DMARDs

Disease and Pharmacotherapy Overview

UMPQUA HEALTH

Overview

Introduction

Major Conditions

Treatment Guidelines

Newer Therapies from the last 5 Years

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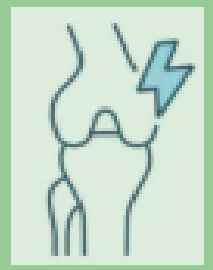
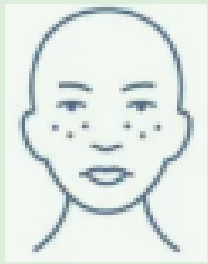
Common Rheumatic Diseases

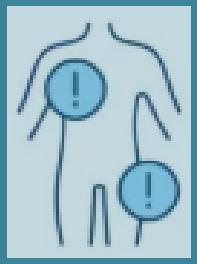
Rheumatoid Arthritis



Psoriatic Arthritis



Ankylosing Spondylitis



Other common diseases include:

- osteoarthritis, systemic lupus erythematosus, Sjogren's syndrome, gout, and scleroderma

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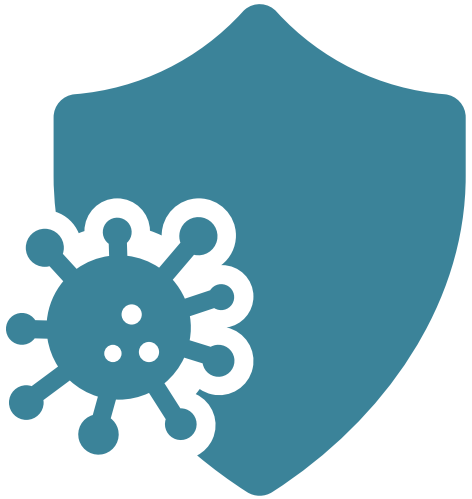
Disease-Modifying Antirheumatic Drugs (DMARDs)



csDMARDs

- **Conventional synthetic**
- **Traditional, broad-spectrum immune suppressants**
- **Ex: methotrexate**

bDMARDs

- **Biologic (larger, protein-based molecules)**
- **Target specific immune cells or proteins (e.g., TNF, IL-6)**
  - Subcategorized as anti-TNF biologics or non-TNF biologics
- **End in “-mab” or “-cept” (e.g., adalimumab, etanercept)**

tsDMARDs

- **Targeted synthetic (smaller, synthetic molecules)**
- **Target specific intracellular signaling pathways (e.g., JAK enzymes)**
- **End in “-nib” (e.g., tofacitinib)**
- **Specificity: bDMARDS > tsDMARDs > csDMARDs**

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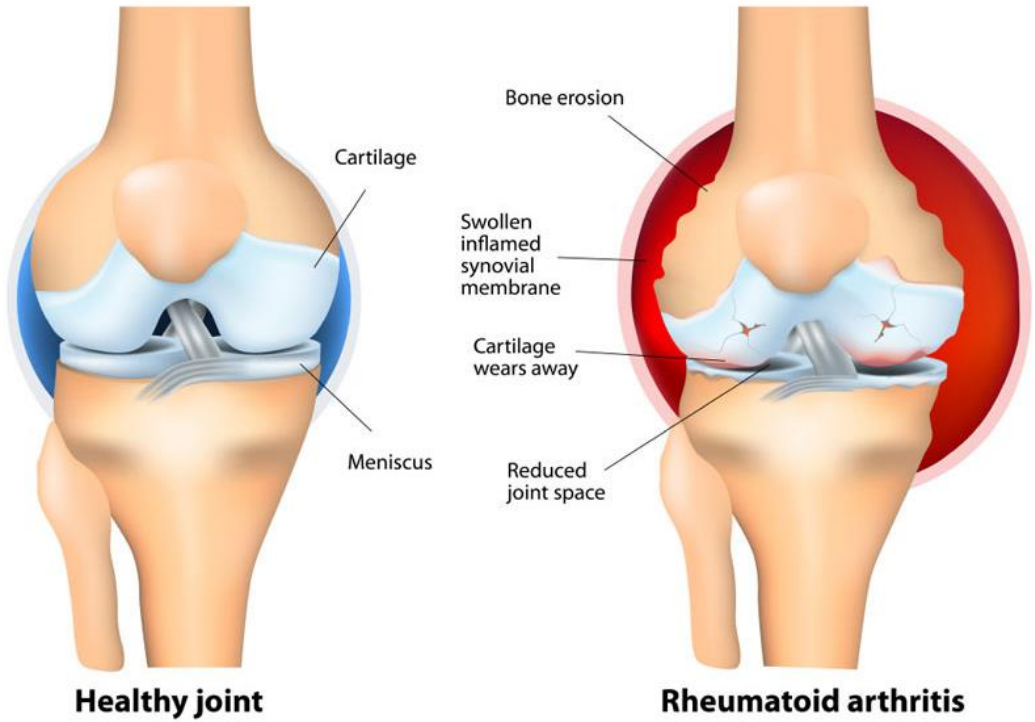
Major Conditions

