	Weekly	Anytime
Sulfasalazine	Once or twice daily	Anytime
Hydroxychloroquine	Once or twice daily	Anytime
Leflunomide (Arava)	Daily	Anytime
Doxycycline	Daily	Anytime
<i>Apremilast (Otezla)</i>	<i>Twice daily</i>	<i>Anytime</i>

SEVERE SLE-SPECIFIC MEDICATIONS††: CONTINUE these medications in the perioperative period in consultation with the treating rheumatologist.	Dosing Interval	Recommended timing of surgery since last medication dose
Mycophenolate mofetil	Twice daily	Anytime
Azathioprine	Daily or twice daily	Anytime
Cyclosporine	Twice daily	Anytime
Tacrolimus	Twice daily (IV and PO)	Anytime

<i>Rituximab (Rituxan)</i>	<i>IV Every 4-6 months</i>	<i>Month 4-6</i>
<i>Belimumab (Benlysta)</i>	<i>Weekly SQ</i>	<i>Anytime</i>
<i>Belimumab (Benlysta)</i>	<i>Monthly IV</i>	<i>Week 4</i>
<i>Anifrolumab (Saphnelo)†</i>	<i>IV Every 4 weeks</i>	<i>Week 4</i>
<i>Voclosporin (Lupkynis)†</i>	<i>Twice daily</i>	<i>Continue</i>

MEDICATIONS TO WITHHOLD PRIOR TO SURGERY***
BIOLOGICS: WITHHOLD these medications through surgery

		Recommended timing of surgery since last medication dose
Infliximab (Remicade)	Every 4, 6, or 8 weeks	Week 5, 7, or 9
Adalimumab (Humira)	Every 2 weeks	Week 3
Etanercept (Enbrel)	Every week	Week 2
Golimumab (Simponi)	Every 4 weeks (SQ) or every 8 weeks (IV)	Week 5 Week 9
Abatacept (Orencia)	Monthly (IV) or weekly (SQ)	Week 5 Week 2
Certolizumab (Cimzia)	Every 2 or 4 weeks	Week 3 or 5
Rituximab (Rituxan)	2 doses 2 weeks apart every 4-6 months	Month 7
Tocilizumab (Actemra)	Every week (SQ) or every 4 weeks (IV)	Week 2 Week 5
Anakinra (Kineret)	Daily	Day 2
IL-17-Secukinumab (Cosentyx)	Every 4 weeks	Week 5
Ustekinumab (Stelara)	Every 12 weeks	Week 13
<i>Ixekizumab (Taltz)†</i>	<i>Every 4 weeks</i>	<i>Week 5</i>
<i>IL-23 Guselkumab (Tremfya)†</i>	<i>Every 8 weeks</i>	<i>Week 9</i>

JAK inhibitors WITHHOLD this medication 3 days prior to surgery**

<i>Tofacitinib (Xeljanz):</i>	<i>Daily or twice daily</i>	<i>Day 4</i>
<i>Baricitinib (Olumiant)†</i>	<i>Daily</i>	<i>Day 4</i>
<i>Upadacitinib (Rinvoq)†</i>	<i>Daily</i>	<i>Day 4</i>

NOT-SEVERE SLE: WITHHOLD these medications 1 week prior to surgery

	Dosing Interval	1 week after last dose
Mycophenolate mofetil	Twice daily	1 week after last dose
Azathioprine	Daily or twice daily	1 week after last dose
Cyclosporine	Twice daily	1 week after last dose
Tacrolimus	Twice daily (IV and PO)	1 week after last dose
Rituximab (Rituxan)	Every 4-6 months	Month 7
<i>Belimumab IV (Benlysta)</i>	<i>Monthly</i>	<i>Week 5</i>
<i>Belimumab SQ (Benlysta)</i>	<i>Weekly</i>	<i>Week 2</i>

Dosing intervals obtained from prescribing information provided online by pharmaceutical companies.

