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Smoking cessation. Selegiline has been investigated as an aid to smoking cessation (p.2354).

References.

1. George TP, *et al.* A preliminary placebo-controlled trial of selegiline hydrochloride for smoking cessation. *Biol Psychiatry* 2003; **53:** 136–43.
2. Biberman R, *et al.* A randomized controlled trial of oral selegiline plus nicotine skin patch compared with placebo plus nicotine skin patch for smoking cessation. *Addiction* 2003; **98:** 1403–7.

Preparations

BP 2008: Selegiline Oral Solution; Selegiline Tablets;
USP 31: Selegiline Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

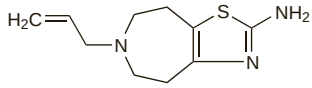
Arg.: Brintenal; Jumex; Kinabide†; Zelapar; ***Austral.:*** Eldepryl; Selgene; ***Austria:*** Amboneural; Cognitiv; Jumex; Regepar; Xilopar; ***Belg.:*** Eldepryl; ***Braz.:*** Deprilan; Elepril; Jumexil; Niar; Parkexin; ***Canad.:*** Eldepryl†; ***Chile:*** Selgina; ***Cz.:*** Apo-Seleg; Cognitiv; Jumex; Niar; Segalin†; Sepatrem†; ***Denm.:*** Eldepryl; ***Fin.:*** Eldepryl; ***Fr.:*** Deprenyl; Otrasel; ***Ger.:*** Amindan†; Antiparkin; Jutagilin; MAOtil†; Movergan; Selegam†; Selemerck; Selepark; Selgimed; Xilopar; ***Gr.:*** Cosmopril; Ermolax; Feliselin; Krautin; Legil; Procythol; Resostyl; ***Hong Kong:*** Julab; Jumex; Sefmex; Selegos; ***Hung.:*** Cognitiv; Jumex; Primulex†; ***India:*** Selerin; Selgin; ***Indon.:*** Jumex; ***Irl.:*** Eldepryl; ***Israel:*** Jumex; ***Ital.:*** Egibren; Jumex; Selecom; Seledat; Xilopar; ***Jpn:*** FP Tab; ***Malaysia:*** Ginex†; Jumex; Sefmex; Selegos†; ***Mex.:*** Niar; ***Neth.:*** Eldepryl; ***Norw.:*** Eldepryl; ***NZ:*** Eldepryl; Selgene†; ***Philipp.:*** Jumex; ***Pol.:*** Apo-Selin; Jumex; Parkinil†; Segan; Selerin; Selgin; Selgres; ***Port.:*** Jumex; Niponeurin; Xilopar; ***Rus.:*** Cognitiv (Когнитив); Segan (Сеган); Selegos (Селегос); ***S.Afr.:*** Eldepryl; Parkilyne; ***Singapore:*** Jumex; Selegos; ***Spain:*** Plurimen; ***Swed.:*** Eldepryl; ***Switz.:*** Jumexal; Selecim†; ***Thai.:*** Elegelin†; Julab; Jumex; Kinline†; Sefmex; Seline†; ***Turk.:*** Moverdin; Seldepar; ***UK:*** Eldepryl; Zelapar; ***USA:*** Atapryl; Carbex; Eldepryl; Emsam; Zelapar; ***Venez.:*** Jumex.

Talipexole Hydrochloride *(rINNM)*

Alefexole Hydrochloride; B-HT-920; Hidrocloruro de talipexol; Talipexole, Chlorhydrate de; Talipexoli Hydrochloridum. 6-Allyl-2-amino-5,6,7,8-tetrahydro-4*H*-thiazolo[4,5-*d*]azepine dihydrochloride.

Талипексола Гидрохлорид

$C_{10}H_{15}N_3S,2HCl$ = 282.2.
CAS — 101626-70-4 (talipexole); 36085-73-1 (talipexole hydrochloride).



(talipexole)

Profile

Talipexole hydrochloride is a dopamine D_2-agonist that is used in the management of parkinsonism (p.791) in usual oral doses of 1.2 to 3.6 mg daily, in divided doses. It has also been investigated in the treatment of schizophrenia.

Preparations

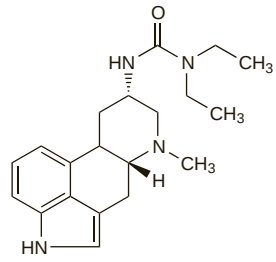
Proprietary Preparations (details are given in Part 3)
Jpn: Domin.

Terguride *(rINN)*

Tergurida; Terguridum. 1,1-Diethyl-3-(6-methylergolin-8α-yl) urea.

Тергурид

$C_{20}H_{28}N_4O$ = 340.5.
CAS — 37686-84-3.



Profile

Terguride, an ergot derivative, is a partial dopamine agonist with general properties similar to those of bromocriptine (p.798). It is used in the treatment of disorders related to hyperprolactinaemia (p.2079) in a usual oral dose of 500 micrograms twice daily. It is also being investigated in the management of parkinsonism.

◊ References.

1. Krause W, *et al.* Pharmacokinetics and endocrine effects of terguride in healthy subjects. *Eur J Clin Pharmacol* 1990; **38:** 609–15.
2. Baronti F, *et al.* Partial dopamine agonist therapy of levodopa-induced dyskinesias. *Neurology* 1992; **42:** 1241–3.

