

Acne

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This presentation

- Overview of acne
- Topical management
- Conventional oral therapies
- Role of isotretinoin
- When to refer

What is acne?

- Folliculocentric inflammatory skin disease
- Characterised by polymorphic lesions
 - Non-inflamed comedones, cysts
 - Inflamed papules, pustules, nodules
 - Secondary crusting, macules, scars
- Face, neck, trunk and sometimes elsewhere

Pathogenesis

- Androgenic stimulation for sebum production
- Hyperkeratinisation of hair follicle
- Colonisation of blocked follicle with *Propionibacterium acnes*
- Free fatty acids from sebum breakdown
- Proteases from bacteria
- Inflammatory cytokines targeting bacteria

What is the role of diet?

- Remains controversial!
- Acne is rare in certain communities
- Western diet associated with higher rates of acne
- Inadequate studies indicate an association with milk and high glycaemic foods
- Stone-age diet appears of modest benefit but difficult to adhere to
- If the patient is interested in dietary measures, then recommend low-dairy, low-glycaemic index diet

Grading acne

- Grading scales available e.g., Leeds
 - These relate to inflammatory lesions on face
- Ask the patient!
 - Clinically mild acne may have serious impact
 - Clinically severe acne may not bother him/her

Mild acne:

- <20 comedones
- <15 inflammatory lesions
- Or, total lesion count <30

Moderate acne:

- 20-100 comedones
- 15-50 inflammatory lesions
- or, total lesion count 30-125

Severe acne:

- >5 cysts
- Total comedo count >100
- Total inflammatory count >50
- Or total lesion count >125

Mild acne <30 lesions



Moderate acne: 30-125 lesions



Severe acne: >125 lesions
Nodules, cysts, scars



Acne grading scales



Comedonal acne

Closed comedones



Open comedones



Inflammatory acne

Papulopustular acne



Sandpaper acne



Acne excorié

Hyperpigmentation



Hypopigmentation



Nodulocystic acne

Mixed lesions



Nodules and cysts



Acne conglobata

Draining sinuses



Crusted sores



Acne fulminans

- Severe inflammatory acne
- Fever, malaise
- Arthralgia, myalgia
- Bone pain
- Neutrophil leucocytosis



Postinflammatory changes

Erythema - weeks



Pigment - months



Acne scarring

Ice pick



Perifollicular elastolysis



Acne scarring

Hypertrophic / keloidal



Atrophic / boxcar



Management: washing

- Wash face twice daily with non-soap non-greasy cleanser
 - Examples: Cetaphil, Neutrogena, Sebamed, QV ...
- Consider cleanser containing salicylic acid or benzoyl peroxide
 - Examples: Neutrogena oil-free cleanser, Benzac Wash
 - May cause irritant dermatitis
- Role of cleansers containing antiseptic is uncertain (triclosan)
- Do not scrub, squeeze or pick spots

Management: cosmetics

- Cosmetics should be non-comedogenic
 - Sunscreens designed for facial use
 - Powder or water-based foundation
 - Avoid hair pomades
- Apply moisturiser only if skin dry
 - E.g. when provoked by treatment
 - Choose non-oily, non-irritating product

