



Complete Summary

GUIDELINE TITLE

Psoriasis.

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Psoriasis. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2005 May 25 [Various].

GUIDELINE STATUS

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references drug(s) for which important revised regulatory and/or warning information has been released.

- October 17, 2008, Raptiva (efalizumab): The U.S. Food and Drug Administration (FDA) notified healthcare professionals of extensive labeling changes, including a Boxed Warning, to highlight the risks of life-threatening infections, including bacterial sepsis, viral meningitis, invasive fungal disease, progressive multifocal leukoencephalopathy and other opportunistic infections with the use of Raptiva. In addition, the prescribing information will be updated to describe a potential risk for the permanent suppression of the immune system with repeat administration of Raptiva in children. Raptiva is not approved for children under 18 years of age.
- <u>May 1, 2008, Enbrel (etanercept)</u>: Amgen and Wyeth Pharmaceuticals informed healthcare professionals of changes to the BOXED WARNING section of the prescribing information for Enbrel regarding the risk of serious infections, including bacterial sepsis and tuberculosis, leading to hospitalization or death. The ADVERSE REACTIONS section of the label was updated to include information regarding global clinical studies and the rate of occurrence of tuberculosis in patients treated with Enbrel.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT ** SCOPE METHODOLOGY - including Rating Scheme and Cost Analysis RECOMMENDATIONS EVIDENCE SUPPORTING THE RECOMMENDATIONS BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS CONTRAINDICATIONS IMPLEMENTATION OF THE GUIDELINE INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES IDENTIFYING INFORMATION AND AVAILABILITY DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Psoriasis

GUIDELINE CATEGORY

Diagnosis Treatment

CLINICAL SPECIALTY

Dermatology Family Practice Internal Medicine

INTENDED USERS

Health Care Providers Physicians

GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

TARGET POPULATION

Patients who have psoriasis or cutaneous lesions suspicious for psoriasis

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

- 1. Assessment of clinical features and patterns of cutaneous lesions
- 2. Assessment for family history of psoriasis
- 3. Biopsy, if needed

Treatment

- 1. No treatment, if minor localized psoriasis on the elbows or knees
- 2. Topical treatment including creams or ointments:
 - Emollients
 - Topical corticosteroids
 - Dithranol (Anthralin)
 - Coal tar
 - Vitamin D derivatives (Calcipotriol [calcipotriene], calcitriol)
 - Combination of calcipotriol with a potent topical corticosteroid
 - Calcitriol
 - Tazarotene
- 3. Phototherapy including:
 - Ultraviolet A with a psoralen (PUVA)
 - Ultraviolet B (UVB) radiation
 - Combination of phototherapy with retinoids
 - Climatotherapy (heliotherapy)
- 4. Systemic treatment including:
 - Acitretin, methotrexate, hydroxycarbamide, cyclosporine, and sulfasalazine
 - Biologicals, such as alefacept, efalizumab, etanercept, and infliximab
- 5. Referral to specialist

Note: Antistreptococcal therapy is considered but not recommended.

MAJOR OUTCOMES CONSIDERED

- Psoriasis clearance rate
- Remission rate
- Adverse effects of (tolerance to) treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources) Hand-searches of Published Literature (Secondary Sources) Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogeneous results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary. The recommendations that follow are based on the previous version of the guideline.

The levels of evidence [A-D] supporting the recommendations are defined at the end of the "Major Recommendations" field.

Definition and Prevalence

- Psoriasis is a chronic disease of the skin caused by genetic and environmental factors. It is characterized by well-defined plaques bearing adherent, silvery scales.
- The prevalence of psoriasis in Scandinavia and Western Europe is approximately 2%. It is rare below 5 years of age. (see picture 1*) There are two peaks of onset: between 16 and 22 years of age in Type I psoriasis and between 57 and 60 years of age in Type II psoriasis. The genetic background of these two types differ (Elder et al., 1994).
- Genetic predisposition to psoriasis follows a multifactorial pattern. Approximately ten susceptibility genes (locus) have been identified. The most significant locus (PSORS1) lies within chromosome 6p21.3 (Asumalahti et al., 2003). Only about 10% of the susceptibility gene carriers will develop the disease (low penetrance) (Swanbeck et al., 1997; Elder et al., 1994).
- Psoriasis is characterized by an abnormal regulation of the interaction between T cells and keratinocytes. T cell cytokine secretion profile resembles that of Th-1 (Lebwohl, 2003).
- External factors (infections, streptococcal in particular, skin injuries, certain drugs) often trigger the onset of psoriasis (Lebwohl, 2003). Stress, smoking, and excessive alcohol consumption may also be connected with the onset of psoriasis.

