# BIOLOGICS IN RHEUMATIC DISEASES – UPDATE 2020

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| Class | Drug | Treatment guidelines and Dosing | |
|---|---|---|---|
| **ANTI TNF**<br><br>**- cept = receptor molecules**<br>**- mab = monoclonal antibodies**<br><br>**- omab = murine;**<br>**- ximab = chimeric;**<br>**- zumab = humanized;**<br>**- umab = human.** | infliximab (Remicade, Inflectra**, Renflexis**) | 3 mg/kg @ wk 0, 2, 6, then 8 weekly IV over 2 hrs; max 6 maintenance doses per year<br>RA, AS, 2nd line for polyarticular JIA, J SpA . (Also IBD and PsO) | LU Code<br>Inflectra: RA 468, AS 469, PsA 470<br>Renflexis: RA 541, AS 542, PsA 543 |
| | etanercept (Enbrel*, Brenzys**, Erelzi #) | 50mg SC weekly or 25 mg SC twice a week for RA, PsA, AS<br>0.8 mg/kg per week (up to a maximum of 50mg per week) for JIA (JSpA, JIA poly) | LU Code<br>Brenzys: RA 499, AS 498<br>Erelzi: RA 512, AS 513, PsA 563 |
| | adalimumab (Humira) | 40 mg SC every 2 weeks (dosing for JIA 24 mg per m2)<br>RA, AS, PsA, polyarticular JIA (Also uveitis, IBD and PsO) | |
| | golimumab (Simponi) | 50 mg SC every month for RA, AS, PsA<br>or 2 mg/kg over 30 minutes at weeks 0, 4, then every 8 weeks thereafter for RA# | |
| | certolizumab (Cimzia) | 400 mg SC at weeks 0, 2, 4 then<br>200 mg every 2 weeks, or 400 mg every 4 weeks for RA, PsA, AS | |
| **ANTI CD20** | rituximab (Rituxan) | RA 1000 mg IV day 1 and day 15 - RA (post 1 anti TNF or see list of specific indications for primary use.<br>GPA / MPA 375 mg/m2 once weekly for 4 weeks, see EAP criteria | |
| **ANTI IL6 receptor** | tocilizumab (Actemra) ### | IV for RA : 4/mg/kg 4 weekly IV over 1 hr – increase to 8 mg based on response.<br>SC for RA : <100kg, 162 mg every other week; increase to every week based on clinical response; in patients 100 kg or greater, use 162 mg administered every week. See EAP criteria for , sJIA , polyarticular JIA | ★ |
| | sarilumab (Kevzara) | 200 mg s.c. every two weeks (cut to 150 mg if AE) | ★ |
| **Selective T Cell Co-stimulatory inhibitor** | abatacept (Orencia) | 30 min IV at 0, 2, 4 weeks then every 4 weeks after. Dose by weight: 500 mg for patients < 60 kg, 750 mg 60–100 kg, 1000 mg > 100 kg or SC 125 mg weekly RA, 2nd line for polyarticular JIA | |
| **ANTI IL17 inhibitor** | secukinumab (Cosentyx) | Dose once a week for 5 weeks, then 4 weekly. Dosing: AS: 150 mg SC PsA: 150 mg SC for bio-naive patients; 300 mg SC for anti TNF inadequate responders or for patients with moderate to severe PsO; PsO: 300 mg SC (LU code | |
| | ixekizumab (Taltz#) | 160mg by subcutaneous injection (two 80 mg injections) at Week 0, followed by 80mg every 4 weeks | |
| **JAK 1/3 inhibitor** | tofacitinib (Xeljanz) | 5 mg PO BID RA | LU Code<br>RA 480 (BID), 565 (OD) ★ |
| **JAK 1/2 inhibitor** | baricitinib# | 2 mg PO daily | ★ |
| **JAK 1 inhibitor** | upadacitinib (Rinvoq) | 15mg PO Daily | ★ |
| **Anti IL 1** | Anakinra (Kineret) | 100 mg SC daily . For cryopyrin associated periodic syndrome 1-2 mg per kg SC daily starting dose | |
| **ANTI IL12 and IL23** | ustekinumab (Stelara) | 45 mg SC at weeks 0 and 4, then every 12 weeks thereafter. (90 mg with body weight > 100 Kg PsA) | |
| **PDE4 Inhibitor** | apremilast (Otezla)# | 30 mg PO BID: 2 week starter pack PsO and PsA | |

## EAP Criteria

**RA**
≥ 5 swollen joints AND RF/ CCP positive AND/OR radiographic evidence of rheumatoid arthritis despite the optimal use of DMARDs, defined as:
- Methotrexate [MTX] (20 mg/week) AND Leflunomide [LEF] each 3 months AND one combination with other DMARD OR
- LEF (20 mg/day) + MTX for at least 3 months OR
- MTX + Sulfasalazine (SFZ) + OH Chloroquine triple therapy for at least 3 months

**Renewal**
20% reduction in SJC and a minimum reduction of 2 swollen joints.

**PsA**
5 swollen joints and radiographic evidence of psoriatic arthritis despite treatment with MTX (20 mg/week) for at least 3 months and one of LEF (20 mg/day) or SAS(1 g twice daily) for at least 3 months.
If the patient has documented contraindication or intolerance to MTX then only one of LEF (20 mg/day) or SAS(1 g twice daily) for at least 3 months is required.
**Renewal**
20% reduction in SJC and a minimum of improvement in 2 swollen joints.

