described on p.1492. For recommendations concerning the correct use of corticosteroids on the skin, and a rough guide to the clinical potencies of topical corticosteroids, see p.1497.

Preparations

Proprietary Preparations (details are given in Part 3) Spain: Cutanit.

Fludrocortisone Acetate (BANM, rINNM)

Acetato de fludrocortisona; Fludrocortisone, acétate de; Fludrocortisoni acetas; Fludrokortison acetát; Fludrokortisonacetat; Fludrokortisoniasetaatti: Fludrokortizon-acetát: Fludrokortizono acetatas; Fludrokortyzonu octan; 9α -Fluorohydrocortisone 21-Acetate. 9α-Fluoro-11β,17α,21-trihydroxypregn-4-ene-3,20-dione 21-acetate.

Флудрокортизона Ацетат

 $C_{23}H_{31}FO_6 = 422.5.$

CAS — 127-31-1 (fludrocortisone); 514-36-3 (fludrocortisone acetate).

ATC - H02AA02

ATC Vet — QH02AA02.

(fludrocortisone)

Pharmacopoeias. In Chin., Eur. (see p.vii), Int., and US. Ph. Eur. 6.2 (Fludrocortisone Acetate). A white or almost white, crystalline powder. Practically insoluble in water; sparingly soluble in dehydrated alcohol.

USP 31 (Fludrocortisone Acetate). White to pale yellow, odourless or practically odourless, hygroscopic, crystals or crystalline powder. Insoluble in water; sparingly soluble in alcohol and in chloroform; slightly soluble in ether. Protect from light.

Adverse Effects, Treatment, Withdrawal, and Precautions

Fludrocortisone acetate has glucocorticoid actions about 10 times as potent as hydrocortisone and mineralocorticoid effects more than 100 times as potent. Adverse effects are mainly those due to mineralocorticoid activity, as described on p.1490.

When applied topically, particularly to large areas, when the skin is broken, or under occlusive dressings, corticosteroids may be absorbed in sufficient amounts to cause systemic effects. Prolonged use of ophthalmic preparations containing corticosteroids has caused raised intra-ocular pressure and reduced visual function.

Interactions

The interactions of corticosteroids in general are described on p.1494.

Pharmacokinetics

For a brief outline of the pharmacokinetics of corticosteroids, see p.1495.

Fludrocortisone is readily absorbed from the gastrointestinal tract. The plasma half-life is about 3.5 hours or more, but fludrocortisone exhibits a more prolonged biological half-life of 18 to 36 hours.

Uses and Administration

Fludrocortisone is a corticosteroid with glucocorticoid and highly potent mineralocorticoid activity (p.1490).

Fludrocortisone acetate is given orally to provide mineralocorticoid replacement in primary adrenocortical insufficiency (p.1498), with glucocorticoids. It is used in a dose range of 50 to 300 micrograms daily.

Fludrocortisone acetate may also be given with glucocorticoid therapy in doses of up to 200 micrograms daily in the salt-losing form of congenital adrenal hyperplasia (p.1502).

It is also given in the management of severe orthostatic hypotension (see below).

Fludrocortisone acetate is applied topically for its glucocorticoid actions in the treatment of various disorders. It is used as an ingredient of eye ointment or ear drops, usually in a concentration of 0.1%. Fludrocortisone acetate has also been included in topical preparations used for skin disorders. For recommendations concerning the correct use of corticosteroids on the skin, see p.1497.

Administration. A study of fludrocortisone requirements in 10 patients with Addison's disease indicated that dosage was often inadequate. Nine were initially on fludrocortisone 50 to 100 micrograms daily in addition to cortisone or hydrocortisone; 5 were also taking levothyroxine for an associated auto-immune thyroid disease; one, who had detectable levels of aldosterone, was not initially receiving fludrocortisone. All the patients had evidence of sodium and water depletion and fludrocortisone was started at 300 micrograms daily, with downwards adjustments. Most patients required 200 micrograms daily; 2 patients elected to remain on 300 micrograms daily, but in most this dose caused pronounced sodium and water retention. The patient with detectable aldosterone levels required 50 micrograms daily. Eight of the 10 patients felt better on the higher fludrocortisone doses while 2 felt no change.