Global Alliance to Improve Outcomes

- Recommendations for management of acne 2003
- Updated 2009

Global Alliance Acne Treatment Algorithm

Acne Severity	MILD → MODERATE → SEVERE				
	Comedonal	Mixed and Papular/pustular	Mixed and Papular/pustular	Nodular(2)	Nodular/Conglobate
1 ST Choice	Topical Retinoid	Topical Retinoid + Topical Antimicrobial	Oral Antibiotic + Topical Retinoid +/- BPO	Oral Antibiotic + Topical Retinoid + BPO	Oral Isotretinoin⁽⁵⁾
Alternatives (1)	Alt. Topical Retinoid or Azelaic acid* or Salicylic acid	Alt. Topical Retinoid Antimicrobial Agent + Alt. Topical Retinoid or Azelaic Acid*	Alt. Oral Antibiotic + Alt. Topical Retinoid +/- BPO	Oral Isotretinoin or + Alt. Topical Retinoid +/- BPO/Azelaic Acid*	High Dose Oral Antibiotic + Topical Retinoid + BPO
Alternatives for Females (1,4)	See 1st Choice	See 1st Choice	Oral Antiandrogen ⁽³⁾ + Topical Retinoid/ Azelaic Acid* +/- Topical Antimicrobial	Oral Antiandrogen ⁽³⁾ + Topical Retinoid/ +/- Oral Antibiotic +/- Alt. Antimicrobial	High Dose Oral Antiandrogen ⁽³⁾ + Topical Retinoid +/- Alt. Topical Antimicrobial
Maintenance Therapy	Topical Retinoid		Topical Retinoid +/- BPO		

1. Consider physical removal of comedones. 2. With small nodules (<0.5 cm). 3. Second course in case of relapse. 4. For pregnancy, options are limited. 5. For full discussion, see Gollnick H, et al. JAAD. 2003.49 (Suppl):1-37.

Mild acne: treatment - topicals first

- Topical retinoid
- Benzoyl peroxide
- Combined products
 - Duac®
 - Epiduo®
- Salicylic acid
- Azelaic acid



How to apply topical tx for acne

- Apply to entire affected area, sparingly at first
- If irritates:
 - Wash off after 5 minutes; reapply tomorrow for one hour
 - Apply alternate days
 - Use hydrocortisone cream short-term
 - Try alternate formulation
 - Newer formulations may be better tolerated

Topical retinoids

- Tretinoin
 - ReTrieve® cream 50g 0.5mg/g
 - PHARMAC fully funded from 1 July 2010
 - Retin-A® cream 20g
 - Retinova® emollient cream 20g
- Isotretinoin
 - Isotrex® gel 30g
- Adapalene
 - Differin® gel, cream 30g
 - PHARMAC fully funded from 1 October 2010

Topical retinoids may cause irritant dermatitis: stinging, redness, dryness



Mild acne: treatment failure

- Has the patient followed the treatment plan?
- Add another topical
- Combination treatments effective, well tolerated but not funded
 - Adapalene or tretinoin + erythromycin or benzoyl peroxide

Isotretinoin if persistent, patient over 25 years, significant distress

Moderate acne: treatment – add oral

- Topical retinoids + benzoyl peroxide
- Oral antibiotic
 - Doxycycline
 - Others
- OCP
 - Combined
 - Yasmin / Yaz
 - Ginet-84 / Estelle 35 / Diane-35



Doxycycline

- Prescribe for 3 to 6 months
- Dose is usually 100 mg daily (range 50 to 200 mg)
- Take with glass water after meals, stay upright 30 minutes
- Warn re side effects:
 - Oesophagitis
 - Sunburn
 - Thrush
- Allergy is uncommon
- Warn that slow to be effective: maximum at 6-24 weeks

Hormones

- Any combined ocp may be helpful
- Ethinyl oestrodiol/cyproterone acetate ?more effective
- Ethinyl oestrodiol/drospirenone ?better tolerated
- Progesterone not helpful & may aggravate acne
 - Minipill
 - Depo Provera®
 - Mirena®

Moderate acne: treatment failure

- Is the patient following the treatment plan?
- Higher dose antibiotic
- In females, antibiotic + OCP

Isotretinoin if persistent, > 6 months tx, patient over 25 years, significant distress

Severe acne treatment: refer

- Topical retinoid + benzoyl peroxide may not be tolerated
- Oral antibiotic high dose
- Contact the dermatologist!
- These are high priority patients & will be seen quickly if your concern is communicated



Isotretinoin treatment mandatory but can be very tricky to manage!

When to refer

- If you don't feel confident to prescribe isotretinoin
- If you haven't read all the resources

- Macrocomedones
- Acne conglobata
- Acne fulminans
- Bad nodulocystic disease
- Children

Macrocomedones



Risks in children



Use in Lactation

Owing to its lipophilicity, there is a high probability that isotretinoin is secreted into the breast milk. Isotretinoin must not be given to nursing mothers.