Preparations

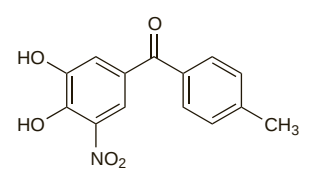
Proprietary Preparations (details are given in Part 3)
Cz.: Mysalfon†; ***Jpn:*** Teluron.

Tolcapone *(BAN, USAN, rINN)*

Ro-40-7592; Tolcapona; Tolcaponum; Tolkapon; Tolkaponi. 3,4-Dihydroxy-4′-methyl-5-nitrobenzophenone; 3,4-Dihydroxy-5-nitrophenyl(4-methylphenyl)methanone.

Толкапон

$C_{14}H_{11}NO_5$ = 273.2.
CAS — 134308-13-7.
ATC — N04BX01.
ATC Vet — QN04BX01.



Pharmacopoeias. In *US.*

USP 31 (Tolcapone). A yellow, fine powder or fine powder with lumps. Insoluble in water and in *n*-hexane; Freely soluble in acetone and in tetrahydrofuran; sparingly soluble in chloroform and in dichloromethane; soluble in methyl alcohol and in ethyl acetate. Store in airtight containers at a temperature between 20° and 25°. Protect from light.

Adverse Effects

The most common adverse effects associated with tolcapone are diarrhoea, nausea, vomiting, constipation, abdominal pain, dry mouth, anorexia, dyskinesia, dystonia, dizziness, orthostatic hypotension, hallucinations, confusion, excessive dreaming, somnolence, headache, increased sweating, and sleep disorders. Diarrhoea may be severe enough for treatment to be stopped. Increases in liver enzyme values have occurred and hepatitis and hepatic failure, sometimes fatal, have been reported. Isolated cases of neuroleptic malignant syndrome have also been reported following dose reduction or stopping tolcapone; rhabdomyolysis may develop as a complication of the syndrome. Tolcapone and its metabolites can produce a yellow intensification in the colour of urine.

Effects on the liver. The UK CSM had noted[1] that, after a report[2] in September 1998 of fatal acute hepatic failure associated with tolcapone, the European Committee for Proprietary Medicinal Products (CPMP) had reviewed all reports of hepatic injury with tolcapone. There had been 10 reports of serious hepatic adverse reactions since tolcapone was marketed in October 1997, which included 7 reports of hepatitis, 3 of which had a fatal outcome. Serious hepatic reactions occurred unpredictably and their development was not always predicted by liver function monitoring. Consequently, in the EU, the marketing authorisation for tolcapone was suspended in November 1998. This suspension was lifted in April 2004 by the CPMP after further review.

In some countries such as the USA, tolcapone has always remained available albeit with restricted indications and strict monitoring requirements (see Precautions, below). Up to 2003, there had been no further reports of fatal hepatic failure following the introduction of these measures although the number of patients eligible to receive the drug has been reduced.[3]

1. CSM/MCA. Withdrawal of tolcapone (Tasmar). *Current Problems* 1999; **25:** 2. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2023233&RevisionSelectionMethod=LatestReleased (accessed 11/08/08)
2. Assal F, *et al.* Tolcapone and fulminant hepatitis. *Lancet* 1998; **352:** 958.
3. Borges N. Tolcapone-related liver dysfunction: implications for use in Parkinson's disease therapy. *Drug Safety* 2003; **26:** 743–7.

Effects on the skin. For reference to the development of vitiligo in a patient following addition of tolcapone to levodopa/carbidopa treatment, see under Levodopa, p.806.

Precautions

Tolcapone should not be given to patients with hepatic impairment or raised liver enzyme values. Liver enzymes should be monitored:

- when starting treatment with tolcapone or on increasing the dose to 200 mg three times daily
- every 2 weeks during the first year of therapy
- every 4 weeks for a further 6 months
- every 8 weeks thereafter

Tolcapone should be stopped if liver enzyme levels exceed the upper limit of normal or if signs or symptoms suggestive of the onset of hepatic failure occur. Patients who have developed evidence of hepatic injury while receiving tolcapone should not be given the drug again.

Tolcapone should be used with caution in patients with severe renal impairment.

It is contra-indicated in patients with severe dyskinesia or with a history of neuroleptic malignant syndrome (NMS). It is also contra-indicated in patients with a history of nontraumatic rhabdomyolysis or symptoms of hyperpyrexia and confusion possibly related to NMS. Patients with phaeochromocytoma should not be given tolcapone.

Use with levodopa may cause dizziness and orthostatic hypotension; if affected patients should not drive or operate machinery. Excessive daytime sleepiness and sudden onset of sleep may also occur with combination use (see Effects on Mental Function, under Adverse Effects of Levodopa, p.805) and again, caution is advised when driving or operating machinery; patients who suffer such effects should not drive or operate machinery until the effects have stopped recurring.

Abrupt withdrawal or dose reduction of tolcapone should be monitored carefully because of the risk of developing symptoms resembling NMS.

The elderly. Confusion occurred in 3 elderly patients with severe Parkinson's disease after the addition of tolcapone to their antiparkinsonian therapy.[1] It was suggested that a starting dose of tolcapone 100 mg daily might be more suitable in frail patients with severe disease. It was noted[2] that a reduction in levodopa dosage is generally recommended when tolcapone is given to patients such as these, who were receiving 500 to 600 mg of levodopa daily.

1. Henry C, Wilson JA. Catechol-O-methyltransferase inhibitors in Parkinson's disease. *Lancet* 1998; **351:** 1965–6.
2. Harper J, Vieira B. Catechol-O-methyltransferase inhibitors in Parkinson's disease. *Lancet* 1998; **352:** 578.