RHEUMATOID ARTHRITIS: DMARD Comparison Chart [1-22]

www.RxFiles.ca — Brent Jensen BSP — Sept 04

Generic/ TRADE — Pregnancy Category	✓ USES / Comments / Onset — Contraindications CI	Side Effects (Common & Rare) — Monitor (ACR 2002 Guidelines) M	Drug INTERACTIONS [11,12]	Rheumatoid Dose: USUAL & MAX	$/Year
Anakinra KINERET (100mg/0.67ml syr ☎⊗) B -Human IL-1 antagonist	✓ Adult Mono Tx +/- DMARDs [non TNF] **Onset**: 2-3 months **CI:** active infections, neutropenia	**Common**: **inj site reaction** ~75% esp. during 1st 4 wks, severe infection [2%], headache, nausea **Rare**: **neutropenia** **M:** CBC(q1mon x3→q3mon[22])	**Enbrel** (& ? with Remicade): ↓ WBC [3%], ↑ infections [7%]	100mg SC od (↓**dose** if ↓**renal** fx) (store in Fridge)	☎ 16,900 ⊗
Etanercept ENBREL (25mg vial ☎✆) B -recombinant soluble TNF fusion receptor protein **Adalimumab** HUMIRA [avail. USA] TNF ∝ inhibitor, 40mg SC every other Week	✓**Mono Tx & with MTX** [FDA] ✓Psoriasis [plaque,arthritis], ankylosing [spondylitis] **Onset**: 1-2 **weeks** (Up to 3 months) ↓joint erosions, May ↓steroid & MTX [doses] **CI:** MS, sepsis, HF. Dx flare if drug D/C	**Common**:headache, nausea, rhinitis, cough, burning @**inj site**~50%1st dose →↓ after 5 doses, antibody to drug **Rare**: pancytopenia, Lupus like, demyelination [9 cases], tuberculosis [reactive], optic [neuritis], severe infection [4.3/100 pt. yr] **M:** CBC, tuberculin test	Anakinra & live vaccines: ↑ risk of infection	**25mg SC twice/wk** (50mg SC weekly [FDA]) **Peds** [FDA & Canada] (Age 4-17): 0.4 mg/kg (Max 25mg) SC twice/wk or {0.8 mg/kg (Max 50mg) SC weekly [FDA]}	☎ **17,400** ✆
Hydroxychloroquine PLAQUENIL **(HCQ)** C (200mg tab)	✓ **mild RA**, Lupus; Well tolerated Not slow radiologic damage **Onset**: 2-6 months (trial~ 4months) **CI:** G6PDH [hemolysis], vision changes	**Common**: GI (cramps & diarrhea), rash, headache **Rare**:**ocular** toxicity,myopathy,skin pigment changes **M:** CBC; **eye** exam (funduscopic & visual field/yr)	digoxin: ↑ digoxin levels methotrexate: ?↓ methotrexate levels Beta blockers: ↑ β-blocker effect	200mg po od (with food/milk) **200mg po bid, 400mg po hs** (Max ≤ 6.5mg/kg/day)	230 **370**
Infliximab REMICADE (100mg VIAL ☎ ✆) B -**mouse**-human anti TNF α monoclonal antibody	✓ **With MTX only** [FDA] ; ↓ joint erosions & ↑ physical functioning ✓ Crohn's disease **CI:** MS, sepsis, acute HF, watch for Dx flare if drug stopped **Onset**: 1-2 **weeks** (Up to 4 months)	**Common**: headache, nausea, lung infections, **infusion reaction** [fever, urticaria, dyspnea,↓ BP for 1st few inj. (10%→ antinuclear & DNA antibodies)] antibody reaction **Rare**:histoplasmosis, extrapulmonary TB, Lupus, HF, severe infection, demyelinating Dx [70 cases],aplastic anemia **M:** CBC, tuberculin test **Pretreatment** at injection clinics (acetaminophen 650mg po & diphenhydramine 50mg po x1) ↓'s infusion reactions. Give over ≥ 2hr in 250ml normal saline.	Anakinra & live vaccines: ↑ risk of infection	200mg [3mg/kg x ~70kg] IV q 8 wks **300mg** [5mg/kg x ~60kg] **IV q 8 wks** (Start Week 0, 2, 6, then every 8 wks) Range: 3-10mg/kg IV q8 wk or 3-5mg/kg IV q4 wk	☎ 11,800 ✆ **17,600**