Use in Children

Long term use in children under 13 years should be avoided because of a risk of premature epiphyseal closure.

Shared care

- Get to know your local dermatologist(s)
 - Find out if he / she is comfortable with this idea
- Dermatologist initiates treatment with isotretinoin
 - Reviews after 3 months
- When access difficult (geographic, financial), GP reviews and prescribes as required
- Good communication required
 - To manage mucocutaneous side effects
 - To determine duration of therapy

GP initiation of isotretinoin

- When criteria fulfilled
 - Moderate or persistent acne
 - Recurrent acne after previous successful course
 - Failure or long duration of standard therapy
 - GP self-assesses as adequately trained
 - Use decision support tool if you like
 - Males, or females-that-are-not-going-to-get-pregnant

What is isotretinoin used for?

Dermatologists prescribe isotretinoin for patients with acne in the following circumstances:

- Nodular or **nodulocystic acne** (i.e. where there are large deep lumps)
- **Acne conglobata** or **acne fulminans**
- Severe disfiguring inflammatory **acne vulgaris**
- Acne which is resulting in **scarring**
- Moderate acne which has failed to respond to **topical agents** combined with oral **antibiotics**, or in women, **hormonal treatment**
- Acne which relapses rapidly on discontinuing treatment
- Acne which has persisted for several years, or arises in an individual over 25 years old
- **Dysmorphophobic acne**
- When the acne has a significant adverse occupational, social or **psychological** effect on the patient's life

Isotretinoin is also useful for patients severely affected by other follicular conditions. These include:

- **Acne keloidalis nuchae**
- **Chloracne**
- **Gram negative folliculitis**
- **Hidradenitis suppurativa**
- **Oil folliculitis**
- **Pityrosporum folliculitis**
- **Pseudofolliculitis barbae**
- **Pyoderma faciale**
- **Rosacea & rhinophyma**
- **Scalp folliculitis & acne necrotica**
- **Sebaceous hyperplasia**
- **Seborrhoea**
- **Steatocystoma multiplex**

Isotretinoin has proved helpful as a second-line treatment for scaly skin conditions and other inflammatory skin diseases such as:

- **Darier disease**
- **Discoid lupus erythematosus**
- **Epidermal naevi**
- **Folliculitis decalvans**
- **Granuloma annulare**
- **Grover's disease**
- **Hidradenitis suppurativa**
- **Ichthyosis**
- **Sarcoidosis**
- **Skin cancers** especially when they arise in those with organ transplants or **xeroderma pigmentosa**

What are its registered indications?

Indications

Severe forms of nodulo-cystic acne which are resistant to therapy, particularly cystic acne and acne conglobata, especially when the lesions involve the trunk. ORATANE should only be prescribed by physicians who are experienced in the use of systemic retinoids, preferably dermatologists, and understand the risk of teratogenicity if ORATANE is used during pregnancy.



• SA0955 – Isotretinoin (1 page, 3 KB)

<http://www.pharmac.govt.nz/2010/06/01/SA0955.pdf>

Ministry of Health
Phone 0800 243 696

**APPLICATION FOR SUBSIDY
BY SPECIAL AUTHORITY**

Page 1
Form SA0955
May 2010

APPLICANT (stamp or sticker acceptable) **PATIENT NHI:** _____ **REFERRER** Reg No: _____

Reg No: _____ First Name: _____ First Name: _____

Name: _____ Surname: _____ Surname: _____

Address: _____ DCE: _____ Address: _____

_____ Address: _____

Fax Number: _____ Fax Number: _____

Isotretinoin

INITIAL APPLICATION
Applications from any relevant practitioner. Approvals valid for 1 year.

