APPENDIX F

Evidence Review for NHS Surrey Area Prescribing Committee

Treatment: Anti- TNFs (Etanercept, Adalimumab & Infliximab) in Hand & Foot Psoriasis

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VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
1.0	07/03/2011	Clare Johns	Draft	First draft for circulation for comments
2.0	15/03/2011	Clare Johns	Draft	Following circulation, comments received from clinicians & on available trials from drug companies

1. Purpose of the Review

To confirm a Surrey-wide position on the use of Etanercept or Infliximab for Hand & Foot Psoriasis

2. Appropriateness

2.1 The patient:

Those patients who have trialled and failed treatments as per NICE guidance for plaque psoriasis.

2.2 The problem:

What is Hand & Foot Psoriasis?

Hand and foot psoriasis (HFP) is a disabling condition that can appear in a hyperkeratotic plaque-type, pustular form or combination.[i] Palmoplantar pustular psoriasis (PPP) may be a distinct entity in epidemiology and pathophysiology because there is a lack of association with the PSOR gene locus.[ii] In addition, it commonly affects patients lacking psoriasis elsewhere on the body.[i] However, the hyperkeratotic variant is frequently part of the general spectrum of psoriasis vulgaris and is associated with classic plaques elsewhere on the body in many cases. Palmoplantar disease severity occurs independently from the degree of body surface area involvement.[i] Although the palms and soles represent only 4 percent of the total body surface area, significant morbidity can have a debilitating effect on the patient's daily functions. Impaired mobility, pain, disability, pruritus, and embarrassment are common complaints. Hand and foot psoriasis usually represents a difficult-to-treat form of psoriasis.[iii]

Diagnosis:

The Psoriasis Area Severity Index (PASI) is the most widely used measurement tool for psoriasis in clinical trials. PASI combines the assessment of the severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease). A PASI score of more than ten has been shown to correlate with a number of indicators commonly associated with severe disease such as the need for hospital admission. Trial outcomes are generally reported in terms of the number of people reaching a specified percentage reduction in PASI from their baseline score (for example, PASI 75 is a 75% reduction from baseline score). The European Medicines Agency (EMEA) recognises the achievement of a PASI 75 as an indicator in clinical trials that severe psoriasis has responded to treatment.[iv] ***In patients with hand & foot psoriasis PASI is not an appropriate measure because the psoriasis is on the patient's hands & feet only.***

Palmoplantar Pustulosis area severity index (PPPASI) is used in some of the trials/case reports discussed below.

APPENDIX F

The Dermatology Life Quality Index (DLQI) is a validated tool for the measurement of quality of life across all skin diseases, including psoriasis, and has been used in both trial and clinical practice settings. A score of > 10 (range 0–30) has been shown to correlate with at least 'a very large effect' on an individual's quality of life[v]. ***In patients with hand & foot psoriasis DLQI is used but not all the questions apply (information from consultant dermatologist)***

2.3 The Intervention:

There are currently two approved groups of biologic agents that target Tumour necrosis factor (TNF):

- anti-TNF monoclonal antibodies (Adalimumab & infliximab)
- sTNF receptors (etanercept).

How does it work:

TNF is a cytokine that is released from T lymphocytes; it mediates inflammation and modulates the cellular immune response.

Etanercept (Wyeth Pharmaceuticals) is a recombinant human tumour necrosis factor (TNF) receptor fusion protein that inhibits the activity of TNF. Infliximab is a chimeric human-murine monoclonal antibody that binds with high affinity to TNF-α and inhibits its functional activity. Adalimumab is a recombinant human monoclonal antibody that binds specifically to tumour necrosis factor alpha (TNF-α), blocking interaction with its cell-surface receptors and thereby limiting the promotion of inflammatory pathways[iv]

Care setting: Should be initiated and supervised by a specialists experienced in the diagnosis & management of Psoriasis. Infliximab is given as a 2 hour infusions and would be usually given in an outpatient setting. Etanercept & Adalimumab are available in prefilled syringes and can be provided by a home care company. The patient can be trained to give themselves the injections at home.