Leflunomide ARAVA X (10, 20mg tab ☎ ✆) -pyrimidine synthesis inhibitor (prodrug)	✓ **Active/severe RA**, **Mono Tx** [FDA] Slow RA progression;↑ physical fx Drug in body up to 2yr after D/C→ **Questran** [8g TID x 11d] if toxic/pregnant **Onset**: 1-3 months **CI:** obstructive biliary & hepatic Dx, viral hepatitis, impaired immune Dx	**Common**:GI (**diarrhea**, nausea,↓weight), rash, ↑BP, alopecia [8%, reversible & dose related], ↑ LFT [5%], lung infection **Rare**: aplastic **anemia**, TENS,Stevens-Johnson [12 cases], hepatotoxic(130pts BMJ [2002] esp if **with MTX**) & pancytopenia, peripheral neuropathy, interstitial lung dx **M:** CBC, LFT, Scr q1mon x6 →q1-2(3 [20])mon	**↑ leflunomide level/toxicity by: methotrexate**(2-3x ↑ of LFTs), **rifampin** **leflunomide ↑ effects of:** NSAIDS, tolbutamide, warfarin **↓ leflunomide level by:** activated charcoal, **cholestyramine** live vaccines: ↑ risk of infection	10mg po od **20mg po od** (?**Loading dose**= 100mg/day x 3 days but ↑ GI intolerance)	4,070 ☎ **4,070** ✆
Methotrexate (MTX) AMETHOPTERIN/ Generics X (2.5mg tab;20 & 50mg/2ml inj ✗▼)	✓ **Active/severe RA** to ↓radiologic progression ✓ Psoriasis If AST or ALT [↑ 2-3x N]→D/C & biopsy **Onset**: **1-2 months** adding Folic acid [1-5mg/d]: ↓ mouth[ulcers] **CI:** liver, renal & lung Dx; ↑ alcohol	**Common**:GI-nausea & diarrhea, stomatitis, rash, alopecia, pulmonary infiltrates→**cough** **Rare**: hypersensitivity **pneumonitis** [<2%], nephrotoxic, **myelosuppression**, hepatotoxic, **hepatic** & pulmonary **fibrosis**, phototoxicity & skin necrotizing vasculitis. **M:** CBC, LFT, Scr, Plt, Alb q1mon x6 →q1-**2** mon	**↑ MTX level/toxicity by:** Bactrim, **cyclosporine**, doxycycline, ethanol, **leflunomide**, live vaccines, **NSAIDs**, omeprazole, probenecid **↑ myelosuppression with:** Bactrim, sulfasalazine, trimethoprim **↓ MTX levels by**: cholestyramine, neomycin	7.5-10mg po weekly(↓**dose** if ↓**renal** fx) **15mg po weekly** (Max 25mg/wk) 7.5mg IM/SC weekly (Max 25mg/wk) Peds: 10mg/square meter per week	200-235 **300** 840
Sulfasalazine (SSZ) SALAZOPYRIN/generic (500ᶜmg tab; 500mg EC tab) B	✓ **mild RA** slows radiologic progression **Onset**: 1-3 months **CI:** G6PDH, sulfa allergy, GI obstruction	**Common**:**GI**(nausea/abd pain),**rash**, photosensitivity **Rare**: leukopenia, **myelosuppression**,hepatitis,lupus, ↓sperm,↑Scr **M:** CBC, LFT q2-4wk x3mon →q3mon	digoxin [↓ dig level], warfarin [↓INR], azathioprine [↑ toxic] **↓ sulfasalazine levels by:** cholestyramine, iron, phenobarb, rifampin	500mg EC po bid -start low to ↓ side effects **1000mg EC po bid (after meals)** 1000mg EC po tid Peds: 30-50 [mg/kg/day]	180 **280** 360
