Tamarind

Tamarindo; West Indian Tamarind.

Индийский Финик; Плоды Тамаринда; Тамаринд

Pharmacopoeias. In *Fr.*

Profile

Tamarind is the fruits of *Tamarindus indica* (Leguminosae) freed from the brittle outer part of the pericarp and preserved with sugar or syrup. It contains tartaric, citric, and malic acid and their salts. Tamarind is used as a laxative with senna.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Delabarre.

Multi-ingredient: ***Arg.:*** Tamarine†; ***Austria:*** Frugelletten; Neda Fruchtewurfel; ***Braz.:*** Fitolax; Florlax; Fontolax; Frutalax†; Laxarine†; Laxtam; Naturetti; Tamanl; Tamarine; Tamarix†; ***Chile:*** Tamarine; ***Fr.:*** Carres Parapsyllium; Laxarine; Tamarine; ***Ital.:*** Ortisan; Tamarine; ***Mex.:*** Naturetti†; ***Spain:*** Dentomicin; Pruina.

Tegaserod Maleate *(BANM, USAN, rINNM)*

HTF-919; Maleato de tegaserod; SDZ-HTF-919; Tégasérod, Maléate de; Tegaserodi Maleas. 1-{[(5-Methoxyindol-3-yl)methylene]amino}-3-pentylguanidine maleate.

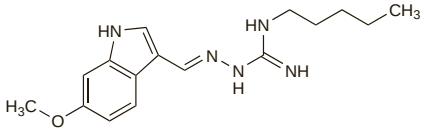
Тегасерода Малеат

$C_{16}H_{23}N_5O,C_4H_4O_4$ = 417.5.

CAS — 145158-71-0 (tegaserod); 189188-57-6 (tegaserod maleate).

ATC — A03AE02.

ATC Vet — QA03AE02.



(tegaserod)

Stability and compatibility. Crushed tablets of tegaserod were found to be stable in water, and apple juice; the latter may mask the taste of the drug. Orange juice, milk, or yogurt were not recommended as vehicles because of incomplete dissolution or uncertainty about stability.[1]

1. Carrier M-N, *et al.* Stability and compatibility of tegaserod from crushed tablets mixed in beverages and foods. *Am J Health-Syst Pharm* 2004; **61:** 1135–42.

Adverse Effects

The most common adverse effects of tegaserod are gastrointestinal disturbances including abdominal pain, diarrhoea, nausea, vomiting, and flatulence. Diarrhoea generally occurs within the first week of treatment and is usually transient but may be severe. Ischaemic colitis has been reported. Headache, dizziness, migraine, insomnia, fatigue, leg or back pain, and arthropathy have also been commonly reported. Cardiovascular adverse effects include hypotension and arrhythmias. Serious cardiovascular ischaemic events such as myocardial infarction, unstable angina pectoris, and stroke have occurred; fatalities have been reported. Other adverse effects include effects on the nervous system such as depression, and other gastrointestinal effects including cholelithiasis and dyspepsia.

◊ References.

1. Hasler WL, Schoenfeld P. Safety profile of tegaserod, a 5-HT receptor agonist, for the treatment of irritable bowel syndrome. *Drug Safety* 2004; **27:** 619–31.
2. Quigley EM, *et al.* Safety and tolerability of tegaserod in patients with chronic constipation: pooled data from two phase III studies. *Clin Gastroenterol Hepatol* 2006; **4:** 605–13.

Effects on the gastrointestinal tract. Severe diarrhoea, leading to hypovolaemia, hypotension, and syncope has been seen occasionally in patients receiving tegaserod. Some patients required hospitalisation for rehydration, and patients should be advised to stop taking the drug and seek medical attention if severe diarrhoea or associated dizziness or lightheadedness develop. In addition, ischaemic colitis has been reported rarely, and the drug should be stopped immediately in patients who develop symptoms such as rectal bleeding, bloody diarrhoea, or new and worsening abdominal pain.[1] The FDA noted that it had received 20 reports of ischaemic colitis in patients taking tegaserod between August 2002 and March 2004; in 3 cases, the effect only developed after several months (7 to 13) of therapy.[2] However, in reply the manufacturer (*Novartis*) suggested that there was no evidence from postmarketing surveillance to support an increased rate of ischaemic colitis over that normally seen in patients with irritable bowel syndrome, who are at increased risk of this diagnosis, nor any obvious pharmacological mechanism for such an adverse effect.[3]

1. Novartis, Canada. Important safety update: diarrhea and ischemic colitis in patients using Zelnorm (tegaserod hydrogen maleate) (issued 28/04/04). Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/zelnorm_hpc-cps_e.pdf (accessed 07/07/06)
2. Brinker AD, *et al.* Tegaserod and ischemic colitis. *N Engl J Med* 2004; **351:** 1361–3.
3. Joelsson BE, *et al.* Tegaserod and ischemic colitis. *N Engl J Med* 2004; **351:** 1363–4.