Frequency:

Etanercept can be given as a single weekly 50mg dose (or 25mg biweekly)[vi]. Adalimumab is given as an initial 80 mg dose administered by subcutaneous injection, followed by 40 mg given subcutaneously every other week starting 1 week after the initial dose. Adalimumab is available in two presentations: a prefilled syringe and an autoinjection pen.[vi]

Infliximab is given as a 5 mg/kg dose given as an intravenous infusion over a 2 – hour period followed by additional 5 mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter[vi]

2.4 Alternative treatments:

Patients would normally have trialled and failed standard anti-psoriatic treatments including topical treatments (vitamin D derivatives, tar preparations, Dithranol, Vitamin A, corticosteroids) PUVA treatment & systemic medications (methotrexate, acitretin, ciclosporin, hydroxycarbamide).

The technology appraisals from NICE for the treatment of Psoriasis with biologic treatment state that the above therapies should have been trialled and failed prior to treatment (or be contraindicated)

3. Effectiveness

The effectiveness of biologic agents as first line treatment after failure of conventional treatments has been established by NICE for plaque psoriasis. This particular type of psoriasis was not discussed by NICE in making their recommendations.

3.1 Expected benefits

Reduction of DLQI or PPPASI and clearance of skin

3.2 Side-effects/complications

Etanercept, Adalimumab & Infliximab have been associated with infections, sometimes severe, including tuberculosis, septicaemia and hepatitis B reactivation. Other side-effects include nausea,

abdominal pain, worsening heart failure, hypersensitivity reactions, fever, headache, depression, antibody formations, pruritus, injection site reactions and blood disorders[vi].

3.4 Review of evidence
(Please see appendix 2 for hierarchy of evidence quality)

Treatment with Infliximab
Palmoplantar Pustulososis Bissonnette R et al. Treatment with Infliximab for palmoplantar psoriasis. This pilot study did not reach its primary endpoint of m-PPPASI 75 at week 14. However, infliximab was observed to be more efficacious than placebo in improving PPSA and with respect to the percentage of patients reaching m-PPPASI 50 at week 14. Larger and longer term studies are needed for severe patients to better assess the efficacy of infliximab in palmoplantar psoriasis

Case reports (unknown type)
Clinical data of 4 patients with HFP treated with infliximab[vii]

Patient Age/sex	Additional body sites involved	Comorbidity	Previous treatments*	PPPASI	PPPASI 24 weeks	Duration of treatment with infliximab (months)	Interruption/causes
1) 38, F	Face , forearms, buttocks	Di George Syndrome, alcoholic fatty liver disease	Ciclosporin	48	0	16	No
2) 61, M	Elbows, knees	HCV chronic infection	Ciclosporin Acitretin Efalizumab	33.6	8	10	Yes/urticaria
3) F	Legs		Ciclosporin Methotrexate	24	6	12	No
4) M	Elbows, legs		Ciclosporin Acitretin Methotrexate	13	4,8	12	No

Treatment with Etanercept
Bissonnette R et al. Etanercept in the treatment of palmoplantar pustulosis. This study showed that etanercept was well tolerated in subjects with PPP and suggests that some PPP subjects might benefit from etanercept therapy. Larger studies are needed to assess PPP response to etanercept including the influence of smoking and the presence or absence of psoriasis outside palms and soles

Case reports
After unsuccessful treatment with topical steroids and PUVA therapy, a 59-year-old patient with palmoplantar psoriasis and arthritic symptoms in her □ngers and feet was prescribed Etanercept 25 mg SC BIW [xxiii]. The patient noted almost total clearing of the hands, mild–to–moderate scaling of the feet and a resolution of arthritic symptoms after 19 weeks of therapy. No AEs were reported by the authors.

A 58-year-old patient with pustules, □ssures, and scaling of her hands and feet was started on etanercept 25 mg SC BIW after failing topical treatments and oral MTX [xxiv]. After 2 weeks of treatment, improvement of her skin lesions was noted. Etanercept was stopped 6 months later due to insurance complications and within 8 days the patient experienced an exacerbation of plantar pustulation, limiting her ability to walk and work. Etanercept was eventually restarted and improvement was noted after 1 week. The patient reported a reduction in exacerbation periods

from 4 to 2 weeks compared with previous treatments and an improvement in her quality of life. Local injection site reaction was the only AE observed. Routine blood analysis was normal.

