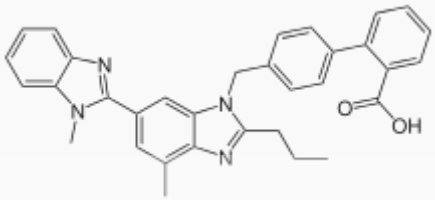
Telmisartan

Telmisartan

Systematic (IUPAC) name
2-(4-{[4-Methyl-6-(1-methyl-1*H*-1,3-benzodiazol-2-yl)-2-propyl-1*H*-1,3-benzodiazol-1-yl]methyl}phenyl)benzoic acid
Clinical data
Trade names — Micardis
AHFS/Drugs.com — monograph
MedlinePlus — a601249
Pregnancy cat. — D (Au), D (U.S.)
Legal status — S4 (Au), POM (UK), ℞-only (U.S.)
Routes — Oral
Pharmacokinetic data
Bioavailability — 42–100%
Protein binding — ≥99.5%
Metabolism — Minimal hepatic
Half-life — 24 hours
Excretion — Faecal 97%
Identifiers
CAS number — 144701-48-4
ATC code — C09CA07
PubChem — CID 65999
IUPHAR ligand — 592
DrugBank — DB00966
ChemSpider — 59391
UNII — U5SYW473RQ

KEGG	D00627
ChEBI	CHEBI:9434
ChEMBL	CHEMBL1017
Chemical data	
Formula	$C_{33}H_{30}N_4O_2$
Mol. mass	514.617 g/mol
SMILES	• O=C(O)c1ccccc1c2ccc(cc2)Cn3c4cc(cc(c4nc3CCC)C)c5nc6ccccc6n5C
InChI	InChI=1S/C33H30N4O2/c1-4-9-30-35-31-21(2)18-24(32-34-27-12-7-8-13-28(27)36(32)3)19-29(31)37(30)20-22-14-16-23(17-15-22)25-10-5-6-11-26(25)33(38)39/h5-8,10-19H,4,9,20H2,1-3H3,(H,38,39) Key:RMMXLENWKUUMAY-UHFFFAOYSA-N

Telmisartan (INN) /tɛlmɪˈsɑrtən/ is an angiotensin II receptor antagonist (angiotensin receptor blocker, ARB) used in the management of hypertension. It is marketed under the trade name **Micardis** (by Boehringer Ingelheim), among others.

Indication

Telmisartan is indicated in the treatment of essential hypertension.[1][2]

Administration

The usually effective dose telmisartan is 40–80 mg once daily. Some patients may already benefit at a daily dose of 20 mg. In cases where the target blood pressure is not achieved, telmisartan dose can be increased to a maximum of 80 mg once daily.[1]

Contraindications

Telmisartan is contraindicated during pregnancy. Like other drugs affecting the renin-angiotensin system (RAS), telmisartan can cause birth defects, stillbirths, and neonatal deaths. It is not

known whether the drug passes into the breast milk.[3] Also it is contraindicated in bilateral renal artery stenosis in which it can cause renal failure.

Side effects

Side effects are similar to other angiotensin II receptor antagonists and include tachycardia and bradycardia (fast or slow heartbeat), hypotension (low blood pressure), edema (swelling of arms, legs, lips, tongue, or throat, the latter leading to breathing problems), and allergic reactions.[3]

Mode of action

Telmisartan is an angiotensin II receptor blocker that shows high affinity for the angiotensin II receptor type 1 (AT_1), with a binding affinity 3000 times greater for AT_1 than AT_2. It has the longest half-life of any ARB (24 hours)[1][4] and the largest volume of distribution among ARBs (500 liters).[5][6]

In addition to blocking the RAs, telmisartan acts as a selective modulator of peroxisome proliferator-activated receptor gamma (PPAR-γ), a central regulator of insulin and glucose metabolism. It is believed that telmisartan's dual mode of action may provide protective benefits against the vascular and renal damage caused by diabetes and cardiovascular disease (CVD).[4]

Telmisartan's activity at the PPAR-γ receptor has prompted speculation around its potential as a sport doping agent as an alternative to GW 501516.[7] Telmisartan activates PPARδ receptors in several tissues.[8][9][10][11]

Clinical trials

ONTARGET

The Ongoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial (ONTARGET) was one of the largest ARB clinical studies ever undertaken;[12] 25,620 patients from 733 centres in 41 countries were randomised for 5.5 years of treatment of either telmisartan, the ACE inhibitor ramipril or a combination of the two. The study aimed to investigate the role of telmisartan in cardiovascular (CV) protection through the primary composite outcome of death from CV causes, myocardial infarction, stroke or hospilization for heart failure, in high CV risk patients.

