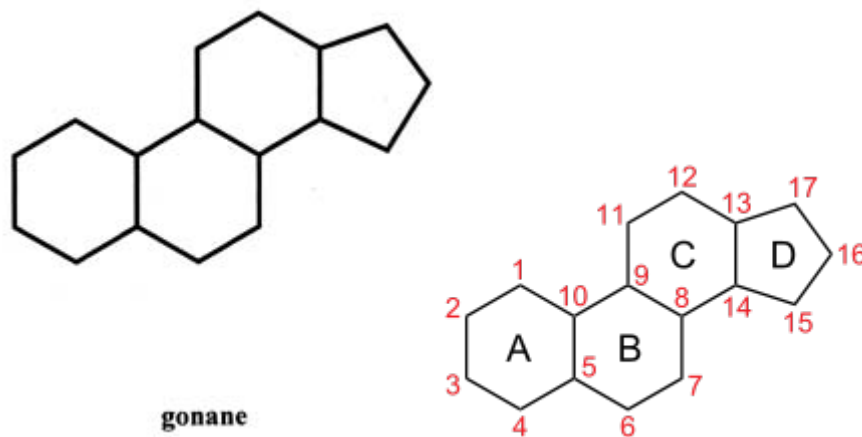


# Topical and Intralesional Corticosteroids

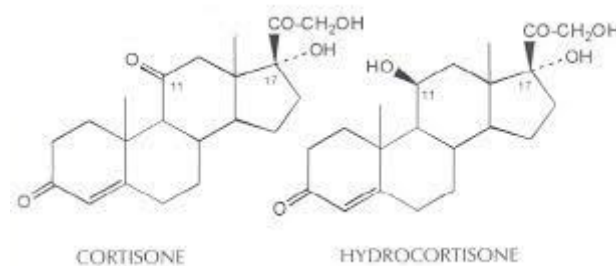
By Matheen Mohamed (2021 update)

## 1. Basic Pharmacology essentials:

- a. Steroid nucleus is based on a Gonane or Cyclopentanoperhydrophenanthrene ring: contains 17 carbons which are arranged as three six-member carbon rings to which a five-member carbon ring is attached



- b. Inactive Cortisone has a Ketone group at position 11: to become active, it requires a hydroxyl group at position 11 (Hydrocortisone). This conversion does not occur spontaneously in the skin, hence needs to be manufactured with -OH group (instead of ketone group) to make it topically active.



- c. Halogenation (Fluorination and Chlorination) increases potency.

## 2. Clinical effects

- a. Anti-inflammatory
- b. Anti-proliferative & Atrophogenic
- c. As the above 2 are hard to measure: Vasoconstrictor assay is used as a *de facto* marker of clinical efficacy (potency).

Anti-inflammatory	Anti-proliferative & Atrophogenic
<ul style="list-style-type: none"> <li>• Stabilise Lysosomes</li> <li>• Enhance Vasoconstriction</li> <li>• Inhibit Vasodilatation</li> <li>• Reduces Vascular permeability</li> <li>• Reduces Endothelial Adhesion, Chemotaxis and Migration of inflammatory cells.</li> <li>• Stabilise Mast cells / Inhibit their sensitisation</li> <li>• Inhibit Inflammatory products such as arachidonic acid metabolites (Prostaglandins Leukotrienes, HETE, Platelet activating factor)</li> <li>• Inhibits Monocytes / Macrophages: Reduced Phagocytosis, Bactericidal &amp; Fungicidal activity</li> <li>• Inhibits Lymphocytes</li> <li>• Inhibits Langerhans cells</li> <li>• Reduces production of Inflammatory Cytokines: Decreases IL-1, IL-2, INF-gamma, TNF etc.</li> </ul>	<ul style="list-style-type: none"> <li>• Reduces Keratinocyte turnover in epidermis → thinning of epidermal layers and cells</li> <li>• <i>(Basement membrane is unaffected!)</i></li> <li>• Reduces Dermal thickness</li> <li>• Early Dermal changes: due to water and glycosaminoglycan loss. <i>(no Collagen/Elastin changes early!)</i></li> <li>• Later dermal changes: due to Collagen, Elastin reduction and reduced fibroblast activity.</li> </ul>

