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5.1 DRY SKIN

L85.3

DESCRIPTION

» The skin is dry and rough, together with varying degrees of scaling.
» Severe forms are mainly inherited, e.g. ichthyosis.
» Milder forms (xeroderma), seen as dryness with only slight scaling are common in the elderly and some chronic conditions, e.g. HIV disease, malignancies and atopic eczema.

GENERAL MEASURES

» Avoid the use of soap.

MEDICINE TREATMENT

- Soap substitutes, e.g.:
- Aqueous cream (UEA)
  - Rub on skin, before rinsing off completely.
  - Aqueous cream should not be used as an emollient.
- Emollient, e.g.:
- Emulsifying ointment (UE)

5.2 ITCHING (PRURITUS)

L29.0-3/L29.8-9

DESCRIPTION

Itching may be:

» localised or generalised
» accompanied by obvious skin lesions or skin conditions e.g. eczema, chicken pox.
» accompanied by many systemic diseases, e.g. hepatitis
» caused by scabies and insect bites

GENERAL MEASURES

» Diagnose and treat the underlying condition.
» Trim fingernails.
» Avoid scratching.

MEDICINE TREATMENT

- Calamine lotion, apply when needed.

For pruritus associated with dry skin:

- Emollient, e.g.:
- Emulsifying ointment (UE).

If pruritis is severe and requires short term control:

Children

- Chlorphenamine, oral, 0.1 mg/kg/dose 6–8 hourly. See chlorphenamine dosing table, chapter 23.

Adults *LoE:IVb*[1]

- Chlorphenamine, oral, 4 mg, 6–8 hourly.

Note: Chlorphenamine is sedating and may only be required in the evening for mild cases.

If pruritis is severe and requires long term control, e.g. for chronic pruritus:

Children: 2–6 years of age

- Cetirizine, oral, 5 mg once daily. See cetirizine dosing table, chapter 23.

Children > 6 years of age and adults

- Cetirizine, oral, 10 mg once daily.

REFERRAL

» No improvement after 2 weeks.
» Underlying malignancy or systemic disease suspected.

5.3 ACNE VULGARIS

L70.0-5/L70.8-9

DESCRIPTION

» Acne is an inflammatory condition of the hair follicle.
» It is caused by hormones and sebum gland keratinisation, leading to follicular plugging producing comedomes and proliferation of Propioni bacterium acnes.
» Distributed on face, chest and back.
» Occurs more commonly in adolescence, but may also occur in adulthood.
» May also occur as a result of the inappropriate use of topical steroids, or as a side effect of medicine e.g. Isoniazid.

Mild acne:
Predominantly consists of non-inflammatory comedones.

Moderate acne:
Consists of a mixture of non-inflammatory comedones and inflammatory papules and pustules.

Severe acne:
It is characterised by the presence of widespread nodules and cysts, as well as a preponderance of inflammatory papules and pustules.

GENERAL MEASURES

» Do not squeeze lesions.
» Avoid greasy or oily cosmetics and hair grooming products that block the hair follicle openings.
» Discourage excessive facial washing.

MEDICINE TREATMENT

Mild inflammatory acne:

- Benzoyl peroxide 5%, gel, apply in the morning to affected areas as tolerated.
  - Wash off in the evening.
  - If ineffective and tolerated, increase application to 12 hourly.
  - Avoid contact with eyes, mouth, angles of the nose and mucous membranes.

LoE:IVb[2]

Moderate inflammatory acne:

- Benzoyl peroxide 5%, gel, apply in the morning to affected areas as tolerated.
  - Wash off in the evening.
  - If ineffective and tolerated, increase application to 12 hourly.
  - Avoid contact with eyes, mouth, angles of the nose and mucous membranes.

LoE:IVb [3]

AND

- Doxycycline, oral, 100 mg daily for 3 months.
  - Review patient after 3 months of treatment.
  - It should be taken with meals.
  - Do not take it together with iron preparations and antacids.

LoE:IVb[4]

Note: Doxycyline should always be used with a topical agent and should not be used as monotherapy.

For non-inflammatory acne:

Topical retinoids

» Main therapeutic objective is to control comedone formation.
» Introduce topical retinoids gradually as a night-time application to limit skin irritant effects, as they are not photo-stable and degrade when exposed to sunlight (e.g. start twice a week and titrate up).

CAUTION

Do not use if pregnant or planning pregnancy.
Limit exposure to sunlight. If sunburn occurs, discontinue therapy until the skin has recovered.

LoE:IIIa[5]

- Tretinoin, topical, apply at night to affected areas for at least 6 weeks.
  - Review patient after 6 weeks' treatment.
  - Minimise exposure to sunlight. If sunburn occurs, discontinue therapy until the skin has recovered.
  - Acne may worsen during the first few weeks.
  - Apply about a pea-sized amount to entire face. Avoid contact with eyes and area around mouth and nose.

REFERRAL
» All severe cases.
» Poor response to treatment.

5.4 BACTERIAL INFECTIONS OF THE SKIN

5.4.1 BOIL, ABSCESS
L02.0-4/L02.8-9/H00.0/H60.0/N76.4/J34.0 + (B95.6)

DESCRIPTION
» Localised bacterial skin infection of hair follicles or dermis, usually with S. aureus.
» The surrounding skin becomes:
- swollen
- red
- hot
- tender to touch

Note:
» Check blood glucose level if diabetes is suspected or if the boils are recurrent. Boils in diabetic or immunocompromised patients require careful management.
» For axillary abscesses and pustules, see Section 5.17: Hidradenitis suppurativa.

GENERAL MEASURES
» Encourage general hygiene e.g.: frequent showering, keeping nails short.
» Drainage of abscess is the treatment of choice. Perform surgical incision only when the lesion is fluctuant.

MEDICINE TREATMENT

Systemic antibiotics are seldom necessary, unless the following features are present:
» swollen, tender lymph nodes in the area
» fever
» extensive surrounding cellulitis
» boils on the face

Antibiotics are also indicated in immunocompromised patients, diabetic patients, and neonates:

Children ≤ 7 years of age:
- Cefalexin, oral, 25 mg/kg/dose 12 hourly for 5 days See cefalexin dosing table, chapter 23.

OR
- Flucloxacillin, oral, 12–25 mg/kg/dose 6 hourly for 5 days. See flucloxacillin dosing table, chapter 23.

Children > 7 years of age and adults:
- Cefalexin, oral, 500 mg 6 hourly for 5 days.

OR
- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

For severe penicillin allergy:
Z88.0

Children
- Macrolide, e.g.:
- Azithromycin, oral, 10 mg /kg/dose daily for 3 days. See azithromycin dosing table, chapter 23.

Adults
- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days.

REFERRAL
» Poor response to treatment.
» Abscesses of the palm of the hand and pulp space abscess of the fingers.
» Features of severe sepsis requiring intravenous antibiotics.
» Deep abscess e.g. ischiorectal and breast abscess.

5.4.2 IMPETIGO
L01.0-1

DESCRIPTION
» A common contagious skin infection caused by streptococci or staphylococci.
» Predominantly occurs in children.
» Often secondary to scabies, insect bite, eczema or tinea capitis.
» Clinical features:
- pus containing blisters
- commonly starts on the face or buttocks
- erosion of blisters with honey-coloured crusts
- spreads to neck, hands, arms and legs

» Post-streptococcal glomerulonephritis is a potential complication.

GENERAL MEASURES
» Counsel on good personal and household hygiene to avoid spread of the infection and to reduce carriage of organisms.
» Trim finger nails.
» Wash and soak sores in soapy water to soften and remove crusts.
» Continue with general measures until the sores are completely healed.
» Check urine for blood if the sores have been present for more than a week.

MEDICINE TREATMENT
- Povidone iodine 5%, cream or 10% ointment, apply 8 hourly.

If extensive or systemic signs of infection (fever, unwell, fatigued), ADD:

Children ≤ 7 years of age:
- Cefalexin, oral, 25 mg/kg/dose 12 hourly for 5 days. See cefalexin dosing table, chapter 23.

OR

- Flucloxacillin, oral, 12–25 mg/kg/dose 6 hourly for 5 days. See flucloxacillin dosing table, chapter 23.

Children > 7 years of age and adults:

- Cefalexin, oral, 500 mg 6 hourly for 5 days.

OR

- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

LoE:IVb[6]

For severe penicillin allergy:
Z88.0

Children

- Macrolide, e.g.:
- Azithromycin, oral, 10 mg/kg/dose daily for 3 days. See azithromycin dosing table, chapter 23.

Adults

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days.

Note: If impetigo has improved, but has not completely cured, give a 2nd 5-day course of antibiotics.

REFERRAL

» No improvement after second course of antibiotics.
» Presence of blood on urine test strip for longer than 5-7 days.
» Clinical features of glomerulonephritis. See Section 8.3.1: Nephritic syndrome.

5.4.3 CELLULITIS

L03.0-3/L03.8-9

DESCRIPTION

» A diffuse, spreading, acute infection within skin and soft tissues, commonly caused by streptococci.
» Characterised by:
- Oedema
- redness
- increased local temperature
- no suppuration

» Frequently associated with lymphangitis and regional lymph node involvement.
» Commonly occurs on the lower legs, but may occur elsewhere.
» May follow minor trauma.
» May present as an acute fulminant or chronic condition.
» May occur with systemic manifestations of infection:
- fever
- tachycardia
- chills
- delirium/altered mental state
- hypotension

GENERAL MEASURES

» Elevate the affected limb to reduce swelling and discomfort.

MEDICINE TREATMENT

Children ≤ 7 years of age

- Cefalexin, oral, 25 mg/kg/dose 12 hourly for 5 days. See cefalexin fosing table, chapter 23.

OR

- Flucloxacillin, oral, 12–25 mg/kg/dose 6 hourly for 5 days. See flucloxacillin dosing table, chapter 23.

Children > 7 years of age and adults

- Cefalexin, oral, 500 mg 6 hourly for 5 days.

OR

- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

LoE:IVb[7]

For severe penicillin allergy:
Z88.0

Children:

- Macrolide, e.g.:
- Azithromycin, oral, 10 mg/kg/dose daily for 3 days. See azithromycin dosing table, chapter 23.

Adults:

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days.

Severe cellulitis:
Refer for parenteral antibiotics.

REFERRAL

Urgent

» Children who have significant pain, swelling or loss of function (to exclude osteomyelitis).
» Haemorrhagic bullae, gas in the tissues or gangrene.
» Extensive cellulitis.
» Recurrent cellulitis associated with underlying conditions, e.g. lymphoedema.
» Cellulitis with systemic manifestations, e.g. confusion, hypotension.
» Poorly controlled diabetic patients.
» Involvement of the hand, face and scalp.

Non-urgent

» Inadequate response to initial antibiotic treatment.

5.4.4 CHRONIC LOWER LEG ULCERS

L97

DESCRIPTION

» A chronic relapsing disorder of the lower limbs.
» Associated with vascular insufficiency (predominantly venous insufficiency) and patient immobility.
» Commonly associated with neuropathy, infections, neoplasia, trauma or other rare conditions.

GENERAL MEASURES

» If the ulcer is oedema- or stasis-related, rest the leg in an elevated position.
» In venous insufficiency, compression (bandages or stockings) are essential to achieve and maintain healing, provided the arterial supply is normal.
» In patients with arterial insufficiency, avoid pressure on bony prominences and toes.
» In patients with neuropathy, relieve pressure from the area.
» Exclude diabetes with finger prick blood glucose test.
» Avoid topical application of home remedies.
» Stress meticulous foot care and avoidance of minor trauma. Encourage patients with neuropathy not to walk barefoot, check their shoes for foreign objects, examine their feet daily for trauma and to test bath water before bathing to prevent getting burnt.
» Avoid excessive local heat.
» Walking and exercises are recommended.

MEDICINE TREATMENT

Refer for assessment and initiation of treatment.

Local wound care:

Topical cleansing:
Use bland, non-toxic products to clean the ulcer and surrounding skin.

For clean uninfected wounds:

- Sodium chloride, 0.9% or sterile water.

Dress frequently with:

- Moistened dressing e.g. gauze with sodium chloride, 0.9%. *LoE: IIIb*[8]

For exudative, infected wounds:

- Povidone-iodine 5% cream, topical apply daily *LoE: IVb*[9]

For venous ulcers:

- Paraffin gauze dressing.

REFERRAL

» No improvement after 1 month.
» All foot ulcers.
» Ulcers with atypical appearance.
» Venous ulcers that are persistently infected, or have offensive odour.

5.5 FUNGAL INFECTIONS OF THE SKIN

5.5.1 CANDIDIASIS, SKIN

B37.2

Vaginal candidiasis: See Section 12.1: Vaginal discharge syndrome (VDS).

DESCRIPTION

A skin infection caused by *C. albicans*.

Most common sites for infection are skin folds such as:

» under the breasts
» axillae
» nail folds
» natal cleft
» groins
» neck folds, peri-anal, perineum and groins in infants

The skin lesions or sores:

» are red raw-looking patches
» appear moist (weeping)
» have peripheral outlying white pustules, red scaly lesions which become confluent

GENERAL MEASURES

» Exclude diabetes.

MEDICINE TREATMENT

- Imidazole, e.g.:
- Clotrimazole 1%, topical, apply 3 times daily for 14 days.

5.5.2 RINGWORM AND OTHER TINEAS

Fungal infections affecting the body (tinea corporis; tinea versicolor), feet (tinea pedis), scalp (tinea capitis) and nails (tinea unguium). These infections may be contagious.

5.5.2.1 RINGWORM – TINEA CORPORIS

B35.4

DESCRIPTION

» Clinical features include:
- itchy ring-like patches
- patches slowly grow bigger
- raised borders

» As the patch extends a clear area develops in the center which may become hyper-pigmented in dark skin.
» Extensive disease is common in HIV, often with no evidence of the patches developing clear centres.

GENERAL MEASURES

» Prevent spreading the infection to others.

- Do not share clothes, towels, or toiletries (especially combs and hair brushes).

» Wash skin well and dry before applying medicine treatment.

MEDICINE TREATMENT

- Imidazole, e.g.:
- Clotrimazole 1%, topical, apply 3 times daily.
  - Continue using cream for at least 2 weeks after lesions have cleared.

Note: Treat any secondary skin infection with antibiotics. See Section 5.4.2: Impetigo.

REFERRAL

» Extensive disease.