Rheumatoid Arthritis (RA)



- RA occurs when the immune system attacks the synovium, the lining of joints

- Symptoms
  - Pain and swelling in multiple joints (usually bilateral)
  - Joint stiffness, especially in the AM
  - Fatigue
  - Problems in other organs
    - Eyes
    - Lungs
    - Skin
    - Heart

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RA Guideline Recommendations

- **Treat-to-Target:** Goal is to reduce disease activity or achieve remission within 6 months
- Frequent monitoring (e.g., q 3 months) to assess efficacy and tolerability of treatment regimen
  - Adjust treatments as needed to achieve goal

RA Guideline Recommendations

csDMARD monotherapy

* mild disease: HCQ > SSZ > MTX > LFN
* mod-high disease: MTX (monotherapy) is preferred

Glucocorticosteroids (GC)

* bridge to DMARD therapy
* no GC > short term GC (ie < 3 mon) > long term GC (ie ≥ 3 mon)

bDMARD or tsDMARD +/- MTX

* not at target: switch to bDMARD or tsDMARD of a different class

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RA Guideline Recommendations

- **Treat-to-Target:** Goal is to reduce disease activity or achieve remission within 6 months
- Frequent monitoring (e.g., q 3 months) to assess efficacy and tolerability of treatment regimen
  - Adjust treatments as needed to achieve goal
- Patients should be at target for at least 6 months prior to tapering
- DMARDs: continuation at current dose > dose reduction > gradual discontinuation > abrupt discontinuation
- MTX +/- bDMARD or tsDMARD: gradual d/c of MTX preferred

Biologic DMARDs: TNF-α Inhibitors

Drug	Dose & Route	Time to Effect	Considerations/Pearls	Screening/Monitoring
Efficacy: ACR 20 response rates - ~50-70%; guidelines consider all agents equally effective			Class effect- see safety slide; ↑ risk of infection	TB screening, hepatitis B/C, hx of demyelinating dx CBC, ESR, CRP, RF, joint counts, steroid use Vaccines- Influenza and pneumococcal (No LIVE) Signs of infection- counseling not to delay care; hold during infections Skin checks (slight increased risk of NMSC) Cancer/lymphoma screenings (studies support negligible risk of solid tumors)
Etanercept	50mg **SC** weekly	4-6 weeks	Injection site reactions (ISR)	
Infliximab	3-10 mg/kg @ 0,2, and 6 weeks then every 6-8 weeks; **IV infusion (2 hr)**	4-6 weeks	Infusion rxn (rash, N, SOB urticaria, HA, fever, chills); may need pre-meds; risk of **anti-drug antibodies (ADA)** if used a monotherapy	
Adalimumab	40mg **SC** every 2 weeks	4-6 weeks	ISR, ↑ risk of infection; **8 biosimilars!!!!** **Risk of ADAs**	
Golimumab	50mg **SC** every 4 weeks; 2mg/kg **IV infusion (30 mins)**	4-6 weeks	ISR; infusion rxn less common; clinically a "wearing off effect seen with approved dosing"	
Certolizumab pegol	400mg **SC** @ 0, 2, 4 weeks then q4 weeks (or 200mg SC q2 weeks)	4-6 weeks	ISR less common; **drug of choice in pregnancy;** very viscous so PFS not autoinjector	

IL-1 & IL-6 Antagonists, T-cell & B-cell Modulators

Drug	Dose & Route	Time to Effect	ADRs	Monitoring
Anakinra *IL-1 inhibitor*	100mg daily; **SC** ****not very effective in RA**	1-4 weeks	HA, N/V/D, ****Injection site reactions (70%)**	Screen for TB, signs of infection; injection site rxn
Abatacept *T-cell Costimulation Modulator*	500mg (<60kg), 750mg (60-100kg), 1000mg (>100kg), **IV (over 30 min)** @ 0, 2, 4 then every 4 weeks 125 mg **SC** weekly after loading dose	12-20 weeks; ACR 20 response ~50-60% (time to full effect 6months)	Injec.site rxn, HA, dizziness, cough, nasopharyngitis	Screen for TB, Signs of infection, respiratory w/ COPD pts. ****infection risk clinically lower than other biologics**
Rituximab *B-cell Modulator*	1,000mg **IV infusion(~6 hr)** twice, given 2 wks apart = 1 cycle	Response usually seen by 16 wks	Infusion rxn (rash, N, SOB, urticaria, HA, fever, chills) Methylpred 100mg 30 min prior & diphenhydramine	Signs of infection, post infusion rxn, **Progressive multifocal leukoencephalopathy (PML)-** neurology s/sx
Tocilizumab *IL-6 inhibitor*	4-8mg/kg **IV infusion (over 1 hr)** q 4weeks; <100kg: 162mg **SC** every other wk; >100kg: weekly	1-4 weeks; ACR 20 response ~50-80%	Infus. rxn, ↑ risk of infection, anemias, **↑ lipids/ liver enzymes, GI sx**	↑ risk of infection ANC, LFTs, platelets, lipids, GI symptoms; **drug intx**
Sarilumab *IL-6 inhibitor*	200 mg **SC** once every 2 weeks	1-4 weeks; ACR 20 response ~50-70%	↑ risk of infection, **anemias, ↑ lipids/ liver enzymes, GI symptoms**	↑ risk of infection ANC, LFTs, platelets, lipids, GI symptoms; **drug intx**

