Pain. Antidepressants, usually amitriptyline or another tricyclic, are useful in alleviating some types of pain (see Choice of Analgesic, p.2). Nortriptyline has also been tried and may produce fewer adverse effects than amitriptyline. An initial oral dose of 10 to 25 mg at night has been suggested by the *BNF* for the management of **neuropathic pain**.

References to the use of nortriptyline.

1. Atkinson JH, *et al.* A placebo-controlled randomized clinical trial of nortriptyline for chronic low back pain. *Pain* 1998; **76:** 287–96.
2. Watson CP, *et al.* Nortriptyline versus amitriptyline in postherpetic neuralgia: a randomized trial. *Neurology* 1998; **51:** 1166–71.

Smoking cessation. For reference to the use of nortriptyline in management of smoking cessation, see under Amitriptyline, p.382.

Preparations

BP 2008: Nortriptyline Capsules; Nortriptyline Tablets;
USP 31: Nortriptyline Hydrochloride Capsules; Nortriptyline Hydrochloride Oral Solution.

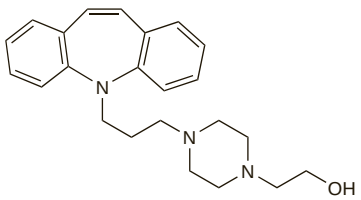
Proprietary Preparations (details are given in Part 3)
Arg.: Ateben†; ***Austral.:*** Allegron; ***Austria:*** Nortrilen; ***Belg.:*** Nortrilen; ***Braz.:*** Nortrip; Pamelor; ***Canad.:*** Aventyl; Norventyl†; ***Cz.:*** Nortrilen; ***Denm.:*** Noritren; ***Fin.:*** Noritren; ***Ger.:*** Nortrilen; ***Gr.:*** Nortrilen; ***Hong Kong:*** Nortrilen; ***India:*** Sensival; ***Israel:*** Nortylin; ***Ital.:*** Noritren; ***Neth.:*** Nortrilen; ***Norw.:*** Noritren; ***NZ:*** Norpress; ***Port.:*** Norterol; ***Spain:*** Norfenazin; Paxtibi; ***Swed.:*** Sensaval; ***Switz.:*** Nortrilen; ***Thai.:*** Norline; Nortrilen; Nortyline; Ortrip; ***UK:*** Allegron; ***USA:*** Aventyl; Pamelor.

Multi-ingredient: ***Arg.:*** Karile; ***Chile:*** Motitrel; ***Indon.:*** Motival; ***Irl.:*** Motival; ***Ital.:*** Dominans; ***Mex.:*** Motival; ***S.Afr.:*** Motival; ***Spain:*** Tropargal; ***Thai.:*** Cetavol; ***UK:*** Motival†.

Opipramol Hydrochloride *(BANM, USAN, rINNM)*

G-33040; Hidrocloruro de opipramol; Opipramol, Chlorhydrate d'; Opipramol Hidroklorür; Opipramoli Dihydrochloridum; Opipramoli Hydrochloridum; Opipramolu dichlorowodorek. 2-[4-(3-5*H*-Dibenz[*b,f*]azepin-5-ylpropyl)piperazin-1-yl]ethanol dihydrochloride.

Опипрамола Гидрохлорид
$C_{23}H_{29}N_3O,2HCl$ = 436.4.
CAS — 315-72-0 (opipramol); 909-39-7 (opipramol dihydrochloride).
ATC — N06AA05.
ATC Vet — QN06AA05.



(opipramol)

Pharmacopoeias. In *Pol.*

Profile

Opipramol hydrochloride is a dibenzazepine tricyclic antidepressant (see Amitriptyline, p.376) given in oral doses of 50 to 300 mg daily in the treatment of depression.

It should be withdrawn gradually to reduce the risk of withdrawal symptoms.

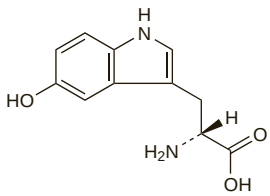
Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Insidon; ***Ger.:*** Insidon; ***Israel:*** Oprimol; ***Pol.:*** Pramolan; ***Switz.:*** Insidon; ***Turk.:*** Deprenil; Insidon; Insomin; Inzeton; Opridon; Oprimol.