5.5.2.2 ATHLETE'S FOOT – TINEA PEDIS

B35.3

DESCRIPTION

» A common contagious fungal infection of the foot, characterised by itching, burning and stinging between the toes or on the sole.
» The skin between the toes is moist and white (maceration) and may become fissured. There is also associated erythema, scaling and peeling.
» Secondary eczema of the hands may be an associated condition. See Section 5.8.1: Eczema, atopic.
» Vesicles may occur in inflammatory cases.
» Pain and tenderness in the web spaces may indicate secondary bacterial infection.
» Re-infection is common.

GENERAL MEASURES

» Discourage the use of shared bathing or swimming areas, whilst infected.
» Keep feet dry:
  - wear open sandals
  - do not wear socks of synthetic material
  - dry between toes after washing the feet or walking in water
» Wash and dry feet twice daily before applying medicine treatment.

MEDICINE TREATMENT

- Imidazole, e.g.:
- Clotrimazole 1%, topical, apply twice daily for 4 weeks.

Note: For nail infection, See Section 5.6.3: Nail infections – *tinea unguium*.

REFERRAL

» No improvement after 4 weeks.

5.5.2.3 SCALP INFECTIONS – TINEA CAPITIS

B35.0

DESCRIPTION

» Round or patchy bald areas with scales and stumps of broken off hair.

GENERAL MEASURES

» Avoid shaving head in children.
» Do not share toiletries such as combs and hair brushes.

MEDICINE TREATMENT

Children:

- Fluconazole, oral, 6 mg/kg once daily, for 28 days. See fluconazole dosing table, chapter 23. *LoE: IIb*[10]

Adults:

- Fluconazole, oral, 200 mg weekly, for 6 weeks. *LoE:IIIb*[11]

Note: Do not give to women of child-bearing age unless they are on effective contraceptive.

5.5.2.4 PITYRIASIS VERSICOLOR – TINEA VERSICOLOR

B36.0

DESCRIPTION

» Round macules which are often lighter than normal skin (but may be darker).
» Mostly found on the upper chest and back, less common on the neck, face, abdomen and upper limbs.
» Macules on the chest and back often coalesce, and the condition spreads with the formation of new macules on the periphery.
» Pigmentation may take months to return to normal after treatment.
» Recurrences are common, especially in hot weather.

GENERAL MEASURES

» Avoid wearing clothing that impairs ventilation in hot weather to reduce perspiration.

MEDICINE TREATMENT

» Oral antifungal therapy is not indicated.

- Selenium sulfide, 2.5% suspension, apply once weekly for three weeks.
  - Lather shampoo on affected parts.
  - Leave on overnight, then wash off the following day.

LoE:IVb[12]

5.5.2.5 NAIL INFECTIONS – TINEA UNGUIUM

See Section 5.6.3: Nail infections – *tinea unguium*.

5.6 NAILFOLD AND NAIL INFECTIONS

5.6.1 PARONYCHIA, ACUTE

L03.0

DESCRIPTION

» Small subcutaneous collection of pus under the nailfold.
» Often associated with cutting nails too short, or nail biting.

GENERAL MEASURES

» Avoid cutting finger nails too short.
» Avoid nail biting.

MEDICINE TREATMENT

» Drain abscess by puncture or incision.

Adults:

- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

5.6.2 PARONYCHIA, CHRONIC

L03.0

DESCRIPTION

» Chronic, red, swollen nailfold, lifted off the nail plate with whitish pus.
» Commonly caused by working in water and contact with household detergents.

GENERAL MEASURES

» Avoid hand contact with household detergents, washing powders and fabric softeners.
» Wear rubber gloves when washing clothes, linen and kitchen utensils to keep hands clean and dry as far as possible.

MEDICINE TREATMENT

- Corticosteroid, potent, topical, e.g.: (Doctor prescribed)
- Betamethasone 0.1%, topical, apply at night until lesions have cleared.
  - Wash hands, then massage cream into the nailfold.

If secondary infection is present, indicated by pain and tenderness in the nail fold, treat with antibiotics (See Section 5.4.2: Impetigo).

LoE: IIIb[13]

REFERRAL

» No response to treatment.

5.6.3 NAIL INFECTIONS – TINEA UNGUIUM

B35.1

DESCRIPTION

» Nails are lifted, distorted, crumbling and discoloured.

» One or more nails may be affected.

GENERAL MEASURES
» Topical treatment is generally ineffective for fungal nail infections.
» Systemic treatment is often unsuccessful and recurrent infections are common if repeat exposure is not prevented.

REFERRAL
» Patients that are distressed by cosmetic appearance.

5.7 PARASITIC INFESTATIONS OF THE SKIN

5.7.1 LICE (PEDICULOSIS)

DESCRIPTION
An infestation of the body with parasitic lice.
Clinical features include:
» itching
» bite marks
» presence of secondary eczema, or secondary infection

CAUTION
Do not use commercial insect sprays as they are toxic.
Lotions used for the treatment of lice are toxic when swallowed.

Note: Treat secondary infection with antibiotics. See Section 5.4.2: Impetigo.

5.7.1.1 HEAD LICE
B85.0

DESCRIPTION
Head lice are common in children. The eggs (nits) appear as fixed white specks on the hair.

GENERAL MEASURES
» Use a fine tooth comb to comb out the nits after washing hair.
» Shaving of the head may expedite treatment, where socially acceptable.
» Prevent spread by treating other contacts.
» Remove nits from eyelashes by application of white soft paraffin.

MEDICINE TREATMENT
- Permethrin 5%, topical
  - Apply permethrin 5% lotion to towel-dried or dry hair. Comb into hair repeatedly with a normal comb until scalp is covered completely.
  - Remove lice and nymphs with fine lice comb by dividing scalp into sections and combing away from scalp.

- Rinse lice comb in a white bowl filled with hot water between hair strokes to identify removed lice, or detach on white tissue paper. Paralysed and dead lice will present as dark spots (like ground pepper).
- Take note of the physical size of removed lice and nymphs, as the size should get smaller with consecutive treatments.
- Keep on combing with fine lice comb, rinsing or wiping comb frequently.
- Permethrin 5% lotion is safe and can be left in the hair for up to one hour.
- After combing, rinse hair with lukewarm water and wash permethrin 5% lotion out with normal shampoo (more than one foaming might be needed).
- Repeat this procedure every 5 days for 3 weeks.
- Thereafter, carry out frequent inspections to detect new infestations early.
- **Do not** apply to broken skin or sores.
- **Avoid** contact with eyes.

LoE: IIIb[14]

5.7.1.2 BODY LICE

B85.1/B85.4

DESCRIPTION

» Body lice live in the seams of clothing and only come to the skin to feed.
» **Note:** Body lice may carry typhus fever.

GENERAL MEASURES

» Regularly wash bed linen and underclothes in hot water and expose to sunlight.

MEDICINE TREATMENT

Adolescents and adults:

- Benzoyl benzoate 25% lotion, undiluted, once weekly for 3 weeks.
  - Apply over the whole body, excluding the neck and face.
  - Leave on overnight and wash off the next day.
  - **Note:**
  - Avoid contact with eyes and broken skin or sores.
  - The lotion is toxic if swallowed.
  - Do not continue if a rash or swelling develops.
  - Itching may continue for 2–3 weeks after treatment.

LoE:IIIb[15]

5.7.1.3 PUBIC LICE

B85.3/B85.4

DESCRIPTION

» Pubic lice are acquired as STIs and nits are found on pubic hair and eyelashes.

GENERAL MEASURES

» Prevent spread by treating other contacts.

MEDICINE TREATMENT

- Benzoyl benzoate 25% lotion, apply once weekly for two weeks

- Apply to affected area.
- Leave on for 24 hours, then wash thoroughly.
- Repeat in 7 days.

For pediculosis of the eyelashes or eyebrows:

- Yellow petroleum jelly (Note: Do not use white petroleum jelly near the eyes).
  - Apply to the eyelid margins (cover the eyelashes) daily for 10 days to smother lice and nits.
  - Do not apply to eyes. *LoE: IVb*

REFERRAL

» Lice infestation of eyelashes in children to exclude suspected sexual abuse.

5.7.2 SCABIES

B86

DESCRIPTION

» An infestation with the parasite Sarcoptes scabei.
» Commonly occurs in the skin folds. The infestation spreads easily, usually affecting more than one person in the household.
» Clinical features include:
  - intense itching, which is more severe at night
  - small burrows between fingers, toes, elbow areas and buttocks where the parasite has burrowed under the skin
  - secondary infection which may occur due to scratching with dirty nails
  - vesicles and pustules on the palms, soles, and sometimes scalp, in small babies

GENERAL MEASURES

» Treat all close contacts simultaneously even if they are not itchy.
» Cut finger nails and keep them clean.
» Wash all linen and underclothes in hot water.
» Expose all bedding to direct sunlight.
» Put on clean, washed clothes after medicine treatment.

MEDICINE TREATMENT

<u>Children < 6 years of age:</u>

- Permethrin 5%, topical, apply lotion undiluted to the whole body from neck to feet
  - Leave on overnight (8–12 hours) and wash off the following morning. *LoE: IVb*[16]

If permethrin is unavailable for children < 6 years of age:

- Benzoyl benzoate 25% lotion:
  - Children 0 months to 1 year of age:
    - Dilute 1 part of benzoyl benzoate to 3 parts of water to form an emulsion of 6%.

- Apply diluted emulsion to the whole body from neck to feet as described above.

– Children 1 to 6 years of age:
  - Dilute 1 part of benzoyl benzoate with an equal amount of water to form an emulsion of 12.5%.
  - Apply diluted emulsion to the whole body from neck to feet as described above. *LoE:IVb*[17]

Children ≥ 6 years of age and adults:

- Benzoyl benzoate 25% lotion, applied undiluted to the whole body from neck to feet.
  – Allow the lotion to remain on the body for 24 hours, then wash off using soap and water.
  – Treatment may be repeated after 24 hours **once** within 5 days for severe infestations.
  – All infested persons living in the household, or likely to contract the infestation, should be treated at the same time.

If benzoyl benzoate is unsuccessful:

- Permethrin 5%, topical, apply lotion undiluted to the whole body from neck to feet.
  – Leave on overnight (8–12 hours) and wash off the following morning. *LoE: IIIb*[18]

  Note:
  – Benzoyl benzoate and permethrin are toxic if swallowed.
  – Avoid contact with eyes and broken skin or sores.
  – Do not continue if rash or swelling develops.
  – Itching may continue for 2–3 weeks after treatment.
  – Treatment may need to be repeated againafter one week.
  – Treat secondary infection with antibiotics. See Section 5.4.2: Impetigo.

5.7.3 SANDWORM

B76.0

DESCRIPTION

» Creeping eruption (cutaneous larva migrans) caused by Ancylostoma braziliense, a hookworm of dog or cat.
» Larvae of ova in soil penetrate skin commonly through the feet, legs, buttocks or back and cause a winding thread-like trail of inflammation with itching, scratching dermatitis and bacterial infection.

MEDICINE TREATMENT

- Albendazole, oral:
  – Children < 2 years of age: 200 mg daily for 3 days
  – Children ≥ 2 years of age and adults: 400 mg daily for 3 days

AND

Children

- Chlorphenamine, oral, 0.1 mg/kg/dose 6–8 hourly. See chlorphenamine dosing table, chapter 23.

Adults *LoE:IVb*[19]

- Chlorphenamine, oral, 4 mg, 6–8 hourly.

Note: Chlorphenamine is sedating and may only be required in the evening for mild cases.

5.8 ECZEMA AND DERMATITIS

5.8.1 ECZEMA, ATOPIC

L20.0/L20.8-9

DESCRIPTION

» An inflammatory disorder with an itchy red rash or dry rough skin.
» In babies it appears at approximately 3 months.
» Family history of asthma, hay fever or atopic dermatitis is common.
» Clinical features:
  - occurs on the inner (flexural) surfaces of elbows and knees, the face and neck
  - can become chronic with thickened scaly skin (lichenification)
  - secondary bacterial infection may occur with impetigo or pustules
  - can be extensive in infants
  - very itchy at night
» Eczema is usually a chronic condition and requires long-term care.
» Sufferers of atopic eczema are particularly susceptible to herpes simplex and may present with large areas of involvement with numerous vesicles and crusting surrounded by erythema (eczema herpeticum). See Section 5.13: Herpes simplex.

GENERAL MEASURES

» Avoid direct skin contact with woollen or rough clothes.
» Avoid overheating by blankets at night.
» Trim fingernails to prevent scratching.
» Counsel on good personal hygiene with regular washing to remove crusts and accretions, and to avoid secondary infection.
» Diet modification has no role in atopic eczema treatment.
» Avoid soap on affected areas.

MEDICINE TREATMENT

(For management of severe eczema, start at step 3).

STEP 1

- Avoid soap, use soap substitutes such as aqueous cream (UEA).
  – Rub on skin, then rinse off completely.
  – Do not use aqueous cream as an emollient.

- Emollient, e.g.:
- Emulsifying ointment (UE).

If no response within seven days/worsening symptoms:

STEP 2

- Hydrocortisone 1% topical, applied twice daily for 7 days.
  - Apply sparingly to the face.
  - Do not apply around the eyes.

If there is a response:
Reduce the use of the hydrocortisone cream to once daily for a further few days, then stop and maintain treatment with:

- Aqueous cream (UEA) as a wash-off soap.

AND

- Emollient, e.g.:
- Emulsifying ointment (UE).

If no response within seven days or severe eczema:

STEP 3

- Corticosteroid, potent, topical, e.g.: (Doctor prescribed)
- Betamethasone 0.1%, topical, apply ointment once daily for 7 days
  - **Do not** apply to face, neck and flexures. *LoE: IIb*[20]

If there is a response:
Reduce use of corticosteroid ointment for a further few days, then stop and maintain treatment with:

- Aqueous cream (UEA) as a soap.

AND

- Emollient, e.g.:
- Emulsifying ointment (UE).

If the patient is itching:

Children:

- Chlorphenamine, oral, 0.1 mg/kg/dose at night for a maximum of 2 weeks. See chlorphenamine dosing table, chapter 23.

LoE:IVb[21]

Adults:

- Chlorphenamine, oral, 4 mg, at night for a maximum of 2 weeks.
  - **Note:** Chlorphenamine is sedating.

If itch is not controlled or is more severe during the day, switch to:

Children: 2–6 years of age:

- Cetirizine, oral, 5 mg once daily. See cetirizine dosing table, chapter 23.

Children > 6 years of age and adults:

- Cetirizine, oral, 10 mg once daily. *LoE:IVb*

REFERRAL

» No improvement in 2 weeks.
» Infants and children requiring more than 1% hydrocortisone cream.
» Extensive involvement.
» Eczema herpeticum.

