reduced by urinary alkalinisers, which may enhance or prolong their effects; excretion is increased by urinary acidifiers.

Amfetamines may delay the absorption of ethosuximide, phenobarbital, and phenytoin. The stimulant effects of amfetamines are inhibited by chlorpromazine, haloperidol, and lithium. Disulfiram may inhibit the metabolism and excretion of amfetamines.

Use of sympathomimetics with volatile liquid anaesthetics such as halothane is associated with an increased risk of cardiac arrhythmias.

Pharmacokinetics

Amfetamines are readily absorbed from the gastrointestinal tract and are distributed into most body tissues with high concentrations in the brain and CSF. They are partially metabolised in the liver but a considerable fraction may be excreted in the urine unchanged. Urinary elimination is pH-dependent and enhanced in acid urine. Amfetamines are distributed into breast milk.

◊ References.

1. Steiner E, *et al*. Amphetamine secretion in breast milk. *Eur J Clin Pharmacol* 1984; **27:** 123–4.
2. de la Torre R, *et al*. Clinical pharmacokinetics of amfetamine and related substances: monitoring in conventional and non-conventional matrices. *Clin Pharmacokinet* 2004; **43:** 157–85.
3. Ilett KF, *et al*. Transfer of dexamphetamine into breast milk during treatment for attention deficit hyperactivity disorder. *Br J Clin Pharmacol* 2007; **63:** 371–5.

Uses and Administration

Dexamfetamine, the dextrorotatory isomer of amfetamine, is an indirect-acting sympathomimetic with alpha- and beta-adrenergic agonist activity. It has a marked stimulant effect on the CNS, particularly the cerebral cortex.

Dexamfetamine is used in the treatment of narcolepsy (p.2148). It is also used in the treatment of attention deficit hyperactivity disorder (p.2148); in the UK, this use is limited to refractory hyperactivity disorders in children. Dexamfetamine has been given in the treatment of obesity (p.2149), although amfetamines are no longer recommended for this indication. Amfetamines have also been used to overcome fatigue but, again, such use is considered undesirable. In some countries dexamfetamine has been tried for motion sickness (p.1700), but safer drugs are available.

Dexamfetamine is generally used as the sulfate and is given by mouth.

In the treatment of **narcolepsy**, the usual initial dose is 5 to 10 mg daily in divided doses, increased if necessary by 5 to 10 mg at weekly intervals to a maximum of 60 mg daily. The lower initial dose of 5 mg daily is recommended for the elderly and any weekly increments should also be restricted to 5 mg in such patients.

In children with **hyperactivity** individualisation of treatment is especially important. Children aged 6 years and over usually start with a dose of 5 mg once or twice daily; the dose may be increased if necessary by 5 mg at weekly intervals to an upper limit of 20 mg daily, although older children might require up to 40 mg or more daily. Although dexamfetamine is licensed for the treatment of children younger than 6 years of age in some countries, including the UK and the USA, many authorities consider that stimulants should not be used in young children.

In the USA, an immediate-release, combination preparation containing dexamfetamine sulfate and saccharate, with amfetamine sulfate and amfetamine aspartate monohydrate (*Adderall*, *Shire*), is licensed for the treatment of narcolepsy and attention deficit hyperactivity disorder. This formulation is given by mouth in doses similar to those for dexamfetamine (see above). A modified-release formulation is also available for the treatment of attention deficit hyperactivity disorder in adults and children. The initial dose in adults is 20 mg of total amfetamine salts once daily. In children, it is given as for dexamfetamine in initial doses of 10 mg of total amfetamine salts once daily increased gradually up to a maximum of 30 mg daily; in older children aged 13 to 17 years the dose may be increased to a maximum of 20 mg once daily after 1 week if necessary.

Preparations

BP 2008: Dexamfetamine Tablets.

Proprietary Preparations (details are given in Part 3)
Canad.: Dexedrine; ***Switz.:*** Dexamin†; ***UK:*** Dexedrine; ***USA:*** Dexedrine; Dextrostat.

Multi-ingredient: ***Canad.:*** Adderall; ***USA:*** Adderall.

Dexfenfluramine Hydrochloride ⊗

(BANM, USAN, rINNM) ⊗

Deksfenfluramiinihydrokloridi; Dexfenfluramine, Chlorhydrate de; Dexfenfluraminhydroklorid; Dexfenfluramini Hydrochloridum; Hidrocloruro de dexfenfluramina; S-5614 (dexfenfluramine). (*S*)-*N*-Ethyl-α-methyl-3-trifluoromethylphenethylamine hydrochloride.

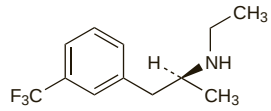
Дексфенфлурамина Гидрохлорид

$C_{12}H_{16}F_3N$,HCl = 267.7.

CAS — 3239-44-9 (dexfenfluramine); 3239-45-0 (dexfenfluramine hydrochloride).

ATC — A08AA04.

ATC Vet — QA08AA04.



(dexfenfluramine)

Profile

Dexfenfluramine is the *S*-isomer of fenfluramine (p.2156). It stimulates the release of serotonin and selectively inhibits its reuptake, but differs from fenfluramine in not possessing any catecholamine agonist activity.

Dexfenfluramine was formerly given orally as the hydrochloride in the treatment of obesity but, like fenfluramine, was withdrawn worldwide after reports of valvular heart defects.