Antoniou *et al*. reported that a 27-year-old patient with palmoplantar pustulosis and arthroosteitis received etanercept 50 mg SC BIW after failing therapy with prednisolone, indomethacin, MTX, and cyclosporine [xxxx]. The patient experienced improvement in skeletal pain; however, some pustules remained on his palms and soles despite the addition of topical therapy. Etanercept was reduced to 25 mg SC BIW. Six months after disease-onset, he experienced a deterioration of the palmoplantar pustular eruptions and severe skeletal pain on the anterior chest wall. Etanercept was increased to 50 mg SC BIW and acitretin 35 mg/day was added to his current medication regimen. The patient subsequently experienced a gradual improvement in both skeletal pain and skin lesions. At the time of publication, the patient had been maintained on combination therapy with etanercept 25 mg SC BIW and acitretin 35 mg/day for 18 months without disease complications or adverse events.
Additional case reports documenting improvement in non–plaque palmoplantar lesions after treatment with etanercept have been published [xxv-xxx]. However, one case report described a patient with palmoplantar pustular psoriasis who failed to respond to etanercept treatment and subsequently discontinued therapy [xxxi].

Occurrence of new onset or exacerbation of palmoplantar psoriasis
Case reports of patients who have experienced new onset [xxxii – xxxv] or exacerbation [xxxvi - xxxx] of palmoplantar psoriasis after beginning or switching to etanercept treatment have been published. The cases describe lesions that developed on the palms and/or soles one week to 26 months after initiating etanercept for arthritis symptoms or ankylosing spondylitis. Improvement or resolution of the palmoplantar lesions was seen in most patients who discontinued etanercept therapy. However, improvement or resolution of palmoplantar lesions was also seen in patients who elected to continue therapy. Psoriasis flare was noted in one patient who restarted etanercept therapy due to disease severity.

Treatment with Adalimumab [xxii]

Craig Leonardi, MD et al. Adalimumab for the treatment of Moderate to Severe Chronic Plaque Psoriasis of the Hands and Feet.
Patients were excluded if they had received prior treatment with adalimumab or if they had been diagnosed as having palmoplantar pustulosis; however, patients who presented with pustules were not necessarily excluded (unless the pustules were the predominant feature of psoriasis). Adalimumab is efficacious and well tolerated for treatment of chronic plaque psoriasis of hands and/or feet, with efficacy largely maintained to 28 weeks.

3.4.1 National Guidance:
NICE has issued guidance for the use of adalimumab, etanercept and ustekinumab in the treatment of psoriasis (TA 146, 103 and 180). Each drug is recommended for first line use after failure of standard treatment (with PASI and DLQI ≥ 10). Infliximab (TA 134) is recommended for very severe plaque psoriasis where PASI ≥ 20 and DLQI >18. No recommendations have been made for hand & foot psoriasis where these measurement tools for severity do not apply[viii]

3.4.2 Cochrane Library systematic review and meta-analysis
Interventions for chronic palmoplantar pustulosis (2006)

Many different interventions were reported to produce "improvement" in PPP. There is, however, no standardised method for assessing response to treatment, and reductions in pustule counts or other empirical semi-quantitative scoring systems may be of little relevance to the patient. This review has shown that the ideal treatment for PPP remains elusive and that the standards of study design and reporting need to be improved to inform patients and those treating them of the relative merits of the many treatments available to them

APPENDIX F

No review found for hyperkeratotic plaque-type hand & foot psoriasis[ix].

British association of dermatologist's guidelines for biologic interventions for psoriasis 2009. Please see excerpt below from these psoriasis guidelines

How effective are biologic therapies in pustular psoriasis and palmoplantar pustulosis?

'There are two disabling and difficult-to-treat conditions affecting the hands and feet in which localized pustules are associated with psoriasis elsewhere on the body.

