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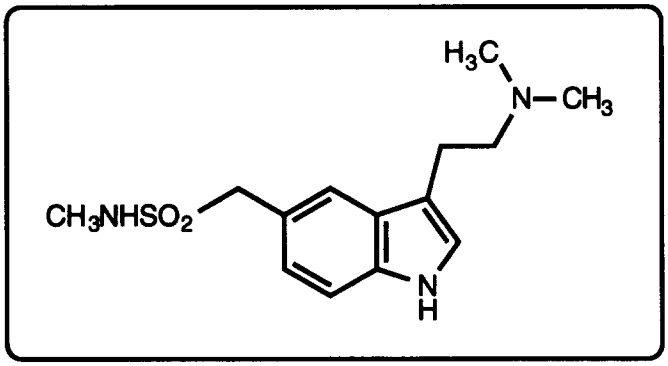
NEW DRUGS—REPORTS OF NEW DRUGS RECENTLY APPROVED BY THE FDA

Sumatriptan



Structure
$C_{14}H_{21}N_3O_2S$

3-[2-(Dimethylamino)ethyl]-*N*-methyl-1*H*-indole-5-methanesulfonamide

Supply: Succinate, $C_{14}H_{21}N_3O_2S{\cdot}C_4H_6O_4$, mp 165–166 °C

GR-43175, SN 308
IMIGRAN®, SUMADOL®, IMIJECT®, ARCOIRAN®
IMITREX® Injection: subcutaneous use only.
IMITREX®: oral formulation.

Mechanism of action: Serotonin $5HT_1$-receptor agonist.

Therapeutic category: Antimigraine.

Synthesis: This compound can be obtained by several different ways.

Summary: Although the mechanism of action of sumatriptan[1] has not been entirely explained, it has been established that it selectively stimulates a subpopulation of serotonin 5HT-1 receptors, specifically the $5HT\text{-}1_D$ receptor with no significant affinity or pharmacological activity at other receptor subtypes.[2,3] Sumatriptan is very effective and well-tolerated in the treatment of common migraine and classical migraine. Subcutaneous administration of sumatriptan 2 to 6 mg results in complete resolution of symptoms, including photophobia, nausea and vomiting, within 20 to 40 min in the majority of patients.[4] Oral sumatriptan is also effective in the treatment of acute migraine, however, single doses of 25 mg are recommended with a maximum single dose of 100 mg.[5] Sumatriptan is rapidly absorbed after oral or subcutaneous administration and is widely distributed to tissues, but passage across the blood–brain barrier is limited; its plasma half-life is approximately 2 h. Oral bioavailability is poor (only about 14%) due to extensive hepatic first-pass metabolism.[6,7] Peak serum sumatriptan levels occur 0.25 h after a single 2 mg iv dose of sumatriptan, and approximately 2 h after a 100 mg oral dose[8] sumatriptan is approximately 10 to 21% protein bound.[7] Single oral dose of 100 to 200 mg have been shown to be effective within 2 h for treatment of migraine. The oral formulation of sumatriptan has now received an approval (June 1995) and a launch is expected in September 1995 in the U.S.A. After two intranasal insufflations of sumatriptan 20 mg spaced 15 min apart, significant relief of pain was observed 60 min after administration; at 120 min, 75% of patients reported headache relief and 53% were completely pain-free.[9] Sumatriptan may prove to be a major therapeutic advance in the acute treatment of migraine. The structure of sumatriptan differs markedly from that of ergot alkaloids. The drug has a more desirable side effect profile than the ergot derivatives, which interact with many

types of receptors, and which thereby may exacerbate the nausea and vomiting accompanying acute migraine. The manufacturer advises[10] avoiding concurrent use of sumatriptan and ergot-containing drugs because an additive vasospastic reaction may occur.

Manufacturer: Glaxo Group Res., Ltd (U.K.).

References

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10. Product Information: Imitrex(R), sumatriptan. Cerenex, Research Triangle Park, NC, 1994.