Preparations

BP 2008: Doxapram Injection;
USP 31: Doxapram Hydrochloride Injection.

Proprietary Preparations (details are given in Part 3)

Austral.: Dopram†; ***Austria:*** Dopram; ***Belg.:*** Dopram; ***Denm.:*** Dopram; ***Fin.:*** Dopram; ***Fr.:*** Dopram; ***Ger.:*** Dopram; ***Gr.:*** Dopram; ***Hong Kong:*** Dopram†; ***Irl.:*** Dopram; ***Neth.:*** Dopram; ***Norw.:*** Dopram; ***NZ:*** Dopram†; ***S.Afr.:*** Dopram; ***Spain:*** Docatone†; ***Switz.:*** Dopram†; ***UK:*** Dopram; ***USA:*** Dopram.

Etamivan *(BAN, rINN)* ⊗

Etamivaani; Étamivan; Etamiván; Etamivanum; Ethamivan *(USAN)*; NSC-406087; Vanillic Acid Diethylamide; Vanillic Diethylamide. *N,N*-Diethylvanillamide.

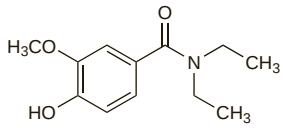
Этамиван

$C_{12}H_{17}NO_3$ = 223.3.

CAS — 304-84-7.

ATC — R07AB04.

ATC Vet — QR07AB04.



Profile

Etamivan has actions similar to those of doxapram (above). It was formerly used as a respiratory stimulant, but the risk of toxicity associated with effective doses is now considered to be unacceptable.

Etamivan is available in oral compound preparations for cerebrovascular and circulatory disorders and hypotension, but such use is not recommended.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Dosulfin Bronquial; ***Austria:*** Cinnarplus; Instenon; ***Ger.:*** Normotin-R†; ***Hong Kong:*** Instenon; ***Rus.:*** Instenon (Инстенон); ***Thai.:*** Instenon†.

Etilamfetamine Hydrochloride *(rINNM)* ⊗

Ethylamphetamine Hydrochloride; Étilamfétamine, Chlorhydrate d'; Etilamfetamini Hydrochloridum; Hidrocloruro de etilanfetamina. *N*-Ethyl-α-methylphenethylamine hydrochloride.

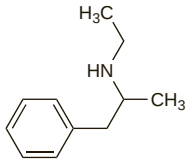
Этиламфетамина Гидрохлорид

$C_{11}H_{17}N,HCl$ = 199.7.

CAS — 457-87-4 (etilamfetamine); 1858-47-5 (etilamfetamine hydrochloride).

ATC — A08AA06.

ATC Vet — QA08AA06.



(etilamfetamine)

Profile

Etilamfetamine hydrochloride is a central stimulant with properties similar to those of dexamfetamine (p.2153). It has been used as an anorectic in the treatment of obesity.

Fencamfamin Hydrochloride *(BANM, rINNM)* ⊗

Fencamfamine, Chlorhydrate de; Fencamfamini Hydrochloridum; H-610; Hidrocloruro de fencanfamina. *N*-Ethyl-3-phenylbicyclo[2.2.1]hept-2-ylamine hydrochloride.

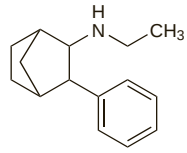
Фенкамфамина Гидрохлорид

$C_{15}H_{21}N,HCl$ = 251.8.

CAS — 1209-98-9 (fencamfamin); 2240-14-4 (fencamfamin hydrochloride).

ATC — N06BA06.

ATC Vet — QN06BA06.



(fencamfamin)

Profile

Fencamfamin hydrochloride has been given orally as a central stimulant.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***S.Afr.:*** Reactivan.

Fenetylline Hydrochloride *(BANM, rINNM)* ⊗

Amfetyline Hydrochloride; 7-Ethyltheophylline Amphetamine Hydrochloride; Fenethylline Hydrochloride *(USAN)*; Fénétylline, Chlorhydrate de; Fenetyllini Hydrochloridum; H-814; Hidrocloruro de fenetilina; R-720-11. 7-[2-(α-Methylphenethylamino)ethyl]theophylline hydrochloride.