3. Potency Chart

# CORTICOSTEROID POTENCY CHART

Topical corticosteroids available in Australia

BRAND NAME	GENERIC
<b>Mild (Class I)</b>	
Dermaid: C 30g	Hydrocortisone (alcohol) 0.5%
Cortic-DS: O 30g 50g, C 30g 50g Dermaid: C 30g SC: 30g, Sp 30mls, Sol 30mls Sigmacort: O 30g & 50g, C 30g & 50g	Hydrocortisone (alcohol or acetate) 1%
<b>Moderately Potent (Class II)</b>	
Desowen: AqL 60ml	Desonide 0.05%
Eumovate: C 30g Kloxema: C 30g	Clobetasone butyrate 0.05%
Aristocort: O C 100g 2tubes Tricortone O C 100g 2tubes	Triamcinolone acetonide 0.02%
Antroquoril: C100g 2tubes Betnovate 1/5: C 100g 2tubes Celestone-M: C 100g 2tubes Cortival 1/5: C 100g 2tubes	Betamethasone valerate 0.02%
Betonvate ½: C 15g Cortival ½: O C 15g	Betamethasone valerate 0.05%
<b>Potent (Class III)</b>	
Advantan FO 15g, O 15g, C 15g, AqL* 20g (not ml)	Methylprednisolone aceponate 0.1%
Betnovate O C 30g	Betamethasone valerate 0.1%
Elocon: O 15g, O 50g, L 30ml Elocon Alcohol Free Cream: C 15g, C 50g Novasone: O 15g, C 15g, C 45g, L 30ml Zatamil: HG 15g & 45 g, O 15g 45g, L 30ml	Mometasone furoate 0.1%
Diprosone: O 15g, O 50g, C 15g, O 50g, L 30ml Eleuphrat: O 15 g, C 15g	Betamethasone dipropionate 0.05%
<b>Very Potent (Class IV)</b>	
Diprosone OV: O 30g, C 30g	Betamethasone dipropionate 0.05% in optimized vehicle
Clobex Shampoo 125ml	Clobetasol propionate 0.05%

- O=Ointment
  - FO=Fatty Ointment
  - C=Cream
  - SC=Soft Cream
  - Sp=Spray
  - Sol=Solution
  - HG=Hydrogel
  - L=Lotion
  - AqL=Aqueous Lotion
  - Green= PBS/RPBS
  - \*=PBS for eczema only
  - Red=RPBS only
  - Black=Not on PBS
- OTC** Over the counter

4. How to identify topical steroids being used: ask about the size of the tube and whether it required a prescription. 0.5% & 1% hydrocortisone and Clobetasone butyrate do not need prescriptions! Everything else requires a prescription. In general 15 g tubes means a class III steroid such as Advantan, Elocon, Novasone, Diprosone et cetera. In general 100 g tube means a class II steroid such as Aristocort, Tricortone, Celestone-M, Betnovate 1/5. Most over-the-counter steroids (class I) come in 30 g or 50 g tubes and are low potency. They include 0.5% & 1% hydrocortisone and Clobetasone butyrate (Eumovate). Clobetasone butyrate and Clobetasol propionate can be confused because both of them are usually supplied in 30 g quantities and pharmacists are known to dispense Eumovate when Clobetasol propionate has been prescribed. Ask patient if the steroid came in the tube or in a jar. Tube = Clobetasone butyrate (over-the-counter, no prescription required), jar = Clobetasol propionate. A 30 g tube which requires a prescription is generally Diprosone OV.
5. Clinical use: topical and intralesional steroid use is considered here.
  - a. Factors to consider when choosing topical steroid
    - i. patient factors such as age and pregnancy
    - ii. site to be treated
    - iii. the skin condition being treated
    - iv. the formulation
6. Patient factors
  - a. Age:
    1. In neonates and infants start with low potency steroids whenever possible. Atopic eczema is the most common indication in this age group. By the time such patients have been seen by a dermatologist most of them have already been given 1% (or 0.5%) hydrocortisone cream or ointment which has proven ineffective. Those who have not previously received any topical steroids should first be trialed on 1% hydrocortisone on the face. If unsuccessful, on the face, Advantan cream for short term (regular use for one to 2 weeks followed by intermittent use) and intermittent use (maximum two or three applications a fortnight on a regular basis) is generally safe. If this needs to be exceeded to maintain control: consider topical Calcineurin inhibitors. Advantan fatty ointment is usually quite effective and safe on the trunk and limbs. Long-term usage should be restricted to one tube or less per month in infants and neonates. In difficult cases consider the use of Elocon or Diprosone ointment. In such cases monitor carefully for skin atrophy by reviewing every 2 to three months.
    2. In older children and adults, the same comments about Advantan cream usage for face are applicable. Use only short-term or intermittently, otherwise consider switching to Calcineurin inhibitors. The use of Advantan fatty ointment, Elocon ointment and Diprosone ointment on the trunk and limbs is generally safe provided a maximum quantity of two tubes per month is not exceeded in the long run. Prophylactic usage after the dermatosis has settled once or twice a week can sometimes be useful to prevent relapse. However atrophy can occur rarely.