Clinical Features

- Characteristic cutaneous lesions facilitate diagnosis.
 - The plaques are sharply demarcated, slightly elevated, and covered with silvery scales (see pictures 1, 3, and 2*).
 - Gentle scraping of the scales reveals minute capillary bleeding points (Auspitz sign) (see picture 4*).
 - The elbows (see picture 5*), knees (see picture 6*), legs, lower back, scalp (see pictures 7 and 8*), and glans penis (see picture 9*) are the sites of predilection.
- Involvement of the nails is common.
 - Pitting
 - Separation of the distal nail plate from the nail bed (onycholysis), yellowish flecks beneath the nail plate ("oily macules"), and subungual hyperkeratosis (see pictures 11, 12, and 10*).
 - Acrodermatitis continua of Hallopeau is a painful, localized pustular form of psoriasis which often leads to nail deformity (see pictures 14 and 13*).

Common Manifestations of Psoriasis

- The most common type is plaque psoriasis, which is a stationary form of the disease with the lesions often covered with thick silvery scales.
- Guttate psoriasis is often triggered by tonsillitis. It is widely distributed throughout the body.
- Flexural psoriasis is localized within the main skin folds (genitocrural area [see picture 15*], navel, axillae, submammary region).
- Erythrodermic psoriasis (see picture 16*) is a generalized form of the disease and is most refractory to treatment. It may also appear in a pustular form (pustular psoriasis).
- Psoriasis may also affect joints in 5 to 10% of cases.

Differential Diagnosis

- Diagnosis is based on the clinical picture (Lebwohl, 2003).
- A biopsy may exclude some other skin diseases resembling psoriasis, but it rarely is pathognomic (Lebwohl, 2003).
- A family history of psoriasis may help in diagnosis: up to 50% of patients report an affected relative (Swanbeck et al., 1997).

Scalp

- In **seborrhoeic dermatitis** (see the Finnish Medical Society Duodecim guideline "Seborrhoeic dermatitis" (see picture 17*) the flakes are thinner, "greasier," and the condition responds better to treatment. It is often difficult to differentiate seborrhoeic dermatitis from psoriasis unless other skin areas offer additional information.
- **Fungal infection** of the scalp (see the Finnish Medical Society Duodecim guideline "Dermatomycoses") is uncommon in the Western populations. It mostly affects children. This diagnosis can be excluded by microscopy and negative culture for fungi.
- **Neurodermatitis** of the neck (lichen simplex nuchae) is characterised by an isolated, itchy plaque covered with thin scales.

Flexures

- **Seborrhoeic dermatitis** may resemble flexural psoriasis. Examine other skin areas. It is not necessary to differentiate between these two conditions, as the treatment is the same.
- **Fungal infection** (tinea) (see the Finnish Medical Society Duodecim guideline "Dermatomycoses") may resemble psoriasis; however, it usually heals in the centre and expands peripherally. Potassium hydroxide (KOH) and fungal culture are diagnostic.
- **Candidiasis** is not often seen in the young and middle-aged patients. It presents as a moist area of erythema and maceration with outlying "satellite eruptions."
- **Erythrasma** is a macular brown area with few symptoms, most often found in the armpits or groin. It is caused by overgrowth of diphtheroids of the normal skin flora. These areas fluoresce coral pink under long-wave ultraviolet radiation (Wood's light).

Hands, Feet

- **Hyperkeratotic eczema** of the palms and **palmoplantar pustulosis** may be difficult to differentiate from psoriasis (see picture 18*). Examine the entire skin.
- **Fungal infection** (see the Finnish Medical Society Duodecim guideline "Dermatomycoses") can easily be diagnosed with microscopic examination and culture.