Rheumatology, 2022, 00, 1–41
<https://doi.org/10.1093/rheumatology/keac551>
Guidelines



British Society for
Rheumatology

RHEUMATOLOGY

OXFORD

Guidelines

British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids

**Mark D. Russell ¹, Mrinalini Dey², Julia Flint³, Philippa Davie¹, Alexander Allen⁴, Amy Crossley⁵,
Margreta Frishman⁶, Mary Gayed⁷, Kenneth Hodson⁸, Munther Khamashta⁹, Louise Moore¹⁰,
Sonia Panchal¹¹, Madeleine Piper¹², Clare Reid⁵, Katherine Saxby¹³, Karen Schreiber^{14,15,16}, Naz Senvar¹⁷,
Sofia Tosounidou¹⁸, Maud van de Venne¹⁹, Louise Warburton²⁰, David Williams²¹, Chee-Seng Yee ²²,
Caroline Gordon ²³, Ian Giles^{24,*}; for the BSR Standards, Audit and Guidelines Working Group[†]**

Table 1. Summary of drug compatibility in pregnancy and breastmilk exposure

	Peri-conception	First trimester	Second/third trimester	Breastfeeding	Paternal exposure
Corticosteroids					
Prednisolone	Yes	Yes	Yes	Yes	Yes
Antimalarials					
Hydroxychloroquine (≤ 400 mg/day)	Yes	Yes	Yes	Yes	Yes
Conventional synthetic DMARDs					
Methotrexate (≤ 25 mg/week)	Stop ≥ 1 month pre-conception	No	No	No	Yes
Sulfasalazine (with folic acid 5 mg/day in first trimester)	Yes	Yes	Yes	Yes ^a	Yes ^b
Leflunomide	No: Cholestyramine washout	No	No	No	Yes
Azathioprine	Yes	Yes	Yes	Yes	Yes
Ciclosporin	Yes	Yes ^c	Yes ^c	Yes	Yes
Tacrolimus	Yes	Yes ^c	Yes ^c	Yes	Yes
Cyclophosphamide	Exceptional circumstances ^d	Exceptional circumstances ^d	Exceptional circumstances ^d	No	No
Mycophenolate mofetil	Stop ≥ 6 weeks pre-conception	No	No	No	Yes
Intravenous immunoglobulin	Yes	Yes	Yes	Yes	Yes
Anti-TNFα medications					
Infliximab	Yes	Yes	Yes ^e	Yes	Yes
Etanercept	Yes	Yes	Yes ^f	Yes	Yes
Adalimumab	Yes	Yes	Yes ^g	Yes	Yes
Certolizumab	Yes	Yes	Yes	Yes	Yes
Golimumab	Yes	Yes	Yes ^g	Yes	Yes
Other biologic DMARDs					
Rituximab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-6 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-1 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Abatacept	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Belimumab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-17 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-12/23 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Targeted synthetic DMARDs					
JAK-inhibitors	Stop ≥ 2 weeks pre-conception	No	No	No	Yes ^j

