

Emerging Therapies for Psoriasis

19th May 2011 – North West Region

Presented by:

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Agenda

- Overview of psoriasis
 - Psoriasis treatments
 - How to measure psoriasis severity
 - Biologic therapy and safety
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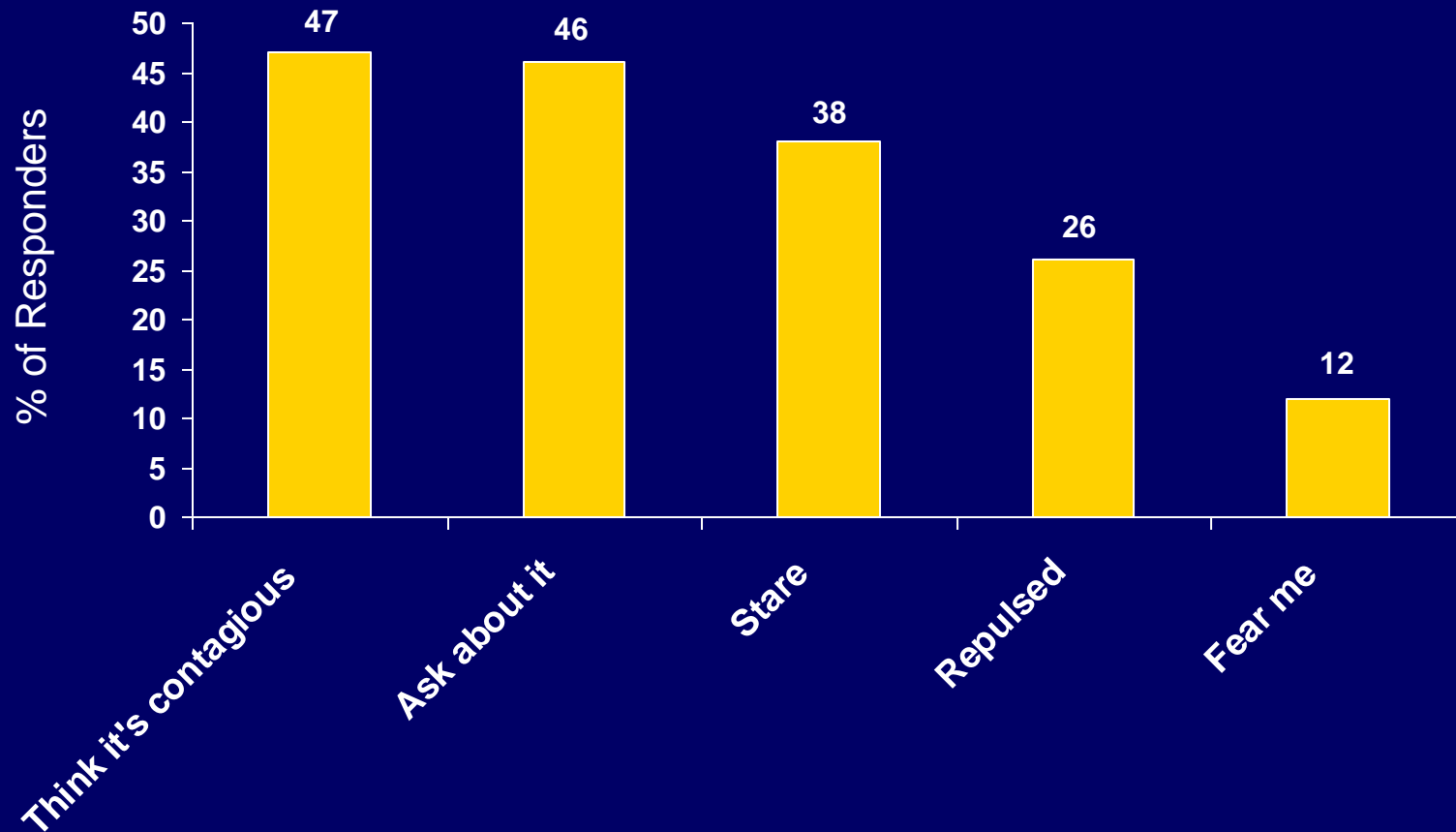
Overview of Psoriasis



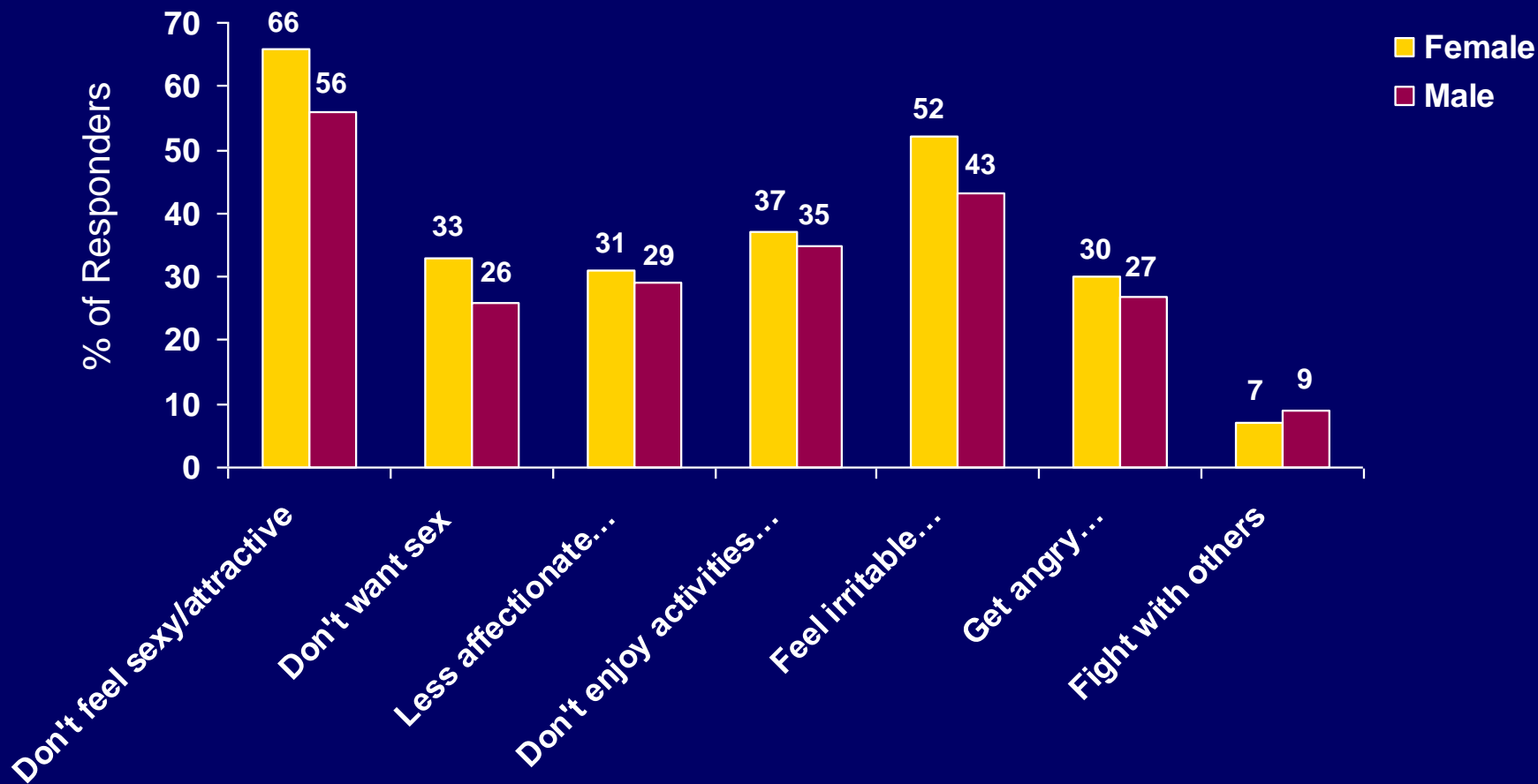
“Because of its high visibility, psoriasis results in a significant impact on quality of life, with social and psychological consequences in addition to the physical signs and symptoms”

