PSORIASIS: Management of Psoriasis and Psoriatic Arthritis: Clinical Recommendations

American Academy of Dermatology
Patients with non-deforming psoriatic arthritis without any radiographic changes, loss of range of motion, or interference with tasks of daily living should not automatically be treated with tumor necrosis factor (TNF) inhibitors. It would be reasonable to treat these patients with a non-steroidal anti-inflammatory agent or to consult a rheumatologist for therapeutic options.

Patients with limited skin disease should not automatically be treated with systemic treatment if they do not improve, because treatment with systemic therapy may carry more risk than the disease itself.

1 Patients with non-deforming psoriatic arthritis without any radiographic changes, loss of range of motion, or interference with tasks of daily living should not automatically be treated with tumor necrosis factor (TNF) inhibitors. It would be reasonable to treat these patients with a non-steroidal anti-inflammatory agent or to consult a rheumatologist for therapeutic options.

2 Patients with limited skin disease should not automatically be treated with systemic treatment if they do not improve, because treatment with systemic therapy may carry more risk than the disease itself.
Recommendations for topical corticosteroids

> Indication: Plaque type psoriasis

> Dosing:
  • Can be used as mono-therapy 1-2 times daily
  • Can be combined with other topical agents, UV light and systemic agents

> Potency of Topical Steroids:
  • Stoughton-Cornell classification system divides steroids into 7 classes

> Duration of Dosing:
  • Class 1 steroids: available data for 2-4 weeks of treatment
  • Less potent agents: Optimal endpoint unknown
  • Gradual reduction in usage recommended following clinical response; while optimal endpoint is unknown unsupervised continuous use is not recommended
  • For clobetasol and halobetasol maximal weekly use should be 50 gms or less

> Short-term Results:
  • Highly potent agents have greater efficacy than less potent agents
  • Vehicle, usage area, patient preference, patient age, and cost alter efficacy

> Long-term Results:
  • True efficacy and risks associated with long-term use are unknown as most clinical trials are of short duration
  • Tachyphylaxis, while not demonstrated in clinical trials, may affect the long-term results achieved in a given patient
  • Combination with other topicals and variations in dosing schedules may lessen risk of long-term side effects

> Toxicities:
  • Local - skin atrophy, telangiectasias, striae, purpura, contact dermatitis, rosacea
  • Systemic - hypothalamic-pituitary-adrenal axis suppression may occur with use of medium and high potency topical steroids. This will be lessened by intermittent or localized use. Unilateral or bilateral avascular necrosis of the femoral head rarely occurs. Increased intraocular pressure, glaucoma and cataracts have been reported with use around the eye.
  • Risks increase when used with excessive frequency or duration
  • It is unknown if there is an increased risk of infection with chronic use

> Baseline Monitoring: None

> Ongoing Monitoring:
  • Assessment of growth in children using for long term
  • Regular skin checks for all patients on long term therapy to assess for atrophy

> Pregnancy: Category C

> Nursing: Unknown safety
  • Pediatric Use: Because of the increased skin surface/body mass ratio, the risks to infants and children may be higher for systemic effects secondary to enhanced absorption. Growth retardation is also a potential concern.
Recommendations for Vitamin D analogues

- Indication: Plaque type psoriasis
- Dosing: Twice daily to affected areas
- Efficacy:
  - In two large studies of plaque type psoriasis of the body, 70-74% of patients treated with calcitriol or calcipotriene ointment showed either 75% improvement or marked improvement to clearing as compared with 18-19% of patients treated with placebo. 60% of scalp psoriasis patients treated with calcipotriene solution showed clearance or marked improvement as compared to 17% of placebo patients.
  - Combination of calcipotriene and betamethasone ointment — In a 4 week trial of patients with mild to severe plaque psoriasis - 48% of patients treated with the combination agent achieved absent or mild psoriasis, compared to 16.5% of patients treated with calcipotriene once daily, 26.3% of patients treated with betamethasone once daily, and 7.6% of patients treated with placebo. A 52 week clinical practice usage study showed 70-80% of patients achieving clear or almost clear status with no drug-related serious adverse events such as HPA axis oppression or stria when used on an as needed basis.
- Use in combination with topical corticosteroids gives added benefit
- Contraindications/Adverse Reactions:
  - Irritation in lesional and peri-lesional skin that is transient
  - Reversible elevation of serum calcium – more likely to occur in patients treated with greater than 100 g/week
  - Causes photosensitivity, but no contraindications to combining with UVB phototherapy
  - When using combination calcipotriene/betametasone, the side effects of high potency topical corticosteroids including HPA axis suppression, skin atrophy, among others (see above) may occasionally occur
- Pregnancy and nursing:
  - Category C
  - No information on excretion in breast milk and pregnant and nursing mothers were excluded from clinical studies
- Pediatric use: Appears to be safe

Recommendations for topical tazarotene

- Indication: Plaque type psoriasis
- Dosing: Applied once daily
- Efficacy: 50% or more improvement, seen in 63% and 50% of patients treated with tazarotene 0.1% gel and 0.05% gel used once daily for 12 weeks, compared to 31% of patients treated with vehicle. Overall lesional assessment of none, minimal or mild found in 40 – 51% of patients treated with tazarotene 0.1% cream and 0.05% cream used once daily for 12 weeks, compared to 25% of patients treated with vehicle.
- Best used in combination with topical corticosteroids
- Contraindications/Adverse Reactions:
  - Most common side effect is skin irritation in lesional and perilesional skin
  - Photosensitizing
- Pregnancy and nursing:
  - Pregnancy category X
  - Excreted in mammalian milk, but quantity in human milk is unclear
- Pediatric use: No available data in psoriasis patients under age 18; for acne, approved to age 12

Recommendations for topical tacrolimus and pimecrolimus

- Indications: No FDA approved indications for psoriasis. Primary indications for off label use are for facial and intertriginous psoriasis.
- Dosing: Applied twice daily to affected areas. No length of course is specified.
- Efficacy:
  - Plaque psoriasis – not generally effective
  - Intertriginous and facial psoriasis: 65% of patients treated with tacrolimus 0.1% ointment were clear or almost clear after 8 weeks of therapy compared with 31% of patients treated with placebo. 71% of the patients treated with pimecrolimus 0.1% cream were clear or almost clear after 8 weeks of therapy as compared to 21% of patients treated with placebo.
- Contraindications/Adverse reactions:
  - There are no specific contraindications/adverse reactions for psoriasis
  - Most common side effect for both medications is burning and itching
  - A controversial lymphoma “black box” warning has been issued by the FDA
- Pregnancy and nursing:
  - Category C
  -Tacrolimus and pimecrolimus are found in human milk and are not recommended for nursing mothers
- Pediatric use: Topical tacrolimus (0.03%) and topical pimecrolimus are approved for patients age 2 years or older for atopic dermatitis
Recommendations for emollients

- Indications: The use of emollients represents an internationally accepted standard adjunctive therapeutic approach to the treatment of psoriasis
- Dosing: Applied once to three times daily
- Efficacy: Two controlled studies of aloe vera with conflicting results
- Contraindications/Adverse reactions: No known contraindications
- Pregnancy and nursing: Generally considered safe
- Pediatric use: Generally considered safe