Prerequisites (tick boxes where appropriate)

Patient has had an adequate trial on other available treatments and has failed these treatments or these are contraindicated
and
 Applicant is a vocationally registered dermatologist, vocationally registered general practitioner, or nurse practitioner working in a relevant scope of practice
and
 Applicant has an up to date knowledge of the treatment options for acne and is aware of the safety issues around isotretinoin and is competent to prescribe isotretinoin
and

Patient is female and has been counselled and understands the risk of teratogenicity if isotretinoin is used during pregnancy and the applicant has ensured that the possibility of pregnancy has been excluded prior to the commencement of the treatment and that the patient is informed that she must not become pregnant during treatment and for a period of one month after the completion of the treatment
or
 Patient is male

Note:
Applicants are recommended to either have used or be familiar with using a decision support tool accredited by their professional body.

RENEWAL
Current approval Number (if known): _____
Applications from any relevant practitioner. Approvals valid for 1 year.

Prerequisites (tick boxes where appropriate)

Patient has had an adequate trial on other available treatments and has failed these treatments or these are contraindicated
and
 Applicant is a vocationally registered dermatologist, vocationally registered general practitioner, or nurse practitioner working in a relevant scope of practice
and
 Applicant has an up to date knowledge of the treatment options for acne and is aware of the safety issues around isotretinoin and is competent to prescribe isotretinoin
and

Patient is female and has been counselled and understands the risk of teratogenicity if isotretinoin is used during pregnancy and the applicant has ensured that the possibility of pregnancy has been excluded prior to the commencement of the treatment and that the patient is informed that she must not become pregnant during treatment and for a period of one month after the completion of the treatment
or
 Patient is male

Note:
Applicants are recommended to either have used or be familiar with using a decision support tool accredited by their professional body.

I confirm the above details are correct and that in signing this form I understand I may be audited.

Signed: _____ Date: _____

Post application to Ministry of Health, Private Bag 3015, Wanganui – Fax: 0800 100 131

Rules for Special Authority funding

Isotretinoin

INITIAL APPLICATION

Applications from any relevant practitioner. Approvals valid for 1 year.

Prerequisites (tick boxes where appropriate)

Patient has had an adequate trial on other available treatments and has failed these treatments or these are contraindicated

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Applicant is a vocationally registered dermatologist, vocationally registered general practitioner, or nurse practitioner working in a relevant scope of practice

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or

Patient is male

Note:

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Training for GPs

- BMJ Learning
- BPAC article
- BPAC Decision support tool

- DermnetNZ

<http://dermnetnz.org>

- Drug company information

<http://www.oratane.co.nz>

- Medsafe data sheet

<http://medsafe.govt.nz/profs/datasheet/o/oratanecap.pdf>

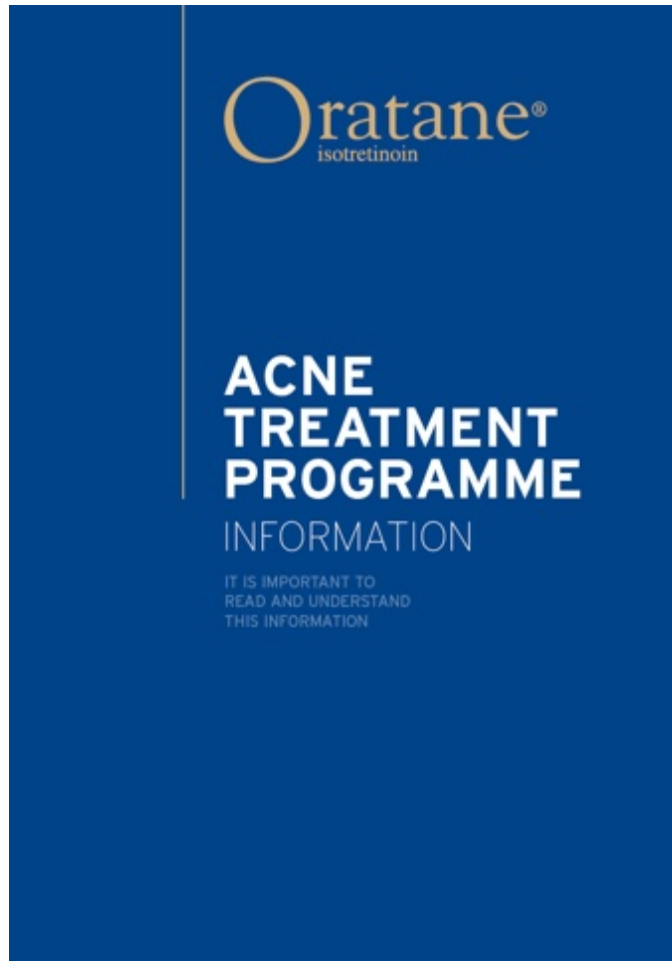
Gaining experience

- 4 years supervision for dermatology trainees
 - No independent prescribing for 6 months
 - All acne patients discussed with dermatologist
 - Consultant applies for Special Authority
- 300 acne consults / 12 mths at Waikato Hospital
 - Most patients are prescribed isotretinoin
- Equivalent training not achievable for GPs
 - Could develop acne as a subspecialty interest if >50 patients per year

Prior to treatment

- Prolonged consultation with patient
- Assess type, severity & extent of acne
- Provide written material about isotretinoin
- Discuss & arrange contraception for females
- Assess mental status & record in notes
- Arrange blood tests: CBC, LFT, lipids, beta-HCG
- Apply for Special Authority funding

Written information



FACE AND BODY MOISTURISERS



QV CREAM



QV LOTION



DRY NOSE

Face Moisturisers

Using a moisturiser on your face regularly will help keep the dryness that may be seen with Oratane treatment under control. The best type of moisturiser is an oil free face moisturiser for sensitive skin, you should avoid greasy moisturisers. Products you could try are: QV Lotion, Clinique Oil-Free Moisturiser, Hamilton Dry Skin Treatment and Avene Skin Recovery Cream.

Body Moisturisers

Body moisturisers should not be used on the face, unless they are also included in the Face Moisturisers section. To keep your skin in good condition you should use a moisturising lotion on your whole body, even if you don't seem to have any dryness, prevention is always better than cure. For extremely dry areas use a cream, rather than a lotion. Products you could try are: QV Skin Lotion, QV Cream, Hydraderm Lotion, Vaseline Intensive Care Lotion, Hamilton Dry Skin Treatment and Innoxia Sensitivity Soothing Moisture Lotion.

Dry lips

Your lips are particularly sensitive to the drying effects of Oratane. This makes it important to look after them well. This can be achieved very simply by applying a lip balm regularly.

By applying a lip balm every one to two hours you can prevent your lips from becoming dry and cracked. Make sure you also pay attention to the corners of your mouth, this area is prone to cracking. A lip balm that contains a sunscreen is best. You should carry a tube of lip balm with you during the day. You should see your local doctor if your lips become very cracked or begin bleeding.

Products you could try are:

QV Lip Balm, Vaseline Lip Therapy, Lip Sed, Blistex, Hamilton Lipz Lip Ointment and Avene Lip Balm with Cold Cream.

Dry Nose

The inside of your nose can also become dry while you are taking Oratane. If this becomes severe it can result in nosebleeds. To keep the inside of your nose moist you should apply a small amount of petroleum jelly a few times a day using a cotton bud. If you suffer from persistent nose bleeds or your nose bleeds are difficult to stop, you will need to see your pharmacist or your doctor. Severe nose bleeds can be treated with prescription products.

Dry Eyes

If you find that your eyes feel dry or sore then you may need to use eyedrops to keep them moist. Dry eyes can be a particular problem for people who wear contact lenses or people who work in air-conditioned areas. If you wear contact lenses you may find that you

<http://www.oratane.co.nz/>

Obtain consent

- Discuss birth control
- Discuss depression

CONFIRMATION OF RECEIPT OF INFORMATION ON THE TREATMENT OF SEVERE ACNE WITH ORATANE® (isotretinoin)

Female Patients

I understand that I must not be pregnant in order to start this medicine. I understand that I must not become pregnant while being treated with Oratane and for one month after the end of Oratane treatment.