1. Smith SJ, et al. Evidence that patients with Addison's disease are undertreated with fludrocortisone. Lancet 1984; i: 11-14

Neurally mediated hypotension. Fludrocortisone may be used in the management of neurally mediated hypotension in patients who require drug therapy (see p.1174) but there is limited evidence to support its use.

Orthostatic hypotension. Orthostatic (postural) hypotension¹⁻⁸ is a fall in blood pressure that occurs upon rising abruptly to an erect position, although it may also occur after a period of prolonged standing. Characteristic symptoms include lightheadedness, dizziness, blurred vision, weakness in the limbs, and syncope.

The causes of orthostatic hypotension are wide-ranging and include autonomic dysfunction, such as in the Shy-Drager syndrome, diabetes mellitus, and Parkinson's disease, circulating volume depletion, phaeochromocytoma, and Addison's disease. Orthostatic hypotension may also occur following a period of prolonged bed rest or after meals.

Orthostatic hypotension may result from the adverse effects of a range of drugs, such as antihypertensives, diuretics, tricyclic antidepressants, phenothiazines, and MAOIs.

In mild cases nonpharmacological treatment alone may be adequate. This includes increasing salt intake if not contra-indicated, maintaining adequate hydration, the use of elastic stockings to improve venous return and increase cardiac output, and elevating the head of the bed to reduce early morning symptoms. Druginduced orthostatic hypotension should be treated by withdrawing the drug or by dose reduction.

Pharmacological treatment. No pharmacological treatment is entirely satisfactory: responses and tolerance vary greatly between patients. Fludrocortisone acetate is usually tried first; it increases sodium retention and thus plasma volume. Most reports indicate some response in about 80% of patients, but hypokalaemia, fluid retention, and supine hypertension may limit its use. In patients who fail to respond adequately an NSAID (usually indometacin) may be tried, alone or with fludrocortisone. In patients with overt autonomic failure a beta blocker with some partial agonist activity, such as pindolol, may be tried although they are potentially dangerous.

Sympathomimetics may be useful in some patients with autonomic failure; the direct acting drugs such as phenylephrine or midodrine are usually more consistently effective than the indirect such as ephedrine, but even so, responses tend to vary with the degree of denervation. Ambulatory noradrenaline infusion therapy is under investigation for severe refractory orthostatic hypotension. Patients with central neurological abnormalities may respond to desmopressin, while drugs such as ergotamine or dihydroergotamine may be useful for resistant disease.

Other drugs that have been tried include metoclopramide, which may be useful for autonomic symptoms in patients with diabetes mellitus, fluoxetine, octreotide, yohimbine, clonidine, and in patients with concurrent anaemia, erythropoietin. Caffeine has been tried in postprandial hypotension but its value in all but the mildest cases is dubious.5 The use of MAOIs (which given alone can induce orthostatic hypotension) with a sympathomimetic to

induce a pressor reaction is controversial. Most of these drugs have potentially serious adverse effects and few are well evalu-

- 1. Ahmad RAS, Watson RDS. Treatment of postural hypotension: a review. Drugs 1990; 39: 74-85.
- Tonkin AL, Wing LMH. Hypotension: assessment and management. Med J Aust 1990; 153: 474–85.
- 3. Schoenberger JA. Drug-induced orthostatic hypotension. Drug Safety 1991; 6: 402-7
- Stumpf JL, Mitrzyk B. Management of orthostatic hypotension Am J Hosp Pharm 1994; 51: 648–60. 5. Mathias CJ. Orthostatic hypotension. Prescribers' J 1995; 35:
- 6. Frishman WH, et al. Drug treatment of orthostatic hypotension and vasovagal syncope. Heart Dis 2003; 5: 49–64. 7. Freeman R. Treatment of orthostatic hypotension. Semin Neurol
- 2003; 23: 435-42. 8. Gupta V, Lipsitz LA. Orthostatic hypotension in the elderly: diagnosis and treatment. Am J Med 2007; 120: 841-7.

Preparations

BP 2008: Fludrocortisone Tablets; **USP 31:** Fludrocortisone Acetate Tablets.