Table 1. Summary of drug compatibility in pregnancy and breastmilk exposure

	Peri-conception	First trimester	Second/third trimester	Breastfeeding	Paternal exposure
Corticosteroids					
Prednisolone	Yes	Yes	Yes	Yes	Yes
Antimalarials					
Hydroxychloroquine (≤ 400 mg/day)	Yes	Yes	Yes	Yes	Yes
Conventional synthetic DMARDs					
Methotrexate (≤ 25 mg/week)	Stop ≥ 1 month pre-conception	No	No	No	Yes
Sulfasalazine (with folic acid 5 mg/day in first trimester)	Yes	Yes	Yes	Yes ^a	Yes ^b
Leflunomide	No: Cholestyramine washout	No	No	No	Yes
Azathioprine	Yes	Yes	Yes	Yes	Yes
Ciclosporin	Yes	Yes ^c	Yes ^c	Yes	Yes
Tacrolimus	Yes	Yes ^c	Yes ^c	Yes	Yes
Cyclophosphamide	Exceptional circumstances ^d	Exceptional circumstances ^d	Exceptional circumstances ^d	No	No
Mycophenolate mofetil	Stop ≥ 6 weeks pre-conception	No	No	No	Yes
Intravenous immunoglobulin	Yes	Yes	Yes	Yes	Yes
Anti-TNFα medications					
Infliximab	Yes	Yes	Yes ^e	Yes	Yes
Etanercept	Yes	Yes	Yes ^f	Yes	Yes
Adalimumab	Yes	Yes	Yes ^g	Yes	Yes
Certolizumab	Yes	Yes	Yes	Yes	Yes
Golimumab	Yes	Yes	Yes ^g	Yes	Yes
Other biologic DMARDs					
Rituximab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-6 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-1 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Abatacept	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Belimumab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-17 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-12/23 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Targeted synthetic DMARDs					
JAK-inhibitors	Stop ≥ 2 weeks pre-conception	No	No	No	Yes ^j

Table 1. Summary of drug compatibility in pregnancy and breastmilk exposure

	Peri-conception	First trimester	Second/third trimester	Breastfeeding	Paternal exposure
Corticosteroids					
Prednisolone	Yes	Yes	Yes	Yes	Yes
Antimalarials					
Hydroxychloroquine (≤ 400 mg/day)	Yes	Yes	Yes	Yes	Yes
Conventional synthetic DMARDs					
Methotrexate (< 25 mg/week)	Stop > 1 month pre-conception	No	No	No	Yes
Sulfasalazine (with folic acid 5 mg/day in first trimester)	Yes	Yes	Yes	Yes ^a	Yes ^b
Leflunomide	No: Cholestyramine washout	No	No	No	Yes
Azathioprine	Yes	Yes	Yes	Yes	Yes
Ciclosporin	Yes	Yes ^c	Yes ^c	Yes	Yes
Tacrolimus	Yes	Yes ^c	Yes ^c	Yes	Yes
Cyclophosphamide	Exceptional circumstances ^d	Exceptional circumstances ^d	Exceptional circumstances ^d	No	No
Mycophenolate mofetil	Stop ≥ 6 weeks pre-conception	No	No	No	Yes
Intravenous immunoglobulin	Yes	Yes	Yes	Yes	Yes
Anti-TNFα medications					
Infliximab	Yes	Yes	Yes ^e	Yes	Yes
Etanercept	Yes	Yes	Yes ^f	Yes	Yes
Adalimumab	Yes	Yes	Yes ^g	Yes	Yes
Certolizumab	Yes	Yes	Yes	Yes	Yes
Golimumab	Yes	Yes	Yes ^g	Yes	Yes
Other biologic DMARDs					
Rituximab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-6 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-1 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Abatacept	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Belimumab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-17 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-12/23 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Targeted synthetic DMARDs					
JAK-inhibitors	Stop ≥ 2 weeks pre-conception	No	No	No	Yes ^j