Porphyria. Dexfenfluramine is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Isolipan†; ***Hung.:*** Isolipan†.

Dexmethylphenidate Hydrochloride

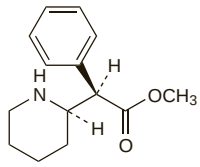
(USAN, rINNM) ⊗

Dexméthylphénidate, Chlorhydrate de; Dexmethylphenidati Hydrochloridum; d-MPH; Hidrocloruro de dexmetilfenidato; *d-threo*-Methylphenidate; *d*-Methylphenidate Hydrochloride. Methyl (2*R*)-phenyl[(2*R*)-piperidin-2-yl]acetate hydrochloride.

Дексметилфенидата Гидрохлорид

$C_{14}H_{19}NO_2$,HCl = 269.8.

CAS — 40431-64-9 (dexmethylphenidate); 19262-68-1 (dexmethylphenidate hydrochloride).



(dexmethylphenidate)

Profile

Dexmethylphenidate hydrochloride is the *d-threo*-enantiomer of racemic methylphenidate hydrochloride (p.2159). It is used as a central stimulant in the treatment of attention deficit hyperactivity disorders.

Dexmethylphenidate hydrochloride is licensed for use in children aged 6 years and older. For patients new to methylphenidate the starting dose of dexmethylphenidate hydrochloride is 2.5 mg twice daily. Each dose should be given at least four hours apart. Dosage may be adjusted in 2.5 to 5 mg increments weekly to a maximum of 10 mg twice daily.

For patients currently using methylphenidate the starting dose of dexmethylphenidate hydrochloride is half the dose of the racemic substance. The maximum recommended dose is 10 mg twice daily.

A modified-release formulation is also available for once-daily dosing.

Dexmethylphenidate should be stopped if there is no improvement in symptoms after appropriate adjustments in dosage over one month. It also needs to be stopped from time to time in those who do respond to assess the patient's condition.

◊ References.

1. Robinson DM, Keating GM. Dexmethylphenidate extended release: in attention-deficit hyperactivity disorder. *Drugs* 2006; **66:** 661–8.

Preparations

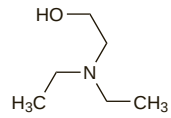
Proprietary Preparations (details are given in Part 3)
USA: Focalin.

Diethylaminoethanol ⊗

Dietilaminoetanol. 2-Diethylaminoethanol.

$C_6H_{15}NO$ = 117.2.

CAS — 100-37-8.



Profile

Diethylaminoethanol is an analogue of deanol (p.2152) and has been used similarly as the malate. The hydrochloride has also been used.

Preparations

Proprietary Preparations (details are given in Part 3)
Gr.: Durobion.

Multi-ingredient: ***Austria:*** Barokaton.

Diethylpropion Hydrochloride *(BANM)* ⊗

Amfepramone Hydrochloride *(pINNM)*; Amfépramone, Chlorhydrate d'; Amfepramoni Hydrochloridum; Hidrocloruro de anfepramona. *N*-(1-Benzoylethyl)-*NN*-diethylammonium chloride; 2-Diethylaminopropiophenone hydrochloride; (*RS*)-α-Diethylaminopropiophenone hydrochloride.

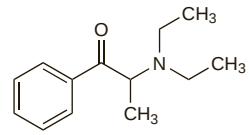
Амфепрамона Гидрохлорид

$C_{13}H_{19}NO$,HCl = 241.8.

CAS — 90-84-6 (diethylpropion); 134-80-5 (diethylpropion hydrochloride).

ATC — A08AA03.

ATC Vet — QA08AA03.



(diethylpropion)

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of diethylpropion: Blue; Blues.

Pharmacopoeias. In *US*.
USP 31 (Diethylpropion Hydrochloride). A white to off-white, fine crystalline powder. Is odourless or has a slight characteristic odour. It may contain tartaric acid as a stabilising agent. Soluble 1 in 0.5 of water, 1 in 3 of alcohol, and 1 in 3 of chloroform; practically insoluble in ether. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Dexamfetamine Sulfate, p.2153. In addition gynaecomastia has been reported rarely. The incidence of central adverse effects may be lower with diethylpropion than with dexamfetamine. Diethylpropion should not be given to patients with emotional instability or a history of psychiatric illness. It should be avoided in children and the elderly. Diethylpropion hydrochloride is subject to abuse.

Porphyria. Diethylpropion is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Interactions

Diethylpropion is an indirect-acting sympathomimetic and, similarly to dexamfetamine (p.2153), may interact with a number of other drugs.

Pharmacokinetics

Diethylpropion is readily absorbed from the gastrointestinal tract. It is extensively metabolised in the liver and possibly the gastrointestinal tract and is excreted in the urine. Diethylpropion crosses the blood-brain barrier and the placenta. Diethylpropion and its metabolites are distributed into breast milk.

Uses and Administration

Diethylpropion hydrochloride is a central stimulant and indirect-acting sympathomimetic with the actions of dexamfetamine (p.2154). It is used as an oral anorectic in the short-term treatment of obesity (p.2149), although stimulants are not generally recommended for this indication.

Doses of 25 mg three times daily 1 hour before meals or 75 mg once daily in mid-morning as a modified-release preparation, are given. To reduce the risk of dependence, diethylpropion should not be given for more than a few weeks at a time.

Regulatory authorities in the EU have called for the withdrawal of diethylpropion from the market (see under Effects on the Cardiovascular System in Fenfluramine, p.2156).