5.8.2 ECZEMA, ACUTE, MOIST OR WEEPING

L20.0/L20.8-9

DESCRIPTION

» A form of eczema with small or large vesicles, associated with oozing and eventual crusting and scaling.
» Yellow pustules with crust indicate secondary sepsis.

GENERAL MEASURES

» Sodium chloride, 0.9% dressings, applied daily or twice daily.
Avoid use of soap on affected areas.

MEDICINE TREATMENT

- Topical steroids, e.g.:
- Hydrocortisone 1% topical, applied 12 hourly, until improved.
  - Topical steroids should be applied to both moist and dry inflamed areas.

Antibiotic treatment if secondary infection is present:

Children ≤ 7 years of age:

- Cefalexin, oral, 25 mg/kg/dose 12 hourly for 5 days. See cefalexin dosing table, chapter 23.

OR

- Flucloxacillin, oral, 12–25 mg/kg/dose 6 hourly for 5 days. See flucloxacillin dosing table, chapter 23.

Children > 7 years of age and adults:

- Cefalexin, oral, 500 mg 6 hourly for 5 days.

OR

- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

Severe penicillin allergy:
Z88.0

Children:

- Macrolide, e.g.:

- Azithromycin, oral, 10 mg /kg/dose daily for 3 days. See azithromycin dosing table, chapter 23.

Adults:
- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days.

If the patient is itching:

Children
- Chlorphenamine, oral, 0.1 mg/kg/dose at night. See chlorphenamine dosing table, chapter 23.

Adults
- Chlorphenamine, oral, 4 mg, at night. *LoE: IVb*[22]

Note: Chlorphenamine is sedating.

If itch is not controlled or is more severe during the day, switch to:

Children: 2–6 years of age
- Cetirizine, oral, 5 mg once daily. See cetirizine dosing table, chapter 23.

Children > 6 years of age and adults
- Cetirizine, oral, 10 mg once daily. *LoE: IVb*

For itching in children < 2 years of age:
- Calamine lotion, applied on the skin.

REFERRAL
» No improvement after a week.
» Severe acute moist or weeping eczema.

5.8.3 DERMATITIS, SEBORRHOEIC
L21.0-1/L21.8-9

DESCRIPTION
» Dandruff is an uninflamed form of seborrhoeic dermatitis.
» Pruritus may or may not be present in seborrhoeic dermatitis.
» The scalp, face, ears and skin folds e.g. axillae, groins, under the breasts are commonly affected.
» May become very extensive, particularly in infants and HIV infected patients.

GENERAL MEASURES
» Trim nails.
» Avoid scratching affected areas.
» Avoid perfumed soap.

MEDICINE TREATMENT

- Hydrocortisone 1% topical, apply twice daily until improved.
  - Then apply once or twice weekly for maintenance as needed.

For severe dermatitis:

- Corticosteroid, potent, topical, e.g.: (Doctor prescribed)
- Betamethasone 0.1%, topical, apply ointment once daily for 5–7 days.
  - Do not apply to face neck and flexures.

LoE: IIb[23]

For itching scalp, scaling and dandruff:

- Selenium sulphide, 2.5% suspension, apply weekly.
  - Lather on the scalp.
  - Rinse off after 10 minutes.
  - Apply weekly, until improved, then every second week to maintain control.

5.9 NAPPY RASH

L22

DESCRIPTION

» A diffuse reddish eruption in the nappy area, usually caused by irritation from:
  - persistent moisture and irregular cleaning and drying of the nappy area,
  - diarrhoeal stools,
  - underlying skin conditions in some cases, or
  - improper rinsing of nappies to remove urine and stool breakdown products.

» Rash is predominantly on areas in contact with the nappy, and spares the flexures.

GENERAL MEASURES

» Prompt changing of soiled nappies.
» Avoid waterproof pants.
» Expose nappy area to air if possible especially with severe nappy dermatitis.
» Educate caregiver on washing, rinsing and drying of the nappy when soiled.

MEDICINE TREATMENT

- Zinc emollient, e.g.:
- Zinc and castor oil, topical, apply ointment after each nappy change.

<u>If rash involves the flexures, suspect candida:</u>

- Imidazole, e.g.:
- Clotrimazole 1%, topical, apply cream beneath zinc and castor oil ointment after each nappy change until symptoms are resolved.

REFERRAL

» No improvement after 3 days of treatment.

5.10 ALLERGIES

5.10.1 URTICARIA

L50.0-6/L50.8-9

DESCRIPTION

» Urticaria is a skin disorder characterised by itchy wheals (hives).
» There are many causes, including allergic, toxic or physical:
  - Allergic urticaria may be caused by drugs, plant pollen, insect bites or foodstuffs, e.g. fish, eggs, fruit, milk and meat.
  - Commonly caused by medicines e.g. aspirin, NSAIDs, or codeine.

GENERAL MEASURES

» Take detailed history to determine trigger factors.
» Lifestyle adjustment.

MEDICINE TREATMENT

Note: Avoid the use of oral corticosteroids. *LoE: IVb*

Children

- Chlorphenamine, oral, 0.1 mg/kg/dose at night See chlorphenamine dosing table, chapter 23. *LoE:IVb*[24]

Adults

- Chlorphenamine, oral, 4 mg, 6–8 hourly.

For long term use in adults and school going children:

Children: 2–6 years of age

- Cetirizine, oral, 5 mg once daily. See cetirizine dosing table, chapter 23.

Children > 6 years of age and adults

- Cetirizine, oral, 10 mg once daily.

- Calamine lotion, applied on the skin.

REFERRAL

» No improvement or response after 24 hours.

5.10.2 ANGIOEDEMA

T78.3 + (Y14.99/Y34/Y57.9)

DESCRIPTION

» Localised oedema of the subcutaneous tissue affecting particular parts of the face i.e. lips, eyes and tongue. May also affect the larynx, causing life threatening airway obstruction and anaphylaxis.
» ACE-inhibitors are the most common cause in adults. Other causes include other medicines and allergies.

GENERAL MEASURES

» Stop all suspected agents e.g. ACE-inhibitor.
» In the case of airway obstruction, a definitive airway must be established if oedema is extensive or progressing.

MEDICINE TREATMENT

If urticaria and/or itch present (no imminent airway compromise):

- Cetirizine, oral, 10 mg as a single dose. *LoE:IVb*

OR

- Promethazine, IM, 25–50 mg immediately.

In severe cases where airway obstruction is present:

Adults

- Adrenaline (epinephrine), 1:1000 solution, 0.5 mL into the lateral thigh, administered immediately and repeated every 5 to 15 minutes as needed.

Children

- Adrenaline (epinephrine), IM, 0.01 mL/kg of 1:1000 solution, administered immediately.
  - Maximum dose of 0.3 mL

AND

- Hydrocortisone, IV, 100 mg as a single dose.

Note: Observe all cases until resolution.

REFERRAL

» Failure to respond.
» No obvious cause found.
» Severe ACE-inhibitor induced angioedema.

5.10.3 FIXED DRUG ERUPTIONS

L27.0-1

DESCRIPTION

» Dark coloured round macules that can occur anywhere on the body following the ingestion of a medicine to which the patient has become allergic.
» They recur on the same spot and increase in number with each successive attack.
» In the acute stage they are itchy, red around the edge or even bullous.

GENERAL MEASURES

» Stop the suspected offending medicine(s).

MEDICINE TREATMENT

Acute/active stage

- Hydrocortisone 1%, topical, apply daily for 5 days. *LoE: IVb*

REFERRAL

» Widespread eruptions.

5.10.4 PAPULAR URTICARIA

L50.8

DESCRIPTION

» Hypersensitivity response to insect bites.
» Initial lesion is a red papule, which may blister, become excoriated, and then heal with hyperpigmentation. Usually occur in crops over several months.
» Common and often severe in HIV infections (See Section 11.3.12: Papular pruritic eruption).

GENERAL MEASURES

» Reduce exposure to insects by treating pets, using mosquito nets and fumigating houses regularly. Use of insect repellents may be helpful.

MEDICINE TREATMENT

New, inflamed lesions:

- Hydrocortisone 1%, topical, apply daily for 5 days.

For relief of itch:

Children

- Chlorphenamine, oral, 0.1 mg/kg/dose 6–8 hourly. See chlorphenamine dosing table, chapter 23. *LoE:IVb*[25]

Adults

- Chlorphenamine, oral, 4 mg, 6–8 hourly.

Note: Chlorphenamine is sedating and may only be required in the evening for mild cases.

For long term use in adults and school going children:

Children 2–6 years of age:

- Cetirizine, oral, 5 mg once daily. See cetirizine dosing table, chapter 23..

Children > 6 years of age and adults:

- Cetirizine, oral, 10 mg once daily.

REFERRAL

» Non-responsive and chronic cases.

5.10.5 ERYTHEMA MULTIFORME

L51.0/L51.8-9

DESCRIPTION

» A self-limiting and commonly recurrent inflammatory eruption of the skin.
» May involve mucous membrane (but not more than one surface), and usually without systemic symptoms.
» Usually lasts for 10–14 days before complete recovery occurs.
» Symmetrically distributed crops of target lesions (dark centre, an inner, pale ring surrounded by an outer red ring) occur on the extremities, and in particular, on the backs of the hands and forearms, palms and soles.
» This condition is usually due to an infection, commonly herpes simplex or mycoplasma.

REFERRAL

» All patients with systemic symptoms or mucosal involvement.
» Unsure of the diagnosis.

5.10.6 SEVERE CUTANEOUS ADVERSE DRUG REACTIONS

5.10.6.1 STEVENS-JOHNSON SYNDROME (SJS)/TOXIC EPIDERMAL NECROLYSIS (TEN)

L51.1/ L51.2

DESCRIPTION

» An acute, systemic condition with vesico-bullous lesions involving the skin and mucous membranes (≥ 2 mucosal surfaces), but occasionally only the mucous membranes.
» The eruption may start as widespread red irregular macules and patches. There may be a vesicle or bulla in the central area of the lesion. The blisters rupture leaving denuded areas of skin. Mucous membrane erosions often with slough covering the surface are frequently seen.
» Toxic epidermal necrolysis (TEN) is a more severe form of the condition and is suggested if the skin lesions cover > 30% of the body surface area. The mucous membranes such as the mouth, eyes and vagina are also more severely affected.
» The condition is usually caused by medicines e.g. sulphonamides, anti-retrovirals (nevirapine), anti-epileptics (phenytoin, phenobarbitone, carbamazepine, lamotrigine).
» Systemic involvement with multi-organ dysfunction is common.

GENERAL MEASURES

» Immediate withdrawal of offending medicine.
» Patients usually require care in a high or intensive care unit with dedicated nursing.

REFERRAL
» All patients.

5.10.6.2 DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS)
L27.0 + (D72.1)

DESCRIPTION
» Severe hypersensitivity reaction to a medicine.
» Typically occurs within 3 months of starting the offending medicine.
» Clinical symptoms include:
  - maculopapular rash
  - lymphadenopathy
  - eosinophilia and/or other blood count abnormalities
  - fever > 38°C
  - hepatitis or other organ involvement
» Medicines that commonly induce the DRESS syndrome include phenobarbital, carbamazepine, phenytoin, lamotrigine, allopurinol, sulphonamides, abacavir, nevirapine.

REFERRAL
» All patients.

5.11 PITYRIASIS ROSEA
L42

DESCRIPTION
» A common disease of unknown cause, probably due to a viral infection as it occurs in minor epidemics.
» Most common in young adults but any age may be affected.
» The rash involves the trunk, neck and mainly proximal parts of the limbs.
» Presents as pink papules and macules. The macules are oval and have a thin collar of scale towards, but not at, the periphery of the lesions.
» The eruption is usually preceded by a few days by one larger, oval, slightly scaly area ("herald patch"), commonly found in the scapular area or abdomen. The macules on the thorax characteristically lie parallel to the long axis of the ribs ("Christmas tree" distribution).
» The itch is usually mild and there are few or no constitutional symptoms. It is self-limiting and resolves within about 6–8 weeks.

GENERAL MEASURES
» Counsel on the benign but prolonged nature of the condition.

MEDICINE TREATMENT

Children

- Chlorphenamine, oral, 0.1 mg/kg/dose at night. See chlorphenamine dosing table, chapter 23. *LoE:IVb*[26]

Adults

- Chlorphenamine, oral, 4 mg at night.

Note: Chlorphenamine is sedating.

If itch is not controlled or more severe during the day, switch to:

Children: 2–6 years of age

- Cetirizine, oral, 5 mg once daily. See cetirizine dosing table, chapter 23.

Children > 6 years of age and adults:

- Cetirizine, oral, 10 mg once daily. *LoE: IVb*

5.12 MOLLUSCUM CONTAGIOSUM

B08.1

DESCRIPTION

» Infectious disease caused by a poxvirus.
» Presents with dome-shaped papules with a central depression (umbilication). Varies from occasional lesions to large crops of lesions particularly in immunocompromised or HIV-infected patients.
» Papules are commonly seen on the face in children, but may be found at any skin site, except on the palms and soles. They may also occur on the genitalia as an STI.
» Most infections resolve spontaneously except in the immunocompromised.

GENERAL MEASURES

In non-genital molluscum contagiosum:

» Allow lesions to heal spontaneously if the lesions are few in number and the patient not immunocompromised.
» Manual removal of lesions or expression of contents is not recommended as it may result in unintentional inoculation of other parts of the body, increase the risk of spread to others, or result in secondary bacterial infection.

LoE:IVb[27]

In genital molluscum contagiosum:

» Counsel on risk reduction for transmission of STIs.
» Counsel that the partner(s) should be notified, examined, and treated.

MEDICINE TREATMENT

- Tincture of iodine BP, applied to core of individual lesions using an applicator. *LoE:IIIb*[28]

CAUTION
Beware of hypersensitivity to iodine.

REFERRAL
» Extensive disease.
» Those failing to respond to simple measures.
» Peri-ocular lesions to an ophthalmologist.

5.13 HERPES SIMPLEX
B00.0-4/B00.7-9

DESCRIPTION
» Infection caused by herpes simplex virus type 1 or 2.
» Primary herpes infection involving gingivostomatitis (usually type 1) or the genital area (usually type 2) may be extensive, and may occur at other sites, e.g. the face.
» It is characterised by grouped crusted vesicles surrounded by erythema. The vesicles rupture soon after forming, producing discrete ulcers.
» Recurrences are usually mild and last a few days, except in immunosuppressed patients. Recurrences of oral herpes may be triggered by other respiratory tract infections or exposure to ultraviolet light.
» Sufferers of atopic eczema are particularly susceptible to the virus and may present with large areas of involvement with numerous vesicles and crusting surrounded by erythema (eczema herpeticum).
» Herpes simplex mucocutaneous ulceration that persists for > 1 month is an AIDS–defining illness. See Section 11.3.10: Herpes simplex ulcers, chronic.
» Herpes simplex infection may be the precipitating event in many cases of erythema multiforme.