A/Prof Peter Foley, Dermatologist

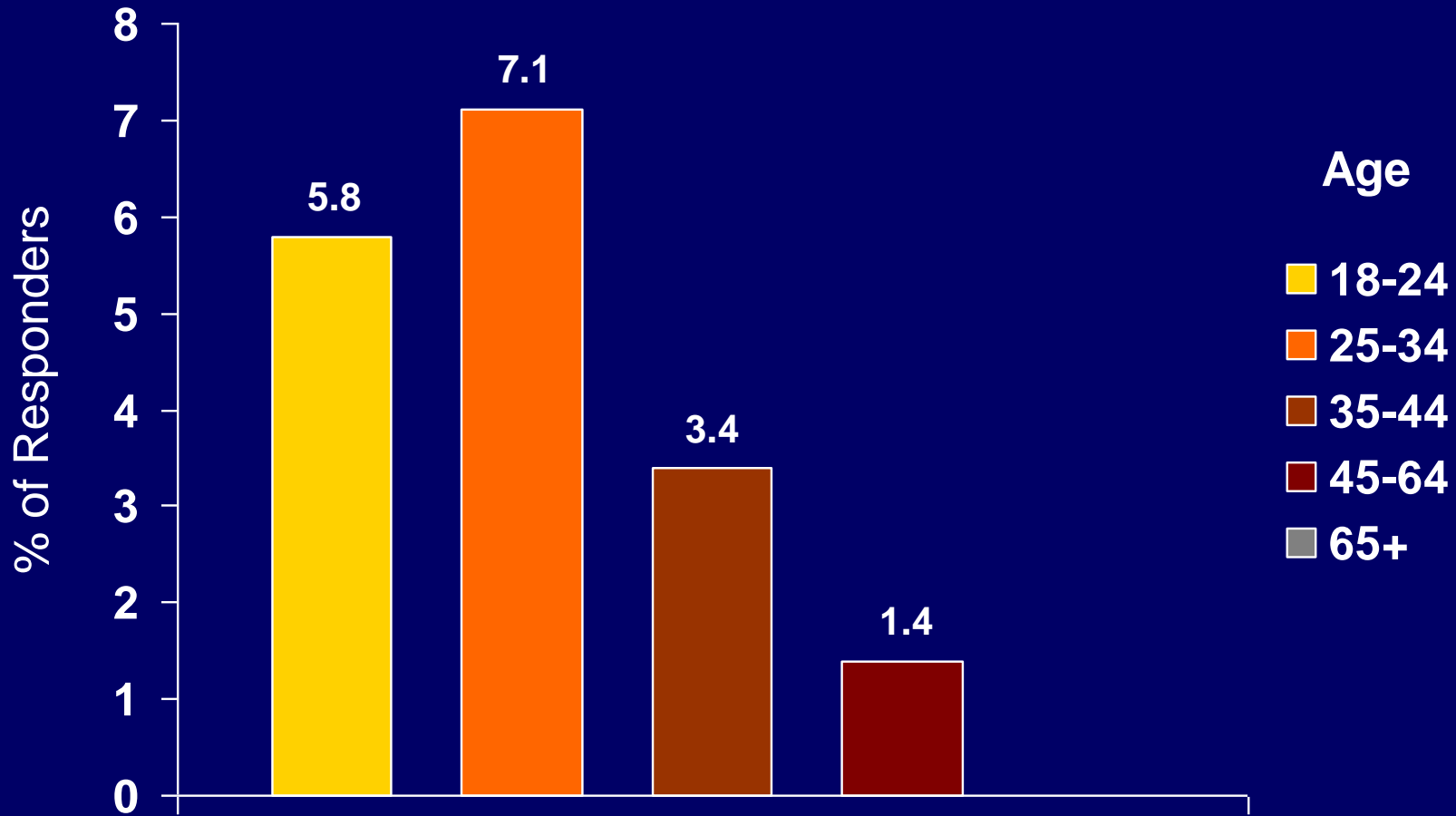
Australian Survey: What is the response of the general public to your psoriasis¹?



Australian Survey: In which of these ways does psoriasis impact on your relationships¹?

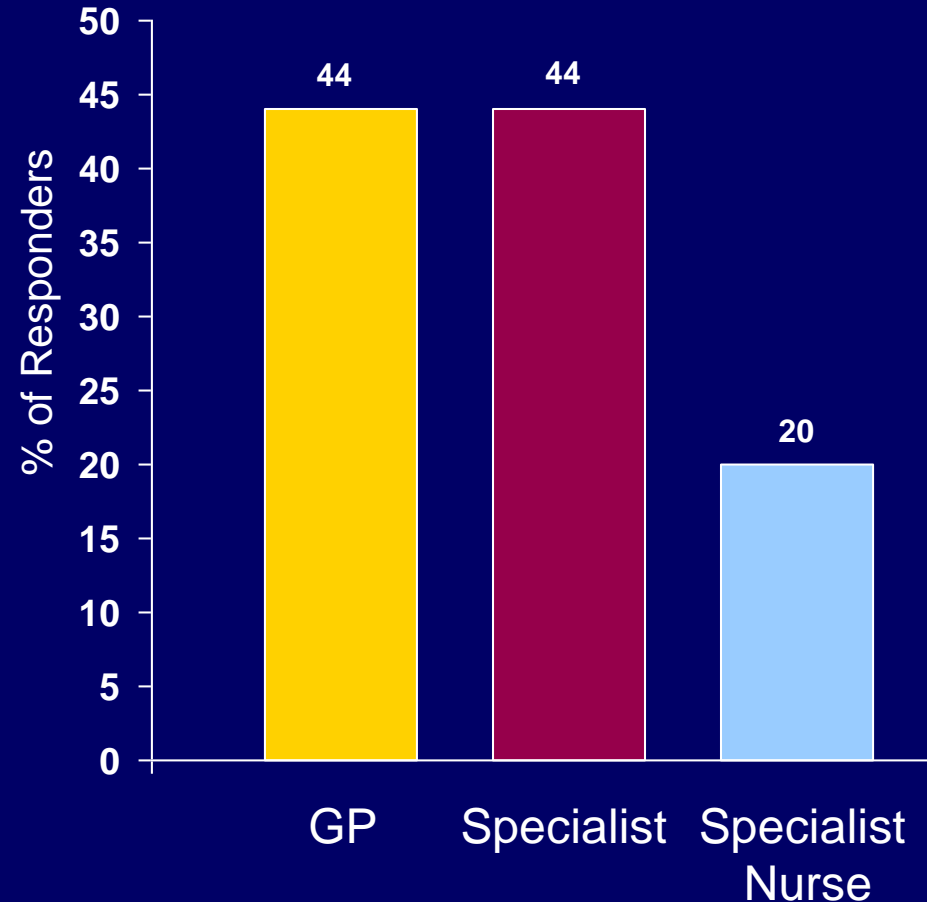


Australian Survey: How many days are missed from work/study per year because of your psoriasis¹?