Proprietary Preparations (details are given in Part 3)

Proprietary Preparations (details are given in Part 3)
Arg.: Lonlian, Australi. Florinef, Austria: Astonin Hs Braz.: Borinefe; Canad.: Borinef, Chile: Florinef, Denm.: Florinef: Fin.: Florinef Ger.: Astonin H, Gr.: Florinef; Hong Kong: Florinef, Hung.: Astonin H; Irl.: Florinef; Israel: Florinef; Malaysia: Florinef, Mex.: Florinef, Neth.: Florinef, Now.: Florinef, NZ: Florinef, Pol.: Cortineff, Rus.: Cortineff (Kopru-leph): S.Afr.: Florinef, Spagore: Florinef, Spain: Astonin; Swed.: Florinef, Spain: Astonin; Swed.: Florinef; Florinef; UK: Florinef; USA: Florinef; Venez.: Florinefe;

Multi-ingredient: Belg.: Panotile; Braz.: Otodol†; Panotil; Fr.: Panotile; Ger.: Panotile N†; Gr.: Paroticin; Indon.: Nelicort; Otopian; Otopian; Otopraf; Oto-zambon; Neth.: Panotile; Pol.: Dicortineff; Spain: Fludronef; Panotile; Switz.: Panotile; Thai.: Otosamthong.

Fludroxycortide (BAN, rINN) ⊗

33379; Fludroksikortidi; Fludroxicortida; Fludroxikortid; Fludroxycortidum; Fluorandrenolone; 6α-Fluoro-16α-hydroxyhydrocortisone 16,17-Acetonide; Flurandrenolide (USAN); Flurandrenolone. 6α -Fluoro-11 β ,21-dihydroxy-16 α ,17 α -isopropylidenedioxypregn-4-ene-3,20-dione.

Флудроксикортид

 $C_{24}H_{33}FO_6 = 436.5.$ CAS — 1524-88-5. ATC - D07AC07. ATC Vet — QD07AC07.

Pharmacopoeias. In US.

USP 31 (Flurandrenolide). A white to off-white, fluffy, odourless, crystalline powder. Practically insoluble in water and in ether; soluble 1 in 72 of alcohol, 1 in 10 of chloroform, and 1 in 25 of methyl alcohol. Store in airtight containers at a temperature not exceeding 8°. Protect from light.

Profile

Fludroxycortide is a corticosteroid used topically for its glucocorticoid activity (p.1490) in the treatment of various skin disorders. It is usually used as a cream, lotion, or ointment containing 0.0125% or 0.05%. It is also used as an adhesive polyethylene tape impregnated with fludroxycortide 4 micrograms/cm²

When applied topically, particularly to large areas, when the skin is broken, or under occlusive dressings, corticosteroids may be absorbed in sufficient amounts to cause systemic effects (p.1490). The effects of topical corticosteroids on the skin are described on p.1492. For recommendations concerning the correct use of corticosteroids on the skin, and a rough guide to the clinical potencies of topical corticosteroids, see p.1497.

Preparations

USP 31: Flurandrenolide Cream; Flurandrenolide Lotion; Flurandrenolide Ointment; Flurandrenolide Tape; Neomycin Sulfate and Flurandrenolide Cream; Neomycin Sulfate and Flurandrenolide Lotion; Neomycin Sulfate and Flurandrenolide Lotion; Neomycin Sulfate and Flurandrenolide Ointment.

Proprietary Preparations (details are given in Part 3) Braz.: Drenison; UK: Haelan; USA: Cordran.

Multi-ingredient: Braz.: Dreniformio; Drenison N.

Flumetasone Pivalate (BANM, rINNM) &

Flumetason pivalát; Flumétasone, pivalate de; Flumetasoni pivalas; Flumetasonipivalaatti; Flumetasonpivalat; Flumetasonum Pivalas; Flumetazon Pivalat; Flumetazono pivalatas; Flumetazon-pivalát; Flumetazonu piwalan; Flumethasone Pivalate (USAN); Flumethasone Trimethylacetate; NSC-107680; Pivalato de flumetasona. Flumethasone 21-pivalate.

Флуметазона Пивалат

 $C_{27}H_{36}F_2O_6 = 494.6.$ CAS - 2002-29-1. ATC - D07AB03. ATC Vet - QD07AB03.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.