The study showed telmisartan was as effective as ramipril but with lower rates of cough and angioedema, which led to fewer discontinuations. The combination group experienced similar efficacy, but with increased risk of hypotensivesymptoms. Moreover, in a patient population selected to tolerate ACE inhibitors, telmisartan was shown to be better tolerated and associated with higher treatment compliance than ramipril.[13]

TRANSCEND

As part of the ONTARGET study, patients who could not tolerate ACE inhibitors were randomly assigned to receive either telmisartan or placebo as part of the Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease (TRANSCEND) study. An accompanying editorial comments: "Overall, data supporting use of angiotensin-receptor blockers to prevent vascular events in various cardiovascular groups, other than heart failure, are incomplete. TRANSCEND's results challenge the non-inferiority shown in ONTARGET and suggest no more than a modest effect, if any at all."[14]

PRoFESS

The Prevention Regimen For Effectively Avoiding Second Strokes (PRoFESS) study investigated therapy with telmisartan initiated soon after an ischemic stroke and continued for 2.5 years. This treatment did not significantly lower the rate of recurrent stroke, major cardiovascular events, or diabetes.[15]

See also

- Discovery and development of angiotensin receptor blockers
- GW 501516

References

1. ^ [a] [b] [c] Pritor prescribing information
2. ^ Drugs.com: Telmisartan
3. ^ [a] [b] Drugs.com: Micardis
4. ^ [a] [b] Benson, S. C.; Pershadsingh, H.; Ho, C.; Chittiboyina, A.; Desai, P.; Pravenec, M.; Qi, N.; Wang, J.; Avery, M.; Kurtz, T. W. (2004). "Identification of Telmisartan as a Unique Angiotensin II Receptor Antagonist with Selective PPAR -Modulating Activity". *Hypertension* **43** (5): 993–1002. doi:10.1161/01.HYP.0000123072.34629.57. PMID 15007034. edit
5. ^ Department of Pharmacokinetics and Drug Metabolism, Biberach an der Riss, Boehringer Ingelheim Pharma KG, Biberach, Germany (July 2000). "Pharmacokinetics of orally and intravenously administered telmisartan in healthy young and elderly volunteers and in hypertensive patients.". Journal of International Medical Research. Retrieved 18 January 2014.
6. ^ Philippe Gosse (September 2006). "A Review of Telmisartan in the Treatment of Hypertension: Blood Pressure Control in the Early Morning Hours". Vasc Health Risk Manag. Retrieved 18 January 2014.
7. ^ Sanchis-Gomar, F.; Lippi, G. (2011). "Telmisartan as metabolic modulator: A new perspective in sports doping?". *Journal of Strength and Conditioning Research*: 1. doi:10.1519/JSC.0b013e31824301b6. PMID 22130396. edit
8. ^ *Cytoplasmic and Nuclear Receptors: Advances in Research and Application: 2011 Edition*. ScholarlyEditions. 2012. pp. 21–. ISBN 978-1-464-93110-9. Retrieved 2 April 2013.
9. ^ Feng, X.; Luo, Z.; Ma, L.; Ma, S.; Yang, D.; Zhao, Z.; Yan, Z.; He, H.; Cao, T.; Liu, D.; Zhu, Z. (2011). "Angiotensin II receptor blocker telmisartan enhances running endurance of skeletal muscle through activation of the PPAR-δ/AMPK pathway". *Journal of Cellular and Molecular Medicine* **15** (7): 1572–1581. doi:10.1111/j.1582-4934.2010.01085.x. PMID 20477906. edit
10. ^ He, H.; Yang, D.; Ma, L.; Luo, Z.; Ma, S.; Feng, X.; Cao, T.; Yan, Z.; Liu, D.; Tepel, M.; Zhu, Z. (2010). "Telmisartan Prevents Weight Gain and Obesity Through Activation of Peroxisome Proliferator-Activated Receptor- -Dependent Pathways". *Hypertension***55** (4): 869–879. doi:10.1161/HYPERTENSIONAHA.109.143958. PMID 20176998. edit
11. ^ Li, L.; Luo, Z.; Yu, H.; Feng, X.; Wang, P.; Chen, J.; Pu, Y.; Zhao, Y.; He, H.; Zhong, J.; Liu, D.; Zhu, Z. (2012). "Telmisartan Improves Insulin Resistance of Skeletal Muscle Through Peroxisome Proliferator-Activated Receptor- Activation". *Diabetes* **62**(3): 762–774. doi:10.2337/db12-0570. PMC 3581229. PMID 23238297. edit
12. ^ Ontarget, I.; Yusuf, S.; Teo, K.; Pogue, J.; Dyal, L.; Copland, I.; Schumacher, H.; Dagenais, G.; Sleight, P.; Anderson, C. (2008). "Telmisartan, Ramipril, or Both in Patients at High Risk for Vascular Events". *New England Journal of Medicine* **358** (15): 1547–1559. doi:10.1056/NEJMoa0801317. PMID 18378520. edit
13. ^ Bayer Healthcare: Telmisartan approved by the European Commission to reduce the risk of cardiovascular (CV) morbidity in a broad spectrum of at risk patients
14. ^ Ripley, T. L.; Harrison, D. (2008). "The power to TRANSCEND". *The Lancet* **372** (9644): 1128. doi:10.1016/S0140-6736(08)61243-X. PMID 18757086. edit
15. ^ ClinicalTrials.gov *NCT00153062 PRoFESS - Prevention Regimen For Effectively Avoiding Second Strokes*