**Pharmacopoeias.** In *Swiss*.

### Profile
Drofenine hydrochloride is an antimuscarinic available in preparations for the treatment of visceral spasms.

### Preparations
**Proprietary Preparations** (details are given in Part 3)

**Multi-ingredient:** ***Arg.:*** Espasmo Cibalena; ***Austria:*** Spasmoplus; ***Belg.:*** Spasmoplus†; ***Chile:*** Espasmo Cibalgina; Espasmo Cibalgina Compuesta; ***Ger.:*** Spasmo-Cibalgin S†; ***Ital.:*** Spasmo-Cibalgina†; ***Mex.:*** Espasmo Cibalgina; ***Switz.:*** Lunadon; Spasmo-Cibalgin comp†; Spasmo-Cibalgin†.

## Dronabinol *(USAN, rINN)* ⊗

Dronabinolum; NSC-134454; $\Delta^9$-Tetrahydrocannabinol; $\Delta^9$-THC. (6a*R*,10a*R*)-6a,7,8,10a-Tetrahydro-6,6,9-trimethyl-3-pentyl-6*H*-dibenzo[*b*,*d*]pyran-1-ol.

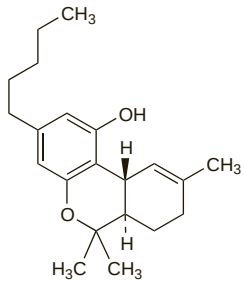
Дронабинол

$C_{21}H_{30}O_2$ = 314.5.

*CAS — 1972-08-3.*

*ATC — A04AD10.*

*ATC Vet — QA04AD10.*



**Pharmacopoeias.** In *US*.

**USP 31** (Dronabinol). Store at a temperature between 8° and 15° in airtight glass containers in an inert atmosphere. Protect from light.

### Adverse Effects and Precautions
As for Nabilone, p.1750. The most frequent adverse effects of dronabinol include abdominal pain, nausea and vomiting, dizziness, euphoria, paranoid reactions, and somnolence. Seizures and seizure-like activity have been reported; dronabinol should be used with caution in those with a history of seizure disorders, and therapy should be stopped if seizures occur.

**Abuse.** The abuse liability of dronabinol was rated as being substantially lower than that of cannabis.[1]

1. WHO. WHO expert committee on drug dependence: thirty-third report. *WHO Tech Rep Ser 915* 2003. Available at: http://libdoc.who.int/trs/WHO_TRS_915.pdf (accessed 03/07/08)

**Breast feeding.** US licensed product information states that dronabinol is concentrated in breast milk and recommends that it should not be used in breast-feeding mothers.

### Pharmacokinetics
After oral doses dronabinol is slowly and erratically absorbed from the gastrointestinal tract; the bioavailability of an oral dose is about 10 to 20%, due to extensive first-pass metabolism. Peak plasma concentrations of dronabinol and its 11-hydroxy metabolite are achieved about 2 to 4 hours after a dose by mouth. It is widely distributed and is extensively protein bound, with a volume of distribution of about 10 litres/kg. Elimination is biphasic, with an initial half-life of about 4 hours, and a terminal half-life of about 25 to 36 hours.

Dronabinol is extensively metabolised, mainly in the liver by cytochrome P450 isoenzymes; the primary metabolite, 11-hydroxydronabinol is also active. The 11-hydroxy metabolite is converted to other, more polar and acidic compounds which are excreted in faeces via the bile, and in the urine. About 50% of an oral dose is recovered in faeces within 72 hours and 10 to 15% in urine. Many of the metabolites have relatively prolonged half-lives, and accumulation may occur with repeated dosage.

Dronabinol is distributed into breast milk and crosses the placenta.

◊ References.

1. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet* 2003; **42:** 327–60.
2. McGilveray IJ. Pharmacokinetics of cannabinoids. *Pain Res Manag* 2005; **10:** 15A–22A.

### Uses and Administration
Dronabinol, the major psychoactive constituent of cannabis (p.2274), has antiemetic properties and is used for the control of **nausea and vomiting** associated with cancer chemotherapy (p.1700) in patients who have failed to respond adequately to conventional antiemetics.

The usual initial oral dose of dronabinol is 5 mg/m$^2$ given 1 to 3 hours before the first dose of the antineoplastic drug with subsequent doses being given every 2 to 4 hours after chemotherapy to a maximum of 4 to 6 doses daily. If necessary, the dose may be increased by increments of 2.5 mg/m$^2$ to a maximum dose of 15 mg/m$^2$, if adverse effects permit.