3. In the elderly the face is *usually not* affected in steroid responsive dermatoses. Exception are photosensitive eruptions such as Chronic actinic dermatitis and drug eruptions. On the trunk and limbs, the use of Advantan fatty ointment, Elocon ointment and Diprosone ointment can be considered for increasing severities of eczematous processes. Long-term usage can cause severe atrophy and bruising. Monitor carefully.
- ii. The pregnancy categorisation of topical steroids is confusing and contradictory in MIMS. In pregnancy only hydrocortisone, betamethasone valerate (Antroquoril, Celestone-M) and betamethasone dipropionate (Diprosone and Diprosone OV) are considered to be Category A steroids. Avoid other topical steroids, especially in a nervous patient. The main risk in pregnancy is foetal growth retardation related to the strength of the topical steroids. Malformations, premature birth and foetal death have not been reported. General principle: use the weakest possible steroid. Although Betnovate is also betamethasone valerate, MIMS lists it as category B3! Methylprednisolone aceponate (Advantan) is listed as category C although methylprednisolone for intravenous use is listed as category A! MIMS says avoid Advantan in first trimester under precautions. This implies that Advantan can be used later in pregnancy. Similarly, Kenacort (triamcinolone acetonide) for intradermal/intralesional use is Category A, whereas triamcinolone acetonide in the form of Aristocort and Tricortone for topical use is listed as category B3. In lactation avoid steroids applied directly to the breast.
- b. Site related factors
1. palms and soles: use class IV steroids such as Diprosone OV, Clobetasol propionate. Generally ointments work better than creams.
  2. On the face: generally 1% hydrocortisone is ineffective for most dermatoses. Short-term and Intermittent use of Advantan cream may be permitted (see above). Desowen lotion is a bit more potent than 1% hydrocortisone and may be suitable in some cases even for long-term use. Otherwise consider using Calcineurin inhibitors such as Tacrolimus. *Pimecrolimus tends to be ineffective except for the mildest dermatoses.*
  3. On the trunk and limbs use class III steroids (Advantan, Elocon, Diprosone) whenever possible. Generally use ointments except for Grover's disease: because this is caused by occlusion of sweat ducts: use a cream. The use of ointments on the hair bearing areas of the trunk and limbs can sometimes lead to secondary folliculitis. Switch to a cream if this happens. Class II steroids such as Aristocort, Tricortone, Celestone-M are generally not effective. GPs tend to prescribe them because they come in large tubes.
  4. On mucous membranes such as in oral conditions: only use creams (generally class III steroids). Creams mix well with aqueous environments. Ointments do not stick to the aqueous environment inside the mouth. Dry the area with a tissue and immediately apply the cream. Ask the patient to keep the cream in the mouth for 2 to 3 minutes and then spit it out. Generally topical steroids are mixed with Daktarin oral gel (in a 50-50 mixture, just prior to application) to prevent secondary Candida. If the condition is not responsive to a 50-50 mixture of class III steroid and Daktarin oral gel, then apply the steroid undiluted

three times a day and use Nilstat oral drops or nystatin lozenges at other times. Alternatively try Diprosone OV cream.

5. In the scalp use lotions. Elocon lotion contains alcohol and can sting. Diprosone lotion is also alcohol-based but it is not PBS listed. Advantan lotion is aqueous and does not sting but is less potent.
6. In the flexures class II steroid creams such as Celestone-M cream should be used. Do not use ointments in flexures. In severe conditions Advantan cream can be used but monitor for atrophy.
7. When steroids are required underneath the nail for example in onycholysis, use an alcohol-based lotion such as Elocon lotion.