Where Australian psoriasis patients seek medical help¹

“Most patients are reasonably satisfied with the medical treatment they are receiving although there is the strong suggestion that they would like their medication to work better and their healthcare professional to know a bit more about their condition²”



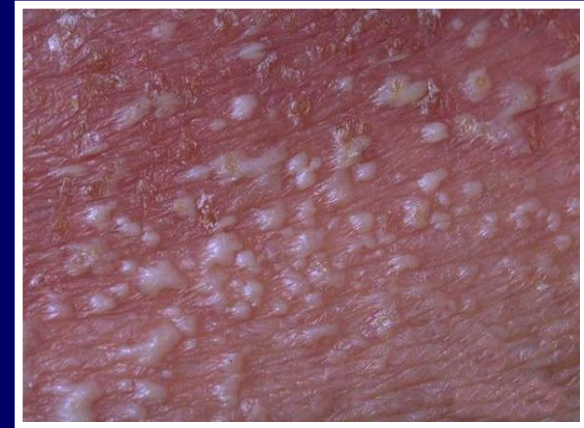
Types of Psoriasis



Plaque Psoriasis



Erythrodermic Psoriasis



Pustular Psoriasis



Guttate Psoriasis



Inverse Psoriasis

Psoriasis Overview

- Psoriasis is an autoimmune condition resulting from chronic activation of the immune system
- Activation of the immune system results in an excess of keratinocytes that mature at a rapid rate
- Usually the skin takes approx. 28 days to renew itself, in patients with psoriasis it only takes ~3-4 days.
- This causes the signs and symptoms characteristic of Psoriasis:
 - Redness
 - Thickened skin
 - Scaling



Psoriasis Overview

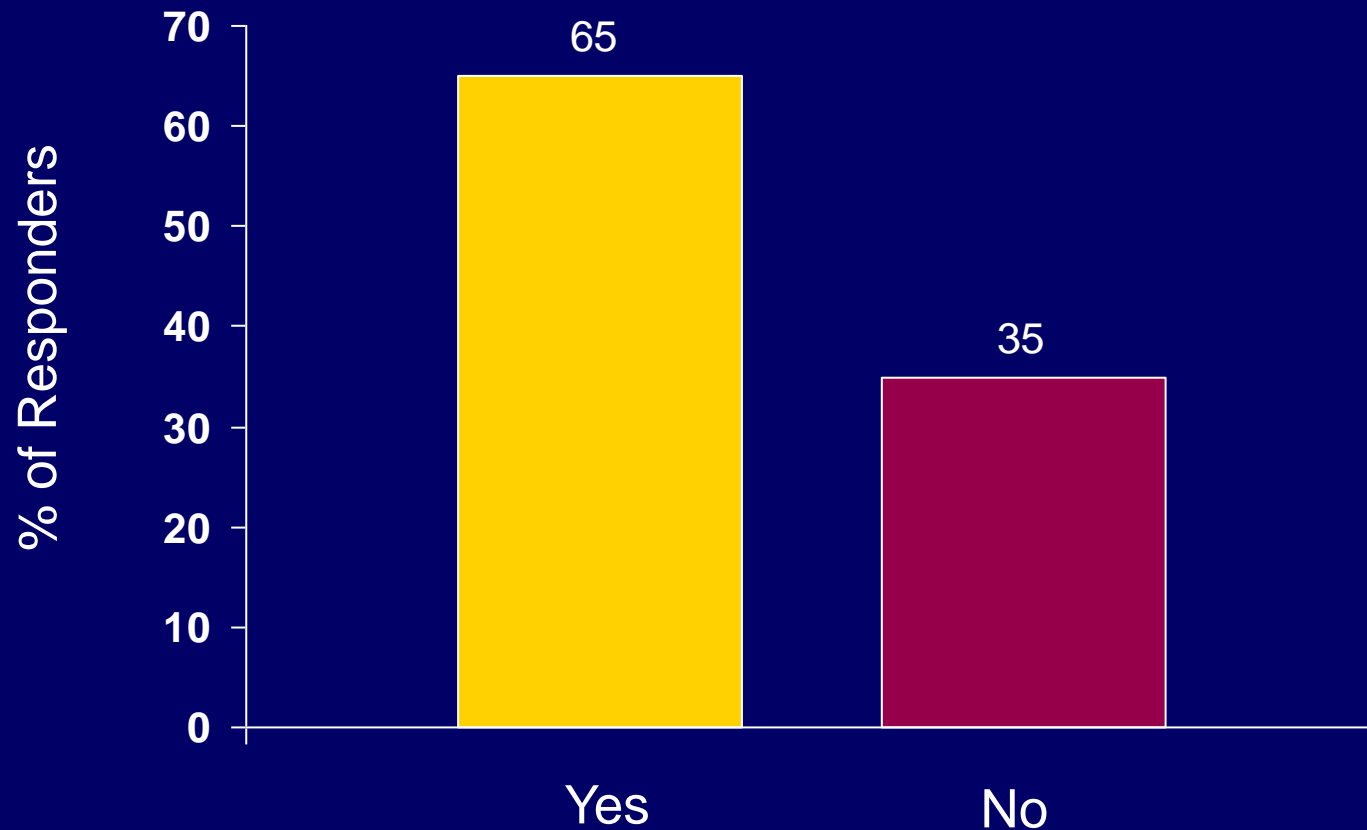
- Occurs most commonly in late teens or early 50's
- Most common type of psoriasis is plaque psoriasis¹
- Prevalence in Australia is 1-3%²
- Possible genetic association – family history¹
- Up to 30% of patients with Psoriasis can develop Psoriatic Arthritis (PsA)³
- In 75% of cases, psoriasis precedes the joint disease in PsA⁴



Psoriatic Arthritis Radiograph Appearance



Australian Survey: Do you suffer from pain and stiffness in your joints¹?



Psoriasis - Flares

- Once Psoriasis is established, disease flares can be triggered by a number of factors including:
 - Stress
 - Climate
 - Skin trauma
 - Viral infections, including HIV
 - Smoking
 - Alcohol