Dronabinol also has appetite-stimulant effects and is used in the treatment of **anorexia** associated with weight loss in patients with AIDS. For this purpose 2.5 mg may be taken twice daily, before lunch and supper, reduced to a single 2.5-mg dose in the evening in patients who tolerate the drug poorly. If necessary, and if adverse effects permit, doses may also be increased up to 20 mg daily in divided doses.

Dronabinol is used with cannabidiol, another cannabinoid, in a buccal spray preparation as adjunctive treatment for the symptomatic relief of **neuropathic pain** in multiple sclerosis in adults; this combination is also used as adjunctive analgesic treatment in adult patients with advanced cancer and is under investigation for a number of other conditions (see under Cannabis, p.2275).

◊ General references.

1. Voth EA, Schwartz RH. Medicinal applications of delta-9-tetrahydrocannabinol and marijuana. *Ann Intern Med* 1997; **126:** 791–8.
2. Williamson EM, Evans FJ. Cannabinoids in clinical practice. *Drugs* 2000; **60:** 1303–14.
3. Tramer MR, *et al.* Cannabinoids for control of chemotherapy induced nausea and vomiting: quantitative systematic review. *BMJ* 2001; **323:** 16–21.
4. Berman JS, *et al.* Efficacy of two cannabis based medicinal extracts for relief of central neuropathic pain from brachial plexus avulsion: results of a randomised controlled trial. *Pain* 2004; **112:** 299–306.
5. Costa B. On the pharmacological properties of Delta9-tetrahydrocannabinol (THC). *Chem Biodivers* 2007; **4:** 1664–77.
6. Beaulieu P, Ware M. Reassessment of the role of cannabinoids in the management of pain. *Curr Opin Anaesthesiol* 2007; **20:** 473–7.

**Alzheimer's disease.** There is some suggestion[1] that dronabinol may decrease agitation in patients with Alzheimer's disease.

1. Volicer L, *et al.* Effects of dronabinol on anorexia and disturbed behavior in patients with Alzheimer's disease. *Int J Geriatr Psychiatry* 1997; **12:** 913–19.

**Anorexia.** Dronabinol is used for the management of anorexia in patients with HIV-associated wasting (p.858). However, although dronabinol may stimulate appetite and prevent weight loss,[1] it does not appear to produce significant weight gain, and may produce less benefit than megestrol acetate.[2] Benefits were also less than those of megestrol in patients with anorexia associated with malignant disease.[3]

1. Beal JE, *et al.* Dronabinol as a treatment for anorexia associated with weight loss in patients with AIDS. *J Pain Symptom Manage* 1995; **10:** 89–97.
2. Timpone JG, *et al.* The safety and pharmacokinetics of single-agent and combination therapy with megestrol acetate and dronabinol for the treatment of HIV wasting syndrome. *AIDS Res Hum Retroviruses* 1997; **13:** 305–15.
3. Jatoi A, *et al.* Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: a North Central Cancer Treatment Group study. *J Clin Oncol* 2002; **20:** 567–73.

**Multiple sclerosis.** Anecdotal evidence has suggested that cannabinoids might improve symptoms in patients with multiple sclerosis (p.892); a review[1] considered evidence of effectiveness to be lacking. In a large placebo-controlled study, treatment with dronabinol or oral cannabis extract had no benefit on objective assessment of spasticity;[2] however, there were improvements in walking time, and subjective improvements in both spasticity and pain. A subsequent small controlled study found dronabinol to have a modest but clinically relevant effect on central neuropathic pain in patients with multiple sclerosis.[3]

Dronabinol is used with cannabidiol, another cannabinoid, in a buccal spray preparation for the symptomatic relief of neuropathic pain in multiple sclerosis in adults.

1. Killestein J, *et al.* Cannabinoids in multiple sclerosis: do they have a therapeutic role? *Drugs* 2004; **64:** 1–11.
2. Zajicek J, *et al.* Cannabinoids for treatment of spasticity and other symptoms related to multiple sclerosis (CAMS study): multicentre randomised placebo-controlled trial. *Lancet* 2003; **362:** 1517–26.
3. Svendsen KB, *et al.* Does the cannabinoid dronabinol reduce central pain in multiple sclerosis? Randomised double blind placebo controlled crossover trial. *BMJ* 2004; **329:** 253–7.

**Tourette's syndrome.** Preliminary studies[1,2] indicate that dronabinol may reduce tic severity in Tourette's syndrome (see Tics, p.954).