c. Factors related to the dermatosis

1. acute weeping dermatoses such as severe allergic contact dermatitis should be treated with a potent class III steroid **cream** such as Diprosone cream. Ointments are oily and hence generally do not stick to weeping dermatoses.
2. Subacute and chronic conditions are generally treated with class III steroid ointments.
3. Extremely lichenified chronic conditions (lichen simplex, hypertrophic lichen planus) should be treated with class IV steroid ointments or intralesional steroids. Use occlusion with cling wrap or wet dressings on limbs to enhance effectiveness of topical steroids.
4. Lichen sclerosis is also treated with class IV steroids in order to bring about a quick remission because there is potential for scarring, acquired phimosis and if untreated malignant transformation.
5. Consider the early use of intralesional steroids in scarring disorders such as discoid lupus of the skin: they work quickly and can prevent irreversible scarring/hair loss. Otherwise use class III or class IV topical steroids depending on the location.
6. Intralesional steroids are generally required for scalp conditions such as alopecia areata, discoid lupus and lichen planopilaris /frontal fibrosing alopecia. This is because the hair follicle is deep seated. If the patient is reluctant for intralesional steroids then class III or IV topical steroids may work in some cases.
7. Intralesional steroids may be necessary around the nail matrix for conditions such as nail psoriasis but are very painful and require a digital block prior to injection.
8. Intralesional steroids are generally required for dermal and deep seated conditions such as granuloma annulare, necrobiosis lipoidica and keloid scars. If the patient is reluctant for intralesional steroids then class IV topical steroids may work in some cases.
9. Most conditions requiring intralesional steroids require repeated injections every 6 to 8 weeks on two or more occasions.
10. There are two types of intralesional steroids for intradermal use: triamcinolone (Kenacort) and betamethasone acetate (Celestone chronodose). Kenacort comes as two strengths: 10 mg per mL (Kenacort A-10, PBS listed) and 40 mg per mL (Kenacort A-40, not PBS) Celestone chronodose is weaker than Kenacort A-10 and is seldom used in dermatology.
11. The strength of intralesional steroids to be used varies from 5 mg per ml (most dermal and hair disorders) to 10 to 40 mg per ml (for keloids). The maximum

dose per "injection session" is ~40-50mg (4-5 ampoules of 10 mg/ml or 1 ampoule of 40 mg/ml)

12. Intralesional steroids are either mixed with lignocaine prior to injection or injected into the lesion, after local anaesthesia has been administered under the lesion for example in a keloid. If a keloid is to be injected in this way, wait for about 10 minutes after injecting the local anaesthetic under the keloid prior to injecting the steroid.

d. Factors related to the formulation

- i. Creams can sting in some dermatoses. Ointments generally do not sting.
- ii. Alcohol-based (ethanol/isopropyl alcohol) lotions (Elocon, Novasone, Zatamil, Diprosone) usually sting due to both the alcohol and the propylene or hexylene glycol. Aqueous lotions such as Advantan lotion do not generally sting. Desowen lotion is water based with liquid paraffin but contains propylene glycol. In most cases it is well tolerated for mild facial eczema and does not sting. Zatamil Hydrogel is hypromellose and water based gel but contains hexylene glycol and stings less than alcohol /ethanol based lotions.
- iii. Advantan and Diprosone do not contain propylene (or hexylene) glycol and do not sting whereas Diprosone OV and Elocon /Novasone/Zatamil do contain propylene (or hexylene) glycol and can cause a mild burning sensation after application.
- iv. When a patient complains of stinging, use an ointment which does not contain propylene (or hexylene) glycol.
- v. Calcineurin inhibitors such as Tacrolimus and Pimecrolimus also cause a stinging sensation when applied in some patients.