**AS**
Age of disease onset < 50; AND
- Low back pain and stiffness for > 3 months that improves with exercise and not relieved by rest; AND
- Failure to respond to or documented intolerance to adequate trials of 2 NSAIDs for at least 4 weeks each; AND
- BASDAI score of 4 for at least 4 weeks while on standard therapy; AND X-ray or CT scan report stating the presence of "SI joint fusion or erosion" OR MRI report stating the presence of "inflammation" or "edema" of the SI joint(s). Send radiology report with application.

**Renewal**
50% reduction in BASDAI score or 2 absolute point reduction in BASDAI score.

**Other notes:**
- * No new starts for RA
- # Awaiting ODB coverage
- ### - See ORA website for GCA criteria

Evaluate need for VZV and HIV serology
Recommend pneumococcal vaccine and annual flu vaccine
RR H. zoster 1.6 with anti TNF and 2 with JAKi

★ Lipids at 2 months then 6 monthly
★ Caution in patients at risk of GI perforation

**Malignancy – If in doubt consult oncologist**
*Recommendations based on ACR 2015 RA Guidelines

**Lymphoproliferative disorder**
Use combination DMARD or Abatacept or Tocilizumab over TNFi, very low quality of evidence.

**Skin cancer (non—melanoma and melanoma):**
Use DMARD over biologic or tofacitinib. Very low level of evidence.
Anti TNF probably does not increase risk. Anti-TNF therapy should be avoided in patients with melanoma.

**Solid tumors:**
Same recommendation as patients without this condition, very low level of evidence.

BSRBR 2016: Patients with prior malignancy selected to receive biologics do not have an increased risk of incident malignancy. It remains unknown whether biologics can be used safely in all patients with prior malignancy

**Hepatitis B Refer ALL to hepatology for classification**

| Hep B Status | HbsAg | HbsAb | Total Hbc-Ab | Hbc-IgM | Hbc-IgG | Abnormal LFT +/- symptoms | Additional Testing | Recommendation |
|---|---|---|---|---|---|---|---|---|
| Susceptible | - | - | - | - | - | - | None | Consider vaccination, start biologic |
| Immune due to prev infection | - | + | + | - | + | - | None | Start biologic |
| Immune due to HBV vaccine | - | + | - | - | - | - | None | Start biologic |
| Acute Infection | + | - | + | + | - | + | None | Hepatology consult, defer biologic |
| Chronic infection | + | - | + | - | + | +/- | HBeAg /Ab, HBV DNA | Start biologic + hepatology |

In asymptomatic HBsAg+ carriers, antiviral prophylaxis is recommended and should be started 2-4 weeks prior to anti-TNF therapy and continued for at least 6-months. In total Hbc-Ab+ patients, routine prophylaxis is not recommended, although individual factors such as degree of immunosuppression, length of therapy, and degree of local HBV endemicity should be taken into account. Rituximab should also be avoided in any patient with active or chronic hepatitis B.

**Hepatitis C - Refer to hepatology - consider pretreatment**
ACR 2015 Guidelines recommend patients receiving antiviral therapy should be treated no differently than those without hepC, however level of evidence is very low. Preference should be given to DMARD over TNFi in those not on antivirals.

**Pregnancy**
Monoclonal antibodies expose the child to the full adult dose when administered in late pregnancy with a risk for adverse effects in the newborn and perinatally.
- No increased risk of congenital malformations with anti TNF; should not affect development of baby's immune system after birth. Certolizumab was shown to have no to minimal placental transfer from mother to infant (CRIB study). This is anti TNF of choice in this population, though data now exists that continuing TNFi through pregnancy is safe, with no increased risk to the developing infant or to pregnancy outcomes.

- Rituximab - data suggests it may be safe to use in early pregnancy. But use in the 2nd and 3rd trimester carries risk of fetal B-cell depletion & immunosuppression.
- JAK inhibitors - Do NOT use. They are small molecules, ≤ 500 Da and cross placenta in the 1st trimester. Teratogenic and abortifacient
- Abatacept , Tocilizumab – still not enough data to use with comfort during pregnancy though some use in first 6 months.
- Apremilast - avoid

Advise NO live vaccines (e.g.rotavirus) until baby is 6 months
www.mothertobaby.org

**Breastfeeding** : minimal amount of biologics is present in breastmilk, clinically insignificant. (CRADLE study tested Cimzia).
- Most expert panels state that the use of biologics should not influence the decision to breastfeed and breastfeeding should not influence the decision to use these medications

**Rituximab**
May be first choice in:
1) Patients with previously treated solid malignancy within the last 5 years
2) Patients with previously treated non-melanoma skin cancer within the last 5 years
3) Patients with previously ever treated melanoma skin cancer
4) Patients with previously ever treated lymphoproliferative malignancy, (e.g., lymphoma, CLL, leukemia)
5) For patients with congestive heart failure NYHA class III or IV with ejection fraction of ≤ 50%
6) For patients with latent tuberculosis with contraindications or intolerance to the use of 2 anti-TB medications
7) For patients with Multiple Sclerosis or family history of MS in first degree relatives
8) For patients with interstitial lung disease where a respirologist opinion is that Methotrexate and Leflunomide are contraindicated, and/ or anti-TNFs are contraindicated.
9) Possibly indicated for Hep C cryoglobulinemic vasculitis.