Treatment

- It is not necessary to treat psoriasis if it has no effect on the patient's quality of life (minor psoriasis on the elbows or knees).
- The choice of treatment depends on the psoriasis subtype and the extent, severity, and site of the lesions and, importantly, on the patient's preferences. In addition to the age of the patient, the availability, feasibility, and cost of the treatment as well as response to earlier treatment also have an influence on the choice.
- Any comorbidity (e.g., hepatic disease, hypertension, alcohol abuse, human immunodeficiency virus [HIV]) or a possible pregnancy of the patient must also be taken into account.

Topical Treatment

- The main form of treatment available for a general practitioner is the use of various ointments and creams.
- Topical treatment may also enhance the effect of other treatment forms.
- The active treatment of mild to moderate plaque psoriasis may consist of vitamin D derivatives (calcipotriol and calcitriol). These are used regularly twice a day. They are suitable for long-term use. Topical corticosteroids are also suitable, but their use should be intermittent.
- **Emollients** may be used as a general treatment in non-acute phases of the disease. They can also be used to soften and remove the scale from the scalp (plenty of emollient rubbed into the scalp in the evening and washed out in the morning). The scalp must not be scratched or rubbed to remove the scale since this may worsen the symptoms (Köbner phenomenon). Salicylic vaseline (5%) or an emollient base with salicylic acid enhances the exfoliating effect.
- **Topical corticosteroid** (Mason, Mason, & Cork, 2002) **[A]** ointments are • usually more effective than creams. On the face and flexures only mild to moderately potent topical corticosteroids should be used. On the other body areas treatment results will only be achieved with potent to very potent ointments. Topical corticosteroids can well be used on the scalp, too. The duration of a course of a corticosteroid ointment may vary from one week up to four weeks, depending on the age of the patient, the area to be treated, and the potency of the preparation. The treatment should then be stopped. Then an emollient can be used or another suitable treatment regime. Corticosteroids are not suitable for the treatment of large skin areas. The treatment of psoriasis in children is usually prescribed only after consulting a dermatologist. Systemic corticosteroids must not be used for the treatment of psoriasis, as disease progression to an extensive form of pustular psoriasis is possible. An experienced dermatologist may deviate from this rule when treating a difficult-to-manage or critically worsened psoriasis (e.g., as a part of combination treatment).

- Preparations of **coal tar** are suitable for the treatment of extensive guttate psoriasis or as follow-up treatment of other treatment forms. At present, coal tar preparations are not much used due to their smell and mess (Lebwohl, 2003).
- **Dithranol** (anthralin) is used as a "short contact" regimen. (Lebwohl & Ali, 2001). 1 to 3% dithranol formula is applied and left on for 20 to 30 minutes. The preparation is washed off after the application time. The preparation may permanently stain the wash basins. Dithranol is also suitable for the treatment of scalp psoriasis.
- **Calcipotriol** (calcipotriene) is a vitamin D analogue. It is available as an ointment or cream as well as scalp solution. Its efficacy is similar to that of a potent topical corticosteroid. The maximum weekly dose is 100 g of 50 micrograms/g ointment, cream, or solution. It must be used regularly twice a day in order to get effect.
- The combination of calcipotriol with a potent topical corticosteroid is more effective than either component alone (Mason, 2002; Douglas et al., 2002) [A]. The combination formula is suitable as an initial treatment of plaque psoriasis in adults. Once daily dosing is sufficient (Guenther et al., 2002), which may improve compliance. The treatment may last for up to four weeks. Follow-up treatment may be carried out with calcipotriol alone, or with calcipotriol on weekdays and combination therapy on weekends. The patient must be observed for corticosteroid-induced signs of skin atrophy (thinning of the skin, papery skin, dilated capillaries, bruising).
- Calcitriol (Ashcroft et al., "Systematic review," 2000; DARE-20008265, 2001) [A] is an active form of vitamin D, and it is available as an ointment. Its efficacy is similar to that of a potent topical corticosteroid (Langner, Stapor, & Ambroziak, 2001). The treated area must be not more than 35% of total body surface area. The maximum dose is 30 g of the ointment (3 micrograms/g) daily or 210 g weekly. It can also be applied lightly to sensitive skin areas, such as the face and flexures (Ortonne et al., 2003). The ointment should be applied twice daily. It has also been used together with a topical corticosteroid (Kowalzick, 2001).
- **Tazarotene** is a topically applied retinoid used as a gel once daily (Weinstein et al., 1997) [**B**]. Its efficacy is similar to that of a potent topical corticosteroid. Irritation is seen in some patients (Lebwohl et al., 1998). The addition of a potent topical corticosteroid to tazarotene therapy increases the treatment success.