GENERAL MEASURES
Keep the skin lesions clean and dry.

MEDICINE TREATMENT

Extensive herpes, eczema herpeticum or chronic mucocutaneous ulcerations:

Children < 15 years of age:
- Antiviral, (active against herpes simplex) e.g.:
- Aciclovir, oral, 250 mg/m^2/dose, 8 hourly for 7 days. See aciclovir dosing table, chapter 23.

Children ≥ 15 years of age and adults:
- Antiviral, (active against herpes simplex) e.g.:
- Aciclovir, oral, 400 mg, 8 hourly for 7 days. *LoE: IIIb*[29]

5.14 HERPES ZOSTER
See Section 11.3.11: Herpes zoster (Shingles).

5.15 WARTS

DESCRIPTION
A common, infectious, self-limiting condition of the skin or mucous membrane caused by human papilloma virus.

5.15.1 COMMON WARTS

B07

DESCRIPTION
» Seen most often on the hands and fingers, but can be found anywhere on the body.
» Raised nodules with a rough 'warty' surface.

GENERAL MEASURES
» Usually does not require treatment as they will resolve spontaneously .

MEDICINE TREATMENT
- Salicylic acid, 15 to 30%, topical liquid application.
  - Protect surrounding skin with petroleum jelly.
  - Apply daily to wart and allow to dry.
  - Occlude for 24 hours.
  - Soften lesions by soaking in warm water and remove loosened keratin by light abrasion.
  - Wash affected area well, dry, reapply the wart paint, and occlude.
  - Repeat process daily until the wart disappears.

LoE: IIIb[30]

REFERRAL
» Extensive warts.

5.15.2 PLANE WARTS

B07

DESCRIPTION
» Very small warts that are just slightly raised.
» Present as smooth, flat, skin-coloured or slightly pigmented surface.
» Frequently present on the face, backs of the hands, and knees.
» Commonly seen in immunocompromised patients.

MEDICINE TREATMENT
These warts are notoriously difficult to treat with a poor response.
- Salicylic acid, 2%, topical.

LoE: III [31]

REFERRAL
» Failure to respond.
» Extensive cases involving the face.

5.15.3 PLANTAR WARTS
B07

DESCRIPTION
» Commonly appear on the pressure-bearing areas of the soles and can be painful and interfere with walking.
» Lesions often have a flat, circular appearance, as pressure on the sole of the foot forces them deep into the dermis. They have a rough surface and are often thick and hard due to increased keratin formation.
» As they are contagious, walking barefoot in communal areas should be discouraged.

MEDICINE TREATMENT
- Salicylic acid, 15 to 30%, topical liquid application.
  – Protect surrounding skin with petroleum jelly.
  – Apply daily to wart and allow to dry.
  – Occlude for 24 hours.
  – Soften lesions by soaking in warm water and remove loosened keratin by light abrasion.
  – Wash affected area well, dry, reapply the wart paint and occlude.
  – Repeat process daily until the wart disappears. *LoE:IIIb*[32]

REFERRAL
» No response to treatment.
» Diabetic patients.

5.15.4 GENITAL WARTS: CONDYLOMATA ACCUMINATA
See Section 12.12: Genital warts (GW): condylomata accuminata.

5.16 PSORIASIS
L40.0-5/L40.8-9

DESCRIPTION
» Inflammatory condition of the skin and joints of unknown aetiology.
Lesions present as scaly, itchy plaques, especially on the extensor surfaces of the knees, elbows, sacrum and scalp.
» Psoriasis may spread to involve other sites, although the face is usually spared.
» The nails and skin folds are often involved.
» Often aggravated by stress, and may be provoked by HIV disease.

GENERAL MEASURES
» Counselling regarding precipitating factors and chronicity.
» HIV test, if acute onset and patient has risk factors for HIV infection.
» Encourage sun exposure as tolerated.

MEDICINE TREATMENT
For flares (if delay experienced in obtaining a dermatological consultation):
- Coal tar (Liquor picis carbonis - LPC) BP 5%, topica one to four times dailyl.

OR

- Corticosteroid, potent, topical, e.g.: (Doctor prescribed) *LoE: IVb*[33]
- Betamethasone 0.1%, topical, apply 12 hourly.
  - Decrease according to severity, reduce to hydrocortisone 1%, topical, and then stop.

REFERRAL
» All patients, if diagnosis is not already confirmed.
» Complications such as pustular psoriasis, acute flares, chronic local plaques.

5.17 HIDRADENITIS SUPPURATIVA
L73.2

DESCRIPTION
» A chronic disorder of the pilosebaceous follicles, involving the formation of abscesses and cysts, often accompanied by scarring and sinus tract formation.
» Commonly found in axillae, groin, between the thighs, perianal and perineal areas.
» Flare-ups may be triggered by perspiration, hormonal changes (such as menstrual cycles), humidity and heat, and friction from clothing.

GENERAL MEASURES
» Avoid tight clothing or clothing made of non-breathable material.

REFERRAL
» All patients with abscesses, infected cysts or sinuses suspected to be due to hidratenitis suppurativa.

5.18 HYPOPIGMENTORY DISORDERS

5.18.1 ALBINISM
E70.3

DESCRIPTION

» Congenital disorder characterised by the complete or partial absence of pigment in the skin, hair and eyes.
» Albinism is associated with a number of visual symptoms or defects such as photophobia, nystagmus, strabismus, and amblyopia.
» Lack of skin pigmentation increases a person's susceptibility to sunburn and skin cancers.

GENERAL MEASURES

To avoid sunburn and skin damage:

» Avoid sun exposure during periods of maximum intensity (i.e. between 10:00 and 15:00).
» Wear a wide-brimmed hat and long-sleeved top when exposed to the sun.
» Wear sunscreens with a high sun protection factor (SPF); a SPF of between 20 and 30 will provide adequate protection. The product should also provide protection against both UVA and UVB rays.
» To reduce photophobia and prevent retinal damage:
  - Wear sunglasses that preferably have UV filters
    Check skin regularly for signs of skin cancer such as a new spot or growth on their skin.

MEDICINE TREATMENT

- Zinc oxide, topical ointment.
  – Apply evenly to all sun exposed areas at least 15 minutes before going out into the sun. *LoE: IVb*[34]

OR

- High potency (SPF) sunblock, topical (UV block).
  – Apply evenly to all sun exposed areas at least 15 minutes before going out into the sun. *LoE: IVb*[35]

REFERRAL

» To dermatologist for regular skin checks.
» To ophthalmologist for visual rehabilitation and regular eye checks.

5.18.2 VITILIGO

L80

» Autoimmune disease characterised by patches of the skin losing their pigment.
» Presents as pale patchy areas of depigmented skin which tend to occur on the extremities.
» They are most prominent on the face, hands and wrists. The loss of pigmentation is particularly noticeable around body orifices such as the mouth, eyes, nostrils, genitalia, and umbilicus.
» The patches often begin in areas of skin that are exposed to the sun.
» New patches appear over time and can occur over large portions of the body, or can be restricted to a particular area.

GENERAL MEASURES
» Encourage sun exposure, moderate sun exposure is beneficial.

MEDICINE TREATMENT
- High potency (SPF) sunblock, topical (UV block)
  - Apply evenly to all sun exposed areas at least 15 minutes before going out into the sun. *LoE: IVb* [36]

REFERRAL
» All patients.

5.19 PRESSURE ULCERS/SORES
L89.0-3/L89.9

DESCRIPTION
» Localised damage to the skin and underlying tissue that usually occurs over bony
» prominences as a result of pressure, or pressure in combination with shear force and/or friction.
» The most common sites are the skin overlying the sacrum, coccyx, heels, and hips, but other sites can also be affected.
» Pressure ulcers most commonly develop in individuals who are immobile, including those bedridden or confined to a wheelchair.
» Other factors increasing the risk of pressure ulcer development are:
  - Skin wetness e.g. incontinence.
  - Reduced blood flow e.g. arteriosclerosis.
  - Reduced skin sensation e.g. paralysis or neuropathy.

GENERAL MEASURES

Skin care
» The skin should be kept clean and dry. Ensure that the skin folds are dried thoroughly.

Wound odour
» Regular cleansing, debridement and management of infection.
» Activated charcoal dressings may be used.

Pressure redistribution
» Repositioning and turning at regular intervals, every 2-4 hours. Individual receiving palliative care should be repositioned in accordance with the individual's wishes, comfort and tolerance.
» Avoid positioning the individual on the wound if erythema is present.

MEDICINE TREATMENT

Cleanse the skin prior to application of a barrier product.

- Zinc and castor oil, topical ointment. *LoE:IIIb*[37]

For pain:
See chapter 20: Pain.

REFERRAL

» Patients with pressure sores or those at high risk of development of pressure sores to rehabilitation services, if available. *LoE:IIb*[38]

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Chapter 6

SOUTH AFRICAN PRIMARY HEALTHCARE & ADULT HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 5: SKIN CONDITIONS
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020-4)

The Primary Health Care (PHC) Skin Conditions chapter underwent detailed clinical editing and editorial changes for clarity.

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the respective standard treatment guideline (STG) and supporting medicine reviews. *All reviews and costing reports may be accessed at:* https://www.health.gov.za/nhi-edp-stgs-eml/.

A: MEDICINE AMENDMENTS:

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED/ NOT ADDED/ RETAINED
5.2 Itching (Pruritus) *and* **5.8.1 Ectopic eczema** *and* **5.8.2 Eczema, acute, moist, or weeping** *and* **5.10.1 Urticaria** *and* **5.10.4 Papular urticaria** *and* **5.11 Pityriasis rosea**	Antihistamines	Caution box for <2 years deleted
	Chlorphenamine, oral	Retained and amended
	Cetirizine, oral	Retained and amended
5.3 Acne vulgaris	Benzoyl peroxide, topical	Retained
	Topical, retinoids	Directions for use amended
	Doxycycline, oral	Directions for use amended
5.4.1 Boils, abscess	Povidone iodine	Not added
	Children ≤ 7 years of age: Cefalexin	The dosing of cefalexin was aligned to the PHC paediatric dosing table, chapter 23 for children ≤ 7 years of age
5.4.2 Impetigo	Flucloxacillin, oral	Indication amended
	Cefalexin, oral	Indication amended
	Children ≤ 7 years of age: Cefalexin	The dosing of cefalexin was aligned to the PHC paediatric dosing table, chapter 23 for children ≤ 7 years of age
5.4.3 Cellulitis	Flucloxacillin, oral	Retained
	Cefalexin, oral	Retained
	Children ≤ 7 years of age: Cefalexin	The dosing of cefalexin was aligned to the PHC paediatric dosing table, chapter 23 for children ≤ 7 years of age
	Amoxicillin, oral	Not added
	Clindamycin, oral	Not added
5.4.4 Chronic lower leg ulcers	Hydrocolloid dressings	Not added
	Moistened dressing e.g., gauze with Sodium chloride, 0.9%.	Retained
5.5.2.4 Pityriasis versicolor – Tinea versicolor	Selenium sulfide, 2.5% suspension	Directions for use amended
5.6.3 Nail infections – Tinea unguium	Fluconazole, oral	Not added
5.7.1.1 Head lice	Permethrin 5%, topical	Retained
5.7.2 Scabies	Permethrin 5% topical	Retained
-children <6 years of age	Benzoyl benzoate 25% lotion	Added
5.8.1 Ectopic eczema	Emollient	Retained as a therapeutic class
	Emulsifying ointment (UE)	Retained as an example of class (emollient) listed in the STG
	Cetamacrogol	Not added as an example of class (emollient) – already included on the therapeutic interchange database
	Corticosteroid, potent, topical	Retained as a therapeutic class

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED/ NOT ADDED/ RETAINED
	Betamethasone 0.1%, topical	Retained as an example of class (potent corticosteroid) listed in the STG
	Fluocinolone, topical	Not added as an example of class (potent corticosteroid) – already included on the therapeutic interchange database
5.8.2 Eczema, acute, moist or weeping	Hydrocortisone 1% topical	Retained
	Betamethasone 0.1%, topical	Not added
	Fluocinolone, topical	Not added
	Children ≤ 7 years of age: Cefalexin	The dosing of cefalexin was aligned to the PHC paediatric dosing table, chapter 23 for children ≤ 7 years of age
5.8.3 Dermatitis, seborrhoeic	Corticosteroid, potent, topical:	retained as a therapeutic class
	Betamethasone 0.1%, topical:	retained as an example of class (potent corticosteroid) listed in the STG
	Fluocinolone, topical:	not added as an example of class (potent corticosteroid) – already included on the therapeutic interchange database
5.9 Nappy Rash	Topical corticosteroid	Not added
5.10.3 Fixed drug eruptions	Potent topical corticosteroid	Not added
5.10.4 Papular urticaria *- new inflamed lesions*	Hydrocortisone 1%, topical	Retained
	Fluocinolone, topical	Not added
	Hydrocortisone 1%, topical	Retained
	LPC 5%	Not added
5.11 Pityriasis rosea	Calamine lotion	Not added
	Hydrocortisone 1%, topical	Not added
	Aqueous cream	Deleted
5.12 Molluscum contagiosum	Benzoyl peroxide, topical	Not added
	Tincture of iodine BP	Retained
5.15.1 Common Warts	Histofreeze	Not added
5.16 Psoriasis	Corticosteroid, potent, topical	Retained as a therapeutic class
	Betamethasone 0.1%, topical	Retained as an example of class (potent corticosteroid) listed in the STG
	Fluocinolone, topical	Not added as an example of class (potent corticosteroid) – already included on the therapeutic interchange database
	Biologics	Not added
5.17 Hidradenitis suppurativa	Monoclonal antibodies	Not added
	Steroids	Not added
	Antibiotics	Not added
5.18.1 Albinism	Zinc oxide, topical	Retained, directions for use not amended
	Titanium dioxide, topical ointment/cream (UV block)	Retained, directions for use not amended, product name revised to high potency (SPF) sunblock, topical (UV Block)
	Titanium dioxide, topical ointment/cream (UV block)	Retained, product name revised to high potency (SPF) sunblock, topical (UV Block)
5.19 Pressure Ulcers/ Sores	Referral criterion (for rehabilitation)	Added

**The dosing of cefalexin in the chapter was aligned to the PHC paediatric dosing table, chapter 23 for children ≤ 7 years of age.*

5.2 ITCHING (PRURITUS) *and* **5.8.1 ECTOPIC ECZEMA** *and* **5.8.2 ECZEMA, ACUTE, MOIST, OR WEEPING** *and* **5.10.4 PAPULAR URTICARIA** *and* **5.11 PITYRIASIS ROSEA**

The NEMLC recommended at the meeting of the 23 June 2022[1] that the PHC/Adult Hospital Level ERC review the caution of restricting chlorphenamine to children older than 2 years of age, and align the dosing with guidance in the Paediatric Hospital Level STGs and EML.