1. Müller-Vahl KR, *et al.* Treatment of Tourette's syndrome with Δ -tetrahydrocannabinol (THC): a randomized crossover trial. *Pharmacopsychiatry* 2002; **35:** 57–61.
2. Müller-Vahl KR, *et al.* Δ -Tetrahydrocannabinol (THC) is effective in the treatment of tics in Tourette syndrome: a 6-week randomized trial. *J Clin Psychiatry* 2003; **64:** 459–65.

### Preparations
***USP 31:*** Dronabinol Capsules.

**Proprietary Preparations** (details are given in Part 3)

***Canad.:*** Marinol; ***Israel:*** Ronabin†; ***S.Afr.:*** Elevat†; ***USA:*** Marinol.

**Multi-ingredient:** ***Canad.:*** Sativex.

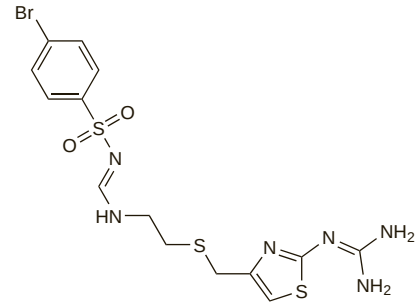
## Ebrotidine *(rINN)*

Ebrotidina; Ébrotidine; Ebrotidinum. *p*-Bromo-*N*-[(*E*)-({2-[({2-[(diaminomethylene)amino]-4-thiazolyl}methyl)thio]ethyl}amino)methylene]benzenesulfonamide.

Эбротидин

$C_{14}H_{17}BrN_6O_2S_3$ = 477.4.

*CAS — 100981-43-9.*



### Profile
Ebrotidine is a histamine $H_2$-antagonist with general properties similar to those of cimetidine (p.1716), but which also has cytoprotective actions. It has been used in peptic ulcer disease. Serious liver damage has been reported.

◊ References.

1. Patel SS, Wilde MI. Ebrotidine. *Drugs* 1996; **51:** 974–80.
2. Various. Ebrotidine: a new generation H -receptor antagonist and gastroprotective agent. *Arzneimittelforschung* 1997; **47:** 427–590.
3. Andrade RJ, *et al.* Acute liver injury associated with the use of ebrotidine, a new H -receptor antagonist. *J Hepatol* 1999; **31:** 641–6.

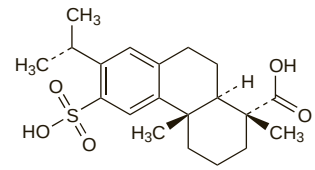
## Ecabet Sodium *(rINNM)*

Ecabet sódico; Écabet Sodique; Natrii Ecabetum; 12-Sulphodehydroabietic Acid, Monosodium Salt; TA-2711. 13-Isopropyl-12-sulphopodocarpa-8,11,13-trien-15-oic acid pentahydrate, sodium salt.

Экабет Натрий

$C_{20}H_{27}NaO_5S,5H_2O$ = 492.6.

*CAS — 33159-27-2 (ecabet); 86408-72-2 (ecabet sodium).*



*(ecabet)*

### Profile
Ecabet sodium is a cytoprotective drug used in the treatment of peptic ulcer disease (p.1702). The suggested oral dose is 1 g of ecabet sodium twice daily.

It is also under investigation as eye drops in the management of dry eye.

◊ References.

1. Murata H, *et al.* Combination therapy of ecabet sodium and cimetidine compared with cimetidine alone for gastric ulcer: prospective randomized multicenter study. *J Gastroenterol Hepatol* 2003; **18:** 1029–33.
2. Lee JH, *et al.* Efficacy and safety of ecabet sodium on functional dyspepsia: a prospective, double-blinded, randomized, multicenter controlled trial. *World J Gastroenterol* 2006; **12:** 2756–61.

**Administration.** The use of ecabet sodium as a rectal enema has been investigated in patients with ulcerative colitis.[1,2]

1. Kono T, *et al.* Effect of ecabet sodium enema on mildly to moderately active ulcerative proctosigmoiditis: an open-label study. *Am J Gastroenterol* 2001; **96:** 793–7.
2. Iizuka M, *et al.* Efficacy of ecabet sodium enema on steroid resistant or steroid dependent ulcerative colitis. *Gut* 2006; **55:** 1523.

### Preparations
**Proprietary Preparations** (details are given in Part 3)

***Jpn:*** Gastrom.