Recommendations for salicylic acid

- Indication: No specific FDA indication
- Dosing: Applied daily
- Efficacy: Data is limited on salicylic acid alone
  - Comparator study of tacrolimus and salicylic acid vs tacrolimus alone in small study (n=24) of psoriasis pts with less than 10% BSA, revealed improved efficacy with addition of salicylic acid
  - Comparator study of 408 pts with moderate - severe psoriasis treated with either mometasone and salicylic acid vs mometasone alone for 3 weeks. Psoriasis severity index measure of erythema, induration, and scaling showed the combination of mometasone furoate-salicylic acid to be more effective than mometasone furoate alone.
- Contraindications/adverse reactions: Do not combine with other salicylate drugs. Systemic absorption although rare, can occur especially when applied to over 20% of body surface or in patients with abnormal hepatic or renal function. Salicylic acid decreases the efficacy of UVB phototherapy due to a filtering effect and should not be used before UVB phototherapy.
- Pregnancy/nursing: Appears to be a safe choice for the control of localized psoriasis in pregnancy
- Pediatric use: Due to greater risk of systemic absorption and toxicity, salicylic acid should be avoided in children

Recommendations for anthralin

- Indications: Was important component of psoriasis treatment for many years
- Dosing: Several doses are available. Now commonly used as short contact therapy starting at 1% concentration with increasing concentration over time as tolerated.
- Efficacy: Limited placebo controlled trial data but as monotherapy, anthralin appears to have lower efficacy than more potent topical corticosteroids or vitamin D derivatives
- Contraindications/adverse reactions: Most common side effects are skin irritation and staining of the skin and other touching objects. Due to skin irritation, important to avoid contact with surrounding normal skin.
- Pregnancy/nursing: Category C
- Pediatric use: Use with caution

Recommendations for coal tar

- Indications: Used in the treatment of psoriasis for over 100 years. Although the use of tar products for treatment of localized psoriasis has decreased over time in the US, they are still often used in other countries.
- Dosing: Many formulations exist
- Efficacy: In double blind randomized controlled trial of 324 patients with mild-moderate psoriasis comparing 1% coal tar lotion with 5% coal tar extract, there was better improvement in both PASI score and TSS (total sign score) in patients treated with 1% lotion than in 5% extract
- Contraindications/Adverse reactions: Often poorly tolerated by patients due to cosmetic issues including staining of clothes and tar odor. Other potential adverse events include irritant contact dermatitis, folliculitis, and photosensitivity. Coal tar is carcinogenic in animals, but in humans there are no convincing data proving carcinogenicity and epidemiologic studies fail to show increased risk of skin cancer in patients who use coal tar.
- Pregnancy and nursing: Risk of topical coal tar used for short periods of time during pregnancy is likely to be small
- Pediatric use: Use with caution
Systemic Agents
Recommendations for methotrexate

> Indication: Severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy

> Dosing: Methotrexate is administered as a weekly single oral dose
  • Doses can be increased gradually until an optimal response is achieved. Total dose should not ordinarily exceed 30mg per week. Doses should be reduced to the lowest possible amount of drug needed to achieve adequate control of psoriasis with concomitant topical therapy.
  • A test dose of 2.5 – 5 mg is recommended

> Duration of Dosing:
  • Treatment can be continued for as long as is necessary provided there are no meaningful signs of liver or bone marrow toxicity with adequate monitoring
  • Folic acid supplementation 1-5mg daily by mouth, except for the day of methotrexate dosing, reduces the frequency of side effects

> Therapeutic Results:
  • In the only placebo-controlled trial of methotrexate for psoriasis, 36% of patients treated with 7.5mg orally per week, increased as needed up to 25mg per week, reached PASI 75 after 16 weeks

> Absolute Contraindications
  • Pregnancy
  • Nursing mothers
  • Alcoholism
  • Alcoholic liver disease or other chronic liver disease
  • Immunodeficiency syndromes
  • Bone marrow hypoplasia, leukopenia, thrombocytopenia or significant anemia
  • Hypersensitivity to methotrexate

> Relative Contraindications
  • Abnormalities in renal function
  • Abnormalities in liver function
  • Active infection
  • Obesity
  • Diabetes mellitus

> Toxicity
  • Elevated LFT’s
    – Minor elevations of LFTs are common. If elevation exceeds 2x normal, must check more frequently; if exceeds 3x normal, consider dose reduction; if exceeds 5x normal discontinue.
  • Anemia, aplastic anemia, leukopenia, thrombocytopenia
  • Interstitial pneumonitis
  • Ulcerative stomatitis
  • Nausea, vomiting, diarrhea
Management of Psoriasis and Psoriatic Arthritis: Clinical Recommendations | American Academy of Dermatology

- Malaise or fatigue
- Chills and fever
- Dizziness
- Decreased resistance to infection
- Gastrointestinal ulceration and bleeding
- Photosensitivity ("radiation recall")
- Alopecia

> Drug Interactions
- Hepatotoxic drugs such as barbiturates
- Acitretin has been used successfully in combination with methotrexate despite the potential for hepatotoxicity from both medications
- Drugs that interfere with renal secretion of methotrexate such as sulfamethoxazole, NSAIDs, and penicillins
- Folic acid antagonists such as trimethoprim

> Liver Biopsy
- Low risk patients – at baseline, not necessary
  - First biopsy: 3.5-4g; subsequent biopsies to be considered after 1.5g
- High-risk patients including history of diabetes, obesity, abnormal LFTs, excessive EtOH ingestion, chronic liver disease, family hx of heritable liver disease
  - Consider baseline biopsy or at 6 months with subsequent biopsies after 1-1.5 grams

> Baseline Monitoring
- History and Physical Examination
- CBC and platelet count
- BUN, creatinine and LFT's
- Liver biopsy is only indicated in patients with a history of significant liver disease
- Pregnancy test and test for HIV in selected patients.
- Consider PPD
- Consider chest x-ray if patient has underlying pulmonary disease

> Ongoing Monitoring
- CBC and platelet count at varying intervals (initially every 2-4 weeks for first few months and then every 1-3 months depending upon dosage adjustments, symptoms, and previous CBC results)
- LFT's at monthly intervals, BUN, creatinine every 2-3 months depending on dosage adjustments, symptoms and previous blood results
- Pregnancy test if indicated
- Consider liver biopsy in high-risk patients including history of diabetes, obesity, abnormal LFTs, excessive EtOH ingestion, chronic liver disease, family hx of heritable liver disease
- For those without risk factors, consider liver biopsy in patients with cumulative doses of more than 3.5-4g methotrexate
- For patients without risk factors, consider repeat liver biopsies after each subsequent 1.5g dosage, based on LFT's, risk factors such as diabetes and obesity, or in consultation with a hepatologist
- The aminoterminal peptide of procollagen III is used in Europe (but is generally not available in the United States) as a test for hepatic fibrosis, reducing the need for frequent liver biopsies
- Pregnancy: Category X; Males and females considering conception should be off methotrexate for 3 months prior to attempting to conceive. Should pregnancy ensue prior to this time period, consider genetic counseling.
- Nursing: Mothers receiving methotrexate should not breast feed
- Pediatric Use: Methotrexate is approved for the treatment of juvenile rheumatoid arthritis. Low dose methotrexate has been used effectively and safely in children for a variety of dermatologic and rheumatologic disorders
- Psoriatic Arthritis: Although there are only two small controlled trials evaluating methotrexate for psoriatic arthritis that are inadequately powered to assess clinical benefit, methotrexate is often used as the primary agent to treat psoriatic arthritis