[1] Minutes of the NEMLC meeting of 23 June 2022

- The Medicines Control Council (MCC) had issued a safety alert in 2007 for promethazine contra-indication in children less than 2 years of age, as serious life-threatening cases of respiratory depression, including fatalities have been reported

Thus, the following caution box was deleted throughout the STGs, and the weight-band dosing tables for chlorphenamine will be updated in chapter 23: Standard paediatric dosing tables to include dosing for children <2 years of age, accordingly.

~~**CAUTION**~~ ~~Do not give an antihistamine to children < 2 years of age.~~

Chlorpheniramine: *retained*
Cetirizine: *retained and amended*

Guidance for antihistamines was made consistent throughout these STGs for short-term use with chlorphenamine and long-term/chronic use with non-sedating antihistamine, cetirizine.

If pruritis is severe and requires short term control:

Children

- Chlorphenamine, oral, 0.1 mg/kg/dose 6–8 hourly. See chlorphenamine dosing table, chapter 23.

Adults

- Chlorphenamine, oral, 4 mg, 6–8 hourly.

Note: Chlorphenamine is sedating and may only be required in the evening for mild cases.

If pruritis is severe and requires long term control, e.g. for chronic pruritus

Children: 2–6 years of age

- Cetirizine, oral, 5 mg once daily. See cetirizine dosing table, chapter 23.

Children > 6 years of age and adults

- Cetirizine, oral, 10 mg once daily.

Level of Evidence: Expert opinion

Several external comments were received to amend management with antihistamines in these clinical settings. However, no supporting evidence was submitted, despite follow-up requests.

5.3 ACNE VULGARIS

Benzoyl peroxide, topical: *retained*
Following consultation with the Paediatric Hospital Level Committee, it was agreed that the current recommendation of benzoyl peroxide for mild acne be retained, which was supported at the NEMLC meeting on 23rd June 2022[2].

Topical, retinoids: *directions for use amended*
External comments on gradual titrated administration of topical retinoids, applying a "pea-sized" amount to the face and avoiding contact with eyes, and the area around the mouth and nose was accepted as pragmatic advice; and the STG text was amended as follows:

https://www.bing.com/ck/a?!&&p=4b3c6391536fd84aJmltdHM9MTY2MTExNjMyMiZpZ3VpZD0xYjBjZDE2OC05OWY0LTQxZDQtYTBmNS01ODBlYmM2NThkMGUmaW5zaWQ9NTE0Mw&ptn=3&hsh=3&fclid=e65d78bc-2195-11ed-accd-88709b8260e8&u=a1aHR0cHM6Ly93d3cuc2FocHJhLm9yZy56YS9zYWZldHktYWxlcnRzL21zYS1wcm9tZXRoYXppbmUtMi8&ntb=1

[2] Minutes of the NEMLC meeting of 23 June 2022

For non-inflammatory acne:
Topical retinoids

Main therapeutic objective is to control comedone formation.

Introduce topical retinoids gradually as a night-time application to limit skin irritant effects, as they are not photo-stable and degrade when exposed to sunlight (e.g. start twice a week and titrate up).

CAUTION
Do not use if pregnant or planning pregnancy.
Limit exposure to sunlight. If sunburn occurs, discontinue therapy until the skin has recovered.

- Tretinoin, topical, apply at night to affected areas for at least 6 weeks.
  - Review patient after 6 weeks' treatment.
  - Minimise exposure to sunlight. If sunburn occurs, discontinue therapy until the skin has recovered.
  - Acne may worsen during the first few weeks.
  - Apply about a pea-sized amount to entire face. Avoid contact with eyes and area around mouth and nose.

Level of Evidence: Expert opinion

Doxycycline: *directions for use amended*

Following an external comment, the STG text was amended as follows:

- Doxycycline, oral, 100 mg daily for 3 months.
- Review patient after 3 months of treatment.
- It should be taken with meals.
- Do not take it together with iron preparations and antacids.

Note: Doxycyline should always be used with a topical agent and should not be used as monotherapy.

However, an external comment to extend the duration of use for doxycycline from 3 months to 6 months was submitted without supporting evidence and was not considered, noting the concerns of antibiotic resistance.

5.4.1 BOIL, ABSCESS

Povidone iodine scrub: *not added*

An external comment was received for povidone iodine scrub as an anti-Staphylococcus measure for recurrent boils, without supporting evidence. Staining of clothing was also a concern. Available evidence[3] that was identified suggests chlorhexidine as a topical antiseptic and an adjunctive interventional strategy for reducing the risk of staphylococcal postoperative surgical site infections.

5.4.2 IMPETIGO

The NEMLC recommended at the meeting of the 25 August 2022[4] that the PHC/Adult Hospital Level ERC review the evidence for the retention and recommendation of cefalexin for *S Aureus* infections in relation to other antibiotics. An evidence review[5] was summarized including two Cochrane Reviews[6,7] (low & moderate quality review) and Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America (IDSA)[8].

[3] Edmiston CE Jr, Bruden B, Rucinski MC, Henen C, Graham MB, Lewis BL. Reducing the risk of surgical site infections: does chlorhexidine gluconate provide a risk reduction benefit? Am J Infect Control. 2013 May;41(5 Suppl):S49-55.

[4] Minutes of the NEMLC meeting of 25 August 2022.

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In September 2022, an additional search brought up a protocol of a study that is still underway entitled antibiotic therapy for skin and soft tissue infections: a protocol for a systematic review and network meta-analysis (biomedcentral.com)[9]. Remaining, studies date back to the 1990's and early 2000's.

In summary:**Error! Bookmark not defined.**

- The Cochrane reviews could not definitively recommend one antibiotic treatment over another
- It was unclear if oral antibiotics are superior to topical antibiotics for the management of impetigo.
- Penicillin was not as effective as other antibiotics as an intervention for the management of impetigo.
- Mostly there was no significant difference between cefalexin and other treatments, however cefalexin was the most effective treatment (significantly different versus penicillin) in the treatment of non-bullous impetigo. In this case *S aureus* was the most common cause of impetigo in a paediatric population and cefalexin was the most effective treatment.

Level of Evidence: Low to Moderate certainty evidence

Cefalexin, oral: retained

The dosing of cefalexin was aligned to the PHC paediatric dosing table, chapter 23 for children ≤ 7 years of age.

Flucloxacillin, oral: *retained & indication amended*

As not all cases of impetigo need antibiotics, the indication for cefalexin/flucloxacillin was amended to: *'If extensive or systemic signs of infection (fever, unwell, fatigued)'*, for clarity purposes.

5.4.3 CELLULITIS

Flucloxacillin, oral: *retained*
Cefalexin, oral*: retained*
Amoxicillin: *not added*
Clindamycin, oral: *not added*

The dosing of cefalexin was aligned to the PHC paediatric dosing table, chapter 23 for children ≤ 7 years of age.

External comment to replace flucloxacillin/cefalexin with amoxicillin/clindamycin without supporting evidence was not considered, noting that macrolides are already included as an alternative for severe penicillin allergy. A summary of the evidence[10] for the use of cefalexin in *S Aureus* skin infections showed that cefalexin might be the more effective treatment (significantly different versus penicillin in a pediatric population). Furthermore, the IDSA guidelines recommend cefalexin in combination with other antibiotics for both streptococci and Methicillin-resistant Staphylococcus aureus (MRSA) but also indicate that cefalexin alone is efficacious in pure cellulitis.[11]

5.4.4 CHRONIC LOWER LEG ULCERS

Hydrocolloid dressings: *not added*
Moistened dressing e.g. gauze with Sodium chloride, 0.9%: *retained*

[9] Bartoszko JJ, Mertz D, Thabane L, Loeb M. Antibiotic therapy for skin and soft tissue infections: a protocol for a systematic review and network meta-analysis. Syst Rev. 2018 Sep 11;7(1):138. doi: 10.1186/s13643-018-0804-8. PMID: 30205844; PMCID: PMC6134765.

[10] Cefalexin: National Department of Health: Affordable Medicines, EDP- Primary Healthcare and Adult Hospital Level. Medicine Review: Evidence summary of the use of cephalexin for S Aureus skin infections, September 2022.

[11] Intravenous antibiotics (severe cellulitis and erysipelas): Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC; Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014 Jul 15;59(2):e10-52. https://www.idsociety.org/practice-guideline/skin-and-soft-tissue-infections/

External comment was submitted without evidence to include hydrocolloid dressings for local wound care. There is no evidence to support the superiority of one dressing type over another when applied under appropriate multilayer compression bandaging[12].

5.5.2.4 PITYRIASIS VERSICOLOR – TINEA VERSICOLOR

Selenium sulfide, 2.5% suspension: *directions for use amended*

Directions for use was amended as follows for pragmatic purposes:

» Oral antifungal therapy is not indicated.
- Selenium sulfide, 2.5% suspension apply once weekly for three weeks .
  - Lather shampoo on affected parts.
  - Leave on overnight, then wash off the following day.

Level of Evidence: Expert opinion

5.6.3 NAIL INFECTIONS – TINEA UNGUIUM

Fluconazole, oral: *not added*

An external comment to include oral fluconazole was not considered, as the STG provides guidance for referral to secondary level of care if patients are distressed by cosmetic appearance.

Fluconazole was historically not added as evidence reviewed by the Expert Review Committee (2014) indicated minimal benefit of fluconazole for tinea unguium with mainly open label RCTs showing higher cure rates. [13] Therapy is also noted as costly.

5.7.1.1 HEAD LICE

Permethrin 5%, topical: *retained*

5.7.2 SCABIES

Children < 6 years of age

Permethrin 5%, topical: *retained*

Benzyl benzoate 25% lotion: *added*

There have been consistent reports of supply issues with permethrin 5%, thus guidance was provided to consider diluted benzyl benzoate in young children, aligned with SAMF[14].

The STG text was updated as follows:

If permethrin is unavailable for children < 6 years of age:
Benzoyl benzoate 25% lotion:
- Children 0 months to 1 year of age:
  - Dilute 1 part of benzoyl benzoate to 3 parts of water to form an emulsion of 6%.
  - Apply diluted emulsion to the whole body from neck to feet as described above.

Level of Evidence: Guidelines

5.8.1 ECZEMA, ATOPIC

Emollient: *retained as a therapeutic class*

Emulsifying ointment (UE): *retained as an example of class (emollient) listed in the STG*

[12] Palfreyman SJ, Nelson EA, Lochiel R, Michaels JA. Dressings for healing venous leg ulcers. Cochrane Database Syst Rev. 2006 Jul 19;(3):CD001103. doi: 10.1002/14651858.CD001103.pub2.

[13] National Essential Medicines List Committee Implementation Slides- 2012

[14] SAMF, 2022

Cetamacrogol: *not added as an example of class (emollient) – already included on the therapeutic interchange database*

Corticosteroid, potent, topical: *retained as a therapeutic class*
Betamethasone 0.1%, topical: *retained as an example of class (potent corticosteroid) listed in the STG*
Fluocinolone, topical: *not added as an example of class (potent corticosteroid) – already included on the therapeutic interchange database*

5.8.2 ECZEMA, ACUTE, MOIST OR WEEPING

Hydrocortisone 1% topical: *retained*
Betamethasone 0.1%, topical: *not added*
Fluocinolone, topical: *not added*

The dosing of cefalexin was aligned to the PHC paediatric dosing table, chapter 23 for children ≤ 7 years of age.

External comment without supporting evidence to replace mild topical corticosteroids with potent topical corticosteroids was not considered, noting that historically, hydrocortisone 1% cream was added as a water based topical steroid for the treatment of acute and weeping eczema[15]; while the PHC STGs and EML recommends doctor prescribing of potent topical corticosteroids.

5.8.3 DERMATITIS, SEBORRHOEIC

Corticosteroid, potent, topical: *retained as a therapeutic class*
Betamethasone 0.1%, topical: *retained as an example of class (potent corticosteroid) listed in the STG*
Fluocinolone, topical: *not added as an example of class (potent corticosteroid) – already included on the therapeutic interchange database*

5.9 NAPPY RASH

Topical corticosteroid: *not added*
External comment without evidence, to include topical steroids for the treatment of nappy rash was not considered, noting that guidance is provided for referral to secondary level of care if there is no improvement after 3 days.

5.10.3 FIXED DRUG ERUPTIONS

Potent topical corticosteroid: *not added*
External comment without evidence, to include potent topical corticosteroids was not considered, noting that the PHC STGs and EML recommends doctor prescribing of potent topical corticosteroids.

5.10.4 PAPULAR URTICARIA

Hydrocortisone 1%, topical: *retained*
Fluocinolone, topical: *not added*
External comment without supporting evidence to replace hydrocortisone 1%, topical with potent topical corticosteroid, fluocinolone, was not considered, noting that the PHC STGs and EML recommends doctor prescribing of potent topical corticosteroids.

LPC 5%: *not added*
External comment without supporting evidence to consider LPC 5% to relieve itching was not considered.

[15] Primary Healthcare Essential Medicines List NEMLC Report. Chapter 5: Skin. 28 November 2013.

5.10.4 PAPULAR URTICARIA

Hydrocortisone 1%, topical: *retained*
Fluocinolone, topical: *not added*

External comment without supporting evidence to replace hydrocortisone 1%, topical with potent topical corticosteroid, fluocinolone, was not considered, noting that the PHC STGs and EML recommends doctor prescribing of potent topical corticosteroids.

LPC 5%: *not added*
External comment without supporting evidence to consider LPC 5% to relieve itching was not considered. Review of the literature did not result in high certainty evidence for the use of LPC 5% in the treatment of papular urticaria.