N/V/D=nausea, vomiting, diarrhea; HA=headache; TB=tuberculosis; ANC=absolute neutrophil count

tsDMARDs: JAKi

- JAKi is 2nd line after TNFi failure d/t increased risk of CV events, cancer, thrombosis and death seen in tofacitinib
  - Important to evaluate CV risk factor before starting
- Baricitinib not as efficacious as the other two for RA treatment
- Should not be used w/ other JAKs, bDMARDs or other potent immunosuppressants
- **Monitor:** anemias, LFT elevations, lipid changes
- **Adverse events:** HA, URTI, nasopharyngitis, cardiovascular effects, GI perforation, serious infections

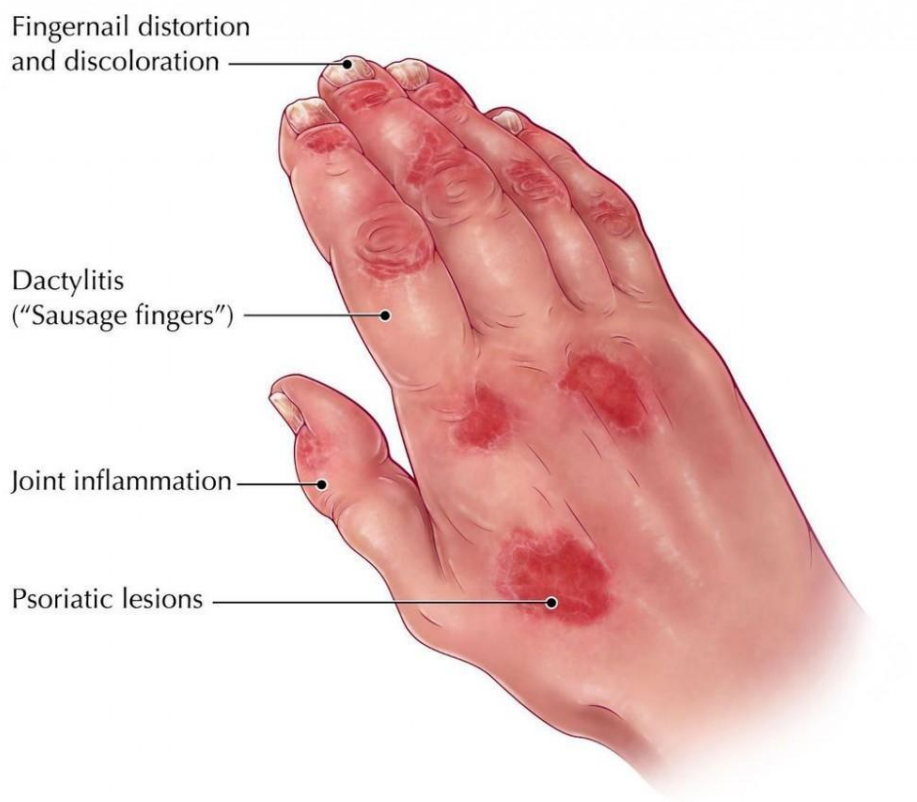
Agents	Tofacitinib (Xeljanz)	Baricitinib (Oluminant)	Upadacitinib (Rinvoq)
JAK target	JAK1, JAK2, JAK3	JAK1, JAK2	JAK1
Dosing	IR: 5 mg by mouth twice daily XR: 11 mg by mouth once daily	2 mg by mouth once daily	15 mg by mouth once daily
Onset	2 weeks (full efficacy 12 weeks)	2-4 weeks (full efficacy 12 weeks)	1-4 weeks (full efficacy 12 weeks)
Indications	RA, PsA, UC, AS, JIA	RA	RA, PsA, AS, UC, nr-AxSpA, atopic derm