**Recommendations for cyclosporine**

> Indication: Adult, non-immunocompromised patients with severe, recalcitrant psoriasis
- Severe is defined by the FDA as extensive or disabling plaque psoriasis
- Recalcitrant is defined by the FDA as those patients who have failed to respond to at least one systemic therapy or in patients for whom other systemic therapies are contraindicated, or cannot be tolerated
- Some guidelines suggest use of cyclosporine in moderate to severe psoriasis
- Efficacy observed in erythrodermic psoriasis, generalized pustular psoriasis and palmoplantar psoriasis

> Dosing: 2.5–5.0 mg/kg/day in two divided doses per day
- Dose adjustments downward (by 0.5 – 1.0 mg/kg) when clearance is achieved or when hypertension or decreased renal function tests are observed

> Duration of Dosing:
- Optimally used as interventional therapy; may be repeated at intervals after a rest period
- US Approval: 1 year continuous treatment; Non-US: 2 years of continuous treatment

> Short-term Results:
- At 3 and 5 mg/kg/d, 36% and 65%, respectively, achieved a clear or almost clear after 8 weeks
- After B-16 weeks, 50-70% of patients achieve PASI 75

> Long-term Results
- Not recommended due to toxicities
- Rapid relapse after abrupt discontinuation of cyclosporine

> Contraindications
- Concomitant PUVA or UVB, methotrexate or other immunosuppressive agents, coal tar, history of >200 PUVA treatments or prior radiation therapy
- Abnormal renal function
• Uncontrolled hypertension
• Malignancy
• Hypersensitivity to cyclosporine
• Avoid live vaccinations
• Caution with major infection and poorly controlled diabetes

> Toxicity
• Renal impairment
  – Acute
  – Chronic (increasing glomerular fibrosis with increasing duration of treatment with higher dosages)
• Hypertension
• Malignancies
  – Cutaneous
  – Lymphoproliferative
• Headache, tremor, paresthesia
• Hypertrichosis
• Gingival hyperplasia
• Worsening acne
• Nausea/vomiting/diarrhea
• Myalgias
• Flu-like symptoms
• Lethargy
• Hypertriglyceridemia
• Hypomagnesemia
• Hyperkalemia
• Hyperbilirubinemia
• Increased risk of infection
• May increase risk of cancer

> Drug Interactions
• Inducers/inhibitors of cytochrome P-450 3A4
• St. John’s Wort decreases cyclosporine concentration
• Cyclosporine may reduce clearance of digoxin, colchicine, prednisolone, statins (increased risk of rhabdomyolysis)
• Potassium-sparing diuretics cause hyperkalemia
• Thiazide diuretics increase nephrotoxicity
• Killed vaccines may have decreased efficacy
• Live vaccination is contraindicated
• Grapefruit juice
• NSAID’s

> Baseline Monitoring
• History and Physical Examination
• Blood Pressure x 2
• BUN and Cr x 2
• Urinalysis

> Ongoing Monitoring
• Every other week during initial 3 months, thereafter at 1 month intervals: Blood pressure, BUN, and Cr
• Monthly CBC, LFTs, lipid profile, magnesium, uric acid and potassium
• Pregnancy testing if indicated

> Pregnancy: Category C; lower birth weight and shorter duration of pregnancy reported in transplant patients. Appears not to be teratogenic in transplant patients

> Nursing: Mothers receiving cyclosporine should not breast-feed

> Pediatric Use: Transplant recipients as young as 1 year old have been treated with no unusual adverse events. While safety and efficacy of cyclosporine for children < 18 yrs with psoriasis has not been established, it may be considered in this patient population with severe psoriasis.

> Psoriatic Arthritis: There are studies demonstrating the efficacy of cyclosporine for psoriatic arthritis

Recommendations for acitretin

> Indication: FDA approved for adults with severe plaque type psoriasis

> Dosing: 10-50 mg/day given as a single dose
• Lower doses (25 mg/day or less) often used to minimize side effects, especially in combination regimens
• When acitretin is added to UV, light dose should be reduced by 30-50%

> Short-term Results:
• Efficacy rates not well defined but are high, based on studies of high dosages that are poorly tolerated
• Efficacy rates when used in combination with phototherapy are higher

> Long-term Results
• Not reported

> Contraindications
• Acitretin is a potent teratogen and must be avoided in women of child-bearing potential
• Severely impaired liver or kidney function
• Chronic abnormally elevated blood lipid values

> Toxicity
• Cheilitis
• Alopecia
• Xerosis, pruritus
• Xerophthalmia, night blindness
• Dry mouth

• Consider PPD
• LFTs, CBC, lipid profile, magnesium, uric acid and potassium
• Pregnancy test if indicated
Systemic Agents

Paronychia
Paresthesias
Headache, pseudotumor cerebri
Nausea, abdominal pain
Joint pain
Myalgia
Hypertriglyceridemia
Abnormal LFT’s

**Drug Interactions**
- Etretinate can be formed with concurrent ingestion of acitretin and ethanol
- Acitretin may potentiate glucose lowering effect of glibenclamide
- May interfere with the contraceptive effect of microdosed progestin minipill
- Acitretin and methotrexate can both cause hepatotoxicity, therefore they should be combined with caution
- Acitretin may reduce the protein binding of phenytoin
- Acitretin and tetracyclines can both increase intracranial pressure. Their combined use should be avoided.
- Concomitant administration of vitamin A and other oral retinoids with acitretin should be avoided

**Baseline Monitoring**
- History and Physical Examination
- Lipid profile, CBC, LFT’s, renal function tests
- Pregnancy test if indicated

**Ongoing Monitoring**
- LFTs, lipid profile at 2 wk intervals for the first 8 weeks, then every 6-12 wks
- CBC, renal function tests every 3 months
- Pregnancy test if indicated

**Pregnancy:** Category X

**Nursing:** Mothers receiving acitretin should not breast-feed

**Pediatric Use:** The safety and efficacy of acitretin in children with psoriasis is not established. High dose, long term oral retinoid use has been associated with ossification of interosseous ligaments and tendons of the extremities, skeletal hyperostoses, decreases in bone mineral density, and premature epiphyseal closure.

**Psoriatic Arthritis:** Generally thought to be ineffective for psoriatic arthritis

---

**Recommendations for azathioprine**

*Indication:* There is no FDA approved use for psoriasis

**Dosing:**
- Thiopurine methyl transferase levels are generally used to guide dosing
- One suggested daily schedule guided by results of TPMT values
  - TPMT <5.0 U do not use azathioprine
  - TPMT 5 -13.7 U 0.5mg/kg max dose
  - TPMT 13.7 - 19.0 U 1.5mg/kg max dose
  - TPMT >19.0 U 2.5mg/kg max dose

  Alternatively, start at 0.5mg/kg, and monitor for cytopenia. If no cytopenia, can increase dose by 0.5 mg/kg/day after 6-8 wks if necessary and increase by 0.5 mg/kg/day every 4 wks thereafter as needed. Generally dosed at 75 – 150 mg/day.