5.11 PITYRIASIS ROSEA

Calamine lotion: n*ot added*
Hydrocortisone 1%, topical: *not added*
Aqueous cream: *deleted*

External comment without supporting evidence to consider calamine lotion and topical mild corticosteroids and to remove aqueous cream for the management of pityriasis rosea was received. Guidelines for management of the condition were sought but evidence to support the addition of calamine or topical corticosteroids for this indication could not be justified.

At the NEMLC meeting on the 25 August 2022 it was raised that there might be a safety issue with the use of aqueous cream due to the ingredient sodium lauryl sulphate which can be irritant[16], and therefore NEMLC recommended the use of aqueous cream should be reconsidered. Although sodium lauryl sulphate free products are available on the market, no evidence could be found for the explicit use of aqueous cream in pityriasis rosea, and therefore aqueous cream was removed from the PHC STG and EML for this indication.

5.12 MOLLUSCUM CONTAGIOSUM

Benzoyl peroxide: not added
Tincture of iodine BP: retained

External comment without supporting evidence for benzoyl peroxide as an irritant to allow lesions to become inflamed and then involute was received. Review of the literature showed that the Centers for Disease Control (CDC) recommendations[17] suggest physical removal of lesions through cryotherapy (freezing the lesion with liquid nitrogen), curettage and laser therapy all outside the scope of PHC level. The CDC guidance does not recommend the patient try and remove lesions or the fluid inside of lesions as it may unintentionally autoinoculate other parts of the body, risk spreading it to others and result in bacterial infection. A Cochrane review showed that iodine is used as a treatment option but no single treatment is convincingly effective in the treatment of molluscum contagiosum[18].

Level of Evidence: Low certainty systematic review evidence and Guidelines

[16] Aqueous cream: may cause skin irritation. https://www.gov.uk/drug-safety-update/aqueous-cream-may-cause-skin-irritation#:~:text=Although%20aqueous%20cream%20is%20useful,%2C%20burning%2C%20itching%20and%20redness. 11 March 2014.
[17] Molluscum contagiosum. Centers for Disease Control. https://www.cdc.gov/poxvirus/molluscum-contagiosum/treatment.html.
[18] van der Wouden JC, van der Sande R, Kruithof EJ, Sollie A, van Suijlekom-Smit LW, Koning S. Interventions for cutaneous molluscum contagiosum. Cochrane Database Syst Rev. 2017 May 17;5(5):CD004767. doi: 10.1002/14651858.CD004767.pub4. PMID: 28513067; PMCID: PMC6481355.

5.15.1 COMMON WARTS

Histofreeze: not added

External comment without supporting evidence for histofreeze was received. Review of the available evidence showed that Histofreeze would require a portable cryosurgical system at a high cost and therefore was not included.

5.16 PSORIASIS

Corticosteroid, potent, topical: *retained as a therapeutic class*
Betamethasone 0.1%, topical: *retained as an example of class (potent corticosteroid) listed in the STG*
Fluocinolone, topical: *not added as an example of class (potent corticosteroid) – already included on the therapeutic interchange database*
Biologics: *not added*
External comments received from two manufacturer motivating for early use of biologics in patients with psoriasis, was not accepted. However, the matter was referred to the Tertiary and Quaternary Expert Review Committee for consideration.

5.17 HIDRADENITIS SUPPURATIVA

Monoclonal antibodies: *not added*
Steroids: *not added*
Antibiotics: *not added*
External comment received from a manufacturer for antibiotic, steroids and biologics for the management of hidradenitis suppurativa. However, individualised management of patients is required with treatment of symptoms and comorbidities. Treatment varies and includes therapeutics such as topical treatment, anti-androgenic medicines and spironolactone. The STGs do provide for management of furuncles and abscesses. Refractory therapy includes the following therapeutic options: rifampicin, dapsone, laser therapy, surgery and monoclonal antibodies. The matter pertaining to monoclonal antibodies was referred to the Tertiary and Quaternary Expert Review Committee for consideration.

In addition, the following text was added to the STG:

Referral
» All patients with abscesses, infected cysts or sinuses suspected to be due to hidratenitis suppurativa

5.18.1 ALBINISM

Zinc oxide, topical ointment: *retained, directions for use not amended*
Titanium dioxide, topical ointment/cream (UV block): *retained, directions for use not amended, product name revised to high potency (SPF) sunblock, topical (UV Block)*

External comment *without* supporting evidence to re-apply sunscreens at least every 2 hours was received. Although sunscreens are recommended for hypo pigmentation,[19] and drug information sites[20] indicate that most sun screens can be easily removed from the skin and therefore should be reapplied every one to two hours for adequate protection (especially after swimming and severe perspiration); the practically of the reapplication at least every 2 hours could not be guided by strong evidence.

[19] Hill JP, Batchelor JM. An approach to hypopigmentation. BMJ. 2017 Jan 12;356:i6534. doi: 10.1136/bmj.i6534. PMID: 28082370.
[20] Sunscreen Agent (Topical application). https://www.drugs.com/cons/sunscreen-agent-topical-application.html

5.18.2 VITILIGO

Titanium dioxide, topical ointment/cream (UV block): retained, product name revised to high potency (SPF) sunblock, topical (UV Block)

External comment *without* supporting evidence to remove UV blocks in vitiligo was received. Review of the available evidence indicated that sunscreens are recommended in the management of vitiligo, and was retained with a revision of the active ingredient of the treatment from titanium dioxide, topical ointment/ cream to high potency (SPF) sunblock, topical (UV Block)

Text encouraging patients to only use sunscreen when the sun is at its strongest was deleted from the STG, as application of sunscreen was deemed appropriate at any time of the day.

The STG was revised a follows:

From

MEDICINE TREATMENT
- Titanium dioxide, topical ointment/cream (UV block),
  - Only use when sun is at it is strongest i.e., between 10:00 and 15:00.
  - Apply evenly to all sun exposed areas at least 15 minutes before going out into the sun during this time

To

MEDICINE TREATMENT
- High potency (SPF) sunblock, topical (UV block)
  - Apply evenly to all sun exposed areas at least 15 minutes before going out into the sun.

5.19 PRESSURE ULCERS/SORES

Referral criterion (for rehabilitation): *added*

Referral criterion was added for referral to rehabilitation on receipt of motivation from RuReSA and Rehabilitation Associations of SA in collaboration with the Department of Health and Rehabilitation Sciences, Stellenbosch University for electrical stimulation for wound management in addition to standard care to improve healing[21]; and for prevention of pressure sores e.g., wheelchair users should be referred to rehabilitation for wheelchair and transfers training[22] [23].

The STG text was amended as follows:

Referral

Refer patients with pressure sores or those at high risk of development of pressure sores to rehabilitation.

[21] Arora M, Harvey LA, Glinsky JV, Nier L, Lavrencic L, Kifley A, Cameron ID. Electrical stimulation for treating pressure ulcers. Cochrane Database Syst Rev. 2020 Jan 22;1(1):CD012196. https://pubmed.ncbi.nlm.nih.gov/35244315/

[22] Harvey LA, Glinsky JV, Bowden JL. The effectiveness of 22 commonly administered physiotherapy interventions for people with spinal cord injury: a systematic review. Spinal Cord. 2016 Nov;54(11):914-923. https://pubmed.ncbi.nlm.nih.gov/27349607/

[23] Wang J, Ren D, Liu Y, Wang Y, Zhang B, Xiao Q. Effects of early mobilization on the prognosis of critically ill patients: A systematic review and meta-analysis. Int J Nurs Stud. 2020 Oct;110:103708. https://pubmed.ncbi.nlm.nih.gov/32736250/

South African National Essential Medicine List
Primary Healthcare and Adult Hospital Level Medication Review Process
Component: Skin Conditions/Dermatology

EVIDENCE SUMMARY

Title: Evidence summary of the use of cephalexin for *S Aureus* skin infections

Date: 8 September 2022

Reviewers: Milli Reddy, Halima Dawood, Zahiera Adam

Affiliation and declaration of interests: MR (Right to Care), HD (Grey's Hospital, Caprisa, University of KwaZulu-Natal, Combined Primary Healthcare/Adult Hospital Level Committee, 2021-2023 & National Essential Medicines List Committee, 2021-2023) & ZA (Right to Care) have no interests to declare pertaining to cephalexin.

Background:
At a recent National Essential Medicines List Committee (NEMLC) meeting (August 2022), the inclusion of cephalexin for Staphylococcus Aureus skin infections was deliberated as an external comment was received to replace flucloxacillin/cephalexin with amoxicillin/clindamycin for the management of impetigo and cellulitis, without supporting evidence.

It is noted that during the 2013 review cycle a request was made to replace cloxacillin with amoxicillin. However, cloxacillin was retained. Cloxacillin supply constraints have been experienced by the Department of Health. Macrolides are included in the Standard Treatment Guidelines (STG) as an alternative for severe penicillin allergy.

A summary of the evidence used in reaching the decision to retain cephalexin on the STG was requested by NEMLC. The evidence includes two Cochrane reviews (2010 & 2012)[i],[ii] and Guidelines from the Infectious Diseases Society of America[iii].

In September 2022, an additional search brought up a protocol of a study that is still underway entitled antibiotic therapy for skin and soft tissue infections: a protocol for a systematic review and network meta-analysis (biomedcentral.com)[iv]. Remaining, studies date back to the 1990's and early 2000's. Therefore, the two Cochrane Reviews[i,ii] and IDSA guideline[iii] were reviewed and summarised here.

Meta-Analysis and Systematic Review of Interventions for cellulitis and erysipelas[i]

A Cochrane review included 25 studies (n=2488) published until May 2010 that included adults or children diagnosed with cellulitis. Treatment regimens included antibiotics or antibiotics with anti-inflammatory agents, or physical treatment (such as topical heat, cold, vibration, or elevation). The primary outcomes included symptoms rated by participant or medical practitioner, e.g., duration and intensity of fever, pain, redness of the affected area, swelling of the skin surface and subcutaneous tissue, blister formation, or proportion symptom-free ('cure'), at a time specified by the study authors; proportion with severe complications (such as severe sepsis, multi-organ failure, death) and quality of life scores (including generic and disease-specific items and return to normal activity). Data was screened and independently extracted by two authors. For studies where similar types of interventions were compared and the same primary outcome measures were used, a meta-analysis was conducted.

The age of participants from the included trials ranged from 16 to 90 years old. Of the 25 studies included 17 studies included skin and skin structure infections (such as abscess, impetigo, folliculitis (inflammation of hair follicles), furunculosis (boils), and wound infection). Cellulitis was included as a subgroup. There were eight studies included

where cellulitis or erysipelas was the main inclusion criteria. Three trials compared a cephalosporin with penicillin, six trials compared different cephalosporins and one trial compared a macrolide against a first-generation cephalosporin.

Results:

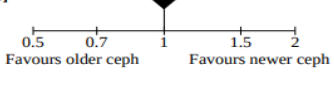
Penicillin versus a cephalosporin: None of the three studies that compared penicillin to a cephalosporin included cephalexin in the comparison. In two studies IV ampicillin/sulbactam was compared with IV cefazolin for the treatment of cellulitis. In the third study IV cefuroxime was compared with IV flucloxacillin. After accounting for heterogeneity, the two studies that reviewed the 1st generation cephalosporins showed no strong evidence of an effect (RR 1.17, 0.91 to 1.50). Similarly, the evidence from the one study using a third-generation cephalosporin also showed no strong effect (RR 0.7, 95% CI 0.48 to 1.00).

Cephalosporin versus cephalosporin

Symptoms rated by participant or medical practitioner (Cure at the end of treatment): Six trials (n=538) compared one cephalosporin with another. Four of these six trials included cephalexin in the comparison. In the meta-analysis comparisons were labelled as new vs old cephalosporin. Overall, no significant differences in treatment effect were noted between the cephalosporins (RR 1.00, 95% CI 0.94 to 1.06).

Analysis 3.1. Comparison 3: Newer vs older generation cephalosporin, Outcome 1: Symptom-free/reduced at the end of treatment

Study or Subgroup	Newer cephalosporin Events	Total	Older cephalosporin Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
3.1.1 2nd vs 1st generation						
Iannini 1985	31	35	9	10	6.5%	0.98 [0.78 , 1.25]
Subtotal (95% CI)		**35**		**10**	**6.5%**	**0.98 [0.78 , 1.25]**
Total events:	31		9			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.13 (P = 0.90)						
3.1.2 3rd vs 1st generation						
Bucko 2002 part 2	50	56	55	66	18.7%	1.07 [0.93 , 1.23]
Grayson 2002	51	59	51	59	18.2%	1.00 [0.87 , 1.15]
Tack 1998	13	17	14	17	3.2%	0.93 [0.66 , 1.31]
Subtotal (95% CI)		**132**		**142**	**40.0%**	**1.03 [0.93 , 1.13]**
Total events:	114		120			
Heterogeneity: Tau² = 0.00; Chi² = 0.82, df = 2 (P = 0.66); I² = 0%						
Test for overall effect: Z = 0.54 (P = 0.59)						
3.1.3 3rd vs 2nd generation						
Bucko 2002 part 1	54	66	69	79	18.6%	0.94 [0.81 , 1.08]
Subtotal (95% CI)		**66**		**79**	**18.6%**	**0.94 [0.81 , 1.08]**
Total events:	54		69			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.91 (P = 0.37)						
3.1.4 4th vs 3rd generation						
Schwartz 1996	49	51	22	23	34.8%	1.00 [0.91 , 1.11]
Subtotal (95% CI)		**51**		**23**	**34.8%**	**1.00 [0.91 , 1.11]**
Total events:	49		22			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.08 (P = 0.93)						
Total (95% CI)		**284**		**254**	**100.0%**	**1.00 [0.94 , 1.06]**
Total events:	248		220			
Heterogeneity: Tau² = 0.00; Chi² = 1.97, df = 5 (P = 0.85); I² = 0%						
Test for overall effect: Z = 0.03 (P = 0.97)						
Test for subgroup differences: Chi² = 1.13, df = 3 (P = 0.77), I² = 0%						



Miscellaneous (Other) antibiotics: One study which provided an analysis for a cellulitis subgroup showed failure rates of 1/24 (4%) for azithromycin vs 1/23 for cephalexin (4%). In this study oral azithromycin was administered as 1 x 500 mg on day 1 and 250 mg once a day on days 2 to 5. Oral cephalexin was dosed 500 mg 2 times a day for 10 days.

Refer to Appendix 1A for AMSTAR review.

Interventions for impetigo (Review)[ii]

Initially 57 trials were included in the review. Following the update of the review, 1 trial was excluded and 12 new trials added. Therefore, the updated review included 68 trials (n=5578), reporting on 50 different treatments, including placebo.