Oxitriptan *(rINN)*

5-HTP; L-5-Hydroxytryptophan; Oxitriptán; Oxitriptanum; Ro-0783/B. L-2-Amino-3-(5-hydroxy-1*H*-indol-3-yl)propionic acid.

Окситриптан
$C_{11}H_{12}N_2O_3$ = 220.2.
CAS — 4350-09-8 (oxitriptan); 56-69-9 (DL-5-hydroxytryptophan).
ATC — N06AX01.
ATC Vet — QN06AX01.



Profile

Oxitriptan is the L form of 5-hydroxytryptophan, a precursor of serotonin. Like tryptophan (p.427) it is used in the treatment of depression; it is given in oral doses of up to 600 mg daily.

Oxitriptan is also used in doses of up to 1 g daily in myoclonic disorders, especially posthypoxic myoclonus (p.470). It has also been used in neurological conditions including migraine, pain syndromes, and sleep disorders, and as an adjunct in epilepsy and parkinsonism.

DL-Oxitriptan has also been used as an antidepressant.

Preparations

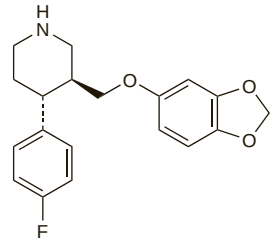
Proprietary Preparations (details are given in Part 3)
Cz.: Tript-OH; ***Fr.:*** Levotonine; ***Ger.:*** Levothym†; ***Ital.:*** Tript-OH; ***Port.:*** Cincofarm; ***Spain:*** Cincofarm; ***Switz.:*** Tript-OH.

Multi-ingredient: ***Indon.:*** Deprex; Menose.

Paroxetine *(BAN, USAN, rINN)*

BRL-29060; FG-7051; Paroksetiini; Paroxetin; Paroxetina; Paroxétine; Paroxetinum. (−)-*trans*-5-(4-*p*-Fluorophenyl-3-piperidylmethoxy)-1,3-benzodioxole.

Пароксетин
$C_{19}H_{20}FNO_3$ = 329.4.
CAS — 61869-08-7.
ATC — N06AB05.
ATC Vet — QN06AB05.



Paroxetine Hydrochloride *(BANM, rINNM)*

BRL-29060A; Hidrocloruro de paroxetina; Paroksetiinihydrokloridihemihydraatti; Paroksetin Hidroklorür; Paroksetino hidrochloridas hemihidratas; Paroksetyny chlorowodorek; Paroxetin hydrochlorid; Paroxétine, chlorhydrate de; Paroxétine (chlorhydrate de) hémihydraté; Paroxetine Hydrochloride Hemihydrate; Paroxetinhydrokloridhemihydrat; Paroxetini hydrochloridum; Paroxetini hydrochloridum hemihydricum.

Пароксетина Гидрохлорид
$C_{19}H_{20}FNO_3,HCl, ½H_2O$ = 374.8.
CAS — 78246-49-8 (anhydrous paroxetine hydrochloride); 110429-35-1 (paroxetine hydrochloride hemihydrate).

Pharmacopoeias. In *Eur.* (see p.vii) and *US*, which permit the anhydrous and hemihydrate forms.
Ph. Eur. 6.2 (Paroxetine Hydrochloride, Anhydrous). A white or almost white, hygroscopic, crystalline powder. It exhibits polymorphism. Slightly soluble in water; sparingly soluble in dehydrated alcohol and in dichloromethane; freely soluble in methyl alcohol. Store in airtight containers at a temperature not exceeding 25°.
Ph. Eur. 6.2 (Paroxetine Hydrochloride Hemihydrate). A white or almost white, crystalline powder. It exhibits pseudopolymorphism. Slightly soluble in water; sparingly soluble in alcohol and in dichloromethane; freely soluble in methyl alcohol. Protect from light.
USP 31 (Paroxetine Hydrochloride). It is anhydrous or contains one-half molecule of water of hydration. A white to off-white solid. Slightly soluble in water; soluble in alcohol and in methyl alcohol. Store the anhydrous form in airtight containers.