**Efficacy:**
In one study 19/29 pts had >75% improvement but in another smaller study 5/10 pts had >25% improvement

**Contraindications**
- **Absolute**
  - Allergy to azathioprine
  - Pregnancy or attempting pregnancy
  - Clinically significant active infection
- **Relative**
  - Concurrent use of allopurinol
  - Prior treatment with cyclophosphamide or chlorambucil

**Toxicity**
- Bone marrow suppression
- Malignancies
  - Cutaneous (SCCs)
  - Lymphoproliferative
- Increased risk of infections
- GI: nausea, vomiting, diarrhea
- Hypersensitivity syndrome
- Pancreatitis
- Hepatitis

**Drug Interactions**
- Allopurinol – increased risk of pancytopenia (if using concurrently, lower azathioprine dose by 75%)
- Captopril – may increase risk of anemia and leukopenia
- Warfarin – may need an increased dose of warfarin
- Pancuronium – may need an increased dose of this for adequate paralysis
- Co-trimoxazole – increased risk of hematologic toxicity
- Rifampicin – decreases azathioprine efficacy, also hepatotoxic
- Clozapine – increased risk of agranulocytosis
Baseline Monitoring
• History and Physical Examination
• LFTs, CBC/diff, serum chemistry profile, urinalysis, PPD, hepatitis B and C screen
• Pregnancy test if indicated

Ongoing Monitoring
• CBC/diff twice/month for the first 2 months, monthly for the next 2 months, every 2 months thereafter
• LFTs monthly for the first 3 months then every 2 months thereafter
• Biannual physical examination focusing on lymph node exam and skin cancer exam (SCC’s in particular)
• Pregnancy testing if indicated

Pregnancy/Nursing: Pregnancy Category D
• Pregnancy and breast-feeding should be avoided during treatment with azathioprine, and patients (including males) must use adequate contraception

Pediatric Use: No data
Psoriatic Arthritis: A small observational cohort study suggests that azathioprine may be of value in psoriatic arthritis

Recommendations for fumaric acid esters
Indications:
• There is no FDA approved use for psoriasis in the US. Fumaric acid esters are approved in Europe.

Dosing:
• Starting dose - one tablet of Fumaderm® Increase over the next 8 weeks to a maximum of 6 tablets daily

Short-term Results:
• Multi-center, randomized, double blind placebo controlled trial of 100 pts showed that after 16 weeks fumarate treated pts reached a mean PASI 50 compared to placebo patients whose PASI was essentially changed
• Randomized, double blind controlled trial of 143 pts given either fumarates plus calcipotriol or fumarates alone found that pts given combination therapy reached PASI 50 in 3 wks vs those treated with fumarates alone reaching PASI 50 in 9 wks

Long-term Results:
• Case series of pts treated up to 14 years suggest no increased risk for infections or malignancies. Large, long term follow-up studies are necessary to confirm these observations.

Contraindications
• Severe liver disease
• Severe or chronic gastrointestinal disease
• Severe or chronic kidney disease
• Malignancy or a history of malignancy

• Leukopenia and other hematologic abnormalities
• Pregnancy
• Breastfeeding

Toxicity
• Gastrointestinal (Abdominal cramps, nausea, diarrhea, fullness and flatulence)
• Flushing
• Malaise
• Fatigue
• Lymphopenia, leukopenia, eosinophilia
• Hepatotoxicity and elevated LFT’s
• Increased cholesterol, triglycerides
• Increased serum creatinine and potassium, and proteinuria
• Rare case reports of renal disease but none in the controlled trials

Drug Interactions
• Other fumaric acid derivatives, methotrexate, cyclosporine, immunosuppressive drugs and cytostatic drugs may potentiate toxicity
• Drugs known to cause renal dysfunction

Baseline Monitoring
• History and physical examination
• CBC, platelet counts
• Chemistry screen
• Urinalysis

Ongoing Monitoring
• CBC, platelet count every other week for the first two months; monthly until month 6, and bimonthly thereafter
• Serum chemistry and urinalysis every 2 weeks for the first month, then monthly for the first 6 months and bimonthly thereafter

Pregnancy: Not recommended in pregnancy (no FDA pregnancy category because it is not approved in the US)
Nursing: There is no data and therefore mothers receiving fumaric acid esters should not breast-feed.
Pediatric Use: No data
Psoriatic Arthritis: One small double blind placebo controlled trial suggested minimal efficacy as evidenced by decreased joint pain and sedimentation rate

Recommendations for hydroxyurea
Indication:
• There is no FDA approved use for psoriasis

Dosing:
• Initial dose of 500 mg PO BID increasing to up to 3 g/day as tolerated
• Weekly dose of 3 - 4.5 g/week has also been utilized
> Short-term Results:
  • Efficacy rates vary widely
  • One study showed that 55% of 31 patients had at least a 70% reduction in PASI score (mean treatment time of 36 weeks), while another study comparing hydroxyurea to methotrexate showed a 48% reduction in PASI score after 12 weeks of hydroxyurea

> Long-term Results
  • One study found that 60% of 85 pts treated for a mean of 16 months had a complete or almost complete clearance

> Contraindications
  • Marked bone marrow depression, including leukopenia, thrombocytopenia or anemia

> Toxicity
  • Bone marrow suppression
  • Gastrointestinal symptoms (stomatitis, anorexia, nausea, vomiting, diarrhea, and constipation)
  • Dermatological reactions (rash, ulceration, dermatomyositis-like skin changes, alopecia)
  • Dysuria may rarely occur
  • Neurological disturbances limited to headache, dizziness, disorientation, hallucinations, and convulsions rarely seen
  • Temporary impairment of renal tubular function accompanied by elevations in serum uric acid, BUN, and creatinine
  • Fever, chills, malaise, edema, asthenia
  • Elevation of hepatic enzymes
  • Pulmonary fibrosis rare
  • Fatal and nonfatal pancreatitis and hepatotoxicity, and severe peripheral neuropathy have been reported in HIV-infected patients who received hydroxyurea in combination with antiretroviral agents

> Drug Interactions
  • Concurrent use of hydroxyurea and other myelosuppressive agents or radiation therapy may increase the likelihood of bone marrow depression
  • Hydroxyurea may raise the serum uric acid level; dosage adjustment of uricosuric medication may be necessary

> Baseline Monitoring
  • History and Physical Examination
  • Complete blood count at baseline and weekly until stable dose is achieved
  • Pregnancy test if indicated

> Ongoing Monitoring
  • Complete blood count at monthly intervals
  • Biannual physical examination focusing on lymph node exam and skin cancer exam (SCC's in particular)
  • Pregnancy testing if indicated

> Pregnancy/Nursing: Pregnancy Category D
  • Pregnancy and breast-feeding should be avoided during treatment and patients (including males) must use adequate contraception

> Pediatric Use: No data

> Psoriatic Arthritis: No data

**Recommendations for leflunomide**

> Indication:
  • There is no FDA approved use for psoriasis

> Dosing:
  • Loading dose of 100 mg/day for 3 days followed by 20 mg/day long term

> Short-term Results:
  • In the only randomized controlled trial of 190 pts, 24 wks of leflunomide dosed as above, led to a PASI 75 of 17% vs placebo response of 8% (p =.048)

> Long-term Results
  • Not reported

> Contraindications
  • Patients with hypersensitivity to leflunomide or its metabolites

> Toxicity
  • Most common side effects include nausea, diarrhea, loss of appetite, weight loss, headache, dizziness
  • Less frequent adverse reactions may include severe liver injury, including fatal outcome. Most cases of severe liver injury occur within 6 months of therapy and in pts with multiple risk factors for hepatotoxicity.
  • Rare reports of pancytopenia, agranulocytosis and thrombocytopenia in patients receiving leflunomide. This occurs in patients who have been treated with methotrexate or other immunosuppressive agents, or who had recently discontinued these.