Azathioprine IMURAN/generic (50ᶜmg tab) D -purine analog immunosuppressant	**Onset**: 2-3 months **CI:** history of treatment with alkylating agents	**Common**: GI, flu-like illness, ↑ LFT **Rare**: **myelosuppression**, hepatotoxic, infection, pancreatitis **M:** CBC, Plt, LFT, Scr q 1-2 wk →q1-3 mon	**azathioprine ↓ effect of**: warfarin **↑ aza level by: allopurinol** (?↓ dose by~70%) **↑ myelosuppression with**: captopril	50mg po od 100mg po od (Max 150mg po od) Range: 1-2.5mg/kg/day	320 550
Cyclosporine NEORAL (10, 25, 50, 100mg cap; 100mg/ml liquid) ☎▼ C **Tacrolimus** ☎▼ PROGRAF (0.5,1,5mg cap; 5mg/ml amp) 3mg po od $3200	✓ RA, Psoriasis (recalcitrant plaque) **Onset**:2-4months. Seldom used alone. **CI:** ↓ renal fx, uncontrolled ↑BP	**Common**: GI, headache, paresthesia, ↑**BP** [dose related] **Rare**: **nephrotoxicity** [dose related], **anemia**, malignancy, hypertrichosis,gingival hyperplasia,tremor,↑ LFT,↑K^+ **M:** Scr [q2wk→q1mon if stable],CBC,LFT,K^+,uric acid,BP,Cp	**↑ cyclo level by:** allopurinol, amiodarone, danazol, diltiazem, erythromycin, flu & ketoconazole, grapefruit juice, verapamil. **↓ cyclo levels by**: aluminum, carbamaz.,orlistat,phenobarbital,phenytoin,rifampin, St. Johns Wort, sulfasalazine. **↑ nephrotoxicity with**: aminoglycosides, amphotericin, methotrexate, NSAIDs	100mg po q12h (↓**dose** if ↓**renal** fx) 150mg po q12h (Max 4-5mg/kg/d) 2.5[mg/kg/d] bid, (↑ 0.5 [mg/kg/d] q 2-4 wk)	☎▼ 4,600 6,800
GOLD: **Sodium aurothiomalate** MYOCHRYSINE (10,25,50 mg/ml inj); **Auranofin** RIDAURA (3mg cap) C	**Onset**:3-6 months(trial ~ 5months) **Oral**: ↓ efficacy & longer to effect than **IM gold** (~25% absorbed) **CI:** blood & skin Dx, lung fibrosis	**Common**:stomatitis,**rash**,**diarrhea**,edema,**proteinuria** **Rare**: **myelosuppression**, ↓platelets, alopecia, colitis **M:** CBC, Plt, Scr, urine protein q1-2 wk x 20wk then when inj or every other inj.{Oral: q1-3 mon}	Aspirin: may ↑ hepatotoxicity Penicillamine: ↑ rash & suppress bone marrow	3mg po bid ⇒ Clinically often IM used 25mg **IM** q2-**4** wks (↓**dose** if ↓**renal** fx) 50mg **IM** q2-**4** wks (Peds: 1 mg/kg) Test dose: 10mg IM→ Load 50mg/**wk** x ~20wk)	1,320 220 300
Minocycline MINOCIN (50 & 100mg cap ☎ ✆) D	**Onset**: 1-3 months **CI:** children <8yr,last ½ of pregnancy	**Common**: GI upset, headache, dizziness, ↑ **pigmentation**, yeast infection **Rare**: vestibular dysfx, lupus, ↑ LFT, photosensitivity **M:** CBC, LFT	antacids, calcium, food, iron: [↓ minocycline levels]; warfarin [↑ bleeding], isotretinoin [↑ BP]	50mg po bid 100mg po bid	☎ ✆ 540 970
Penicillamine CUPRIMINE (125 & 250mg cap, 250ᶜ mg tab) D	**Onset**: 3-6 mon (Note:↓**iron** [esp peds & menstruating ♀]) **CI:** renal impairment,possible penicillin [cross sensitivity]	**Common**: GI (N/V, diarrhea), taste disorders, **rash**, gynecomastia **Rare**: **myelosuppression**, **proteinuria**,Goodpasture's,myasthenia [gravis], neuropathy **M:** CBC,Scr,urinary protein q2wk→ dose stable→ q1-3mon	antacids, calcium, food,iron: [↓ penicillamine levels]; digoxin [↓ digoxin levels], gold [↑ rash & ↓ bone marrow]	250mg po od, 250mg bid -start low & ↑ slowly 250mg po tid **before meals** (Max 1-1.5g/day)	415, 750 1,070