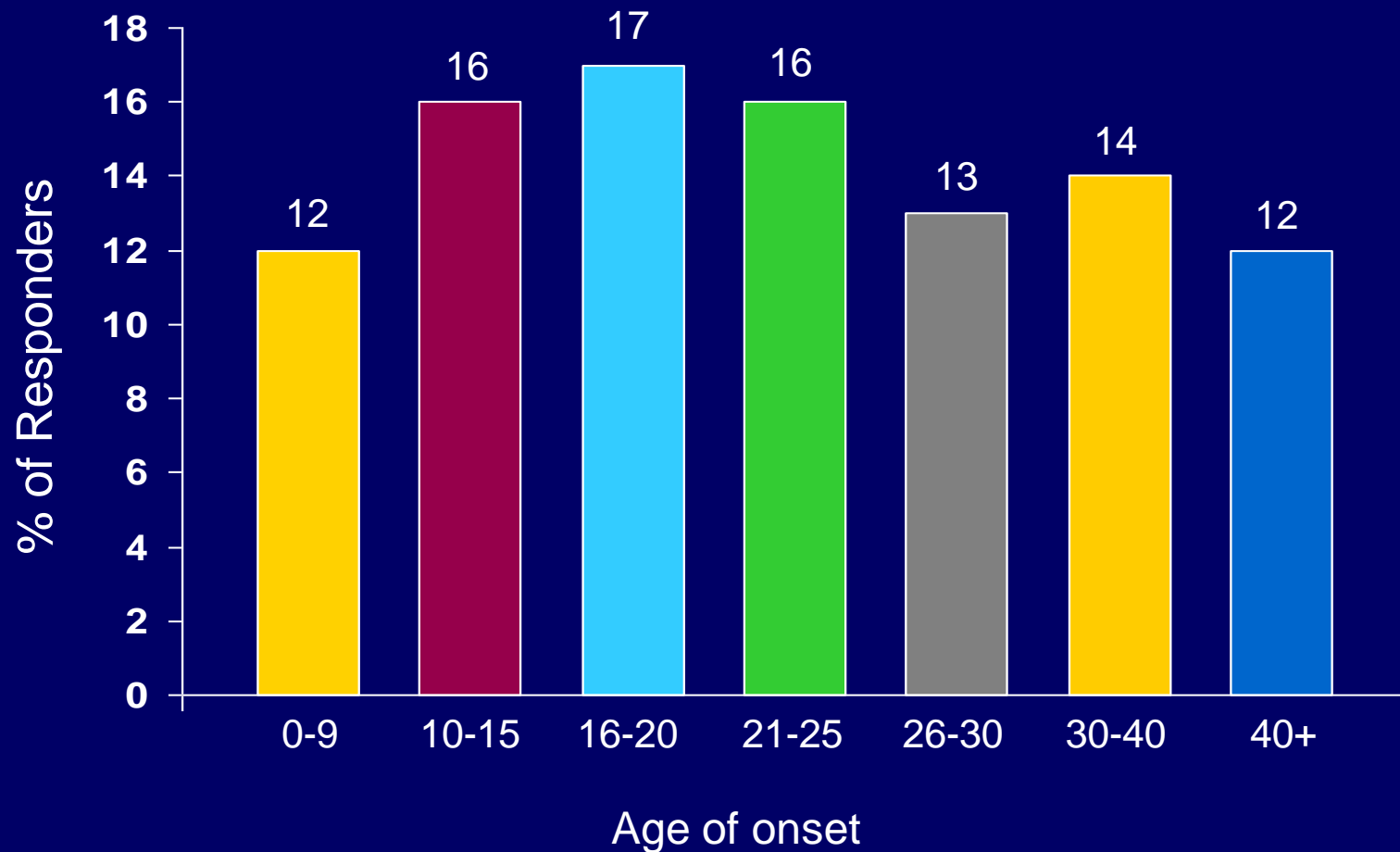
Psoriasis Co-morbidities

- PsA
 - obesity
 - hypertension
 - diabetes
 - hyperlipidemia
 - metabolic syndrome
 - cardiovascular disease
 - Crohn's disease
 - lymphoma
 - multiple sclerosis
 - increased mortality
- } immunopathogenic
-
- smoking
 - alcoholism
 - anxiety
 - depression
- } psychosocial

Cardiovascular Disease and Mortality

- Severe psoriasis and early age of onset is associated with increased risk for cardiovascular death¹.
- Patients with severe psoriasis have a 50% increased risk of mortality².
- Male and female patients with severe psoriasis died 3.5 and 4.4 years younger than the general population².

Age of onset for psoriasis in Australia¹



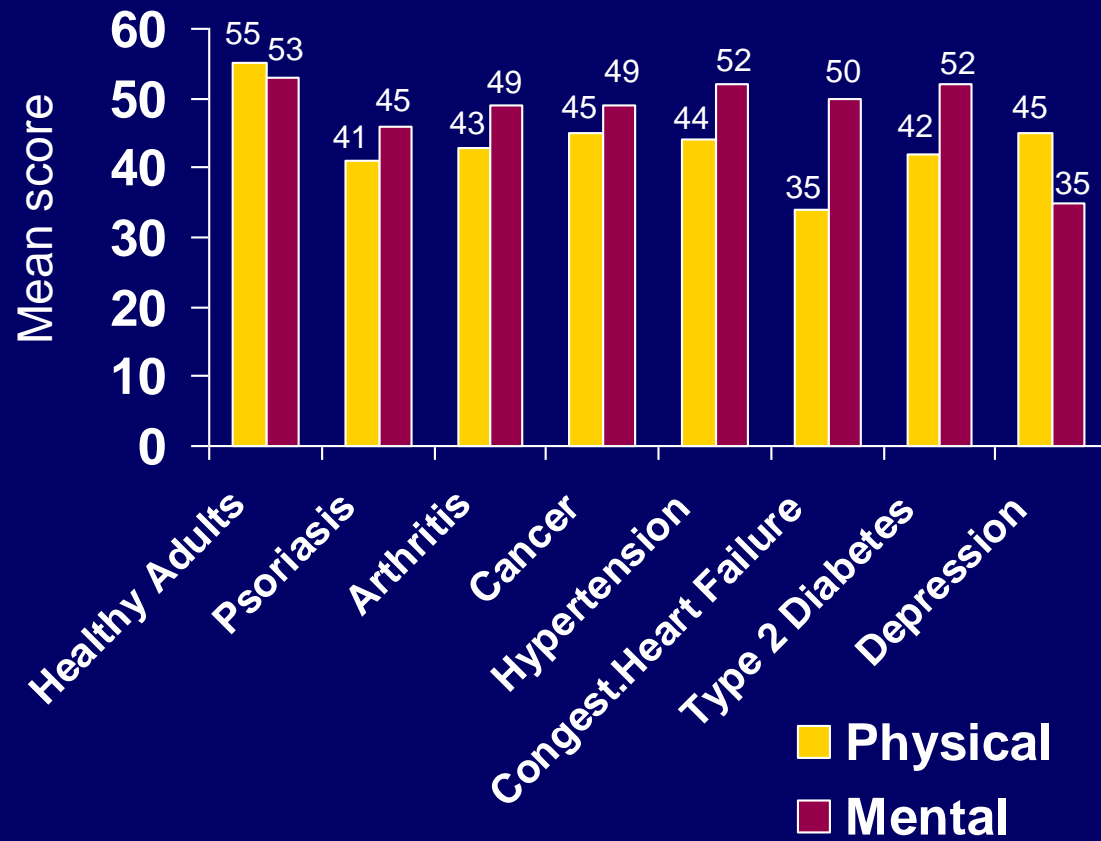
¹ Psoriasis Uncovered: What is it like to have psoriasis? By Stollznow Research for Psoriasis Australia and Abbott Australasia, October 2010, pg 54

Depression and Suicidality

- Psoriasis can have a substantial emotional impact, which is not always related to the extent of skin disease¹.
- The prevalence of depression in patients with psoriasis may be as high as 60%².
- Depression may be severe enough that some patients will contemplate suicide:
 - In one study of 217 patients with psoriasis, almost 10% reported a wish to be dead and 5% reported active suicidal ideation³.

Burden of Disease

- Psoriasis patients reported reduction in physical and mental functioning comparable to that seen in cancer, arthritis, hypertension, heart disease, diabetes and depression



Psoriasis Treatments



Evolution of psoriasis therapies



Four Major Types of Treatment

- Topical therapies
- Phototherapy
- Systemic therapies
- Biologic therapies

Topical Therapies

- Corticosteroids
- Vitamin D analogues
- Retinoids
- Coal tar
- Dithranol

Phototherapy

■ UVB

- Narrowband ultraviolet B radiation

■ PUVA (photochemotherapy)