> Drug Interactions
  • Co-administration of leflunomide with methotrexate demonstrates no pharmacokinetic interaction between the two drugs but can lead to an increased risk of hepatotoxicity
  • When leflunomide is given with rifampin, leflunomide levels are increased

> Baseline Monitoring
  • History and Physical Examination
  • CBC/diff and LFT's
  • Pregnancy test if indicated

> Ongoing Monitoring
  • Monthly complete blood count with differential and liver function tests for the first six months and then every 6 – 8 weeks
  • Pregnancy testing if indicated

> Pregnancy: Category X
> Nursing: Leflunomide should not be used by nursing mothers

> Pediatric Use: No data

> Psoriatic Arthritis: In the only randomized controlled study of 190 pts with psoriasis and psoriatic arthritis, 59% of pts treated with leflunomide vs 30% of placebo pts were responders by the PsARC

**Recommendations for mycophenolate mofetil**

> Indication:
  - There is no FDA approved use for psoriasis

> Dosing:
  - 1.0 – 1.5 gm orally two times per day

> Short-term Results:
  - 47% mean reduction in PASI at 12 weeks in 23 patients with psoriasis treated with 1.0-1.5 gm bid
  - 47% mean reduction in PASI at 6 weeks in 11 psoriasis patients treated with 1 gm bid for 3 weeks then 0.5 gm bid for 3 more weeks

> Long-term Results: No data

> Contraindications
  - Hypersensitivity to mycophenolate mofetil, mycophenolic acid

> Toxicity
  - GI side effects (diarrhea, nausea/vomiting, abdominal cramps). These occur early and decrease with continued use.
  - Hematologic (leukopenia is most common; anemia, thrombocytopenia)
  - Genitourinary (urgency, frequency, dysuria, sterile pyuria).
  - Increased incidence of viral, bacterial and mycobacterial infections
  - Progressive multifocal leukoencephalopathy
  - Hypercholesterolemia, hypophosphatemia, hyperkalemia, hypokalemia
  - Fever and myalgias
  - Headache, insomnia
  - Peripheral edema
  - Hypertension
  - Patients taking mycophenolate mofetil should not be given live attenuated virus vaccines

> Drug Interactions
  - Antacids containing aluminum and magnesium
  - Calcium and iron
  - Cholestyramine
  - Antibiotics including cephalosporins, fluoroquinolones, macrolides, penems, penicillins, sulfonamides inhibit enterohepatic recirculation and decrease mycophenolate mofetil levels
  - High dose salicylates
  - Phenytoin
  - Xanthine bronchodilators
  - Probenecid
  - Acyclovir, ganciclovir, valganciclovir

> Baseline Monitoring
  - History and Physical Examination
  - CBC, platelet counts
  - Chemistry screen, LFT’s
  - Pregnancy test if indicated

> Ongoing Monitoring
  - CBC, platelet count weekly x1 month; then every 2 weeks for 2 months; then monthly thereafter.
  - Monthly chemistry panel and LFT’s
  - Biannual physical examination focusing on lymph node exam and skin cancer exam (SCC’s in particular)
  - Pregnancy testing if indicated

> Pregnancy/Nursing: Pregnancy Category D
  - Pregnancy and breast-feeding should be avoided during treatment and patients (including males) must use adequate contraceptive precautions

> Pediatric Use: No data

> Psoriatic Arthritis: Case reports suggest improvement

**Recommendations for sulfasalazine**

> Indication:
  - There is no FDA approved use for psoriasis

> Dosing for Psoriasis:
  - In psoriasis, initial dose of 500 mg PO BID increased to up to 3-4 g/day as tolerated

> Duration of Dosing:
  - As long as needed. There are no known cumulative toxicities.

> Short-term Results:
  - Efficacy rates not well characterized. In the only randomized controlled trial, 8 wks of 3-4 g/day sulfasalazine led to moderate improvement (global improvement of 30-59%) in 7/17 assessable sulfasalazine pts compared to 1/27 assessable placebo pts.

> Long-term Results
  - Not reported

> Contraindications
  - Patients with intestinal or urinary obstruction, patients with porphyria, patients hypersensitive to sulfasalazine, its metabolites, sulfonamides, or salicylates

> Toxicity
  - Anorexia, headache, gastrointestinal symptoms (including nausea, vomiting, and gastric distress) and oligospermia can occur in up to one third of patients
Systemic Agents

Management of Psoriasis and Psoriatic Arthritis: Clinical Recommendations  
American Academy of Dermatology

> Drug Interactions
> • Reduced absorption of folic acid and digoxin

> Baseline Monitoring
> • History and physical examination
> • CBC/diff and LFT’s
> • Pregnancy test if indicated

> Ongoing Monitoring
> • CBC/diff and LFT’s every other week for the first three months. During the second three months, CBC/diff and LFT’s monthly and thereafter once every three months.
> • Urinalysis and renal function tests should be done periodically.
> • Pregnancy testing if indicated

> Pregnancy: Category B
> • Nursing: Sulfonamides are excreted in the milk. In the newborn, they compete with bilirubin for binding sites on the plasma proteins and may thus cause kernicterus.
> • Pediatric Use: No data
> • Psoriatic Arthritis: In the largest trial of sulfasalazine for psoriatic arthritis, after 36 weeks of treatment with 2 gm/day, 58% of pts given sulfasalazine compared to 45% of pts given placebo achieved PsARC

Recommendations for tacrolimus

> Indication:
> • There is no FDA approved use for psoriasis

> Dosing for Psoriasis:
> • 0.05 – 0.15 mg/kg

> Duration of Dosing:
> • Unknown

> Short-term Results:
> • Efficacy rates are poorly characterized. Pts dosed at 0.05 mg/kg showed no difference from placebo at 3 wks. When dosed at 0.10 – 0.15 mg/kg, by 9 wks there was a statistically significant improvement in PASI compared to placebo.

> Long-term Results
> • Not reported

> Contraindications
> • Patients with hypersensitivity to tacrolimus or its metabolites
> • Side effect profile similar to cyclosporine:
>  • Most common side effects include tremor, headache, nausea, diarrhea, hypertension and abnormal renal function tests

Recommendations for 6-thioguanine

> Indication
> • There is no FDA approved use for psoriasis

> Dosing:
> • Start at 80 mg two times per week. Increase by 20 mg every 2-4 weeks. Maximum dose is 160 mg 3 times per week.

