Thalidomide Therapeutic Cheat Sheet

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TRADE NAME

- Thalomid

MECHANISM OF ACTION

- Thalidomide has multiple mechanisms, which can be grouped into four categories:[1]
  1. Hyponosedative effects: penetrates the central nervous system and causes sedation by unknown mechanism (use: pruritic conditions like prurigo nodularis).[1]
  2. Immunomodulatory effects: thalidomide inhibits Tumor Necrosis Factor alpha, resulting in decreased helper T cells and slightly increased suppressor T cells (uses: Erythema Nodosum Leprosum, sarcoidosis, chronic graft-versus-host disease, prurigo nodularis).[1–3]
  3. Anti-inflammatory effects: decreases neutrophil chemotaxis (uses: chronic cutaneous lupus erythematosus, pyoderma gangrenosum, aphthous stomatitis).[1,4]
  4. Neural and vascular effects: thalidomide is hypothesized to have direct effects of neural tissue (use: prurigo noduarlis).[1] It also inhibits angiogenesis (use: Kaposi Sarcoma).[1]

FDA APPROVED FOR[5]

- Erythema Nodosum Leprosum (ENL)
  - Acute cutaneous manifestations of moderate to severe ENL
  - Maintenance therapy for prevention of ENL recurrence
  - Not indicated for monotherapy in the presence of moderate to severe neuritis
- Multiple myeloma, in combination with dexamethasone

OFF-LABEL USES

- Very effective:[1,6,7]
  - Aphthous stomatitis and HIV-associated oral stomatitis
  - Behçet disease
  - Cutaneous features of lupus erythematosus
  - Prurigo nodularis
- Moderately effective:[1,6,7]
  - Actinic prurigo
  - Uremic pruritus
  - Langerhans cell histiocytosis
  - Cutaneous sarcoidosis
  - Recurrent erythema multiforme
  - Chronic graft-versus-host disease
  - Jessner lymphocytic infiltrate of the skin
- Possibly effective:[1,6,7]
  - Kaposi Sarcoma
  - Lichen planus
  - Pyoderma gangrenosum

DOSING (ORAL)

- ENL: 100 to 300 mg daily (up to 400 mg daily for severe disease);[1,5] for 7 days, followed but another 7 days for non-responders.[8,9]
  - MM: 200 mg daily[5]
  - Doses vary for off label indications, typically 50 to 300 mg daily.[1]

MONITORING

- REMS program: prescribers and pharmacists must be registered.[1,5]
  - Female patients must use 2 reliable forms of birth control.
  - Pregnancy tests required 1 month before therapy, within 24 hours of starting therapy, and 1 month after therapy. During therapy, pregnancy tests are needed weekly for 4 weeks followed by monthly.
  - Fertile men must use latex condoms given thalidomide has been detected in semen.[13,14]
- Perform neurologic exam to monitor for neuropathy monthly for 3 months, then every 3-6 months.[1]
- Baseline CBC and hepatic function panel; monitor monthly until dose is stable, then every 2-3 months.[1]

SIDE EFFECTS

- Teratogenicity (see pregnancy below)
- Peripheral neuropathy: proximal muscle weakness and lower extremity sensory loss (motor changes are often reversible, but sensory function may not be).[1,7,10]
- Thromboembolic events[11]
- Common effects:[1,7,7,12]
  - Drowsiness (very common)
  - Constipation (very common)
  - Nausea
  - Fatigue
  - Mood changes (anxiety or agitation)
  - Xerostomia and xerosis
  - Brittle nails
  - Peripheral edema
  - Pruritus
  - Irregular menses
  - Hyperglycemia
  - Bradycardia
  - Red palms
  - Decreased libido
  - Dizziness and orthostatic hypotension
- Rare effects:[1]
  - Endocrine defects (hypothyroidism, hypoglycemia, adrenocorticotropic hormone stimulation)
  - Leukopenia
  - Seizures
  - Exfoliative or erythrodermic reactions
  - Hypersensitivity reaction

DRUG INTERACTIONS

- Use with caution in combination with other drugs that cause:[1,5]
  - Sedation/CNS depression (alcohol, sedating H1 antihistamines, antipsychotics, benzodiazepines, antidepressants, anticholinergics)
  - Bradycardia
  - Peripheral neuropathy (isoniazid, metronidazole)
  - Thromboembolic events (bisphosphonates, corticosteroids)
    - Oral contraceptive pills are included; benefit may outweigh risk but it is important to consider non-hormonal birth control options.
- High risk use with CYP3A4 inducers (anticonvulsants, rifampin, griseofulvin) that impair the efficacy of oral contraceptive pills.[1]
- Live vaccines: should be given 3 months after completion of therapy.[1]

CONTRAINDICATIONS[1]

- Absolute:
  - Hypersensitivity to thalidomide
  - Patients with peripheral neuropathy
  - Pregnancy and women of childbearing potential without strict contraception or abstinence
  - Men engaging in sexual intercourse with women of childbearing potential without latex condoms
- Relative:
  - Hepatic or renal impairment
  - Neuritis or other neurologic disorders
  - Congestive heart failure or hypertension
  - Significant constipation
  - Hypothyroidism
- Live vaccines: should be given 3 months after completion of therapy.[1]

PREGNANCY

- Category X: severe teratogenic effects. During 21 to 36 weeks gestation, there is almost 100% risk of birth defects, the most common being phecomelia (underdevelopment of arms and legs).[1,7] Birth defects or fetal death can occur after only one dose.[5]
- Thalidomide is only available through a restricted distribution program, THALOMID Risk Evaluation and Mitigation Strategy (REMS) program.