Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Nubevital BB; Nubevital Sunblock Ultra; Refrane Plus; ***Braz.:*** Sunmax Acqua; ***Canad.:*** Hawaiian Tropic Herbal†; ***Chile:*** Hidrafil; Spectraban 55; ***Mex.:*** Spectraban 55; ***USA:*** Hawaiian Tropic Protective Tanning Dry.

T4 Endonuclease V

Bacteriophage T4 Endodeoxyribonuclease V; T4N5. Coliphage T4 endodeoxyribonuclease V.

T4 Эндонуклеаза V

CAS — 52227-85-7.

Profile

T4 endonuclease V is a DNA-repair enzyme that is reported to remove DNA damaged by UV radiation. It is under investigation to reduce the incidence of actinic keratosis and basal cell carcinoma in patients with xeroderma pigmentosum (see Photosensitivity Disorders, p.1581).

◊ References.

1. Wolf P, *et al.* Topical treatment with liposomes containing T4 endonuclease V protects human skin in vivo from ultraviolet-induced upregulation of interleukin-10 and tumor necrosis factor-α. *J Invest Dermatol* 2000; **114:** 149–56.
2. Yarosh D, *et al.* Effect of topically applied T4 endonuclease V in liposomes on skin cancer in xeroderma pigmentosum: a randomised study. *Lancet* 2001; **357:** 926–9.

Tacalcitol *(BAN, rINN)*

1α,24-Dihydroxycholecalciferol; 1α,24-Dihydroxyvitamin D_3; Tacalcitolum; Takalsitol. (+)-(5*Z*,7*E*,24*R*)-9,10-Secocholesta-5,7,10(19)-triene-1α,3β,24-triol monohydrate.

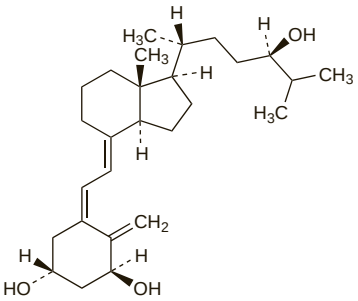
Такальцитол

$C_{27}H_{44}O_3,H_2O$ = 434.7.

CAS — 57333-96-7 (anhydrous tacalcitol); 93129-94-3 (tacalcitol monohydrate).

ATC — D05AX04.

ATC Vet — QD05AX04.



Adverse Effects and Precautions

As for Calcipotriol, p.1591. Paraesthesia may also occur. Tacalcitol may be applied to the face, but care should be taken to avoid the eyes. Tacalcitol may be degraded by UV radiation (see Uses and Administration, below).

Uses and Administration

Tacalcitol is a vitamin D_3 derivative, with actions and uses similar to those of calcipotriol (p.1592).

Tacalcitol is applied topically in the management of plaque psoriasis (p.1583). It is used as the monohydrate, but the concentration is expressed in terms of anhydrous tacalcitol; 4.17 micrograms of tacalcitol monohydrate is equivalent to about 4 micrograms of tacalcitol. It is applied as an ointment containing the equivalent of tacalcitol 4 micrograms/g (0.0004%). Applications are made once daily, preferably at bedtime, and no more than 10 g of ointment should be applied each day. Duration of treatment depends on the severity of the lesions; continuous and intermittent treatments for up to 12 months have been used.

Tacalcitol may be degraded by UV radiation and therefore if combined with UV therapy, the radiation should be given in the morning and tacalcitol applied at bedtime.

◊ References.

1. Peters DC, Balfour JA. Tacalcitol. *Drugs* 1997; **54:** 265–71.
2. Gollnick H, Menke T. Current experience with tacalcitol ointment in the treatment of psoriasis. *Curr Med Res Opin* 1998; **14:** 213–18.
3. Harrison PV. Topical tacalcitol treatment for psoriasis. *Hosp Med* 2000; **61:** 402–5.
4. Van de Kerkhof PCM, *et al.* Long-term efficacy and safety of tacalcitol ointment in patients with chronic plaque psoriasis. *Br J Dermatol* 2002; **146:** 414–22.
5. Lecha M, *et al.* Tacalcitol in the treatment of psoriasis vulgaris: the Spanish experience. *J Eur Acad Dermatol Venereol* 2005; **19:** 414–17.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Bonalfa†; ***Austria:*** Curatoderm; ***Belg.:*** Curatoderm; ***Chile:*** Bonalfa; ***Cz.:*** Curatoderm; ***Fr.:*** Apsor; ***Ger.:*** Curatoderm; ***Hung.:*** Curatoderm; ***Israel:*** Curatoderm; ***Ital.:*** Ticlapsor; Vellutan; ***Jpn:*** Bonalfa; ***Mex.:*** Bonalfa; ***Pol.:*** Curatoderm; ***Port.:*** Bonalfa; ***Spain:*** Bonalfa; ***Switz.:*** Curatoderm; ***UK:*** Curatoderm; ***Venez.:*** Bonalfa†.