> Short-term Results:
> • Open label trial of 14 pts treated with pulse dosing followed by maintenance dosage (120 mg twice a week to 160 mg three times per week). Of 11 pts who became longer term responders, 6/11 showed a response after 2-4 weeks.

> Long-term Results
> • 76 patients followed for over one month. At 24 months, 58% were effectively maintained.
> • Another study showed 14/18 patients had 90% improvement

> Contraindications
> • Pre-existing liver disease
> • Immunosuppression
> • Anemia, leukopenia and/or thrombocytopenia

> Drug Interactions
> • Numerous drug interactions as tacrolimus is metabolized by cytochrome P450 system
> • Do not give tacrolimus and cyclosporine together

> Baseline Monitoring
> • History and Physical Examination
> • CBC/diff, renal and LFT’s
> • Pregnancy test if indicated

> Ongoing Monitoring – proper frequency is not established
> • Blood pressure
> • Serum chemistry
> • Renal function
> • Liver function
> • Pregnancy testing if indicated

> Pregnancy: Category C
> • Nursing: Tacrolimus should not be used by nursing mothers
> • Pediatric Use: No data
> • Psoriatic Arthritis: Case reports suggest improvement
> Toxicity
  • Myelosuppression
  • Liver toxicity from hepatic venoocclusive disease
  • Increased ALT and AST
  • Hyperuricemia
  • Photodermatitis
  • Taste changes
  • Gastroesophageal reflux, gastric ulcers
  • Headache
  • Nausea/Vomiting
  • Aphthous ulcers
  • Fatigue
  • Non-melanoma skin cancer
  • Multiple warts, herpes zoster

> Drug Interactions
  • Aminosalicylate derivatives (olsalazine, mesalazine, or sulfasalazine) may inhibit TPMT

> Baseline Monitoring
  • History and Physical Examination
  • CBC, platelet count, chemistry screen, LFT’s, Hepatatis B and C, PPD
  • Pregnancy test if indicated

> Ongoing Monitoring
  • CBC and platelet count every 2-4 weeks; Serum chemistry every 3 months
  • Biannual physical examination focusing on lymph node exam and skin cancer exam (SCC’s in particular)
  • Pregnancy testing if indicated

> Pregnancy/Nursing: Pregnancy Category D
  • Pregnancy and breast-feeding should be avoided during treatment, and patients (including males) must use adequate contraception.

> Pediatric Use: No data

> Psoriatic Arthritis: No data
Recommendations for ultraviolet B (broadband and narrowband)

> Indication:
  • Generalized psoriasis (including guttate) unresponsive to topicals

> Dosing:
  • BB:
    – Initial dosing according to skin type (20-60 mJ/cm²) or MED (50% of MED)
    – Subsequent dosage increase by 5-30 mJ/cm² or 25% or less of the initial MED
    – Treatment 3-5 times weekly
  • NB:
    – Initial dosing according to skin type (130 to 400 mJ/cm²) or MED (50% of MED)
    – Subsequent dosage increase by 15-65 mJ/cm² or 10% or less of the initial MED
    – Treatment 3-5 times weekly

> Duration of Treatment:
  • BB:
    – Initial improvement often occurs within 4 weeks of therapy
    – A single course is 20-25 treatments
    – Maintenance therapy may prolong remission
  • NB:
    – Response observed at 8 to 10 treatments
    – A single course is 15 to 20 treatments
    – Maintenance therapy may prolong remission

> Short-term results (clearance):
  • BB:
    – Average of 20-25 treatments to induce clearance
  • NB:
    – More effective than BB-UVB, clearance within 2 weeks may be seen
    – Average of 15-20 treatments to achieve clearance

> Long-term results (remission):
  • BB:
    – Remission rate of 5% after 1 year
  • NB:
    – Remission rate of 38% after 1 year

> Contraindications:
  • Patients with known lupus erythematosus, or xeroderma pigmentosum

> Caution should be exercised in:
  • Patients with skin types I and II who tend to burn easily, those with a history of arsenic intake or previous treatment with ionizing radiation therapy, those with a history of melanoma or multiple non-melanoma skin cancers and any medical condition that is severe enough that the patient cannot tolerate heat or prolonged standing in the light box

> Toxicity:
  • Acute:
    – Erythema
    – Pruritus
Phototherapy and Photochemotherapy

> Long Term:
  > - Photo-aging, lentigines, telangectasias
  > - Theoretical risk of photo-carcinogenesis
  > - Advise use of protective goggles and genital shields during treatment

> Drug interactions:
  > • Cautious use with other photosensitizing medications
  > • When used in conjunction with systemic retinoids, the dose of both retinoids and UVB may need to be lowered

> Baseline Monitoring:
  > Full body skin check before initiation of therapy

> Ongoing Monitoring:
  > Regular full skin exam to monitor signs of photo-aging, pigmentation and cutaneous malignancies

> Pregnancy:
  > • Generally considered safe (expert opinion)

> Nursing:
  > • Generally considered safe (expert opinion)

> Pediatric use:
  > No adequate study. May be used with caution in individuals younger than 18 years of age.

> Psoriatic arthritis:
  > No studies

Recommendations for use of topical targeted phototherapy

> Indications:
  > • Adult and Pediatric Patients with Mild, Moderate or Severe Psoriasis with less than 10% BSA involvement

> Dosage:
  > • Initial dose depends on the individual’s skin type (including formal MED testing), plaque characteristics and thickness. (500 to 900 mJ/cm² for the XTRAC®)
  > • Subsequent doses adjusted according to clinical response and/or side effects

> Duration of Treatment:
  > Dosing 2-3x a week until the patient is clear, usually an average of 10-12 treatments are needed.

> Short-term Results:
  > Initial response within 8-10 treatments depends on multiple factors such as device utilized, protocol used, lesion characteristics and site.

> Long-term Results:
  > Mean remission times of 3.5 – 6 months

> Caution should be exercised:
  > • In patients with photosensitivity disorders

> Toxicity:
  > • Erythema
  > • Hyperpigmentation
  > • Blistering, particularly with higher doses

> Drug Interactions:
  > May need to lower dosing based upon presence of photosensitizing medications
  > (Note: the action spectrum of most photosensitizing medications is in the UVA range)

> Baseline Monitoring:
  > None

> Ongoing Monitoring:
  > • For efficacy and for burning

> Pregnancy:
  > • No studies in pregnancy have been performed but expert opinion is that it is safe

> Nursing:
  > • No studies in nursing mothers have been performed but expert opinion is that it is safe to be used

> Pediatric Use:
  > • No large scale studies in children have been performed but expert opinion is that it is safe to be used

> Psoriatic Arthritis:
  > No studies

Recommendations for use of systemic psoralen plus ultraviolet A

> Indications:
  > • Adults with generalized psoriasis who are resistant to topical therapy

> Dosing:
  > • 8-methoxypsoralen (Oxsoralen Ultra), 0.4-0.6 mg/kg, taken 1-2 hour before exposure to UVA
  > • Other available forms of psoralen include 5-methoxypsoralen and trimethylpsoralen
  > • UV protective eye wear should be worn when outdoors for 12 hours post-ingestion
  > • Treatment 2-3 times weekly