The more common of these, chronic palmoplantar pustulosis, has in the past been termed chronic palmoplantar pustular psoriasis. There is, however, evidence to suggest that, although it is associated with psoriasis in up to about 20% of cases, it is a distinct disease with a different clinical and genetic profile[xiii]. This evidence is strengthened by the almost complete lack of reports of benefit from TNF antagonists but, conversely, an increasing number of reports of new onset palmoplantar pustulosis in patients with conditions other than psoriasis treated with these agents.[ixx] [xx] A recent small pilot study found no benefit over placebo of Etanercept 50 mg given twice weekly for 12 weeks[xxi]. TNF antagonists should therefore be avoided in these patients'…….

4. Summary of Key Points for Consideration

4.1 National guidance:

NICE guidance available for treatment of psoriasis but PASI does not apply in patients with psoriasis of the hands & feet and not all questions from DLQI apply.

4.2 Efficacy

There is limited evidence available to support the use of these biologics in this variant of psoriasis. Evidence is limited to case studies and small randomised controlled trials

4.3 Potential disadvantages

Infections: Rheumatology registry data do suggest an increased risk of skin and soft tissue infections compared with standard disease modifying antirhematic drugs (DMARDs). Serious infections including opportunistic infections have also been reported.

Reactivation of tuberculosis: the risk appears to be greater with infliximab as compared with etanercept

Cardiovascular disease: TNF antagonists should be avoided in patients with severe (NYHA class III and IV) cardiac failure

Malignancy: although there is no robust evidence of increased risk of malignancy, all patients should be assessed prior to and during treatment with respect to their past or current history of malignancy and where possible entered into the British association of Dermatologists Biologic Interventions Register (BADBIR)

4.4 Budgetary Impact

Drug	Dose	Frequency	Cost
Etanercept	50mg or 25mg	Weekly or bi-weekly	£9295.00/year
Adalimumab	80mg stat then 40mg every other week (starting one week after stat dose)	Ongoing	£9155.64 (Price of Adalimumab has fallen from 1st January 2011)
Infliximab	5mg/kg	0,2 & 6 weeks followed by 8 weekly infusions thereafter	£16,113.41/1st year (Cost for 60 – 80kg patient including 20% VAT)

4.5 Precedent setting:

Hand and foot psoriasis occurs in approximately one-third of the psoriatic population, and interestingly, many patients with this disease do not have psoriasis on other parts of their body.

The biological basis for the differences in affected body area is not known.[x] [xi] A consultant dermatologist from Surrey has estimated that they are likely to see no more than 5 patients requiring biologic treatment for this uncommon variant of Psoriasis. **Please can I ask other dermatologists for their view on the number of patients that are likely to require biologics for hand & foot psoriasis?**

5. Conclusions and Recommendations

This variant of psoriasis is very difficult to treat, patients are treated with standard treatments but PASI is not an appropriate measure and not all the questions in DLQI are appropriate so patients cannot be treated as per NICE guidance.

One dermatologist estimates numbers for their centre to be in the region of 5/year. **Potential numbers from other centres would be really useful please?**

There is limited evidence available for this uncommon type of psoriasis. Evidence is available from case studies for hand & foot psoriasis (unknown type) and small randomised controlled trials for Palmopustular Psoriasis. The committee are asked to consider the following options

Options for Consideration

- Do not routinely fund Etanercept, Adalimumab or Infliximab for the treatment of hyperkeratotic plaque-type Hand & Foot Psoriasis

- Fund Etanercept Adalimumab or Infliximab for the treatment of hyperkeratotic plaque-type Hand & Foot Psoriasis and Palmoplantar Pustulosis

APPENDIX F

Appendix 1: Evidence search

Search terms used:

Resource	Used in this review?
National Library for Health (NHL) http://www.library.nhs.uk/Default.aspx A gateway site with access to other resources such as Reviews (Bandolier, Cochrane, CRD etc), Guidelines (e.g. NICE), Clinical Knowledge Summaries (CKS) and Journals including AMED, British Nursing Index, CINAHL, E-books, EMBASE, HMIC, MEDLINE, My Journals, PsycINFO, PubMed, Databases from Dialog.	✓
National Institute of Health and Clinical Excellence (NICE) http://www.nice.org.uk/ NICE produces national guidance in three areas of health: 1. Public health - guidance on the promotion of good health and the prevention of ill health 2. Health technologies - guidance on the use of new and existing medicines, treatments and procedures within the NHS 3. Clinical practice - guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS.	✓ (through NHL)
Bandolier http://www.medicine.ox.ac.uk/bandolier/index.html Bandolier is a website about the use of evidence in health, healthcare, and medicine. Information comes from systematic reviews, meta-analyses, randomised trials, and from high quality observational studies.	✓(through NHL)
Centre for Reviews and Dissemination http://www.york.ac.uk/inst/crd/ CRD undertakes high quality systematic reviews that evaluate the effects of health and social care interventions and the delivery and organisation of health care. Databases maintained by CRD include Database of Abstracts of Reviews of Effects (DARE), NHS Economic Evaluation Database (NHS EED), Health Technology Assessment (HTA) Database	✓(through NHL)
Scottish Intercollegiate Guidelines Network (SIGN) http://www.sign.ac.uk/ Scottish equivalent of NICE	✓
Medical Services Advisory Committee (Australia) http://www.msac.gov.au/internet/msac/publishing.nsf/Content/home-1 The principal role of the Medical Services Advisory Committee (MSAC) is to advise the Australian Minister for Health and Ageing on evidence relating to the safety, effectiveness and cost-effectiveness of new medical technologies and procedures.	✓
Canadian Agency for Drugs and Technologies in Health (CADTH) http://www.cadth.ca/index.php/en/home The Canadian Agency for Drugs and Technologies in Health (CADTH) is a national body that provides Canada's federal, provincial and territorial health care decision makers with credible, impartial advice and evidence-based information about the effectiveness and efficiency of drugs and other health technologies.	✓

Study	Design	Number of Participants	Results
Title: Treatment of palmoplantar psoriasis with infliximab: a randomized, double-blind placebo-controlled study. **Citation:** J Eur Acad Dermatol Venereol. 2011 Feb 23. doi: 10.1111/j.1468-3083.2011.03984. **Author:** Bissonnette R et al.	Patients were randomized (1:1) to receive infliximab 5 mg/kg or placebo at weeks 0, 2 and 6. Patients initially randomized to placebo received infliximab at weeks 14, 16 and 20 whereas patients randomized to infliximab received additional infliximab infusions every 8 weeks until week 22.	Patients with non-pustular palmoplantar psoriasis affecting at least 10% of their palms and soles and with a modified palmoplantar psoriasis area and severity index (m-PPPASI) of at least eight were recruited. Twenty four (24) patients were randomized in this study	At week 14, 33.3% and 66.7% of patients treated with infliximab achieved m-PPPASI 75 and m-PPPASI 50 respectively compared to 8.3% for both m-PPPASI 75 (P = 0.317) and m-PPPASI 50 (P = 0.009) for patients randomized to placebo. A reduction of 50.3% in the mean surface area of palms and soles affected with psoriasis was seen at week 14 in patients randomized to infliximab as compared to an increase of 14.9% in patients randomized to placebo (P = 0.009).
Title: Etanercept in the treatment of palmoplantar pustulosis. **Citation:** J Drugs Dermatol. 2008 Oct; 7(10):940-6. **Author:** Bissonnette R et al.	Fifteen subjects with PPP were randomized (2:1) to receive subcutaneous injections of either etanercept 50 mg or a placebo twice a week for 3 months. All subjects then received the etanercept 50 mg injections twice a week for an additional 3 months.		Etanercept was well tolerated by subjects with PPP. The decrease in median Palmoplantar Pustulosis Area and Severity Index (PPPASI) score from baseline to 24 weeks was statistically significant for subjects treated with etanercept for 24 weeks (P = 0.038, n = 10) but not for subjects in the placebo/etanercept cross-over group (P = 0.125, n = 5). Comparison of changes in PPPASI from baseline to week 12 was not statistically significant for subjects assigned to etanercept or to placebo. Some subjects treated with etanercept presented good clinical improvements in PPP severity whereas others showed an increase in PPP severity.