- Ultraviolet A combined with light-sensitising drug psoralen

Systemic immunosuppressive therapies

- Methotrexate

- Acitretin

- Cyclosporin

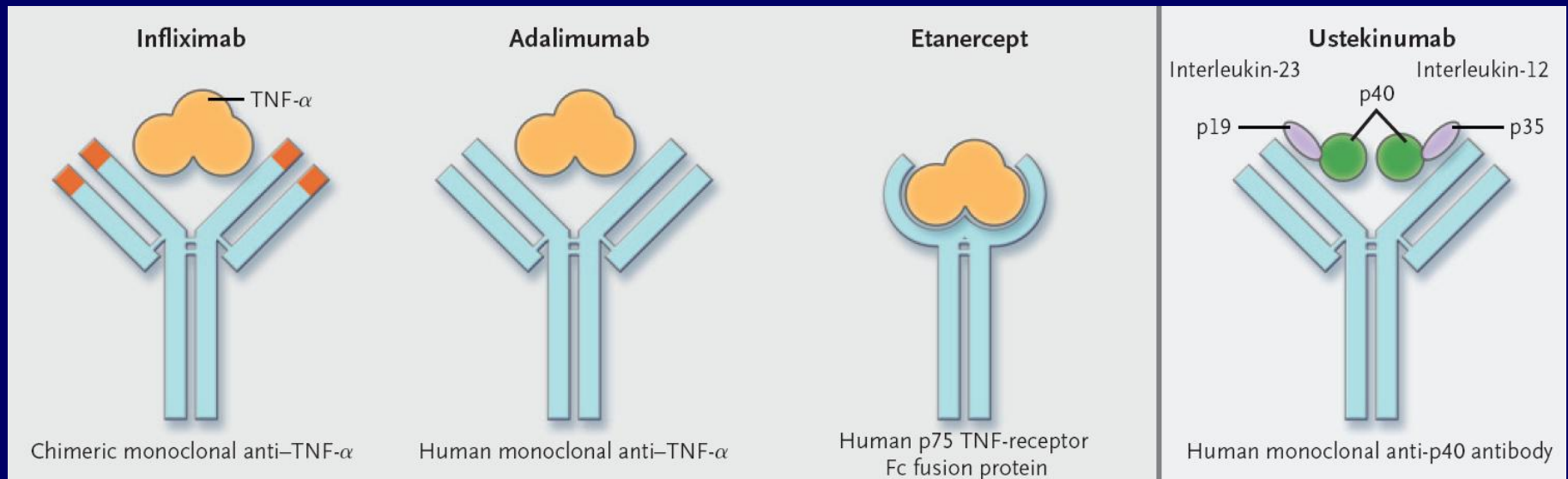
Biological agents

Remicade

Humira

Enbrel

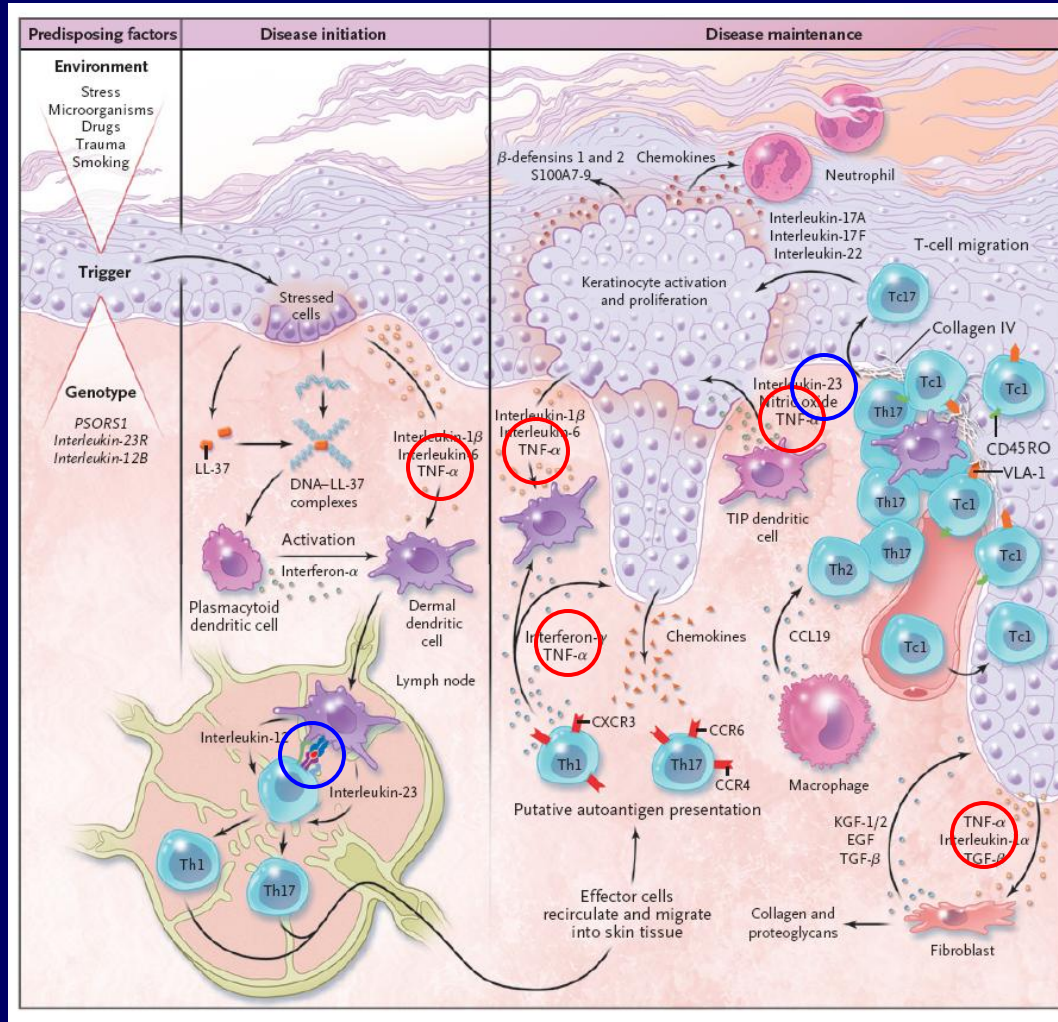
Stelara



Anti-TNF

Anti-IL12/23

Biologic agent mechanism of action in the pathogenesis of psoriasis



Biological Agents in Psoriasis

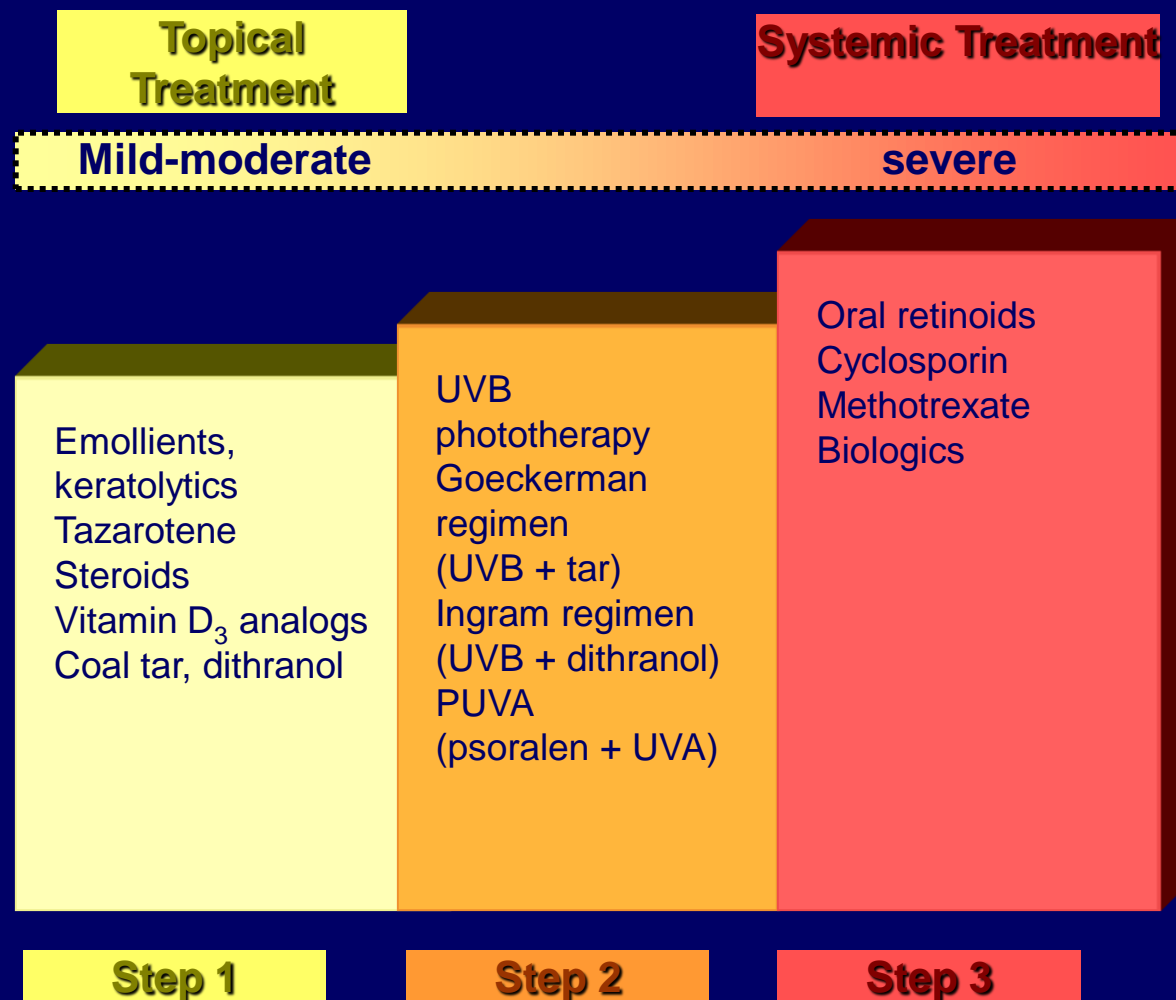
Agent	Dose	t 1/2	PASI 75	Experience*	Indications
Adalimumab	40 mg fortnightly	10-20 days	71 % (week 16)	9 years	Ps, RA, AS, PsA, JIA CD
Etanercept	25 mg Biweekly or 50mg weekly	3.3 days	55 % (week 24)	13 years	Ps, RA, AS, PsA, JIA
Infliximab	5 mg 8 weekly	8 - 9.5 days	80 % (week 10)	13 years	Ps, RA, AS, PsA, CD, UC, FCD, PCD
Ustekinumab	45 mg 12 weekly, 90 mg in patients > 100kg	15-32 days	67 % (45mg) 66% (90mg) (week 12)	3 years	Ps

*Experience based on time since product registration including all indications

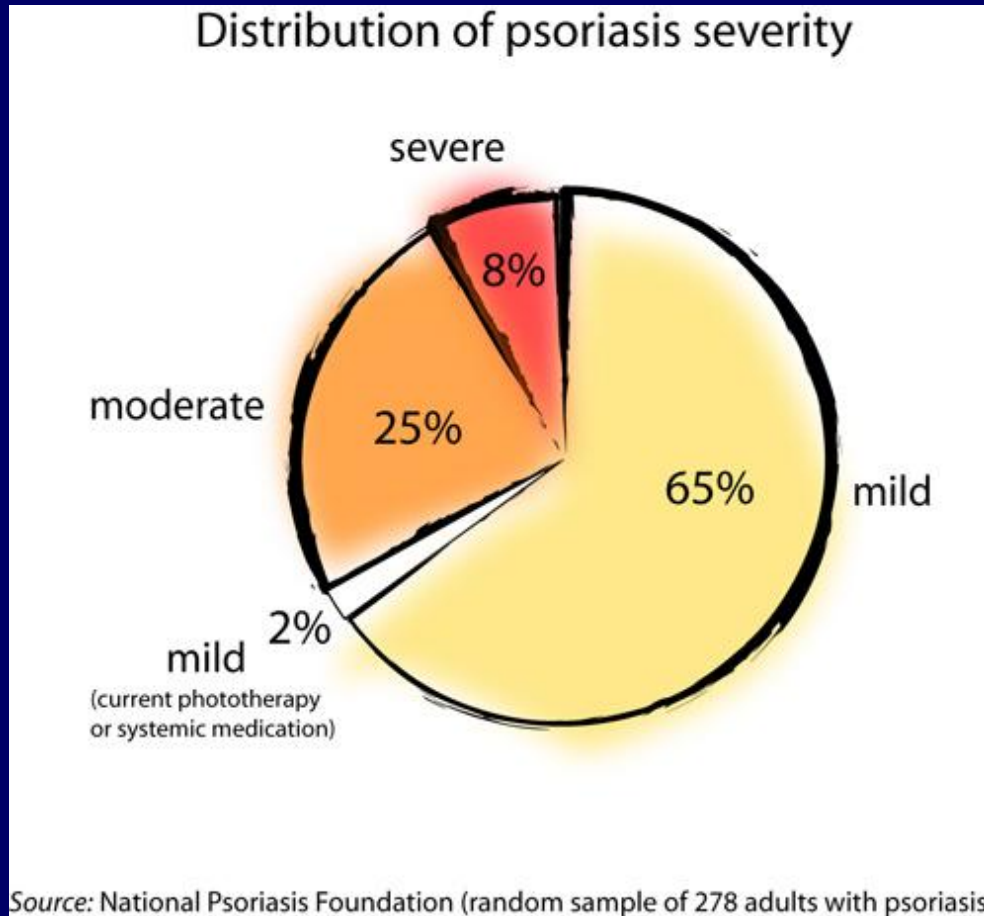
Based on data from REVEAL, Papp et al., 2005, EXPRESS, PHOENIX I, Etanercept Product Information, v CDS28.0; Infliximab Product Information, v 16, Ustekinumab Product Information, v CCDS090217