bDMARD/tsDMARD Safety Information

Class/Drugs	Precautions and Warnings
TNFi	**BW: Infections (including fungal and opportunistic); malignancy, and tuberculosis (TB);** multiple sclerosis (demyelinating dx), hepatitis B (HBV) and C (HCV); heart failure; drug-induced lupus
IL-6 inhibitors	**BW: Infections; TB**; infusion rxn; increased liver enzymes; increased cholesterol; neutropenia; thrombocytopenia; CYP 3A4 inducer
T-cell costimulation modulator	Infections, (***clinically less severe than with TNFi***); COPD exacerbations seen in clinical trials; infusion-related events (mild); TB and hepatitis screening
B-cell modulator rituximab	**BW: Infusion-related rxn; cutaneous rxn; HBV; progressive multifocal leukoencephalopathy (PML)**; infections; decreased response to vaccines?
Janus kinase enzyme inhibitors	**BW: Infections (including fungal and opportunistic); malignancy, TB, thrombosis/CV risk;** liver enzymes; cholesterol; neutropenia; reduce dose in renal/hepatic insufficiency and when used in combination with CYP3A4 inhibitors

*** Boxed Warning (BW)**

Psoriatic Arthritis (PsA)



- PsA occurs when the immune system attacks joint tissues and **skin**
- Occurs in 30% of people with psoriasis
- Symptoms
  - Pain and swelling in multiple joints (uni- or bilateral)
  - Joint stiffness, especially in the AM
  - Fatigue
  - Nail pitting, discoloration, or separation from the nail bed
  - Swollen fingers and toes
  - Tendon or ligament pain
  - Skin sxs

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PsA Guideline Recommendations

- **Treat-to-Target:** Goal is to reduce disease activity or achieve remission within 6 months
- Frequent monitoring (e.g., q 3 months) to assess efficacy and tolerability of treatment regimen
  - Adjust treatments as needed to achieve goal
- Domain-Driven Treatment: Therapy choice depends on predominant symptom
  - (e.g., peripheral arthritis, axial arthritis, dactylitis, enthesitis, skin, nails)

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PsA Guideline Recommendations

- **Symptomatic Relief**
  - NSAIDS
  - Corticorsteroids
- **Oral Small Molecules (OSM)**
  - Methotrexate (MTX)
  - Sulfasalazine (SSZ)
  - Leflunomide (LEF)
  - *Apremilast (APM)*
  - *Cyclosporine (CSA)*
- **bDMARD / tsDMARD**
  - TNFi
  - Non-TNFi
  - JAK inhibitors
- **Adjunct with Topicals**
  - Steroids
  - Retinoids
  - Phototherapy

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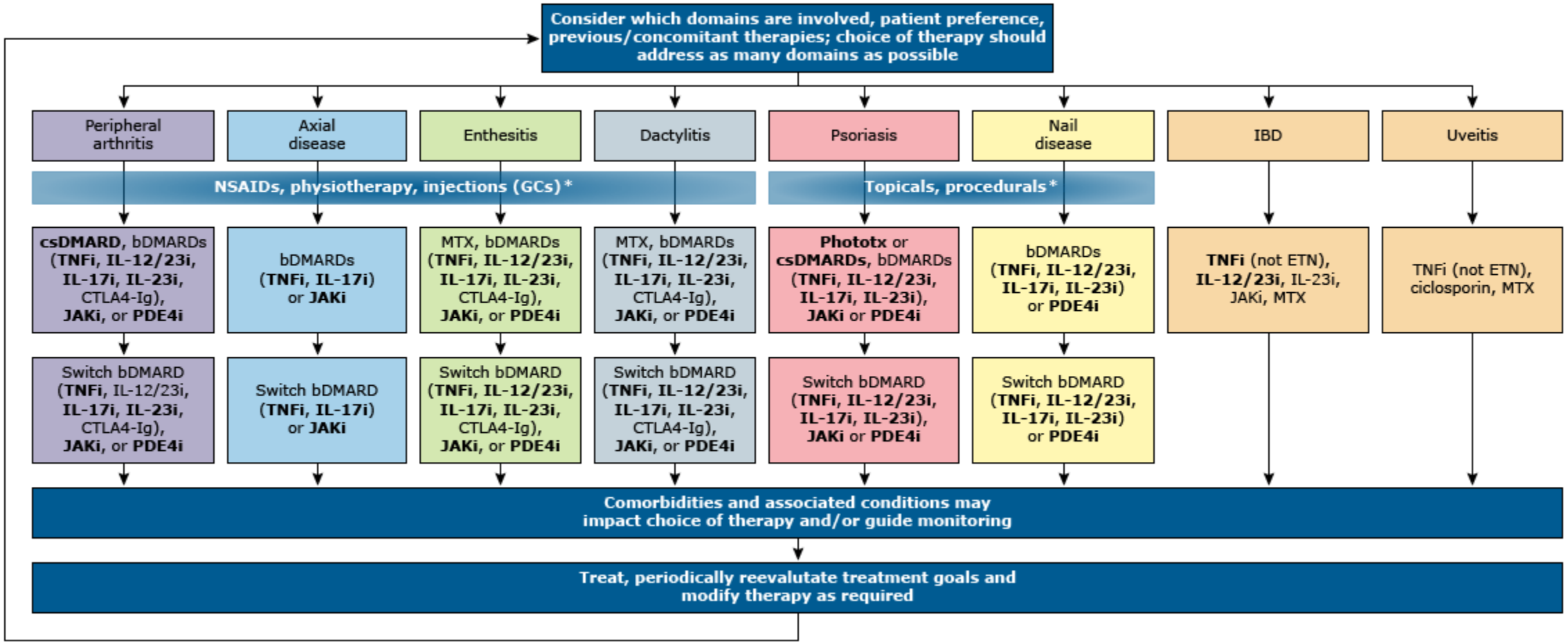
PsA Guideline Recommendations