Paroxetine Mesilate *(BANM, rINNM)*

Mesilato de paroxetina; Paroxétine, Mésilate de; Paroxetine Mesylate *(USAN)*; Paroxetini Mesilas.

Пароксетина Мезилат
$C_{19}H_{20}FNO_3,CH_4O_3S$ = 425.5.
CAS — 217797-14-3.
ATC — N06AB05.
ATC Vet — QN06AB05.

Adverse Effects, Treatment, and Precautions

As for SSRIs in general (see Fluoxetine, p.391).

Extrapyramidal reactions (including orofacial dystonias) and withdrawal symptoms associated with paroxetine have been reported to the UK CSM more commonly than with other SSRIs. For further details, see Extrapyramidal Effects under Adverse Effects of Fluoxetine, p.393 and Withdrawal under Precautions, p.396.

Breast feeding. For comments on the use of SSRIs in breast feeding patients, see under Precautions for Fluoxetine, p.394.

Children. SSRIs are associated with an increased risk of potentially suicidal behaviour when used for the treatment of depression in children and adolescents under 18 years old; for further details, see under Effects on Mental State in Fluoxetine, p.392.

Pregnancy. For discussion of the risks of SSRIs during pregnancy, and whether paroxetine is associated with a greater teratogenic risk than other SSRIs, see under Fluoxetine, p.395.

Interactions

For interactions associated with SSRIs, see Fluoxetine, p.396.

Pharmacokinetics

Paroxetine is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring within about 5 hours of ingestion. It undergoes extensive first-pass metabolism in the liver. The main metabolic pathway is oxidation followed by methylation and formation of glucuronide and sulfate conjugates. The cytochrome P450 isoenzyme CYP2D6 is partly responsible for the metabolism of paroxetine. Paroxetine is widely distributed throughout body tissues and is about 95% bound to plasma proteins. The elimination half-life of paroxetine is reported to be about 21 hours. Excretion is via the urine (about 64%) and the faeces (about 36%), mainly as metabolites in both cases. Paroxetine is distributed into breast milk (see Breast Feeding under Precautions in Fluoxetine, p.394).

◊ References.

1. Dalhoff K, *et al.* Pharmacokinetics of paroxetine in patients with cirrhosis. *Eur J Clin Pharmacol* 1991; **41:** 351–4.
2. Hiemke C, Härtter S. Pharmacokinetics of selective serotonin reuptake inhibitors. *Pharmacol Ther* 2000; **85:** 11–28.

Uses and Administration

Paroxetine, a phenylpiperidine derivative, is an SSRI with actions and uses similar to those of fluoxetine (p.397). It is given orally usually as paroxetine hydrochloride, as a single dose in the morning; it is also given as the mesilate. Doses are expressed in terms of the base; paroxetine hydrochloride 22.8 mg or paroxetine mesilate 25.8 mg are each equivalent to about 20 mg of paroxetine. The doses given below refer to preparations containing paroxetine hydrochloride; similar doses are also used when paroxetine is given as the mesilate.

In the treatment of **depression**, the usual dose of paroxetine is 20 mg daily, increased gradually, if necessary, in weekly increments of 10 mg to a maximum of 50 mg daily (but see Administration, below).

In the treatment of **generalised anxiety disorder**, the initial dose is 20 mg daily; further increases in increments of 10 mg at intervals of at least one week to a maximum of 50 mg have been given (but see Administration, below).

The initial dose in **obsessive-compulsive disorder** is 20 mg daily increased weekly in 10-mg increments to a usual maintenance dose of 40 mg daily; some patients may require up to 60 mg daily (but see Administration, below).

In the treatment of **panic disorder** with or without agoraphobia, the initial dose is 10 mg daily increased weekly in 10-mg increments according to response; the usual recommended maintenance dose is 40 mg daily, although some patients may benefit from 60 mg daily (but see Administration, below).

The recommended starting dose for the treatment of **post-traumatic stress disorder** is 20 mg daily. If necessary this may be increased in increments of 10 mg at intervals of at least one week to a maximum of 50 mg daily (but see Administration, below).

The initial dose for the treatment of **social anxiety disorder** is 20 mg daily increased after several weeks, if necessary, by increments of 10 mg to a maximum of 50 or 60 mg daily (but see Administration, below).