Ps = psoriasis, RA = Rheumatoid Arthritis, AS = Ankylosing Spondylitis, PsA = Psoriatic Arthritis, JIA = Juvenile Idiopathic Arthritis, CD = Crohn's Disease, UC = Ulcerative Colitis, FCD = Fistulising Crohn's Disease, PCD = Paediatric Crohn's Disease,

Escalation or 3-Step Strategy



Distribution of psoriasis severity



Australian population 22.5 million¹

Approx 2 % have psoriasis²
(450,000 people)

Approx 8% have severe psoriasis
(36,000 people)

¹ Australian Bureau of Statistics, ²Raychaudhuri et al., JEADV 2001; 15:20-23.

How to measure psoriasis severity

Psoriasis assessment tools

- BSA: Body Surface Area
- DLQI: Dermatology Life Quality Index
- PASI: Psoriasis Area and severity Index
- 'Rule of Tens' for moderate to severe psoriasis:
 - BSA >10% *or*
 - PASI >10 *or*
 - DLQI >10

Measuring psoriasis severity with PASI

- PASI is a composite score to evaluate severity of Psoriasis and assess treatment efficacy
- Measures body surface area (BSA) and redness, thickness and scaling of Psoriasis
- Calculates score between 0 – 72 (higher PASI = more severe)



PASI Score = 28.7

PASI – How is it calculated?