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Non-TNFi Agents: **IL-17 inhibitors**

Drug	Dose & Route	ADR	Monitoring
Secukinumab *IL-17 inhibitor*	150 mg SC once weekly at weeks 0, 1, 2, 3, and 4 followed by 150 mg every 4 weeks. Some patients may require 300 mg per dose	Infections (nasopharyngitis, upper respiratory tract infection, mucocutaneous candida); neutropenia; exacerbations of Crohn's disease; uticaria; diarrhea	Injection site reactions; Latent TB- TB testing prior to initiation ; Infections (yeast infections); anti-drug antibodies
Ixekizumab *IL-17 inhibitor*	Plaque psoriasis: SubQ: 160 mg once, followed by 80 mg at weeks 2, 4, 6, 8, 10 and 12, and then 80 mg every 4 weeks. Psoriatic arthritis: SubQ: 160 mg once, followed by 80 mg every 4 weeks;	Infections (nasopharyngitis, upper respiratory tract infection, mucocutaneous candida); neutropenia; exacerbations of Crohn's disease; tinea, nausea	Injection site reactions; Latent TB- TB testing prior to initiation; Infections (yeast infections); anti-drug antibodies

Ustekinumab (Stelara) package insert. Horsham, PA: Janssen Biotech, Inc. 2012 May.; Otezla (apremilast) package insert. Summit, NJ: Celegene Corporation; 2014 Sept

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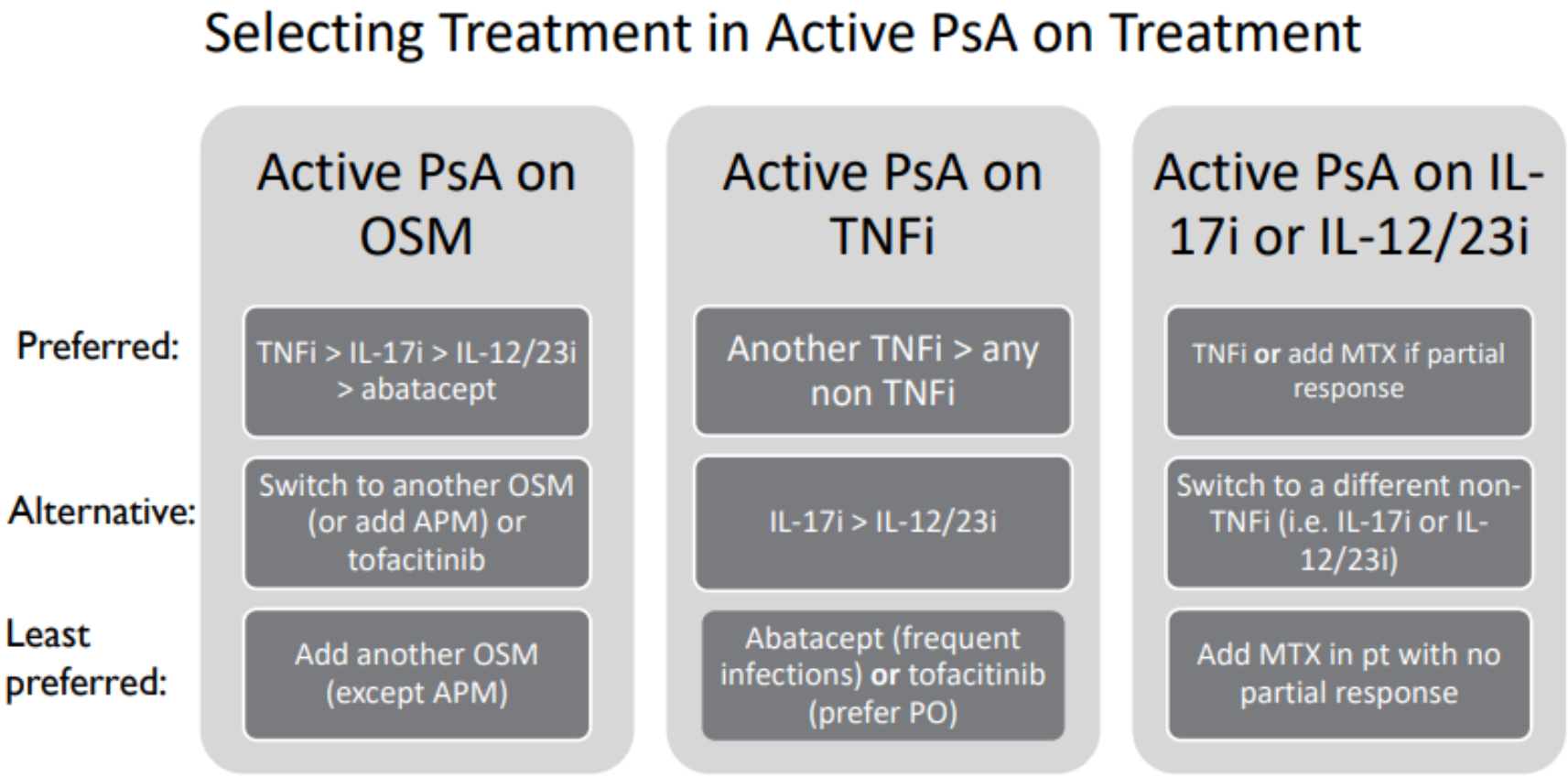
Non-TNFi Agents: IL-12/23 & IL-23 inhibitors