Ph. Eur. 6.2 (Flumetasone Pivalate). A white or almost white, crystalline powder. It shows polymorphism. Practically insoluble in water; slightly soluble in alcohol and in dichloromethane; sparingly soluble in acetone. Protect from light.

(flumetasone)

USP 31 (Flumethasone Pivalate). A white to off-white crystalline powder. Insoluble in water; soluble 1 in 89 of alcohol, 1 in 350 of chloroform, and 1 in 2800 of ether; slightly soluble in methyl alcohol; very slightly soluble in dichloromethane. Store in airtight containers. Protect from light.

Profile

Flumetasone pivalate is a corticosteroid used topically for its glucocorticoid activity (p.1490) in the treatment of various skin disorders. It is usually used as a 0.02% cream, ointment, or lotion. When applied topically, particularly to large areas, when the skin is broken, or under occlusive dressings, corticosteroids may be absorbed in sufficient amounts to cause systemic effects (p.1490). The effects of topical corticosteroids on the skin are described on p.1492. For recommendations concerning the correct use of corticosteroids on the skin, and a rough guide to the clinical potencies of topical corticosteroids, see p.1497.

Flumetasone pivalate is also used in ear drops in a concentration of 0.02% with clioquinol 1%.

Preparations

USP 31: Flumethasone Pivalate Cream.

Proprietary Preparations (details are given in Part 3)

Belg.: Locacortene; Ger.: Cerson; Locacorten; Ital.: Locorten†; Neth.: Locacorten: Pol.: Lorinden: Switz.: Locacorten: Venez.: Lexifalt: Loco-

Multi-ingredient: Arg.: Locorten Vioformo†; Salena†; Tresite F; Austral.: Locacorten Vioform; Austria: Locacorten mit Neomycin; Locacorten Tar; Locacorten Vioform; Locasalen; Belg.: Locacortene Tar†; Locacortene Vioformo†; Locasalen; Braz.: Locorten Vioformo†; Locasalen; Braz.: Locorten†; Loradorten Tar†; Lorinden A†; Loradorten Tar†; Lorinden A†; Lorinden C†; Denm: Locacorten Vioform; Fin: Locacorten Vioform; Fr: Locacorten Vioforme; Locacorten Vioform; Fin: Locacorten Vioforme; Locacorten Vioformi; Locacorten Vioformi; Locacorten Vioformi; Locacorten Vioformi; Locacorten Vioformi; Locacorten Vioformi; Locacorten Vioform; Locacorten Vioforme; Delizion VII: Locacorten Vioform; Locacalen; VII: Locacorten Vioform; Locacalen; VII: Locacorten Vioform; Locacalen; VII: Locacorten Vioform; Locacalen; Colorind, Col Losalen; Vasosterone Oto; Netn.: Locacorten Vioform; Locasalen; N2: Lo-corten Vioform; Philipp.: Locasalen; Pol.: Lorinden A; Lorinden C; Lorind-en N; Port.: Locorten Vioformio†; Losalen†; Rus.: Lorinden A (Лоринден A); Lorinden C (Лоринден С); S.Afr.: Locacorten Vioform; Spain: Lo-salen; Swed.: Locacorten Vioform; Switz.: Locasalen; Thai.: Flumasalen; Locasalen; Turk.: Locacortene Vioform; Locasalene; UK: Locorten Vio-form; Venez.: Flutalon†; Locasalen; Locorten Vioformo.

Flunisolide (BAN, USAN, rINN) ⊗

Flunisolid; Flunisolida; Flunisolidi; Flunisolidum; RS-3999; RS-1320 (flunisolide acetate). 6α -Fluoro-11 β ,21-dihydroxy-1 6α ,17 α -isopropylidenedioxypregna-1,4-diene-3,20-dione.

Флунизолид

 $C_{24}H_{31}FO_6 = 434.5.$

CAS — 3385-03-3 (flunisolide); 77326-96-6 (flunisolide hemihydrate); 4533-89-5 (flunisolide acetate).

ATC - ROTADO4; RO3BAO3.

ATC Vet — QR01AD04; QR03BA03.

CH₃ H_3C H_3C Н Ĥ Ĥ F Ή

Pharmacopoeias. In US which specifies the hemihydrate. USP 31 (Flunisolide). A white to creamy-white crystalline powder. Practically insoluble in water; soluble in acetone; sparingly soluble in chloroform; slightly soluble in methyl alcohol.