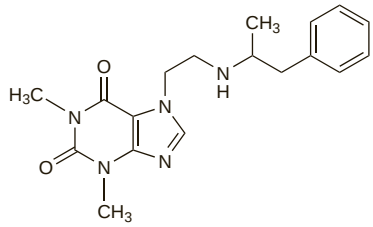
Фенетиллина Гидрохлорид

$C_{18}H_{23}N_5O_2,HCl$ = 377.9.

CAS — 3736-08-1 (fenetylline); 1892-80-4 (fenetylline hydrochloride).

ATC — N06BA10.

ATC Vet — QN06BA10.



(fenetylline)

Profile

Fenetylline is a theophylline derivative of amfetamine with properties similar to those of dexamfetamine (p.2153). It is given orally in the management of narcolepsy in an initial dose of 25 mg daily, increased to usual maintenance doses of 50 to 100 mg daily in 2 divided doses; no more than 150 mg daily should be used. It has also been used in the management of hyperactivity disorders. Fenetylline is subject to abuse.

Preparations

Proprietary Preparations (details are given in Part 3)

Belg.: Captagon; ***Ger.:*** Captagon†.

Fenfluramine Hydrochloride *(BANM, USAN, rINNM)* ⊗

AHR-3002; Fenfluramine, Chlorhydrate de; Fenfluramini Hydrochloridum; Hidrocloruro de fenfluramina; S-768. *N*-Ethyl-α-methyl-3-trifluoromethylphenethylamine hydrochloride.

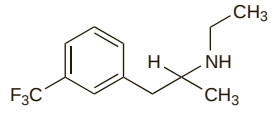
Фенфлюрамина Гидрохлорид

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

CAS — 458-24-2 (fenfluramine); 404-82-0 (fenfluramine hydrochloride).

ATC — A08AA02.

ATC Vet — QA08AA02.



(fenfluramine)

Adverse Effects and Precautions

As for Dexamfetamine, p.2153, but fenfluramine usually depresses rather than stimulates the CNS. Fenfluramine has been associated with serious cardiovascular toxicity. Pulmonary hypertension led to certain precautions being imposed upon its use and subsequent reports of valvular heart defects led to its general withdrawal worldwide.

Effects on the cardiovascular system. The association of primary *pulmonary hypertension* with the use of anorectics including fenfluramine, dexfenfluramine, and phentermine is well recognised.[1-3] Both reversible and irreversible cases have been reported and in some cases it has proved fatal.[1,4-9] The condition appears to be linked to prolonged or repeated therapy.[1,10] In 1992 the UK CSM advised that treatment should not exceed 3 months[1] but later in 1997 it revised its recommendations for fenfluramine and dexfenfluramine allowing treatment for up to 12 months under certain conditions.[2] The CSM stated that treatment could be continued beyond 3 months only if there had been a satisfactory response (more than 10% weight loss) and that this loss was maintained. Patients should also be monitored for symptoms of pulmonary hypertension. For other anorectics such as phentermine the maximum duration of treatment remained 3 months.

However, shortly after this, a report was published[11] that outlined an association between the use of a fenfluramine-phentermine combination and the development of *valvular heart disease* in 24 patients. Initially, the response by the CSM was to advise against the use of combinations of anorectics[12] although subsequently fenfluramine, along with dexfenfluramine, was withdrawn from the world market after more cases became known.[13,14] By September 1997 the FDA in the USA[14] had received 144 reports of valvulopathy, including the original 24, associated with fenfluramine or dexfenfluramine, with or without phentermine; none were associated with phentermine treatment alone. As a consequence the US authorities made recommendations[14] for the screening of all patients who had previously received fenfluramine or dexfenfluramine in order to detect heart valve lesions and to provide optimal care. Further studies[15-20] have supported the association with valvular abnormalities, and suggested that prolonged exposure or exposure to high doses of dexfenfluramine or fenfluramine increased the risk; clinically important disease would probably not develop in most patients with only short-term exposure.[21]

In 2000, the European Commission called for the withdrawal of all anorectics from the European market. Those anorectics involved in the decision included clobenzorex, diethylpropion, fenproporex, mazindol, mefenorex, phendimetrazine, phenmetrazine, and phentermine. However in 2002, after an appeal by some manufacturers, the European Court ruled that the Commission did not have the authority to withdraw marketing authorisations. Subsequently, some anorectics have been allowed back onto the European market.

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