Drug	Dose & Route	ADR	Monitoring
Ustekinumab *IL-12/23 inhibitor*	>100 kg (w/plaque psoriasis): 90 mg SC; repeat dose 4 wks later. Then, give 90 mg SC every 12 weeks starting at week 16. No plaque psoriasis regardless of weight: 45 mg SC; repeat dose 4 wks later. Then, give 45 mg SC every 12 weeks starting at week 16.	Most common: Infections (27% vs 24%), injection site reactions (1-2%), headache (5%), fatigue (3%) Rare: Reversible posterior leukoencephalopathy syndrome (RPLS); pustular psoriasis	Injection site reactions; TB testing prior to initiation ; Infections; Malignancy (1.3%); Worsening psoriasis (pustular)
Guselkumab *IL-23 inhibitor*	100 mg at weeks 0, 4, and then every 8 weeks thereafter; may administer alone or in combination with conventional disease-modifying antirheumatic drugs	Infection (23%), Tinea (1%), Diarrhea (2%), gastroenteritis (1%), increased LFTs(3%), Antibody development (6% to 9%; neutralizing antibodies: 6% to 7%; efficacy of guselkumab may be affected), Herpes simplex infection (1%), Injection site reaction (5%), Headache (5%), Arthralgia (3%), Candidiasis (<1%)	Injection site reactions; TB testing prior to initiation; Infections;
Risankizumab *IL-23 inhibitor*	SubQ: 150 mg (two injections) at weeks 0, 4, and then every 12 weeks thereafter	Antibody development (24%; neutralizing: 14%), Infection (22%), Upper respiratory tract infection (13%), Headache (4%), fatigue (3%, Tinea (1%), Injection site reaction (2%)	Injection site reactions; TB testing prior to initiation; Infections;

PsA Guideline Recommendations



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PsA Guideline Recommendations

- General approach: TNFi > IL-17i > IL-12/23i for biologics
  - OSM for treatment naïve patients without severe disease
  - Combo therapy (i.e. biologic + MTX) generally NOT recommended for PsA per guidelines
    - Unless patients have a partial response to MTX monotherapy
    - In practice, it is done

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PsA “Newer” Therapies

IL-23 Inhibitors

- Risankizumab (Skyrizi) – 2019/2022 for PsA
- Guselkumab (Tremfya) – 2017/2020 for PsA

JAK inhibitors

- upadacitinib (Rinvoq) – 2019/2021 for PsA

Dual IL-17A and IL-17F inhibitor

- Bimekizumab (Bimzelx) – 2023/2024 for PsA

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PsA Newer Therapies

Bimekizumab (Bimzelx)	
Indications	active psoriatic arthritis, active non-radiographic axial spondyloarthritis with objective signs of inflammation, active ankylosing spondylitis, moderate-to-severe plaque psoriasis, and moderate-to-severe hidradenitis suppurativa
Dose	160 mg or 320 mg at various intervals based on indication
Side effects	Increase in: SI/B; infections; liver enzymes nasopharyngitis, upper respiratory tract infection, oral candidiasis, headache, and diarrhea.
Monitor	Liver enzymes, alkaline phosphatase, bilirubin, s/s IBD
Avoid	Liver disease or cirrhosis Active IBD