Purified Talc

E553(b); Mastek; Powdered Talc; Purified French Chalk; Talc; Talco (esteatita); Talco purificado; Talcum; Talcum Purificatum; Talk; Talkas; Talkki; Talkum.

Очищенный Тальк

CAS — 14807-96-6.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Talc; Purified Talc BP 2008). A powdered, selected, natural, hydrated, magnesium silicate. Pure talc has the formula $Mg_3Si_4O_{10}(OH)_2$; it may contain varying amounts of associated minerals. A light, homogeneous, white or almost white powder, greasy to the touch (non-abrasive). It should be free from asbestos. Practically insoluble in water, in alcohol, and in dilute solutions of acids and of alkali hydroxides.

USP 31 (Talc). A powdered, selected, natural, hydrated magnesium silicate. It may contain variable amounts of associated minerals among which chlorites (hydrated aluminium and magnesium silicates), magnesite (magnesium carbonate), calcite (calcium carbonate), and dolomite (calcium and magnesium carbonate) are predominant. A very fine, white or greyish-white, unctuous crystalline powder, which adheres readily to the skin, and is free from grittiness.

Adverse Effects and Precautions

Contamination of wounds or body cavities with talc is liable to cause granulomas and it should not be used for dusting surgical gloves.

Inhalation of talc can cause respiratory irritation; prolonged exposure may produce pneumoconiosis.

The most common adverse effects of talc pleurodesis are chest pain and fever. More serious complications that can occur include empyema, pneumonitis, dyspnoea, hypoxaemia, pulmonary oedema, pulmonary embolism, acute respiratory distress syndrome, and respiratory failure. Cardiovascular complications such as tachycardia, myocardial infarction, hypotension, hypovolaemia, and asystolic arrest have also occurred in patients treated with talc pleurodesis. However, the role of talc in serious complications is not always clear as the underlying condition of patients with malignant pleural effusion and the procedure itself are likely to be contributing factors.

Talc is liable to be heavily contaminated with bacteria, including *Clostridium tetani, Cl. welchii,* and *Bacillus anthracis.* When used in dusting powders or to treat pneumothorax and pleural effusions, it should be sterilised.

Abuse. Adverse pulmonary and ocular effects have been associated with the presence of talc in abused substances. It may be present as an excipient in oral medications that are crushed then dissolved and injected, or it may have been purposely added as a filler to the abused substance. When injected intravenously, the insoluble talc particles can embolise in small pulmonary vessels causing occlusion and pulmonary hypertension. The particles may also then migrate into the pulmonary interstitium, inducing a foreign-body reaction and fibrosis. Irregular nodules can develop in the lungs, which may coalesce to form conglomerate masses.[1] Talc retinopathy is described as deposits of crystalline talc embolising in the retinal microvasculature after intravenous injection.[2-4] Pulmonary granulomas[5] and talc retinopathy[6] have also been described after nasal inhalation of abused substances containing talc.

1. Gotway MB, *et al.* Thoracic complications of illicit drug use: an organ system approach. *Radiographics* 2002; **22** (suppl): S119–S135.
2. Martidis A, *et al.* Talc embolism: a static retinopathy. *Am J Ophthalmol* 1997; **124:** 841–3.
3. Fraser-Bell S, Capon M. Talc retinopathy. *Clin Experiment Ophthalmol* 2002; **30:** 432–3.
4. El-Jabali F, Cohen S. Talc retinopathy. *N Engl J Med* 2006; **354:** e11. Available at: http://content.nejm.org/cgi/reprint/354/12/e11.pdf (accessed 27/09/07)
5. Johnson DC, *et al.* Foreign body pulmonary granulomas in an abuser of nasally inhaled drugs. *Pediatrics* 1991; **88:** 159–61.
6. Kumar RL, *et al.* Crystalline retinopathy from nasal ingestion of methamphetamine. *Retina* 2006; **26:** 823–4.

