BIOLOGICS IN RHEUMATIC DISEASES – UPDATE 2018

**Class** | **Drug** | **Treatment guidelines and Dosing** | **EAP Criteria**
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**ANTI TNF** | infliximab (Remicade*, Inflectra**) | 3 mg/kg @ wk 0, 6, 2, 6 then 8 weekly IV over 2 hrs; max 6 maintenance doses per year RA, AS, 2nd line for polycystic JIA, J SpA. (Also IBD and POI)** | RA 5 swollen joints, RF/ CCP positive and/or radiographic evidence of rheumatoid arthritis despite the optimal use of DMARDs.

Methotrexate (MTX) (20 mg/week) and Leflunomide (LEF) each 3 months plus one combination with other DMARD OR LEF (20 mg/day) + MTX for at least 3 months.

OR MTX + Sulfasalazine (SZF) + Chloroquine - triple therapy for at least 3 months

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

Anti-TNF second line after failing anti-TNF (plus see below)

**ANTI IL6 receptor** | etanercept (Enbrel*, Brenzys**, Enliiz) | 50mg SC weekly or 25 or 50 SC twice a week for RA, PsA, AS 0.8 mg/kg per week (up to a maximum of 50mg per week) for JIA (JSpA, JPA poly)** | PU 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 SASL (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 SASL (g twice daily) for at least 3 months is recommended.

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

**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 RA, 2nd line for polycystic JIA ** | AS Age of disease onset <50; AND

• Low back pain and stiffness for at least 3 months that improves with exercise and not relieved by rest; AND

• Failure to respond to or documented intolerance to adequate trials of 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 “SJ joint fusion or erosion” OR MRI report stating the presence of “stiffening” or “edema” of the SJ joints. Send radiology report with application.

Renewal: 50% reduction in BASDAI score or 2 absolute point reduction in BASDAI score

**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. GPA / MPA 375 mg/m2 once weekly for 4 weeks, see EAP criteria | BSRBR: 5.1 Serious infections per 100 patient years

No increased risk of chromosomal events with tocilizumab

Lipids at 2 months then 6 monthly

Evaluate need for VZV and HIV serology

Evaluate need for ID and PCP prophylaxis

**ANTI JAK** | tofacitinib (Xeljanz**) | 5 mg PO BID RA | **No new starts for RA**

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| 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; breastfeeding is considered safe because anti TNF poorly excreted in breast milk | • Do NOT use rituximab; may result in pre-term, miscarriages, hematological abnormalities, congenital malformations, neonatal B cell depletion

• Do NOT use abatacept, JAK inhibition - lack of data

• Tocilizumab may be reasonable for first two trimesters

• Certolizumab might be considered as the anti TNF of choice in this population (biologic rationale)

• Advise NO live vaccines (e.g. rotavirus) until baby is 6 months old

• www.motherstopbaby.org

**POE Inhibitor** | apremilast (Osela*) | 30 mg PO BID: 2 week starter pack PsO and PsA | P-values for the differences in the ESR (red blood cell sedimentation rate) and CRP (c-reactive protein) were 2.6 x10⁻⁹ and 7.1 x10⁻⁹, respectively; OR:

- 0.8 mg/kg per week (up to a maximum of 50mg per week) for JIA (JSpA, JPA poly)** | **Drug has LU code**

* No new starts for RA

**Awaiting ODB coverage**

Evaluate need for ID and PCP prophylaxis

Evaluate need for VZV and HIV serology

Evaluate need for ID and PCP prophylaxis

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 treated lymphoproliferative malignancy, (e.g., lymphoma, CLL, leukemia)

5) For patients with congestive heart failure NYHA class III or IV with ejection fraction ≤ 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 respiratoryist opinion that is Methotrexate and Leflunomide are contraindicated, and/or anti-TNFs are contraindicated.

9) Possibly indicated for Hep C cryptogenicolemic vasculitis.

**Malignancy** – if in doubt consult oncologist

Lymphoma

Anti-TNF does not increase the risk if lymphoma (BSRBR data)

Abatacept, tocilizumab, and Rituximab should be used with caution, ideally after consult with an oncologist (no evidence)

Solid tumors:

Anti-TNF therapy should be avoided in patients with melanoma only; abatacept, tocilizumab, and Rituximab should be used with caution, ideally after consult with an oncologist (no evidence).

RSBR 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.

**Non-melanoma skin cancer**:

Anti-TNF probably does not increase risk. Abatacept, tocilizumab, and Rituximab should be used with caution, ideally after consult with an oncologist (no evidence).

Solid tumors:

Anti-TNF therapy should be avoided in patients with melanoma only; abatacept, tocilizumab, and Rituximab should be used with caution. Rituximab recommended by ACR for solid tumor and melanoma.

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.

**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 treated lymphoproliferative malignancy, (e.g., lymphoma, CLL, leukemia)

5) For patients with congestive heart failure NYHA class III or IV with ejection fraction ≤ 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 respiratoryist opinion that is Methotrexate and Leflunomide are contraindicated, and/or anti-TNFs are contraindicated.

9) Possibly indicated for Hep C cryptogenicolemic vasculitis.

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**Other notes:**

• Drug has LU code

• * No new starts for RA

• **Awaiting ODB coverage**

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