- severity of symptoms (erythema, scaling and induration) are classified using the following scale:

Score	Grade
0	None
1	Mild
2	Moderate
3	Severe
4	Very severe

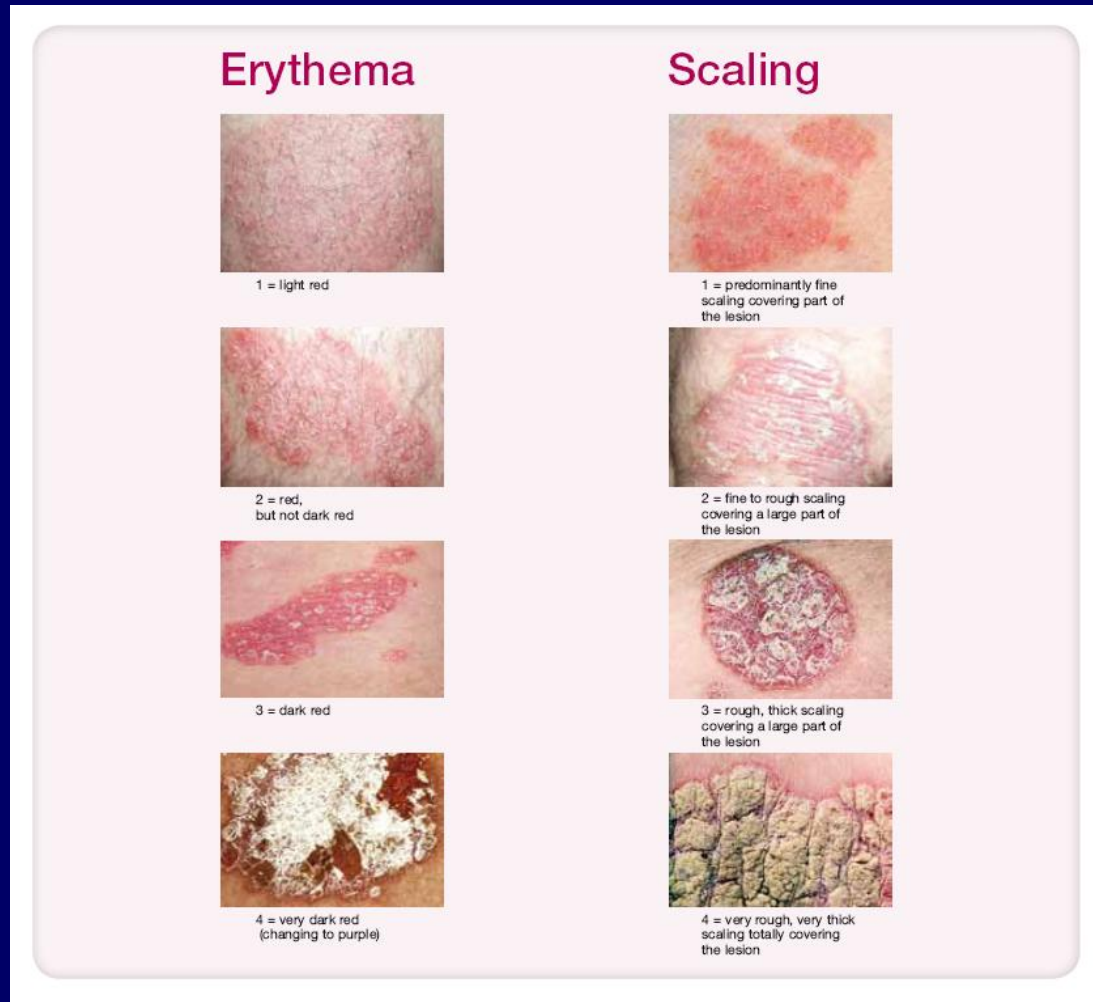
Fredriksson T, Pettersson U, severe psoriasis: oral therapy with a new retinoid. *Dematologica*. 1978;157(4):238-288.

Marks R, Barton SP, Shuttleworth D, Finlay AY. Assessment of disease progress in Psoriasis. *Arch Dermatol*. 1989 Feb;125(2):235-240.

Feldman SR, Krueger GG. Psoriasis assessment tools in clinical trials. *Ann Rheum Dis*. 2005;64(Suppl II):ii65-ii68.

Long CC, Finlay AY, Averill RW. The rule of hand: 4 hand areas = 2 FTU = 1 g. *Arch Dermatol*. 1992;128:11-30.

Visual scales to measure psoriasis severity



Fredriksson T, Pettersson U, severe psoriasis: oral therapy with a new retinoid. *Dematologica*. 1978;157(4):238-288.

Marks R, Barton SP, Shuttleworth D, Finlay AY. Assessment of disease progress in Psoriasis. *Arch Dermatol*. 1989 Feb;125(2):235-240.

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PASI – How is it calculated?

- The extent to which each of the four areas of the body (head, upper extremities, trunk and lower extremities) are affected by psoriasis is assessed according to the following scale:

Score	Grade
0	None
1	1% to 9%
2	10% to 29%
3	30% to 49%
4	50% to 69%
5	70% to 89%
6	90% to 100%

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The “hand method”

- One hand corresponds to approximately:
 - 10% of the head
 - 5% of the arm
 - 3.3% of the trunk
 - 2.5% of the lower extremities



PBS Forms for PASI calculation

A Psoriasis Area and Severity Index (PASI) is a quantitative rating scale for measuring the severity of psoriatic lesions based on area coverage and plaque appearance

Plaque characteristic	Rating score	Body region (and weighting factor)			
		Head	Upper Limbs	Trunk	Lower Limbs
Erythema	0 = None 1 = Slight				
Thickness	2 = Moderate 3 = Severe				
Scaling	4 = Very severe				
Add together each of the 3 scores for each of the body regions to give 4 separate sub totals.					
Sub Totals		A1=	A2=	A3=	A4=
Multiply each sub total by amount of body surface area represented by that region i.e. A1 x 0.1 for head, A2 x 0.2 for upper limbs, A3 x 0.3 for trunk, A4 x 0.4 for lower limbs to give a value B1, B2, B3 and B4 for each body region respectively					
		A1 x 0.1 = B1	A2 x 0.2 = B2	A3 x 0.3 = B3	A4 x 0.4 = B4
		B1=	B2=	B3=	B4=
Degree of involvement as % for each body region affected (score each region with score between 0-6)	0 = None 1 = 1-9% 2 = 10-29% 3 = 30-49% 4 = 50-69% 5 = 70-89% 6 = 90-100%				
For each body region multiply sub total B1, B2, B3 and B4 by the <u>score</u> (0-6) of the % of body region involved to give 4 subtotals C1, C2, C3 and C4					
		B1 x score = C1	B2 x score = C2	B3 x score = C3	B4 x score = C4
		C1=	C2=	C3=	C4=
The patient's PASI score is the sum of C1 +C2+C3+C4				PASI=	