I understand the risks associated with becoming pregnant while on Oratane as explained by my dermatologist. I am aware that significant harm may be caused to my unborn baby should it be exposed to Oratane during pregnancy.

As a precaution I agree to undergo a pregnancy test if necessary and have my doctor confirm that I am not pregnant immediately before starting treatment with Oratane.

I am aware that methods to avoid pregnancy are absolutely essential during my treatment on Oratane. The safest option is an oral contraceptive plus a barrier. If there is any risk that pregnancy may have occurred, I agree to consult my specialist or GP to discuss the need for emergency contraception.

I agree to avoid the possibility of pregnancy for one month before commencing treatment with Oratane, during the whole period of treatment and for one month after completion of treatment. Should I become pregnant, I agree to inform my doctor immediately.

All Patients

I understand that I must not give Oratane to any other person.

I understand that while Oratane may help my skin, it may cause a number of side effects that have been explained to me.

I understand that this medicine may give rise to mood changes. I agree to inform my doctor immediately if I start to feel unhappy or depressed on this medicine.

I confirm that I have been fully informed of the above by:

Doctor: _____

Patient Name: _____

Patient or Guardian Signature: _____

Date of Birth: ____ / ____ / ____ Today's Date: ____ / ____ / ____

Address: _____

Don't use isotretinoin if:

- Pregnancy test positive
- Unmanaged depression
- Unexpected systemic disease
 - E.g. infectious mononucleosis
- Hypertriglyceridaemia >6 mmol/L
- Uncontrolled eczema / dry eyes / nosebleeds etc
- Patient is a pilot – contact Civil Aviation Authority

The teratogenic risks of isotretinoin

If pregnancy occurs either during treatment with isotretinoin or in the month following the end of treatment with isotretinoin there is a great risk of very severe and serious malformation of the foetus.

The foetal malformations associated with exposure to isotretinoin include:

- central nervous system abnormalities (hydrocephalus, cerebellar malformation/ abnormalities, microcephaly)
- facial dysmorphia
- cleft palate
- external ear abnormalities (absence of external ear, small or absent external auditory canals)
- eye abnormalities (microphthalmia)
- cardiovascular abnormalities (conotruncal malformations such as tetralogy of Fallot, transposition of great vessels, septal defects)
- thymus gland abnormality and parathyroid gland abnormalities.

There is also an increased incidence of spontaneous abortion.

Psychiatric side-effects

Depression, aggravation of existing depression, aggressive tendencies, anxiety, and changes in mood have been reported rarely in patients taking isotretinoin (i.e. occurring in one or more of every 10,000 patients, but in fewer than one in every 1,000 patients); abnormal behaviour, psychotic disorder, suicidal ideation, suicide attempt, and suicide have been reported very rarely (ie, in one in every 10,000 patients or fewer).

When to follow up?

- One to three months
- Consider:
 - Patient's character
 - Acne severity
 - Comorbidities
- Always provide a phone number and see patient face to face if there are any concerns
- Train nurse to field calls

What dose?

- 0.1 to 1 mg/kg/day
 - 5 – 60 mg/day for 60kg adult
- Low doses are often effective
 - Start 10-20 mg/day and build up if required
 - Tolerance varies
- Higher doses advocated by many
 - Quicker results
 - Higher long term cure rates
 - Reduced pregnancy-risk

For how long?

- 100-150 mg/kg
 - 125 days at 1 mg/kg
 - 1250 days at 0.1 mg/kg
 - 20-30% relapse
- Individualise
 - Until clearance + some
 - Stop and start again if necessary
 - Long term in adult acne



Additional treatment

- Contraception
- Antibiotics if very inflammatory
 - Not tetracyclines
 - Erythromycin / trimethoprim
- Emollients

Acne getting better

- Great !
 - Keep dose same
 - Reduce dose or frequency
 - Eventually stop ...