Effects on the heart. In an analysis of pooled data from 29 studies, 13 out of 11 614 patients taking tegaserod had serious cardiovascular ischaemic events, compared with 1 out of 7031 patients taking placebo. Events included unstable angina pectoris, stroke, and myocardial infarction, one of which was fatal.[1-3] Most of these patients had at least one cardiovascular risk factor, but for some, no cardiovascular disease or risk had been diagnosed at the onset of treatment with tegaserod.[2] Patients taking tegaserod should seek medical attention if they have severe chest pain, dyspnoea, dizziness, sudden onset of weakness, difficulty walking or talking, or any other symptoms suggestive of myocardial infarction or stroke.[1]

1. FDA Public Health Advisory. Tegaserod maleate (marketed as Zelnorm) (issued 30th March 2007). Available at: http://www.fda.gov/cder/drug/advisory/tegaserod.htm (accessed 31/05/07)
2. Novartis, Canada. Health Canada endorsed important safety information on Zelnorm (tegaserod hydrogen maleate) (issued 30th March 2007). Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/zelnorm_hpc-cps_2_e.pdf (accessed 31/05/07)
3. Novartis, USA. Urgent: marketing and sales suspension notice for Zelnorm® tablets, 2-mg and 6-mg all lots within expiry (issued 30th March 2007). Available at: http://www.zelnorm.com/Dr_Doctor_Letter.pdf (accessed 31/05/07)

Precautions

Tegaserod is contra-indicated in patients with a history of bowel obstruction, symptomatic gallbladder disease, suspected sphincter of Oddi dysfunction, or abdominal adhesions. Tegaserod should also not be given to patients who have diarrhoea or who frequently experience diarrhoea. It should be stopped in patients with new or sudden worsening of abdominal symptoms, hypotension, or syncope. Tegaserod should not be used in patients with severe renal impairment or moderate to severe hepatic impairment. For the possible cardiovascular risks of tegaserod therapy, see above; in the USA use is restricted, and it is contra-indicated in patients with a history of heart disease or symptoms suggestive of cardiac disorders.

Pharmacokinetics

Tegaserod is rapidly absorbed from the gastrointestinal tract with peak plasma levels occurring after about 1 hour. The absolute bioavailability of an oral dose is 10%; this is reduced by the presence of food. Tegaserod is widely distributed into the tissues and is about 98% bound to plasma proteins. Presystemic acid-catalysed hydrolysis in the stomach, and then oxidation and glucuronidation, produces the main metabolite, which is inactive; direct systemic glucuronidation also occurs. Two-thirds of an oral dose is excreted unchanged in the faeces and one-third excreted in the urine primarily as the main metabolite. The terminal half-life of tegaserod is about 11 hours.

◊ Reviews.

1. Appel-Dingemanse S. Clinical pharmacokinetics of tegaserod, a serotonin 5-HT receptor partial agonist with promotile activity. *Clin Pharmacokinet* 2002; **41:** 1021–42.

Uses and Administration

Tegaserod is a partial agonist at 5-HT_4 receptors and has prokinetic properties. It is used in women for the short-term treatment of irritable bowel syndrome (p.1699), particularly the constipation-predominant form. It has also been used for the treatment of chronic idiopathic constipation (p.1693) in men and women less than 65 years of age.

Tegaserod is given orally as the maleate but doses are expressed in terms of the base; 8.31 mg of tegaserod maleate is equivalent to about 6 mg of tegaserod. It is given in a dose of 6 mg twice daily before food. For irritable bowel syndrome, it is given for 4 to 6 weeks; a further 4 to 6 weeks of treatment may be given if a beneficial response is seen.

In March 2007, marketing of tegaserod was suspended in some countries because of a high incidence of cardiovascular ischaemic events (see Effects on the Heart, above). In the USA, the use of tegaserod was subsequently restricted to women younger than 55 years of age who have either constipation-predominant irritable bowel syndrome or chronic idiopathic constipation, and who meet specific guidelines; patients should have no known or pre-existing cardiac problems.

◊ References.