Adverse Effects, Treatment, Withdrawal, and Precautions

As for corticosteroids in general (see p.1490).

Interactions

The interactions of corticosteroids in general are described on p.1494.

Pharmacokinetics

For a brief outline of the pharmacokinetics of corticosteroids, see p.1495. Flunisolide is reported to undergo extensive first-pass metabolism, with only 20% of the dose available systemically if it is given by mouth. The major metabolite, 6β-hydroxyflunisolide has some glucocorticoid activity; it has a half-life of about 4 hours. Only small amounts of flunisolide are absorbed after intranasal doses.

♦ References

- 1. Chaplin MD, et al. Flunisolide metabolism and dynamics of a metabolite. Clin Pharmacol Ther 1980; 27: 402–13.
- 2. Möllmann H, et al. Pharmacokinetic/pharmacodynamic evaluation of systemic effects of flunisolide after inhalation. *J Clin Pharmacol* 1997; **37:** 893–903.

Uses and Administration

Flunisolide is a corticosteroid with glucocorticoid activity (p.1490) used as a nasal spray for the prophylaxis and treatment of allergic rhinitis (p.565). In the UK a formulation containing 25 micrograms per metered spray is available, whereas in the USA each metered spray contains 29 micrograms flunisolide. In adults, the recommended starting dose is 2 sprays into each nostril twice daily, increased if necessary to three times daily, and then reduced for maintenance. In the USA a maximum dose of 8 sprays into each nostril daily has been established. For children aged from about 5 to 14 years, 1 spray into each nostril may be given up to 3 times daily; the USA also allows for an initial 2 sprays into each nostril twice daily (this is the recommended maximum of 4 sprays into each nostril daily).

Flunisolide is also used by inhalation from metereddose aerosols in the management of asthma (p.1108). The usual adult dosage of flunisolide from an aerosol using chlorofluorocarbon (CFC) propellants is 500 micrograms inhaled twice daily. In severe asthma the dosage may be increased but should not exceed a total of 2 mg daily. A dose for children of 6 to 15 years of age is 500 micrograms inhaled twice daily, which should not be exceeded. A hydrofluoroalkane (CFCfree) aerosol, which is also available in some countries, has a lower dose because of different delivery characteristics. The usual adult dose, expressed as flunisolide hemihydrate, is 160 micrograms twice daily, which may be increased after 3 to 4 weeks but should not exceed 320 micrograms twice daily. In children aged 6 to 11 years of age a dose of 80 micrograms twice daily may be used, increased to a maximum of 160 micrograms twice daily if necessary.

Preparations

USP 31: Flunisolide Nasal Solution.

Proprietary Preparations (details are given in Part 3) Arg.: Fluntec†, Austria: Pulmilide; Belg.: Syntaris; Canad.: Rhinalar†, Cz.: Bronilide†; Syntaris; Demm.: Locasyn†; Fr.: Nasalide; Ger.: Inhacort†; Syntaris; Gr.: Bronalide†; Irl.: Syntaris†; Ital.: Aerflu; Aerolid; Asmaflu; Assolid; Careflu; Charlyn; Citiflux; Desaflu; Doricoflu; Eliosid; Euroflu; Fluminex; Flunigar†; Flunitop; Gibiflu; Givair; Inalcort; Kaimil; Levonis; Lunibron; Lunis; Nebulcort; Nereflun; Nisolid; Nisoran; Pantasof†; Plaudit; Pulmist; Syntaris; Turm; Ventoflu; Neth.; Syntaris; Norw: Loklain; Switz: Broncort†; Syntaris†; UK: Syntaris; USA: AeroBid; AeroSpan; Nasalide†; Nasarel.

Multi-ingredient: Ital.: Plenaer.

Fluocinolone Acetonide (BANM, USAN, rINN) ⊗

Acetónido de fluocinolona; 6α,9α-Difluoro-16α-hydroxyprednisolone Acetonide: Fluocinolon acetonid: Fluocinolonacetonid: Fluocinolon-acetonid: Fluocinolone, acétonide de: Fluocinoloni acetonidum; Fluocinolono acetonidas; Fluocynolonu acetonid; Fluosinoloniasetonidi; NSC-92339. 6α , 9α -Difluoro-11 β ,21-dihydroxy-16α,17α-isopropylidenedioxypregna-1,4-diene-3,20-di-

Флуоцинолона Ацетонид

C₂₄H₃₀F₂O₆ = 452.5. CAS — 67-73-2. ATC — C05AA10; D07AC04; S01BA15.