Acne unchanged

- Why?
 - Noncompliance
 - Underlying cause
- Keep dose same: patience!
- Increase dose: quicker response



Acne getting worse

- Why?
 - Underlying cause
 - Herxheimer response
- Reduce dose or stop
- Add antibiotic
- Call for help
- May require systemic steroids



Dry or cracked lips

- Lip balm ++
- Sunscreen
- Don't lick
- Topical antibiotic to angles of mouth & nostrils: 7-day course



Dry or watery eyes

- Wrap-around sunglasses outdoors
- Reduce wearing contact lenses
- Artificial tears
 - Ocular lubricant eg Poly-Tears™



Dry and sensitive skin

- Soapless cleanser
- Regular emollient at least bd
- Careful sun protection
- Don't wax
- For retinoid dermatitis: mild topical steroid for a few days



Muscles, joints and fatigue

- Mild – reassure
- Moderate – reduce dose
- Sometimes, reduce exercise

Headache

- Mild: drink more fluids; may take paracetamol
- Moderate: reduce dose
- Severe: examine for papilloedema & stop isotretinoin
- Ensure patient is not taking additional vitamin A or tetracycline

Contraception

- Combined ocp or IM progesterone + condoms
- IUD, Mirena + condoms
- Vasectomy / tubal ligation
- Abstention

- Not minipill (progesterone-only) reduced efficacy

Depression

- Grumpiness & tiredness common in isotretinoin patients
- Depression usually pre-existing or due to other causes
- Stop isotretinoin if any doubt – try again later
- Treat depression as you would normally

What to do if ... eczema

- Treat eczema first
 - No soap
 - Thick emollients
 - Topical steroids
 - Antibiotic if necessary
- Warn patient will require more emollient and skin will be more sensitive
- Eczema is sometimes **BETTER** on isotretinoin because of its immunosuppressive action



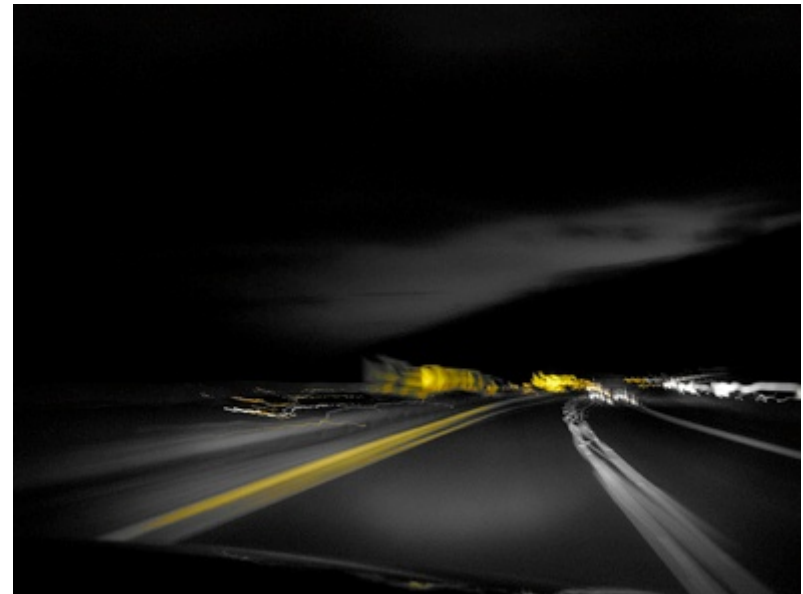
What to do if ... Staph infection

- Topical antiseptic if mild and localised
- Topical antibiotic if moderate and localised
- Flucloxacillin if required



What to do if ... drives at night

- Warn that some individuals lose night vision as retinoids interfere with rods
- Some people have to make a choice: isotretinoin or driving



Relapse

- Start again
- Consider options
- Most patients will choose another course of isotretinoin but some prefer topicals and a few want antibiotics

Long term treatment

- Required for
 - Adult acne – mainly women
 - Seborrhoea
 - Follicular occlusion syndrome
 - Dysmorphophobia
- Adjust dose to minimum
- Re-evaluate every 6 months
 - Blood tests if risk factors for complications