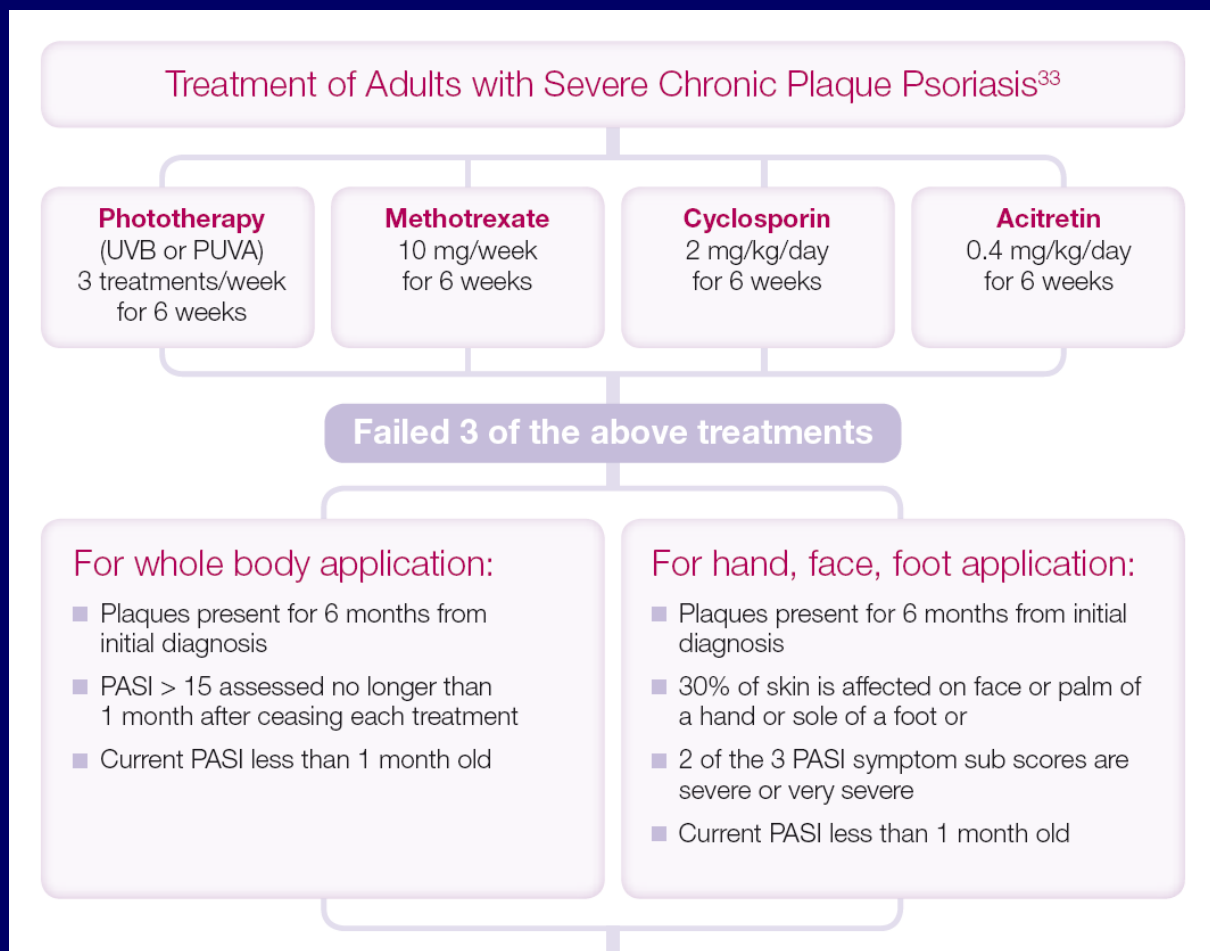
Efficacy standards for biologic therapy



Reduction of at least 75 % in PASI score or **PASI 75** is considered the **gold standard** in biologic trials¹

¹ www.australiandoctor.com.au 19-02-2010; Menter A et al. J Am Acad Dermatol 2008;58:826–50; .

PBS criteria for biologic therapy eligibility



Biologic therapy and Safety

Biologic therapy and safety – Infections

- Infections may also occur as the immune system is suppressed
 - Patients should be advised to be vigilant with seeking treatment at the first sign of infection e.g. common cold
 - Patients who develop a new infection should be monitored closely and undergo a complete diagnostic evaluation.
 - Therapy should be discontinued if a patient develops a new serious infection or sepsis, and appropriate antimicrobial or antifungal therapy should be initiated.

Biologic therapy and safety– injection site reactions

- Injection site reactions are the most common side effect
 - May present as redness and/or itching, bleeding, pain or swelling.
 - Most reactions are mild and do not result in discontinuation
 - Cold press applied to site before injection can reduce reactions

British Association of Dermatology Biologic Guidelines 2009

Live Vaccinations:

- Patients should not receive live or live attenuated vaccinations, less than 2 weeks before, during, and for 6 months after discontinuation of, biologic therapy

Surgery:

- Until there is more evidence availableTNF antagonists should be discontinued at least four half-lives prior to major surgery
- Biologic therapy can be restarted postoperatively if there is no evidence of infection and wound healing is satisfactory

British Association of Dermatology Biologic Guidelines 2009

- Biologic eligibility: severe disease PASI > 10
- TNF antagonists recommended as 1st line intervention for patients fulfilling criteria for treatment with biologic therapy
- For stable plaque psoriasis: adalimumab and etanercept may be considered 1st choice based on favourable risk/benefit profile and ease of administration.
- For rapid disease control: adalimumab or infliximab may be considered due to early onset of action
- For patients who don't respond to their 1st anti-TNF, a 2nd anti- TNF agent may be considered
- Due to the lack of patient-years exposure and long-term safety data, ustekinumab should be reserved as a 2nd line biologic where TNF-therapy has failed or can't be used

PLEASE REVIEW FULL PRODUCT INFORMATION BEFORE PRESCRIBING. Full Product Information is available on request from Abbott Australasia Pty Ltd. ABN 95 000 180 389. 32-34 Lord Street, Botany NSW 2019, or on the TGA website. **Indications: Rheumatoid Arthritis (RA):** Reducing signs & symptoms, and inhibiting structural damage, in adults with moderate to severely active RA; including patients with recently diagnosed moderate to severely active disease who have not received methotrexate. Humira can be used alone or in combination with methotrexate. **Polyarticular Juvenile Idiopathic Arthritis (pJIA):** Humira in combination with methotrexate is indicated for reducing the signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients aged 4 years of age and older. Humira can be given as monotherapy in case of intolerance or when continued treatment with methotrexate is inappropriate. **Psoriatic Arthritis (PsA):** Treatment of signs and symptoms, as well as inhibiting the progression of structural damage, of moderate to severely active PsA in patients where response to previous DMARDS has been inadequate. **Ankylosing Spondylitis (AS):** Reducing signs and symptoms in patients with active AS. **Crohn's Disease (CD):** Treatment of moderate to severe CD in adults to reduce the signs and symptoms of the disease and to induce and maintain clinical remission in patients who have had an inadequate response to conventional therapies, or who have lost response to or are intolerant of infliximab. **Psoriasis:** Treatment of moderate to severe chronic plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. **Contraindications:** Severe infections including sepsis, active TB, opportunistic; concurrent anakinra; moderate to severe heart failure. **Precautions:** Infections (bacterial, mycobacterial, invasive fungal e.g. histoplasmosis, viral or other opportunistic); hepatitis B, latent TB; demyelinating disorders; haematologic events; live vaccines; immunosuppression; new or worsening CHF; renal, hepatic impairment; malignancy; hypersensitivity reactions; latex sensitivity; concurrent abatacept; elderly; pregnancy, lactation, surgery. **Adverse Reactions:** Respiratory tract infections, leucopaenia, anaemia, headache, abdominal pain, nausea and vomiting, elevated liver enzymes, rash, musculoskeletal pain, injection site reaction are very commonly seen adverse events. Benign neoplasm and skin cancer including basal cell and squamous cell carcinoma were commonly reported. Fatal infections such as tuberculosis and invasive opportunistic infections have rarely been reported. For others, see full PI. **Dosage and Method of Use: RA, PsA and AS:** 40 mg sc fortnightly as a single dose. **pJIA:** Paediatric Patients (4 to 17 years) 15 kg to <30 kg 20 mg fortnightly ≥ 30 kg 40 mg fortnightly **CD:** Induction 160mg sc (Four injections on Day 0 or Two injections on Day 0 and 1), 80mg as two sc injections on Day 14, then Maintenance: 40mg sc starting on day 28 and continuing fortnightly **Psoriasis:** Initial dose of 80 mg, followed by 40 mg fortnightly, starting one week after the initial dose. **Date of Preparation:** 1 March 2011 Version 13 HUM 856-0211-1