----------ADVERSE REACTIONS----------

Most common adverse reactions are:

- Psoriasis and Hidradenitis Suppurativa (incidence ≥ 1%): upper respiratory tract infections, oral candidiasis, headache, injection site reactions, tinea infections, gastroenteritis, Herpes simplex infections, acne, folliculitis, other candida infections, and fatigue. (6.1)
- Psoriatic Arthritis (incidence ≥ 2%): upper respiratory tract infections, oral candidiasis, headache, diarrhea, and urinary tract infection. (6.1)
- Non-Radiographic Axial Spondyloarthritis (incidence ≥ 2%): upper respiratory tract infections, oral candidiasis, headache, diarrhea, cough, fatigue, musculoskeletal pain, myalgia, tonsilitis, transaminase increase, and urinary tract infection. (6.1)
- Ankylosing Spondylitis (incidence ≥ 2%): upper respiratory tract infections, oral candidiasis, headache, diarrhea, injection site pain, rash and vulvovaginal mycotic infection. (6.1)

Bimekizumab (Bimzelx)

- BE OPTIMAL: Bimekizumab vs placebo in biologic-naive
  - bimekizumab achieved significantly higher ACR50 response rates compared to placebo at week 16, with responses sustained through week 52
  - More than 70% of patients with concomitant psoriasis reached PASI90, and over 50% achieved complete skin clearance (PASI100) by week 24
- BE COMPLETE: Bimekizumab vs placebo in biologic-exp'd
  - bimekizumab similarly showed superior efficacy versus placebo across all primary and ranked secondary endpoints at week 16.
  - 59% of patients with baseline psoriasis affecting ≥3% body surface area achieved PASI100

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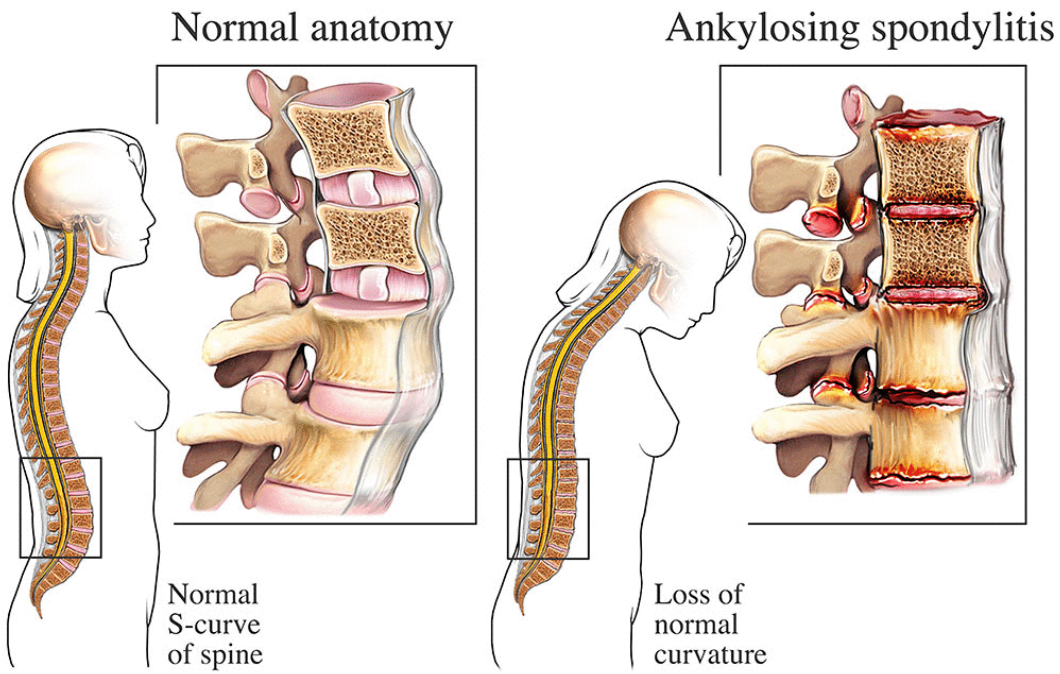
Ankylosing Spondylitis (AS)



- AS occurs when the immune system attacks the joints and ligaments, especially in the spine and sacroiliac joints
- Can also affect other large joints (e.g., shoulders, chest)
- Hunched posture
- Symptoms
  - Stiffness in back, neck, or glutes, especially at rest or period of inactivity
  - Fatigue
  - Swollen fingers and toes
  - Tendon or ligament pain
  - Uveitis (eye inflammation)