Participants included were diagnosed with impetigo or impetigo contagiosa (preferably confirmed by bacterial culture). Treatments included topical or systemic (oral, intramuscular, or intravenous) antibiotics, disinfectants, or any other intervention for impetigo, such as 'awaiting natural response'. Studies that compared different dosages of the same medicine were excluded. Primary outcomes included (1) clearance of crusts, blisters, and redness (i.e., cure as assessed by the investigator), and (2) relief of symptoms such as pain, itching, and soreness as assessed by the participant in the trial.

Topical antibiotics vs oral (systemic) antibiotics (overall n=16 studies, 17 comparisons; n=1 study relevant to cephalexin)

No significant differences were noted between mupirocin and dicloxacillin (n=1 study), cephalexin (n=1 study), or ampicillin (n=1 study). Bacitracin was significantly worse than oral cephalexin in this one small study[v] (n=26 participants), which consisted of three arms.

In this study, cephalexin was reviewed at a dose of 50 mg/kg/day orally in three divided doses (maximum 500mg per dose) plus 30 g of a placebo topical ointment (petrolatum plus glycerin) to be applied to affected areas three times daily in 10 patients, mupirocin ointment 2%, 3 times a day plus an oral liquid placebo matched to oral cephalexin to be given in a dosage comparable with that of cephalexin in 7 patients and bacitracin ointment 500 units/g, three times a day plus an oral liquid placebo matched to oral cephalexin to be given in a dosage comparable with that of cephalexin in three divided daily doses in 9 patients.

S. aureus was cultured from all 22 of 26 patients who had cultures performed of their lesions.

An improvement was noted in 1/10 (1%) participant in the cephalexin group vs 1/7 (14%) in the mupirocin group vs none (n=9 participants) in the bacitracin group. Nine of 10 participants (90%) on cephalexin were cured vs 6/7 (86%) in the mupirocin group vs 3/9 (33%) in the bacitracin group. No treatment failures (0%) were noted for cephalexin and mupirocin groups. However, 6/9 (67%) participants were noted as failing in the bacitracin group.

Comparison of the three treatment groups (Taken from Bass, 1997[v])

Treatment	Initial Lesion(s) Size (cm^2)	Duration of Lesions (Days)	Type of Lesion(s)	Culture Results	Outcome Failure/Improved/ Cured
Cephalexin	6.9 ± 1.8*	7.5 ± 1.8	HC 9, B 1	SA 9	0/1/9
Mupirocin	8.0 ± 3.8	6.1 ± 3.0	HC 4, HC + B1, B1, P1	SA 3, SA + GABHS 2	0/1/6
Bacitracin	4.4 ± 0.9	7.2 ± 1.6	HC 5, HC + B 1, P + B 1, B 2	SA 7, SA + GABHS 1	6/0/3
	6.3 ± 1.3	7.0 ± 1.2	Totals HC 18, HC + B 2, P + B 1, B 4, P 1	Totals SA 19, SA + GABHS 3	Totals 6/2/18

*Mean ± SE.
HC, honey-crusted; NA, not available; GABHS, group A beta-hemolytic streptococci; SA, *Staphylococcus aureus*; B, bullous; S, sensitive; P, pustular; R, resistent.

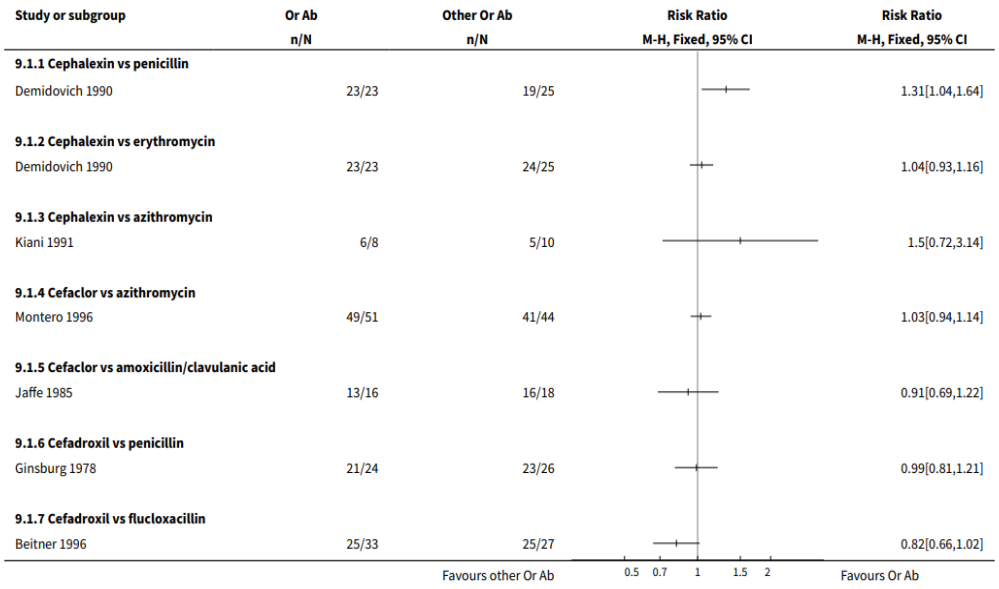
Adverse effects were not reported in the study.

Oral antibiotic vs another oral antibiotic: cephalosporin vs another antibiotic (n=6 studies)

Only one comparison, cephalexin versus penicillin, showed a significant difference in the treatment of non-bullous impetigo (RR 1.31, 95% CI 1.04 to 1.64), favouring cephalexin. Treatment failure occurred in 6/25 (24%) treated with penicillin, 1/25 (4%) treated with erythromycin, and 0/23 (0%) treated with cephalexin. Results showed that *S aureus* was the most common cause of impetigo in this paediatric study population and cephalexin was the most effective treatment. Additionally, erythromycin estolate was nearly equally effective as cephalexin but penicillin was considered

inadequate for treatment of non-bullous impetigo.[vi] There were concerns around randomization, blinding and selective reporting on outcome data and other biases in this study.

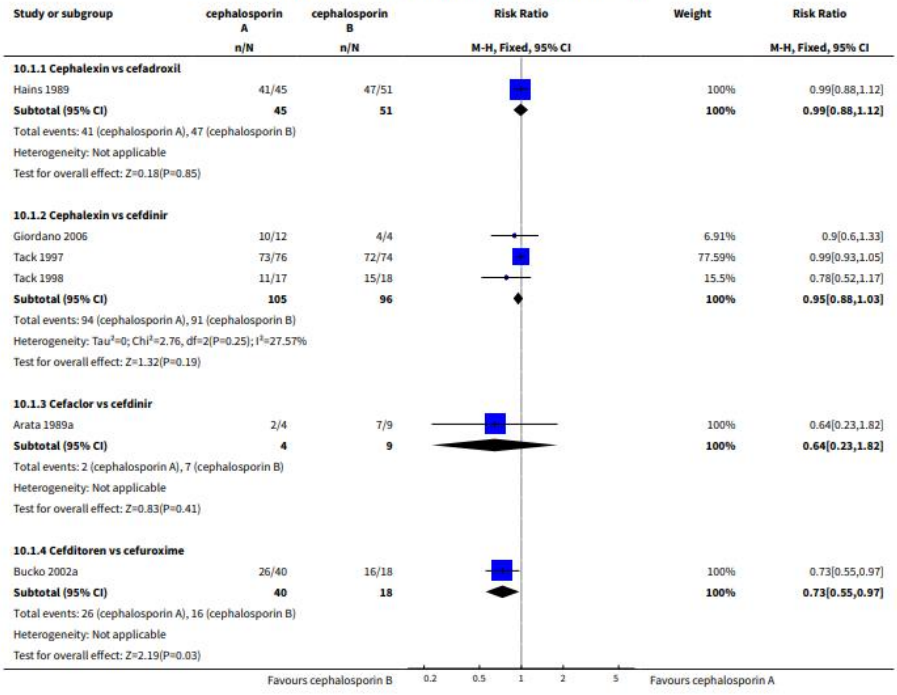
Analysis 9.1. Comparison 9 Non-bullous impetigo: oral (Or) antibiotic (Ab) (cephalosporin) vs another oral (Or) antibiotic (Ab), Outcome 1 Cure/improvement.

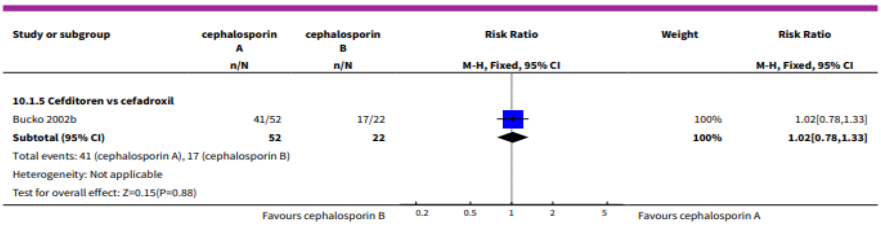


Oral antibiotic vs another oral antibiotic: one cephalosporin vs another cephalosporin (n=7 studies)

No significant differences were noted between cephalexin and cefadroxil, cephalexin vs cefdinir, cefaclor vs cefdinir, or cefditoren vs cefadroxil. The only significant difference for the cephalosporins was noted in the comparison of cefditoren vs cefuroxime, where cefuroxime was more effective (RR 0.73, 99% CI 0.55 to 0.97).

Analysis 10.1. Comparison 10 Non-bullous impetigo: oral (Or) cephalosporin vs other oral (Or) cephalosporin, Outcome 1 Cure/improvement.





Oral antibiotic versus another oral antibiotic (n=1 study)

No significant difference was noted between cephalexin (50 mg/kg/day in 2 divided doses) and dicloxacillin (15 mg/kg/day in 4 divided doses) (RR 1.17, 95% CI 0.95 to 1.45) in the treatment of bullous impetigo.

Topical antibiotic versus oral antibiotic (n=1 study)

No significant difference was noted for cure or improvement between topical mupirocin (44/77 (57%) cured or improved) vs oral cephalexin (52/82; 63%) (RR 1.11, 95% CI 0.86 to 1.43).

Oral antibiotics

In a very small study (n=10), no significant difference was detected between cephalexin and enoxacin for either cure or improvement in secondary impetigo cases (RR 0.75, 96% CI 0.24 to 2.33).

Refer to Appendix 1B for AMSTAR review.

Guidelines

Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America[iii] recommend the following regarding cephalexin and *S Aureus Skin* Infections:

Therapy for Typical Cases of Cellulitis:

- Should include an antibiotic active against streptococci.

- A large percentage of patients can receive oral medications from the start for typical cellulitis, and suitable antibiotics for most patients include penicillin, amoxicillin, amoxicillin-clavulanate, dicloxacillin, cephalexin, or clindamycin.
- In cases of uncomplicated cellulitis, a 5-day course of antimicrobial therapy is as effective as a 10-day course, if clinical improvement has occurred by 5 days
- If coverage for both streptococci and Methicillin-resistant Staphylococcus aureus (MRSA) is desired for oral therapy, options include clindamycin alone or the combination of either sulfamethoxazole and trimethoprim (SMX-TMP) or doxycycline with a β-lactam (e.g., penicillin, cephalexin, or amoxicillin)
- The guidelines mention that a double-blind study showed that a combination of SMX-TMP plus cephalexin was no more efficacious than cephalexin alone in pure cellulitis

Evaluation and Treatment of Impetigo and Ecthyma:

- Because *S. aureus* isolates from impetigo and ecthyma are usually methicillin susceptible dicloxacillin or cephalexin is recommended

Impetigo (Staphylococcus and Streptococcus):

- Adults: Cephalexin - 250mg QID po
- Children 25-50mg/kg/d in 3-4 divided doses po

***Methicillin-Sensitive Staphylococcus. Aureus Skin and soft tissue infections* (*MSSA SSTI)*:** (For penicillin allergic patients except those with immediate hypersensitivity reactions. Availability of a suspension and requirement for less frequent dosing)

- Adults: Cephalexin - 500mg QID po
- Children 25-50mg/kg/d in 4 divided doses po

***Streptococcal skin infections*:**

- Adults: Cephalexin 500 mg every 6 h po

***Antibiotics for Treatment of Incisional Surgical Site Infection*:**

- *Surgery of trunk or extremity away from axilla or perineum:* Cephalexin 500 mg every 6 h po

Refer to Appendix 2 for AGREE II Appraisal.

Conclusions

The Cochrane reviews could not definitively recommend one antibiotic treatment over another, and it was unclear if oral antibiotics are superior to topical antibiotics for the management of impetigo. However, penicillin was not as effective as other antibiotics as an intervention for the management of impetigo. Mostly there was no significant difference between cephalexin and other treatments and cephalexin was the most effective treatment (significantly different versus penicillin) in the treatment of non-bullous impetigo. In this case *S aureus* was the most common cause of impetigo in a paediatric population and cephalexin was the most effective treatment. Previously, also due to supply issues, cephalexin was recommended for S aureus skin infections.

Appendix 1 A: Evaluating the methodological quality of the Kilburn et al (2010)[1] systematic review and meta-analysis – AMSTAR 2 tool (Shea 2017[2])

LOW QUALITY REVIEW

No.	Criteria	Yes/ Partial Yes/ No	Comment
1	Research questions and inclusion criteria for the review included the components of PICO	No	Comparators were not explicitly explained (grouped with interventions)
2*	Report of the review contained an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol	Yes	Report listed deviations from the protocol
3	Review authors explained selection of the study designs for inclusion in the review	Yes	The authors mention that they included studies that allocated participants to groups using randomisation in order to reduce bias.
4*	Review authors used a comprehensive literature search strategy	Partial yes	The authors did not include/consult content experts in the field where relevant
5	Review authors perform study selection in duplicate	Yes	-
6	Review authors perform data extraction in duplicate	Yes	-
7*	Review authors provided a list of excluded studies and justify the exclusions	Yes	-
8	Review authors described the included studies in adequate detail	Partial yes	Comparators included as interventions
9*	Review authors used a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review	Yes	Risk of bias assessed using Cochrane methods – no graphical representation provided
10	Review authors reported on the sources of funding for the studies included in the review.	No	Only mention that a number of drug-company-sponsored studies excluded participants where the bacteria isolated were not sensitive to study antibiotics
11*	For meta-analyses, review authors used appropriate methods for statistical combination of results	Yes	-
12	For meta-analyses, review authors assessed the potential impact of RoB in individual RCTs on the results of the meta-analysis or other evidence synthesis	Yes	The authors mention that they were not able to conduct sensitivity analyses due to the small number of trials available within each category
13*	Review authors accounted for RoB in individual RCTs when interpreting/ discussing the results of the review	Yes	-
14	Review authors provided a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review	Yes	There was heterogeneity in the results
15*	For quantitative synthesis, review authors carried out an adequate investigation of publication bias (small study bias) and discussed its likely impact on the results of the review	No	
16	Review authors reported any potential sources of conflict of interest, including any funding they received for conducting the review	Yes	The authors had no conflicts of interest to disclose

** Critical domains = 2, 4, 7, 9, 11, 13, 15*

Rating overall confidence in the results of the review

- *High:* No or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest
- *Moderate:* More than one non-critical weakness*: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review
- *Low:* One critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest
- *Critically low*: More than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies

(*Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence).