Title: Adalimumab for the treatment of Moderate to Severe Chronic Plaque Psoriasis of the Hands and Feet **Citation:** Arch Dermatol. Published online December 20, 2010. doi:10.1001/archdermatol.2010.384 **Author:** Craig Leonardi, MD et al	Sixteen-week, randomized, double-blind, placebo-controlled evaluation of adalimumab therapy for moderate to severe chronic plaque psoriasis involving the hands and/or feet with a 12-week open-label extension (Randomized Controlled Evaluation of Adalimumab in Treatment of Chronic Plaque Psoriasis of the Hands and Feet [REACH]).	Patients were randomized 2:1 to adalimumab (80 mg at week 0, then 40 mg every other week starting at week 1) or to matching placebo. Overall, 81 patients were enrolled at 17 sites in the United States and Canada,	Seventy-two patients (adalimumab [n=49]; placebo [n=23]) were evaluated. Baseline percentages of patients with moderate and severe Physician's Global Assessment of hands and/or feet (hfPGA) scores were 76% and 24%, respectively, for the adalimumab group and 74% and 26%, respectively, for the placebo group. At week 16, 31% and 4% of patients randomized to adalimumab and placebo, respectively, achieved an hfPGA score of clear or almost clear (P=.01). At week 28, 80% of the hfPGA clear or almost clear response was maintained from week 16 (25% for patients randomized to adalimumab). Adverse events in both groups were generally mild to moderate. In both periods combined, nasopharyngitis (27% and 13% for adalimumab- and placebo-treated patients, respectively) was most frequently reported.

Appendix 2: Grading of evidence

- Ia: systematic review or meta-analysis of randomised controlled trials
- Ib: at least one randomised controlled trial
- IIa: at least one well-designed controlled study without randomisation
- IIb: at least one well-designed quasi-experimental study, such as a cohort study
- III: well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, case–control studies and case series
- IV: expert committee reports, opinions and/or clinical experience of respected authorities

Appendix 3: References

i Farley E, Masrour S, McKey J, Menter A. Palmoplantar psoriasis: a phenotypical and clinical review with introduction of a new quality-of-life assessment tool. J Am Acad Dermatol 2009 Jun;60(6):1024–31.

ii Asumalahti K, Ameen M, Suomela S et al. Genetic analysis of PSOR1 distinguishes guttate psoriasis and palmoplantar pustulosis. J Invest Dermatol 2003 Apr; 120(4):627–32.

iii Marsland AM, Chalmers RJ, Hollis S et al. Interventions for chronic palmoplantar pustulosis. Cochrane Database Syst Rev 2006 Jan 25;(1):CD001433.

iv NICE TA 103 July 2006:Etanercept and efalizumab for the treatment of adults with psoriasis

v Smith, Anstey, Barker. British Association of Dermatologists' guidelines for biologic interventions for psoriasis 2009. Br Jn Dermatology 2009 161, 987-1019

*vi **www.medicines.org.uk***

vii British National Formulary 60 (September 2010)

viii Dermatology online Journal Volume 16 Number 7 July 2010 Successful treatment of hand and foot psoriasis with infliximab Vito Di Lernia MD et al.

*ix **www.nice.org.uk***

x Chalmers R, Hollis S, Leonardi-Bee J, Griffiths CEM, Marsland Bsc MRCP A. Interventions for chronic palmoplantar pustulosis. Cochrane Database of Systematic Reviews 2006, Issue 1. Art. No.: CD001433. DOI: 10.1002/14651858.CD001433.pub2

xi Pettey AA, Balkrishnan R, Rapp SR, et al. Patients with palmoplantar psoriasis have more physical disability and discomfort than patients with other forms of psoriasis: implications for clinical practice. J Am Acad Dermatol 49(2):271-5 (2003 Aug).

xii Enfors W, Molin L. Pustulosis palmaris et plantaris. A follow-up study of a ten-year material. Acta Derm Venereol 51(4):289-94 (1971).

xiii Asumalahti K, Ameen N, Suomela S et al. Genetic analysis of PSORS1 distinguishes guttate psoriasis and palmoplantar pustulosis. J Invest Dermatol 2003; 120:627–32.