ATC Vet — QC05AA10; QD07AC04; QS01BA15.

Pharmacopoeias. In Eur. (see p.vii), Jpn, and Viet. Br. and Viet. have a separate monograph for the dihydrate; US allows either the anhydrous form or the dihydrate.

Ph. Eur. 6.2 (Fluocinolone Acetonide). A white or almost white, crystalline powder. It exhibits polymorphism. Practically insoluble in water; soluble in dehydrated alcohol and in acetone. Protect from light.

BP 2008 (Fluocinolone Acetonide Dihydrate). A white or almost white, crystalline powder. Practically insoluble in water and in hexane; soluble in dehydrated alcohol; freely soluble in acetone; sparingly soluble in dichloromethane and in methyl alcohol. Pro-

USP 31 (Fluocinolone Acetonide). It is anhydrous or contains two molecules of water of hydration. A white or practically white, odourless, crystalline powder. Insoluble in water; soluble 1 in 45 of alcohol, 1 in 25 of chloroform, and 1 in 350 of ether; soluble in methyl alcohol.

Profile

Fluocinolone acetonide is a corticosteroid used topically for its glucocorticoid activity (p.1490) in the treatment of various skin disorders. It is usually used as a cream, gel, lotion, ointment, or scalp application; concentrations normally range from 0.0025 to 0.025% although higher-strength preparations may be available. When applied topically, particularly to large areas, when the skin is broken, or under occlusive dressings, corticosteroids may be absorbed in sufficient amounts to cause systemic effects (p.1490). The effects of topical corticosteroids on the skin are described on p.1492. For recommendations concerning the correct use of corticosteroids on the skin, and a rough guide to the clinical potencies of topical corticosteroids, see p.1497.

Fluocinolone acetonide is also used topically with an antibacterial in the treatment of infective inflammatory eye, ear, and nose disorders

A sterile implant of fluocinolone acetonide is used intravitreally for the treatment of chronic non-infectious posterior uveitis

Formulation. The potency of fluorinolone acetonide varied with the formulation in a study1 involving different Synalar topical preparations, the gel, ointment, and cream. The cream was the most potent followed by the gel, and then the ointment. A comparison of topical vasoconstrictor activity (used as an index of potency) unexpectedly found that the commercial dilutions of the cream (containing 0.00625% and 0.0025%) were indistinguishable in their effects from the full-strength (0.025%) cream.

1. Gao HY, Li Wan Po A. Topical formulations of fluocinolone acetonide: are creams, gels and ointments bioequivalent and does dilution affect activity? Eur J Clin Pharmacol 1994; 46: 71-5.

Preparations

BP 2008: Fluocinolone Cream; Fluocinolone Ointment; **USP 31:** Fluocinolone Acetonide Cream; Fluocinolone Acetonide Ointment; Fluocinolone Acetonide Topical Solution; Neomycin Sulfate and Fluocinolone Acetonide Cream.

Proprietary Preparations (details are given in Part 3)

Proprietary Preparations (details are given in Part 3)
Arg.: Duofit, Flulone; Austria: Synalar; Belg.: Synalar; Canad.: Capex,
Derma-Smoothe/FS; Fluoderm†; Synalar; Chile: Adermina; Cz.: Flucinar;
Gelargin; Synalar†, Denm.: Synalar; Fr.: Synalar†; Ger.: Flucinar; Jellin; Jellisoft; Gr.: Synalar†, Hong Kong: Cinotec†; Flunclone; Pictinar; Synalar†, India: Flucort; Flucort-H; Luci; Indon.: Cinolon; Dermasolon; Esinol; Indem; Licosolon; Irl.: Synalar†; Israel: Dermalar; Ital.
Attoactive; Cortamide†; Dermobeta; Dermolin; Esacinone†; Fluocit;
Fluomix Same; Fluovitef; Fluvean†; Localyn; Localyn SV; Omniderm; Ster-