[1] Kilburn SA, Featherstone P, Higgins B, Brindle R. Interventions for cellulitis and erysipelas. Cochrane Database Syst Rev. 2010 Jun 16;2010(6):CD004299. doi: 10.1002/14651858.CD004299.pub2. PMID: 20556757; PMCID: PMC8693180.

[2] Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008. https://pubmed.ncbi.nlm.nih.gov/28935701/

Appendix 1 B: Evaluating the methodological quality of the Koning et al (2012)[3] systematic review and meta-analysis – AMSTAR 2 tool (Shea 2017[4])

MODERATE QUALITY REVIEW

No.	Criteria	Yes/ Partial Yes/ No	Comment
1	Research questions and inclusion criteria for the review included the components of PICO	No	Comparators were not explicitly explained (grouped with interventions)
2*	Report of the review contained an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol	Yes	Report listed deviations from the protocol Inclusion and exclusion were not explicitly stated in the methods but assessed in the results and summary provided in tables
3	Review authors explained selection of the study designs for inclusion in the review	No	The authors mentioned that they included randomized controlled trials but do not provide an explanation
4*	Review authors used a comprehensive literature search strategy	Partial yes	The authors did not apply any language restrictions. Conducted search on 27 July 2010 and published in 2012
5	Review authors perform study selection in duplicate	Yes	-
6	Review authors perform data extraction in duplicate	Yes	-
7*	Review authors provided a list of excluded studies and justify the exclusions	Yes	-
8	Review authors described the included studies in adequate detail	Partial yes	Comparators included as interventions
9*	Review authors used a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review	Yes	Risk of bias assessed using Cochrane methods
10	Review authors reported on the sources of funding for the studies included in the review.	Yes	
11*	For meta-analyses, review authors used appropriate methods for statistical combination of results	No meta-analyses conducted	Did not conduct meta-analyses
12	For meta-analyses, review authors assessed the potential impact of RoB in individual RCTs on the results of the meta-analysis or other evidence synthesis	No meta-analyses conducted	Did not conduct meta-analyses
13*	Review authors accounted for RoB in individual RCTs when interpreting/ discussing the results of the review	Yes	-
14	Review authors provided a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review	Yes	
15*	For quantitative synthesis, review authors carried out an adequate investigation of publication bias (small study bias) and discussed its likely impact on the results of the review	No meta-analyses conducted	
16	Review authors reported any potential sources of conflict of interest, including any funding they received for conducting the review	Yes	Where there was conflict of interest declared, the authors explained how funds from sponsors were used

** Critical domains = 2, 4, 7, 9, 11, 13, 15*

Rating overall confidence in the results of the review

• *High:* No or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest

• *Moderate:* More than one non-critical weakness*: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review

• *Low:* One critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest

• *Critically low*: More than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies

(*Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence).

[3] Koning S, van der Sande R, Verhagen AP, van Suijlekom-Smit LW, Morris AD, Butler CC, Berger M, van der Wouden JC. Interventions for impetigo. Cochrane Database Syst Rev. 2012 Jan 18;1(1):CD003261. doi: 10.1002/14651858.CD003261.pub3. PMID: 22258953; PMCID: PMC7025440.

[4] Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008. https://pubmed.ncbi.nlm.nih.gov/28935701/

Appendix 2: AGREE II Score Sheet - Evidence-Based Guideline: Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America[iii]

		Reviewer 1 (1 to 7 – Strongly Disagree to Strongly Agree)	Reviewer 2 (1 to 7 – Strongly Disagree to Strongly Agree)
Domain 1	**Scope and purpose**		
Item 1	The overall objective(s) of the guideline is (are) described	5	6
Item 2	The health question(s) covered by the guideline is (are) specifically described	7	7
Item 3	The population (patients, public, etc) to whom the guideline is meant to apply is specifically described	7	4
Domain 2	**Stakeholder involvement**		
Item 4	The guideline development group includes individuals from all relevant professional groups.	6	6
Item 5	The views and preferences of the target population (patients, public, etc.) have been sought.	1	1
Item 6	The target users of the guideline are clearly defined	2	3
Domain 3	**Rigour of development**		
Item 7	Systematic methods were used to search for evidence	4	3
Item 8	The criteria for selecting the evidence are clearly described	4	1
Item 9	The strengths and limitations of the body of evidence are clearly described	3	1
Item 10	The methods for formulating the recommendations are clearly described	6	5
Item 11	The health benefits, side effects, and risks have been considered in formulating the recommendations	4	1
Item 12	There is an explicit link between the recommendations and the supporting evidence	6	6
Item 13	The guideline has been externally reviewed by experts prior to its publication	4	3
Item 14	A procedure for updating the guideline is provided	7	7
Domain 4	**Clarity of presentation**		
Item 15	The recommendations are specific and unambiguous	6	5

		Reviewer 1 (1 to 7 – Strongly Disagree to Strongly Agree)	Reviewer 2 (1 to 7 – Strongly Disagree to Strongly Agree)
Item 16	The different options for management of the condition or health issue are clearly presented	6	5
Item 17	Key recommendations are easily identifiable	6	6
Domain 5	**Applicability**		
Item 18	The guideline describes facilitators and barriers to its applications	1	1
Item 19	The guideline provides advice and/or tools on how the recommendations can be put into practice	4	3
Item 20	The potential resource implications of applying the recommendations have been considered	1	1
Item 21	The guideline presents monitoring and/or auditing criteria	1	1
Domain 6	**Editorial independence**		
Item 22	The views of the funding body have not influenced the content of the guideline	4	4
Item 23	Competing interests of guideline development group members have been recorded and addressed	6	6
Overall assessment	**Assessment**		
	Rate the overall quality of the guideline	5	4
	I would recommend this guideline for use (yes/with modifications/no	Yes, with Modifications	Yes, with Modifications

Appendix 4: Evidence to decision framework

	JUDGEMENT	EVIDENCE & ADDITIONAL CONSIDERATIONS
QUALITY OF EVIDENCE OF BENEFIT	**What is the certainty/quality of evidence?** High ☐ Moderate ☐ Low ☒ Very low ☐ *High quality:* confident in the evidence *Moderate quality:* mostly confident, but further research may change the effect *Low quality:* some confidence, further research likely to change the effect *Very low quality:* findings indicate uncertain effect	The Cochrane reviews could not definitively recommend one antibiotic treatment over another for cellulitis. One comparison, cephalexin versus penicillin, showed a significant difference in the treatment of non-bullous impetigo (RR 1.31, 95% CI 1.04 to 1.64), favouring cephalexin Recommendations are based on one trial
EVIDENCE OF BENEFIT	**What is the size of the effect for beneficial outcomes?** Large ☐ Moderate ☐ Small ☒ None ☐	Overall, no significant differences in treatment effect were noted between the cephalosporins (RR 1.00, 95% CI 0.94 to 1.06). 6 trials (n=538) – only 4 included cephalexin One comparison, cephalexin versus penicillin, showed a significant difference in the treatment of non-bullous impetigo (RR 1.31, 95% CI 1.04 to 1.64), favouring cephalexin (n=1 trial). No significant differences between: • mupirocin, dicloxacillin, cephalexin & ampicillin (n=1 study) • topical mupirocin vs oral cephalexin • cephalexin and enoxacin • cephalosporins
QUALITY OF EVIDENCE OF HARM	**What is the certainty/quality of evidence?** High ☐ Moderate ☐ Low ☒ Very low ☐ *High quality:* confident in the evidence *Moderate quality:* mostly confident, but further research may change the effect *Low quality:* some confidence, further research likely to change the effect *Very low quality:* findings indicate uncertain effect	Failure rates of 1/23 for cephalexin (4%) – 1 trial Concerns around randomization, blinding and selective reporting on outcome data and other biases in the study that favoured cephalexin over penicillin.
EVIDENCE OF HARMS	**What is the size of the effect for harmful outcomes?** **L**arge ☐ Moderate ☐ Small ☐ None ☐	Unknown - Most trials did not consider adverse effects.
BENEFITS & HARMS	**Do the desirable effects outweigh the undesirable harms?** Favours intervention ☒ Favours control ☐ Intervention = Control *or* Uncertain ☐	Most likely favours intervention – as no significant differences with other oral antibiotics and topical treatments. One comparison showed that cephalexin performed significantly better in the treatment of non-bullous impetigo (*S aureus*) compared to penicillin.
THERAPEUTIC INTERCHANGE	Therapeutic alternatives available: n/a	
FEASABILITY	**Is implementation of this recommendation feasible?** Yes ☒ No ☐ Uncertain ☐	In March/April 2022 – there were some supply challenges experienced with cephalexin syrup. No supply challenges with cephalexin capsules May 2022 – no supply issues noted for cephalexin suspension or capsules

<table>
<tr><th></th><th>JUDGEMENT</th><th>EVIDENCE & ADDITIONAL CONSIDERATIONS</th></tr>
<tr><td></td><td></td><td>June 22 – supply issues on cephalexin suspension

July 2022 – No serious supply issues noted on suspension or capsules</td></tr>
<tr><td>RESOURCE USE</td><td>How large are the resource requirements?
More intensive: [ ] Less intensive: [x] Uncertain: [ ]</td><td>Price of medicines/ month
<table><tr><th>Medicine</th><th>Price (ZAR)*</th></tr><tr><td>Cefalexin; 250mg; Capsule; 20 Capsules</td><td>14.95</td></tr><tr><td>Cefalexin; 500mg; Capsule; 20 Capsules</td><td>25.88</td></tr><tr><td>Cefalexin; 125mg/5ml; Suspension; 100 ml</td><td>13.69</td></tr><tr><td>Cefalexin; 250mg/5ml; Suspension; 100 ml</td><td>22.68</td></tr></table>Medicine Procurement Catalogue – September 2022</td></tr>
<tr><td>VALUES, PREFERENCES, ACCEPTABILITY</td><td>Is there important uncertainty or variability about how much people value the options?
Minor: [ ] Major: [ ] Uncertain: [x]

Is the option acceptable to key stakeholders?
Yes: [x] No: [ ] Uncertain: [ ]</td><td>It is uncertain how people value the option. However, cephalexin is available on tender and is used in the public health sector.</td></tr>
<tr><td>EQUITY</td><td>Would there be an impact on health inequity?
Yes: [ ] No: [x] Uncertain: [ ]</td><td></td></tr>
</table>

<table>
<tr><th colspan="6">PHC/ADULT HOSPITAL LEVEL EXPERT REVIEW COMMITEE RECOMMENDATION:</th></tr>
<tr><td>Type of recommendation</td><td>We recommend against the option and for the alternative (strong)</td><td>We suggest not to use the option (conditional)</td><td>We suggest using either the option or the alternative (conditional)</td><td>We suggest using the option (conditional)</td><td>We recommend the option (strong)</td></tr>
<tr><td></td><td></td><td></td><td></td><td>X</td><td></td></tr>
<tr><td colspan="6"><u>PHC/AHL Recommendation: (29 September 2022):</u> The committee suggests that cephalexin be used for management of impetigo as a therapeutic alternative to oral flucloxacillin.
Rationale: Limited evidence showing similar efficacy to alternative antibiotics
Level of Evidence: Low
Review indicator: Completion of an updated Cochrane Review</td></tr>
<tr><td colspan="6"><u>NEMLC RECOMMENDATION: 20 OCTOBER 2022</u>
• The committee suggests that cephalexin be used for management of skin and soft tissue infections as a therapeutic alternative to oral flucloxacillin.</td></tr>
<tr><td colspan="6">Monitoring and evaluation considerations</td></tr>
<tr><td colspan="6">Research priorities</td></tr>
</table>

Version	Date	Reviewer(s)	Recommendation and Rationale
Initial	8 September 2022	MR, HD, ZA	**Cephalexin be used for management of impetigo as a therapeutic alternative to oral flucloxacillin.** *Rationale:* **Limited evidence showing similar efficacy to alternative antibiotics**

References

[i] Kilburn SA, Featherstone P, Higgins B, Brindle R. Interventions for cellulitis and erysipelas. Cochrane Database Syst Rev. 2010 Jun 16;2010(6):CD004299. doi: 10.1002/14651858.CD004299.pub2. PMID: 20556757; PMCID: PMC8693180.

[ii] Koning S, van der Sande R, Verhagen AP, van Suijlekom-Smit LW, Morris AD, Butler CC, Berger M, van der Wouden JC. Interventions for impetigo. Cochrane Database Syst Rev. 2012 Jan 18;1(1):CD003261. doi: 10.1002/14651858.CD003261.pub3. PMID: 22258953; PMCID: PMC7025440

[iii] Intravenous antibiotics (severe cellulitis and erysipelas): Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, Hirschmann JV, Kaplan SL, Montoya JG, Wade JC; Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014 Jul 15;59(2):e10-52. https://www.idsociety.org/practice-guideline/skin-and-soft-tissue-infections/

[iv] Bartoszko JJ, Mertz D, Thabane L, Loeb M. Antibiotic therapy for skin and soft tissue infections: a protocol for a systematic review and network meta-analysis. Syst Rev. 2018 Sep 11;7(1):138. doi: 10.1186/s13643-018-0804-8. PMID: 30205844; PMCID: PMC6134765.

[v] Bass JW, Chan DS, Creamer KM, Thompson MW, Malone FJ, Becker TM, Marks SN. Comparison of oral cephalexin, topical mupirocin and topical bacitracin for treatment of impetigo. Pediatr Infect Dis J. 1997 Jul;16(7):708-10. doi: 10.1097/00006454-199707000-00013. PMID: 9239775.

[vi] Demidovich CW, Wittler RR, Ruff ME, Bass JW, Browning WC. Impetigo. Current etiology and comparison of penicillin, erythromycin, and cephalexin therapies. Am J Dis Child. 1990 Dec;144(12):1313-5. doi: 10.1001/archpedi.1990.02150360037015. PMID: 2244610.