> Duration of Treatment:
  > Initial improvement frequently seen within 1 month of therapy
  > A single course is 20-25 treatments
  > May be repeated as indicated

> Short-term results:
  > • 89% clearing with an average of 25 treatments in the US and 20 treatments in Europe
  > • 11.6 weeks to clear in US studies compared to 5.3 weeks to clear in European studies
Phototherapy and Photochemotherapy

> Long-term results:
  • Once clearance has been achieved, maintenance treatment may or may not be used
  • Remission times: 3-12 months

> Contraindications:
  • Patients with known lupus erythematosus, porphyria, or xeroderma pigmentosum

> Caution should be exercised:
  • In patients with skin types I and II who tend to burn easily, those with a history of arsenic intake or previous treatment with ionizing radiation therapy, those with a history of melanoma or multiple non-melanoma skin cancers, any medical condition that is severe enough that the patient cannot tolerate heat or prolonged standing in the light box, those with severe liver disease that could lead to toxic levels of psoralens, possibly those who have been treated with cyclosporine or methotrexate and patients who are pregnant or nursing

> Toxicity:
  • Acute:
    – Nausea and vomiting are common
    – Dizziness and headache are rare
    – Erythema: peaks at 48-96 hrs
    – Pruritus
    – Tanning: starts 1 wk after PUVA
    – Blisters, photo-onycholysis, melanonychia
  • Chronic:
    – Photo-carcinogenesis (SCC, BCC and possible melanoma)
    – Increased risk of photo-carcinogenesis in Caucasians with skin types 1-3 after 200 treatments. This risk not present for non-Caucasians.
    – Photo-aging and lentigines are common, especially in patients of skin types 1-3 and are cumulative UVA dose dependent

> Drug interactions:
  • Caution when the patient is taking other photosensitizing medication
  • Should decrease the UVA dose by one-third if patient is started on oral retinoids while receiving PUVA

> Baseline monitoring:
  • Skin cancer screening
  • Eye examination. However, recent evidence demonstrates no increased risk of cataract in patients who receive PUVA.
  • If indicated by history:
    - ANA panels (anti-Ro/La antibodies)
    - Liver enzymes

> Ongoing monitoring:
  • Regular full skin exam due to potential increased risk of photo-carcinogenesis in Caucasians
  • In patients who are non-compliant with eye protection, yearly eye exam

> Pregnancy:
  • Category C

> Nursing:
  • Contraindicated for a period of 24 hours after ingesting psoralen

> Pediatric use:
  • No studies. May be used with caution in individuals younger than 18 years of age

> Psoriatic arthritis:
  • No studies

Recommendations for use of topical psoralen plus ultraviolet A

> Indications:
  • Topical PUVA for adults with psoriasis of palms and soles
  • Bath PUVA for adults and children with generalized psoriasis

> Dosing:
  • Topical
    - Use 0.1% 8-methoxypsoralen in emollient and treat 2-3 times per week.
    - Apply 30 minutes before UVA
    - Start at 0.25 – 0.5 J/cm2, increase by 0.25 – 0.5 J/cm2
  • Bath
    - 50mg of 8-methoxypsoralen (Oxsoralen Ultra) in 100L water
    - 20-30 min pre-exposure
    - Schedule similar to oral PUVA

> Duration of Treatment:
  • May take 30 treatments to have noticeable response
  • A single course usually is 30-40 treatments
  • May be repeated as indicated

> Short-term results:
  • Clinically is beneficial

> Long-term results:
  • Once clearance has been achieved, maintenance treatment may be used
  • Remission: 3-12 months.

> Contraindications:
  • Patients with known lupus erythematosus, porphyria, or xeroderma pigmentosum

> Caution should be exercised:
  • In patients with skin types I and II who tend to burn easily, those with a history of arsenic intake or previous treatment with ionizing radiation therapy, those with a history of melanoma or multiple non-melanoma skin cancers and patients who are pregnant or nursing
Toxicity:
• Acute:
  – Erythema, blistering, hyperpigmentation
• Chronic:
  – No increased risk of skin cancer demonstrated

Drug interactions:
• None

Baseline monitoring:
• None

Ongoing monitoring:
• For efficacy and monitor for burning

Pregnancy:
• Category C

Nursing:
• No data available

Pediatric use:
• Safe provided patient can follow instructions, however no systemic absorption studies have been performed

Psoriatic arthritis:
• No studies
Recommendations for ustekinumab

> Indications: moderate - severe psoriasis
> Dosing: 45 mg of ustekinumab at baseline, 4 weeks and every 12 weeks in those < 100 kg, and 90 mg of ustekinumab at the same intervals for those > 100 kg
> Short term efficacy – PASI 75 in 67% at 12 weeks
> Long term efficacy – PASI 75 maintained in 87% of patients at 52 weeks who attained PASI 75 at week 12
> Toxicities:
  • Occasional injection site reactions.
  • Rare reports of serious infections and malignancies including skin cancers.
  • Rare reports of major adverse cardiovascular events (MACE)
> Baseline Monitoring: (similar to other biologic agents)
  • PPD is required
  • LFT, CBC and hepatitis profile
> Ongoing Monitoring:
  • Periodic history and physical examination recommended while on treatment
  • Yearly PPD, and periodic CBC and LFT
> Pregnancy category B

TNF Inhibitors

General recommendations for TNF inhibitors

> Anti-TNF agents are contraindicated in patients with active, serious infections
> Tuberculosis testing (PPD) should be performed on all patients who will be treated with TNF inhibitors as there are reports of tuberculosis reactivation in patients treated with this class of drug
> Do not use with live vaccines; biologically inactive or recombinant vaccines may be considered, although the immune response of these vaccines could be compromised
> Since there is an association between anti-TNF therapy and demyelinating diseases (i.e. multiple sclerosis (MS)) TNF inhibitors should not be used in patients with MS or other demyelinating diseases. First degree relatives of patients with MS have an increased risk of developing MS, with a sibling relative risk of between 18 and 36, evidence strongly suggesting that TNF inhibitors should not be used in first degree relatives of patients with MS.
> Since there have been reports of new onset and worsening of congestive heart failure (CHF) in patients treated with TNF inhibitors, caution should be used when considering TNF inhibitor use in patients with CHF. It is recommended that patients with New York Heart Association Class 3 or 4 CHF avoid all use of TNF inhibitors and patients with Class 1 or 2 CHF undergo echocardiogram testing. If the ejection fraction of these patients is less than 50%, then TNF inhibitor treatment should potentially be avoided.
> Hepatitis B reactivation following treatment with TNF inhibitors has been reported. In the appropriate clinical setting, patients should be screened for hepatitis B infection.
Recommendations for adalimumab