1. Wagstaff AJ, *et al.* Tegaserod: a review of its use in the management of irritable bowel syndrome with constipation in women. *Drugs* 2003; **63:** 1101–20.
2. Lea R, Whorwell PJ. Benefit-risk assessment of tegaserod in irritable bowel syndrome. *Drug Safety* 2004; **27:** 229–42.
3. Johanson JF, *et al.* Effect of tegaserod in chronic constipation: a randomized, double-blind, controlled trial. *Clin Gastroenterol Hepatol* 2004; **2:** 796–805.
4. Müller-Lissner S, *et al.* Tegaserod is effective in the initial and retreatment of irritable bowel syndrome with constipation. *Aliment Pharmacol Ther* 2005; **21:** 11–20.
5. Kamm MA, *et al.* Tegaserod for the treatment of chronic constipation: a randomized, double-blind, placebo-controlled multinational study. *Am J Gastroenterol* 2005; **100:** 362–72.
6. Tack J, *et al.* A randomised controlled trial assessing the efficacy and safety of repeated tegaserod therapy in women with irritable bowel syndrome with constipation. *Gut* 2005; **54:** 1707–13.
7. Muller-Lissner S, *et al.* Safety, tolerability, and efficacy of tegaserod over 13 months in patients with chronic constipation. *Am J Gastroenterol* 2006; **101:** 2558–69.
8. Baun RF, Levy HB. Tegaserod for treating chronic constipation in elderly patients. *Ann Pharmacother* 2007; **41:** 309–13.
9. Evans BW, *et al.* Tegaserod for the treatment of irritable bowel syndrome and chronic constipation. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2007 (accessed 17/03/08).

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Altezerod; Coloserod; Procinet; Tegarod; Zelmac; ***Austral.:*** Zelmac†; ***Braz.:*** Zelmac; ***Canad.:*** Zelnorm; ***Chile:*** Colonaid; Distimax; Tegasir; Ther; Zelmac; ***Cz.:*** Zelmac†; ***Hong Kong:*** Zelmac; ***India:*** Tegibs; Tegod; ***Indon.:*** Zelmac; ***Israel:*** Zelmac; ***Malaysia:*** Zelmac†; ***Mex.:*** Zelmac; ***NZ:*** Zelmac; ***Philipp.:*** Zelnorm; ***Rus.:*** Zelmac (Зелмак)†; ***S.Afr.:*** Zelnorm; ***Singapore:*** Zelmac; ***Switz.:*** Zelmac; ***Thai.:*** Zelmac; ***Turk.:*** Zelmac; ***USA:*** Zelnorm†; ***Venez.:*** Zelmac.

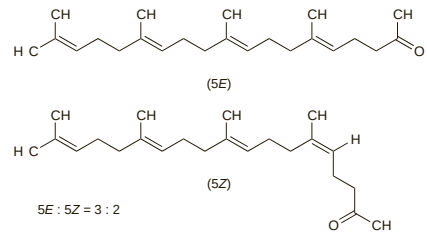
Teprenone *(rINN)*

E-671; Geranylgeranylacetone (5*E*, 9*E*,13*E* isomer); Teprenona; Téprénone; Teprenonum. 6,10,14,18-Tetramethyl-5,9,13,17-nonadecatetraen-2-one, mixture of (5*E*,9*E*,13*E*) and (5*Z*,9*E*,13*E*) isomers.

Тепренон

$C_{23}H_{38}O$ = 330.5.

CAS — 6809-52-5 (teprenone); 3796-63-2 (5E,9E,13E isomer); 3796-64-3 (5Z,9E,13E isomer).



(5*E*)

(5*Z*)

5*E* : 5*Z* = 3 : 2

Profile

Teprenone is a cytoprotective drug that is used in the treatment of gastritis and peptic ulcer disease (p.1702) in a usual oral dose of 50 mg three times daily.

Preparations

Proprietary Preparations (details are given in Part 3)

Indon.: Purubex; ***Jpn:*** Selbex; ***Philipp.:*** Selbex; ***Thai.:*** Selbex.

Tiemonium Iodide *(BAN, rINN)*

Ioduro de tiemonio; TE-114; Tiemonii Iodidum; Tiémonium, Iodure de. 4-[3-Hydroxy-3-phenyl-3-(2-thienyl)propyl]-4-methylmorpholinium iodide.

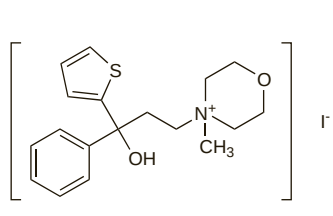
Тиемония Йодид

$C_{18}H_{24}INO_2S$ = 445.4.

CAS — 6252-92-2 (tiemonium); 144-12-7 (tiemonium iodide).

ATC — A03AB17.

ATC Vet — QA03AB17.



Tiemonium Metilsulfate

Tiemonio, metilsulfato de; Tiemonium Methylsulphate. 4-[3-Hydroxy-3-phenyl-3-(2-thienyl)propyl]-4-methyl-morpholinium methylsulphate.

$C_{19}H_{27}NO_6S_2$ = 429.6.

CAS — 6504-57-0.