Carcinogenicity. A review by a working group of the International Agency for Research on Cancer concluded that there was inadequate evidence to confirm whether purified talc was carcinogenic in humans but there was sufficient evidence to confirm that talc containing asbestiform fibres was carcinogenic to man.[1] There have been suggestions of a link between the use of talc and ovarian cancer[2] but although a case-controlled study suggested an approximate doubling of the risk among women after perineal use of talc the working group noted that information was not available on the asbestos content of the talcs.[1] Further case-controlled studies have also reported a positive association between perineal talc use and ovarian cancer, although others have found no association. A large prospective cohort study[3] that included 78 630 women found little support for an association overall, although from an analysis by histological subtype there appeared to be a modest increase in the risk for serous invasive cancer. A meta-analysis[4] that included this cohort study and 15 case-controlled studies did find a positive association between any exposure to perineal talc and the risk of developing ovarian cancer (relative risk 1.33; 95% confidence interval 1.16 to 1.45). However, the authors highlighted possible selection bias and confounding factors that may have resulted in a false-positive association. There was a lack of a clear dose-response relationship, different results for hospital-based and population-based patients, and the timing of exposure to talc in relation to cancer diagnosis was not always known.

An analysis of epidemiological studies in workers involved in milling the raw mineral (not containing asbestos-like fibres) found no evidence of an increased risk of lung cancer; there was some evidence of an excess among miners or other industrial workers exposed to talc, but these populations were also exposed to other potential carcinogens.[5]

1. IARC/WHO. Silica and some silicates. *IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans volume 42* 1987. Available at: http://monographs.iarc.fr/ENG/Monographs/vol42/volume42.pdf (accessed 27/09/07)
2. Longo DL, Young RC. Cosmetic talc and ovarian cancer. *Lancet* 1979; **ii:** 349–51.
3. Gertig DM, *et al.* Prospective study of talc use and ovarian cancer. *J Natl Cancer Inst* 2000; **92:** 249–52.
4. Huncharek M, *et al.* Perineal application of cosmetic talc and risk of invasive epithelial ovarian cancer: a meta-analysis of 11,933 subjects from sixteen observational studies. *Anticancer Res* 2003; **23:** 1955–60.
5. Wild P. Lung cancer risk and talc not containing asbestiform fibres: a review of the epidemiological evidence. *Occup Environ Med* 2006; **63:** 4–9.

Effects on the lungs. Acute respiratory failure has occurred in patients treated with talc pleurodesis, given either as a slurry or by insufflation. In a series of 338 patients treated with insufflation, 4 developed acute respiratory failure and 3 of them died.[1] In another series[2] of 78 patients who underwent 89 procedures using slurry or insufflation, respiratory complications developed after 24 procedures including acute respiratory distress syndrome after 8 procedures in 7 patients of whom 1 died. In a debate based on these and other reports, including some series in which there were no respiratory complications, it was argued[3] that although the risk of acute respiratory distress is small the use of talc for pleurodesis should be abandoned in favour of other drugs such as tetracyclines or bleomycin, or mechanical abrasion of the pleura. The opposing view[4] was that there were many possible causes for acute respiratory distress in these cases, and that talc was still the best pleurodesis agent available. In a prospective randomised comparison in patients with malignant pleural effusion,[5] respiratory complications were more common with insufflation than slurry. The authors noted that the role of talc in causing acute respiratory complications of pleurodesis is unclear and further study is needed.

It has been suggested that acute respiratory distress syndrome after talc pleurodesis may be related to the talc particle size. There were no such reactions in a study[6] of 558 patients given large-particle (mean size 24.5 μm) talc insufflation, and the authors suggested that reported cases appeared to occur in countries where talc products contained higher concentrations of small particles (less than 5 μm).

For other effects on the lungs, see under Abuse, above and Infant Skin Care, below.

1. Campos JRM, *et al.* Respiratory failure due to insufflated talc. *Lancet* 1997; **349:** 251–2.
2. Rehse DH, *et al.* Respiratory failure following talc pleurodesis. *Am J Surg* 1999; **177:** 437–40.
3. Light RW. Talc should not be used for pleurodesis. *Am J Respir Crit Care Med* 2000; **162:** 2024–6.
4. Sahn SA. Talc should be used for pleurodesis. *Am J Respir Crit Care Med* 2000; **162:** 2023–4.
5. Dresler CM, *et al.* Phase III intergroup study of talc poudrage vs talc slurry sclerosis for malignant pleural effusion. *Chest* 2005; **127:** 909–15.
6. Janssen JP, *et al.* Safety of pleurodesis with talc poudrage in malignant pleural effusion: a prospective cohort study. *Lancet* 2007; **369:** 1535–9.

Infant skin care. The routine use of non-medicated powders in the skin care of infants can be hazardous and their use should be discouraged.[1,2] Talc acts as a pulmonary irritant and inhalation of baby-powders by infants has caused severe respiratory difficulties and several deaths have been reported. Careful respiratory monitoring is indicated in children suspected of inhaling talcum powder as the onset of symptoms may be delayed for several