Table 1. Summary of drug compatibility in pregnancy and breastmilk exposure

	Peri-conception	First trimester	Second/third trimester	Breastfeeding	Paternal exposure
Corticosteroids					
Prednisolone	Yes	Yes	Yes	Yes	Yes
Antimalarials					
Hydroxychloroquine (≤400 mg/day)	Yes	Yes	Yes	Yes	Yes
Conventional synthetic DMARDs					
Methotrexate (≤25 mg/week)	Stop ≥1 month pre-conception	No	No	No	Yes
Sulfasalazine (with folic acid 5 mg/day in first trimester)	Yes	Yes	Yes	Yes ^a	Yes ^b
Leflunomide	No: Cholestyramine washout	No	No	No	Yes
Azathioprine	Yes	Yes	Yes	Yes	Yes
Ciclosporin	Yes	Yes ^c	Yes ^c	Yes	Yes
Tacrolimus	Yes	Yes ^c	Yes ^c	Yes	Yes
Cyclophosphamide	Exceptional circumstances ^d	Exceptional circumstances ^d	Exceptional circumstances ^d	No	No
Mycophenolate mofetil	Stop ≥6 weeks pre-conception	No	No	No	Yes
Intravenous immunoglobulin	Yes	Yes	Yes	Yes	Yes
Anti-TNFα medications					
Infliximab	Yes	Yes	Yes ^c	Yes	Yes
Etanercept	Yes	Yes	Yes ^f	Yes	Yes
Adalimumab	Yes	Yes	Yes ^g	Yes	Yes
Certolizumab	Yes	Yes	Yes	Yes	Yes
Golimumab	Yes	Yes	Yes ^g	Yes	Yes
Other biologic DMARDs					
Rituximab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-6 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-1 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Abatacept	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Belimumab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-17 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-12/23 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Targeted synthetic DMARDs					
JAK-inhibitors	Stop ≥2 weeks pre-conception	No	No	No	Yes ^j

Table 1. Summary of drug compatibility in pregnancy and breastmilk exposure

	Peri-conception	First trimester	Second/third trimester	Breastfeeding	Paternal exposure
Corticosteroids					
Prednisolone	Yes	Yes	Yes	Yes	Yes
Antimalarials					
Hydroxychloroquine (≤ 400 mg/day)	Yes	Yes	Yes	Yes	Yes
Conventional synthetic DMARDs					
Methotrexate (≤ 25 mg/week)	Stop ≥ 1 month pre-conception	No	No	No	Yes
Sulfasalazine (with folic acid 5 mg/day in first trimester)	Yes	Yes	Yes	Yes ^a	Yes ^b
Leflunomide	No: Cholestyramine washout	No	No	No	Yes
Azathioprine	Yes	Yes	Yes	Yes	Yes
Ciclosporin	Yes	Yes ^c	Yes ^c	Yes	Yes
Tacrolimus	Yes	Yes ^c	Yes ^c	Yes	Yes
Cyclophosphamide	Exceptional circumstances ^d	Exceptional circumstances ^d	Exceptional circumstances ^d	No	No
Mycophenolate mofetil	Stop ≥ 6 weeks pre-conception	No	No	No	Yes
Intravenous immunoglobulin	Yes	Yes	Yes	Yes	Yes
Anti-TNFα medications					
Infliximab	Yes	Yes	Yes ^c	Yes	Yes
Etanercept	Yes	Yes	Yes ^f	Yes	Yes
Adalimumab	Yes	Yes	Yes ^g	Yes	Yes
Certolizumab	Yes	Yes	Yes	Yes	Yes
Golimumab	Yes	Yes	Yes ^g	Yes	Yes
Other biologic DMARDs					
Rituximab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-6 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-1 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Abatacept	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Belimumab	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-17 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
IL-12/23 inhibitors	Consider stopping at conception ^h	Severe disease if no alternatives ^h	Severe disease if no alternatives ⁱ	Yes ^j	Yes ^j
Targeted synthetic DMARDs					
JAK-inhibitors	Stop ≥ 2 weeks pre-conception	No	No	No	Yes ^j

Case 1:

- 87 yr old lady
- PC Sero+ve RA (RF 78, CCP > 340)
- Early erosions MCP 2,5 R hand
- Pmhx IHD x 3 stents, Stage III COPD, HTN , DM, Depression,
- Dry Cough: HRCT Early ILD, COPD
- Smoker - 60pk yr hx, actively smoking
- 3 IECOPD last year
- Completed x 3/12 cDMARD - Ineffective

Case 2:

- 34 yr old lady
- PC New PsA
- Hands, Knees, Psoriasis- scalp, extremities, ear canals, Nail disease, Enthesitis AT
- Erosive disease DIP of Hands, Large effusions Knees
- PMhx: None
- Non smoker, Minimal Alcohol, Recently Married, Hoping to start a family in next 6 months

Thank you