Phototherapy

- Phototherapy may be used for extensive psoriasis (>10% of the body surface) (Griffiths et al., 2000; Spuls et al., 1997; DARE-980690, 2000) [A]. Phototherapy should only be prescribed with firm criteria. The prescribing physician must be well versed in the prescribed form of phototherapy and the doses necessary for the patient's particular skin type.
- Indications, suitable doses, and frequency of exposure to phototherapies and concomitant treatment require the experience of a dermatologist (Hönigsmann, 2001). Ultraviolet A radiation with a psoralen (PUVA) and retinoids may only be prescribed by dermatologists.
- Various combination regimens (e.g., retinoids) are recommended to reduce the cumulative ultraviolet (UV) dose and with the intention to reduce the long-term adverse effects of phototherapy (Lebwohl et al., 2001).

- Climatotherapy (heliotherapy). Skin must tolerate exposure to the sun (i.e., the skin must be able to tan and it may not burn easily). Sunbathing is started with small UV doses. The time to sunbathe is dependent on the skin phototype and degree of tanning. Furthermore, the geographical location, time of day, season, weather, altitude, and other factors like pollution have a major influence on the time needed for sunbathing. Therefore, no single predetermined time schedule can be given. As regards plaque psoriasis, a three-week course is usually necessary for a good result (Snellman et al., "Effect of heliotherapy," 1993; Snellman et al., "Supervised four-week heliotherapy," 1993). Contraindications include alcoholism and severe mental health problems. Photosensitising medications (e.g., amiodarone, piroxicam, and doxycycline) are also a contraindication, as is poor general health. Heliotherapy is an effective but relatively expensive treatment modality due to the lost working days (Snellman et al., 1998).
- Ultraviolet B (UVB) radiation is particularly beneficial in guttate psoriasis. UVB treatments are divided into the conventional broad-band (TL12) UVB therapy (wavelength 385 to 400 nm) and the narrow-band (TL01) UVB therapy (wavelength 309 to 313 nm). The latter (TL01) is now regarded in most clinics as the treatment of choice in the field of phototherapy.
- The efficacy of narrow-band UVB therapy is at least comparable to that of PUVA. The long-term adverse effects of narrow-band UVB are not yet known.
- The efficacy of UVB therapy may be enhanced with the addition of a systemic retinoid (ReUVB) and various topical agents compatible with phototherapy which may reduce the cumulative UV dose received by the patient (Lebwohl et al., 2001).
- PUVA therapy is an effective but also highly demanding form of phototherapy (Voss et al., 2001). The photosensitising effects of different psoralens vary ten-fold. During RePUVA therapy the patient receives a concomitant systemic retinoid (acitretin). The PUVA therapies have fallen out of favour due to increased risk of skin cancer associated with tablet-PUVA therapy. Despite the associated risks, PUVA may still be the best choice for some patients in problematic cases.