ixx Wollina U, Hansel G, Koch A et al. Tumor necrosis factor-alphainhibitor-induced psoriasis or psoriasiform exanthemata: first 120 cases from the literature including a series of six new patients. Am J Clin Dermatol 2008; 9:1–14.

xx Collamer AN, Guerro KT, Henning JS et al. Psoriatic skin lesions induced by tumor necrosis factor antagonist therapy: a literature review and potential mechanisms of action. Arthritis Care Res 2008; 59:996–1001.

xxi Bissonnette R, Poulin Y, Bolduc C et al. Etanercept in the treatment of palmoplantar pustulosis. J Drugs Dermatol 2008; 7:940–6.

xxii Abbott laboratories medicines information

xxiii Weinberg JM. Successful treatment of recalcitrant palmoplantar psoriasis with etanercept. Cutis. 2003;72:396-398.

xxiv Kasche A et al. Severe psoriasis pustulosa palmaris et plantaris (Barber–Königsbeck) treated successfully with soluble tumour necrosis factor receptor fusion protein (etanercept). J Eur Acad Dermatol Venereol. 2007;21:255-257.

xxv Nikkels AF et al. Etanercept and recalcitrant acrodermatitis continua of Hallopeau. J Drugs Dermatol. 2006;5:705-706.

xxvi Bonish B et al. Etanercept responsive acrodermatitis continua of Hallopeau: is a pattern developing? J Drugs Dermatol. 2006;5:903-904.

xxvii Roux CH et al. New–onset psoriatic palmoplantaris pustulosis following in□iximab therapy: a class effect? J Rheumatol. 2007;34:434-437.

xxvii Wollina U et al. Tumor necrosis factor-α inhibitor–induced psoriasis or psoriasiform exanthemata: □rst 120 cases from the literature including a series of six new patients. Am J Clin Dermatol. 2008;9:1-14.

xxviii Aarão A et al. Successful treatment of acrodermatitis continua of Hallopeau with methotrexate and etanercept. J Am Acad Dermatol. 2009;60:AB163. Abstract P3308.

ixxx Bhargava K et al. A retrospective, case cohort study of antitumour necrosis factor therapy in
severe acral psoriasis. Br J Dermatol. 2009;161(Suppl 1):32-33. Abstract P-25.

xxx Bosch RI et al. Psoriasis induced by anti-TNF probably not so uncommon. J Clin Rheumatol. 2008;14:128.

xxxi Ahmad K et al. Two years of experience with etanercept in recalcitrant psoriasis. Br J Dermatol. 2007;156:1010-1014.

xxxii Weinel S, et al. New onset of palmoplantar pustulosis in a patient with rheumatoid arthritis treated with etanercept. J Am Acad Dermatol. 2007;56(suppl 2):AB52. Abstract P545.

xxxiv Harrison MJ et al. Rates of new-onset psoriasis in patients with rheumatoid arthritis receiving anti– TNFα therapy. Results from the British Society for Rheumatology Biologics Register. Ann Rheum Dis. 2009;68:209-215.

xxxv Kuhara T et al. Psoriasiform and pustular eruption induced by etanercept and infliximab. Eur J Dermatol. 2009;19:388-389.

xxxvi Cohen JD et al. Psoriasis induced by tumor necrosis factor–α antagonist therapy: a case series. J Rheumatol. 2006;34:380-385.

xxxvii Michaëlsson G et a.l In□iximab can precipitate as well as worsen palmoplantar pustulosis: possible linkage to the expression of tumour necrosis factor–α in the normal palmar eccrine sweat duct? Br J Dermatol. 2005;153:1243-1244.

xxxviii Wendling D et al. Onset or exacerbation of cutaneous psoriasis during TNFα antagonist therapy. Joint Bone Spine. 2008;75:315-318.

ixxxx Haibel H et al Unexpected new onset or exacerbation of psoriasis in treatment of active ankylosing spondylitis with TNF-alpha blocking agents: four case reports. Ann Rheum Dis. 2004;64(suppl 1): Abstract SAT0061.

xxxx Antoniou C et al.. Palmoplantar pustulosis with arthro-osteitis: successful treatment with etanercept and acitretin. J Eur Acad Dermatol Venereol. 2009;23:854-855.

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