7. Adverse effects of topical steroids

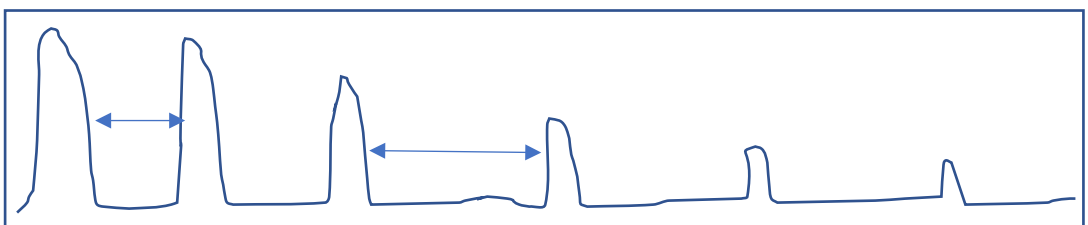
a. Systemic adverse effects

- i. Suppression of HPA axis: test early morning plasma cortisol level (7:30 AM or 8 AM or 9 AM). This seems to occur only if class III and class IV steroids are grossly misused: used in quantities of greater than 30 g per week for several weeks. Many patients in such reports have also used occlusion. Effects have included Cushing syndrome, growth suppression (premature closure of epiphyses), osteopenia and osteoporosis and laboratory abnormalities such as suppression of early morning cortisol level. Risk factors include young age, kidney and liver disease, greater than 30 g of potent and super potent steroid used, occlusion, long-term use without medical supervision. Treatment involves administration of oral corticosteroids whilst gradually withdrawing topical corticosteroids: co-managed with endocrine specialist.

b. Local adverse effects

- i. exacerbation of infections especially fungal and viral. Precipitation of Norwegian scabies. Reactivation of Kaposi sarcoma (HHV-8)
- ii. overgrowth of commensal skin organisms: Perioral dermatitis (Fusobacteria) Steroid induced rosacea (Demodex folliculorum), steroid induced acne (Pityrosporum ovale overgrowth).

- iii. epidermal & dermal atrophy: steroid blush/erythema and visible blood vessels, striate, stellate pseudoscars and purpura. Generally requires potent steroid used for weeks or months without supervision. Reversible: most changes (except for striate and pseudoscars) resolve in four weeks after the cessation. Advantan is the least atrophogenic among the class III steroids. Diprosone is the most atrophogenic in this class and Elocon is intermediate in its atrophogenic potential. If using Elocon on the face for vitiligo, consider using it week on and week off to minimize atrophy. (One week of use, then one week break, then repeat).
- iv. delayed wound healing
- v. ocular side effects include cataract (typically posterior sub-capsular cataract) and precipitation of glaucoma. Glaucoma usually occurs after several weeks of usage on eyelids and in the periocular area. About 1/3<sup>rd</sup> of patients are known as steroid responders and will develop glaucoma with medium to long term usage of topical steroids used around the eyes. The stronger the steroid the greater the risk. Steroid-induced glaucoma was first identified in 1950 and has since been well documented. Studies have demonstrated that about 30% of the population has a moderate response to topical steroid therapy, with IOP increases of 6 to 15 mm Hg or an IOP between 20 and 31 mm Hg. A smaller proportion of the population— approximately 4% to 6%—are high responders, with IOP increases of more than 15 mm Hg or an IOP greater than 31 mm Hg. The remaining two-thirds of the population are considered non-responders, with increases of less than 6 mm Hg and an IOP lower than 20 mm Hg.
- vi. infantile gluteal granuloma and genital ulceration
- vii. tachyphylaxis: consider regimen with two weeks usage and one week off (no usage) to minimise tachyphylaxis.
- viii. allergic contact dermatitis: rare, first rule out allergies to vehicles and preservatives. Creams contain preservatives ointments do not. Consider when there is an exacerbation of the dermatosis with usage of topical steroid. Needs specialised patch testing with delayed reading at day 6 or 7. Five groups of steroids which do not generally cross react with each other: group A: hydrocortisone group, group B triamcinolone group, group C betamethasone group, group D1 betamethasone dipropionate group: this is the biggest group and includes Clobetasol propionate, Clobetasone butyrate and Mometasone furoate. Group D2 methylprednisolone aceponate group.
- ix. steroid addiction: occurs when potent steroids have been used on the face, perianal and genital areas for a long period of time. Characterised by rebound redness when the steroid is stopped. The course of this condition generally involves several intermittent flareups which occur for 12 to 18 months after cessation of the steroid. As time progresses these exacerbations become less intense and more infrequent. Treatment is with a long slow wean off and oral tetracyclines whilst withdrawing the steroid. Sometimes oral cyclosporine can be used in place of tetracycline.





# Identification guide







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**PHARMACIST  
ONLY MEDICINE**  
KEEP OUT OF REACH OF CHILDREN

**sigmacort 1%**  
**cream**

**Hydrocortisone  
acetate cream**

**10 mg/g  
Hydrocortisone  
acetate**  
in a soothing cream  
base for temporary  
relief of redness,  
itching and  
inflammation of  
the skin.  
Hydroxybenzoates free.  
Preserved with  
Chlorocresol 1 mg/g.

**FOR EXTERNAL  
USE ONLY**

**NET 30 g**

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