=↓ dose for renal dysfx ☎ =exception drug status Sask. ✆ prior NIHB ✗ =NonForm. Sk. ⊗=not NIHB ▼ covered NIHB ♀ =females ✓Useful for/in **Alb**=albumin **ALT/AST**=liver tests **BP**=blood pressure **CBC**=complete blood count **CI**=contraindication **Cp**=plasma level **d**=day **Dx**=disease **Dysfx**=dysfunction **EC**=enteric coated **FDA**=USA approved **fx**=function **GI**=stomach **HF**=heart failure **inj**=injection **K**=potassium **LFT**=liver function test **Mon**=month **MS**=multiple sclerosis **N**=normal **Peds**=pediatric **Plt**=platelet **RA**=Rheumatoid arthritis **Scr**=serum creatinine **SE**=side effect **TB**=tuberculosis **TENS**=toxic epidermal necrosis syndrome **TNF**=tissue necrosis factor **Tx**=treatment **WK**=week **yr**=year ς =scored tab

Pregnancy [2,14]: **B**=likely safe **C**=possible fetal risk **D**=fetal human risk **X**=teratogenic. Contraception required for most DMARDs. If possible:D/C med,↓ dose,avoid in 1st trimester. **NSAIDS**:may use until last 6-8 wks of pregnancy. **DMARDs**: relatively safe→ HCQ, prednisone, SSZ. [7]

GOAL: Delay or prevent disability/joint damage, prevent loss of function & ↓ pain. Treat early, aggressive & often with combinations. Give patient info. Trial DMARDs for several months to ensure efficacy. Watch clinical symptoms, ↓ ESR & ↓CRP.

TREAT: **DMARDs main tx** [within 3 months]; NSAIDs [1st few weeks], analgesics, local steroid inj [≥q3mon], prednisone ~ <10mg/day ([↑BP, diabetes, infection, thin skin, ↑ **weight**, cataract, osteoporosis [calcium 1500mg/d, Vit. D 800iu/d & bisphosphonates]). Physio,recreation & occupational **THERAPY** when indicated.

APPROACH: **Mild Dx: HCQ** or **SSZ**; **Active Dx: MTX** or **Leflunomide** or **Combos** {(Common **Triple**=MTX,SSZ,HCQ); or Etanercept/Infliximab/Anakinra +/- MTX/Leflunomide; ...}. **REFER**: for treatment advice (diagnosis or complications).

Diagnostic Criteria [22]: morning stiffness; arthritis: of ≥3 joint areas, hand joints & symmetric -lasting at least 6 weeks; rheumatoid nodules, ↑ serum rheumatoid factor & radiographic changes.

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