- **Indications:** moderate/severe psoriatic arthritis, moderate to severe psoriasis, adult and juvenile rheumatoid arthritis (as young as age 4), ankylosing spondylitis, and Crohn’s disease.
- **Dosing for psoriasis:** 80mg the first week, 40 mg the second week, followed by 40mg every other week given subcutaneously.
- **Short Term Results:** 80% of patients achieve PASI 75 at 12 weeks.
- **Long Term Results:** 68% of patients achieve PASI 75 at 60 weeks.
- **Small percentage of patients lose efficacy with continued use.**
- **Toxicities:**
  - Moderately painful injection site reactions are noted.
  - Rare reports of serious infections (i.e., tuberculosis and opportunistic infections) and malignancies.
  - There are rare reports of drug-induced, reversible side effects including lupus without renal or CNS complications, cytopenias, MS as well as exacerbation of and new onset of CHF.
- **Baseline Monitoring:**
  - PPD is required.
  - Liver function tests, CBC, and hepatitis profile.
- **Ongoing Monitoring:**
  - Periodic history and physical exam are recommended while on treatment.
  - Consider a yearly PPD, and periodic CBC and liver function studies.
- **Pregnancy category B.**

Recommendations for etanercept

- **Indications:** moderate to severe psoriasis, moderate/severe psoriatic arthritis, adult and juvenile rheumatoid arthritis (as young as age 4), and ankylosing spondylitis.
- **Dosing:** 50mg twice weekly given subcutaneously for 3 months followed by 50 mg once weekly.
- **Short Term Results:** 49% of patients given 50 mg twice weekly achieved a PASI 75 at 12 weeks; 34% of patients given 25 mg twice weekly achieved a PASI 75 at 12 weeks.
- **Step-Down Results:** 54% of patients whose dose was decreased from 50 mg twice weekly to 25 mg twice weekly achieved a PASI 75 at 24 weeks; 45% of patients whose dose remained at 25 mg twice weekly achieved a PASI 75 at 24 weeks.
- **Toxicities:**
  - Mildly pruritic injection site reactions may occur.
  - Rare cases of serious infections (i.e., tuberculosis) and malignancies.
  - There are also rare reports of drug-induced, reversible side effects including lupus without renal or CNS complications, cytopenias, MS as well as exacerbation and new onset of CHF.
- **Baseline Monitoring:**
  - PPD, LFT, and CBC.
- **Ongoing Monitoring:**
  - Periodic history and physical exam are recommended while on treatment.
  - Consider yearly PPD, and periodic CBC and liver function studies.
- **Pregnancy category B.**
- **Contraindications:** Sepsis.

Recommendations for infliximab

- **Indications:** severe psoriasis, moderate/severe psoriatic arthritis, adult rheumatoid arthritis, ankylosing spondylitis, ulcerative colitis, and Crohn’s disease.
- **Dosing:** 5mg/kg dose infusion schedule at weeks 0, 2, 6, and then every 6-8 weeks. Dose and interval of infusions may be adjusted as needed.
- **Short Term Response:** 80% of patients achieved a PASI 75 at week 10, 50% PASI improvement noted by 2nd week.
- **Long Term Response:** 61% of patients achieved a PASI 75 at week 50.
- **Toxicities:**
  - Infusion reactions and serum sickness can occur - more commonly in patients who have developed antibodies.
  - The incidence of infusion reactions may be reduced by concurrent administration of methotrexate.
  - Rare cases of serious infections (i.e., tuberculosis) and malignancies including hepatosplenic T-cell lymphoma (in children). There are rare reports of drug-induced, reversible side effects including lupus without renal or CNS complications, cytopenias, MS as well as exacerbation of and new onset of CHF.
- **Baseline Monitoring:**
  - PPD is required.
  - LFT’s, CBC, and hepatitis profile.
- **Ongoing Monitoring:**
  - Periodic history and physical exam are recommended while on treatment.
  - Consider a yearly PPD, and periodic CBC and liver function studies.
- **Pregnancy category B.**
- **Contraindications:** Infliximab at doses of greater than 5 mg/kg should not be given to patients with New York Heart Association Functional Class Type 3 or 4 CHF.
Psoriatic Arthritis
Recommendations for adalimumab

- Indications: Moderate/severe psoriatic arthritis, moderate/severe psoriasis, adult and juvenile rheumatoid arthritis (as young as age 4), ankylosing spondylitis, and adult Crohn’s disease.
- Dosing: 40mg every other week subcutaneously
- Response: ACR 20 at week 12 is 58%
- Toxicities:
  - Moderately painful injection site reactions are noted.
  - Rare reports of serious infections (i.e., tuberculosis and opportunistic infections) and malignancies
  - There are rare reports of drug-induced, reversible side effects including lupus without renal or CNS complications, cytopenias, MS as well as exacerbation of and new onset of CHF

Recommendations for etanercept

- Indications: Moderate/severe psoriatic arthritis, moderate to severe psoriasis, adult and juvenile rheumatoid arthritis (as young as age 4), and ankylosing spondylitis
- Dosing for Psoriatic Arthritis: 25mg twice weekly or 50 mg once weekly given subcutaneously
- Response: ACR 20 at 12 weeks is 59%
- Toxicities:
  - Mildly pruritic injection site reactions may occur
  - Rare cases of serious infections (ie, tuberculosis) and malignancies.
  - There are also rare cases of drug-induced, reversible side effects including lupus without renal or CNS complications, cytopenias, MS, as well as exacerbation and new onset of CHF.
- Baseline Monitoring: PPD, LFT, and CBC
- Ongoing Monitoring: Periodic history and physical exam are recommended while on treatment

Recommendations for golimumab

- Indications: moderate - severe psoriatic arthritis, rheumatoid arthritis, ankylosing spondylitis
- Dosing: 50 mg every 4 weeks subcutaneously
- Efficacy for psoriatic arthritis – ACR 20 - 51% at wk 14
Toxicities:
• Occasional injection site reactions
• Rare reports of serious infections and malignancies
• Although there are rare reports of drug-induced reversible side effects including lupus without CNS or renal complications, cytopenias, multiple sclerosis, and exacerbation as well as new onset congestive heart failure with the other three TNF inhibitors, there have been no reports of these reactions with golimumab to date. However, golimumab is a TNF inhibitor and it should be used cautiously.

Baseline Monitoring:
• PPD is required
• LFT and CBC

Ongoing Monitoring:
• Periodic history and physical examination recommended while on treatment.
• Consider a yearly PPD, and periodic CBC and LFT

Pregnancy Category B

Recommendations for infliximab
> Indications: Moderate/severe psoriatic arthritis, severe psoriasis, adult rheumatoid arthritis, ankylosing spondylitis, and Crohn’s disease (pediatric and adult)
> Dosage: 5mg/kg given intravenously at weeks 0, 2, 6 and then every 6 - 8 weeks. Dose and interval of infusions may be adjusted as needed
> Response: ACR 20 at week 14 is 58%
> Toxicities:
• Infusion reactions and serum sickness can occur - more commonly in patients who have developed antibodies
• The incidence of infusion reactions may be reduced by concurrent administration of methotrexate
• Rare cases of serious infections (i.e., tuberculosis) and malignancies including hepatosplenic T-cell lymphoma (in children). There are rare reports of drug-induced, reversible side effects including lupus without renal or CNS complications, cytopenias, MS as well as exacerbation of and new onset of CHF.

Baseline Monitoring:
• PPD is required
• LFT’s, CBC, and hepatitis profile

Ongoing Monitoring: Periodic history and physical exam are recommended while on treatment
• Consider a yearly PPD, and periodic CBC and liver function studies

References