Systemic Treatment

- Acitretin, methotrexate (Griffiths et al., 2000) [C], hydroxycarbamide (Griffiths et al., 2000) [C], cyclosporin (Griffiths et al., 2000) [A], and sulfasalazine (Griffiths et al., 2000) [B] may be prescribed by a dermatologist to patients with severe psoriasis. Their use requires special experience and regular follow-up. Methotrexate and cyclosporin are equally effective for moderate to severe plaque type psoriasis (Heydendael et al., 2003). An experienced dermatologist who has seen plenty of psoriasis patients may also use combinations of systemic psoriasis medications to treat difficult cases or to get a difficult situation under control.
- Biologicals, such as alefacept, efalizumab, etanercept, and infliximab, may have a role in the treatment of moderate to severe psoriasis refractory to other treatments or when other treatments are contraindicated or unsuitable (Granstein, 2001). Alefacept and efalizumab inhibit T-cell activation. Tumor necrosis factor (TNF)-alpha antagonists infliximab and etanercept are also effective in psoriatic arthritis (Krueger and Callis, 2004). A special risk associated with TNF-alpha antagonists is an activation of latent infections (e.g. tuberculosis).

Referral to Specialist

- Children suffering from psoriasis and adults suffering from psoriasis that does not respond to usual treatment modalities should be referred to a dermatologist.
- An experienced dermatologist can be more helpful in the diagnosis of problematic psoriasis than sending off a skin biopsy.
- If excessive corticosteroid use is suspected, the patient should be referred to a dermatologist.

Related Evidence

- There is no evidence supporting antistreptococcal interventions in psoriasis (Owen et al., 2000) [**C**].
- Combination regimens of topical calcipotriene with acitretin, cyclosporin, and psoralen-UV-A appear not to improve treatment effects in chronic plaque psoriasis but they may reduce the long-term risk of toxic effects (Ashcroft et al., "Combination regimens," 2000; DARE-20010166, 2002) [**B**].

*Note: All pictures identified in this summary can be found in the original guideline document.

Definitions:

Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogeneous results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Accurate diagnosis and effective treatment of psoriasis

POTENTIAL HARMS

Side Effects of Medication

- *Calcipotriol*. In a systematic review, calcipotriol was found to cause significantly more skin irritation than topical corticosteroids.
- *Sulfasalazine*. In one randomized controlled trial (RCT), the efficacy of sulfasalazine was offset to a degree by patient intolerance and side effects, particularly nausea, vomiting, and rashes.
- *Tablet-psoralen-ultraviolet-light (PUVA) therapy* was associated with increased risk of skin cancer.
- Irritation is seen in some patients using *tazarotene*.
- *Topical corticosteroids* can induce skin atrophy (thinning of the skin, papery skin, dilated capillaries, bruising).
- Coal tar preparations are not much used because of their smell and mess.
- A special risk associated with *infliximab* and *etanercept* is activation of latent infections (e.g., tuberculosis)

CONTRAINDICATIONS

CONTRAINDICATIONS

- *Systemic corticosteroids* should not by used for treatment of psoriasis in children, as the disease progression to an extensive form of pustular psoriasis is possible.
- Contraindications to *heliotherapy include* alcoholism, severe mental health problems, photosensitizing medication (e.g., amiodarone, piroxicam, and doxycycline), and poor general health.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Finnish Medical Society Duodecim. Psoriasis. In: EBM Guidelines. Evidence-Based Medicine [Internet]. Helsinki, Finland: Wiley Interscience. John Wiley & Sons; 2005 May 25 [Various].

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 May 7 (revised 2005 May 25)

GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

SOURCE(S) OF FUNDING

Finnish Medical Society Duodecim

GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Erna Snellman

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

GUIDELINE AVAILABILITY

This guideline is included in "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: <u>info@ebm-guidelines.com</u>; Web site: <u>www.ebm-guidelines.com</u>.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 17, 2002. The information was verified by the guideline developer as of February 7, 2003. This NGC guideline was updated by ECRI on October 4, 2004. This summary was updated by ECRI on July 21, 2005 following the Food and Drug Administration (FDA) advisory on Raptiva (efalizumab). This summary was most recently updated on November 14, 2005. This summary was updated by ECRI on February 7, 2006 following the Food and Drug Administration (FDA) advisory on Hydrea and Droxia (hydroxyurea capsules). This summary was updated by ECRI Institute on May 15, 2008 following the U.S. Food and Drug Administration advisory on Enbrel (etanercept). This summary was updated by ECRI Institute on October 30, 2008 following the U.S. Food and Drug Administration advisory on Raptiva (efalizumab).

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