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AS Guideline Recommendations

NSAIDs + physical therapy/exercise

* continuous NSAID treatment for active disease preferred

b**DMARDs:** TNFi > IL-17i

* TNFi: infliximab, etanercept, adalimumab, golimumab, and certolizumab
* IL-17i: secukinumab, ixekizumab, and bimekizumab

tsDMARDs

* JAKi: tofacitinib, upadacitinib

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AS “Newer” Therapies

JAK inhibitors

- upadacitinib (Rinvoq) – 2019/2022 for AS
- tofacitinib (Xeljanz) - 2012/2021 for AS

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References

Bittar, M., & Deodhar, A. (2025). Axial Spondyloarthritis: A Review. *JAMA*, *333*(5), 408–420. https://doi.org/10.1001/jama.2024.20917

Coates, L. C., Soriano, E. R., Corp, N., Bertheussen, H., Callis Duffin, K., Campanholo, C. B., Chau, J., Eder, L., Fernández-Ávila, D. G., FitzGerald, O., Garg, A., Gladman, D. D., Goel, N., Helliwell, P. S., Husni, M. E., Jadon, D. R., Katz, A., Laheru, D., Latella, J., Leung, Y. Y., … GRAPPA Treatment Recommendations domain subcommittees (2022). Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. *Nature reviews. Rheumatology*, *18*(8), 465–479. https://doi.org/10.1038/s41584-022-00798-0

Farrell,J. (2024) Bone/Joint and Rheumatology [PowerPoint Slides}. https://elearning.ashp.org/

Fraenkel, L., Bathon, J. M., England, B. R., St Clair, E. W., Arayssi, T., Carandang, K., Deane, K. D., Genovese, M., Huston, K. K., Kerr, G., Kremer, J., Nakamura, M. C., Russell, L. A., Singh, J. A., Smith, B. J., Sparks, J. A., Venkatachalam, S., Weinblatt, M. E., Al-Gibbawi, M., Baker, J. F., … Akl, E. A. (2021). 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis care & research*, *73*(7), 924–939. https://doi.org/10.1002/acr.24596

McInnes, I. B., Asahina, A., Coates, L. C., Landewé, R., Merola, J. F., Ritchlin, C. T., Tanaka, Y., Gossec, L., Gottlieb, A. B., Warren, R. B., Ink, B., Assudani, D., Bajracharya, R., Shende, V., Coarse, J., & Mease, P. J. (2023). Bimekizumab in patients with psoriatic arthritis, naive to biologic treatment: a randomised, double-blind, placebo-controlled, phase 3 trial (BE OPTIMAL). *Lancet (London, England)*, *401*(10370), 25–37. https://doi.org/10.1016/S0140-6736(22)02302-9

Merola, J. F., Landewé, R., McInnes, I. B., Mease, P. J., Ritchlin, C. T., Tanaka, Y., Asahina, A., Behrens, F., Gladman, D. D., Gossec, L., Gottlieb, A. B., Thaçi, D., Warren, R. B., Ink, B., Assudani, D., Bajracharya, R., Shende, V., Coarse, J., & Coates, L. C. (2023). Bimekizumab in patients with active psoriatic arthritis and previous inadequate response or intolerance to tumour necrosis factor-α inhibitors: a randomised, double-blind, placebo-controlled, phase 3 trial (BE COMPLETE). *Lancet (London, England)*, *401*(10370), 38–48. https://doi.org/10.1016/S0140-6736(22)02303-0

Singh, J. A., Guyatt, G., Ogdie, AUCB, Inc. (2024). *Bimzelx p*., Gladman, D. D., Deal, C., Deodhar, A., Dubreuil, M., Dunham, J., Husni, M. E., Kenny, S., Kwan-Morley, J., Lin, J., Marchetta, P., Mease, P. J., Merola, J. F., Miner, J., Ritchlin, C. T., Siaton, B., Smith, B. J., Van Voorhees, A. S., … Reston, J. (2019). Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis & rheumatology (Hoboken, N.J.)*, *71*(1), 5–32. https://doi.org/10.1002/art.40726

Prescribing information [PDF]. UCB-USA. https://www.ucb-usa.com/bimzelx-prescribing-information.pdf

Ward, M. M., Deodhar, A., Gensler, L. S., Dubreuil, M., Yu, D., Khan, M. A., Haroon, N., Borenstein, D., Wang, R., Biehl, A., Fang, M. A., Louie, G., Majithia, V., Ng, B., Bigham, R., Pianin, M., Shah, A. A., Sullivan, N., Turgunbaev, M., Oristaglio, J., … Caplan, L. (2019). 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis & rheumatology (Hoboken, N.J.)*, *71*(10), 1599–1613. https://doi.org/10.1002/art.41042