Protein binding is at least 98%. Lumiracoxib undergoes extensive hepatic metabolism; several enzymes appear to be involved including glucuronosyltransferase and cytochrome P450 isoenzymes. The main oxidative pathway is mediated by the CYP2C9 isoenzyme; however, this does not appear to be the major pathway. Three major metabolites have been identified: 4′-hydroxy-lumiracoxib, 5-carboxy-lumiracoxib, and 4′-hydroxy-5-carboxy-lumiracoxib. The 4′-hydroxy metabolite is active as a cyclo-oxygenase-2 (COX-2) inhibitor although it is less potent than lumiracoxib. The plasma half-life of lumiracoxib is about 4 hours. Slightly more of a dose is excreted in the urine (54%) than in the faeces (about 43%); only about 5% of a dose is excreted unchanged.

◊ References.

1. Scott G, *et al.* Pharmacokinetics of lumiracoxib in plasma and synovial fluid. *Clin Pharmacokinet* 2004; **43:** 467–78.

Uses and Administration

Lumiracoxib is an NSAID (p.99) reported to be a selective inhibitor of cyclo-oxygenase-2 (COX-2). It has been withdrawn in many countries after reports of hepatotoxicity. In the UK, lumiracoxib was used in the treatment of osteoarthritis of the knee and hip in an oral dose of 100 mg once daily. Higher doses of up to 400 mg daily have been used in some countries but may be associated with an increased risk of hepatotoxicity (see Effects on the Liver, above).

◊ References.

1. Lyseng-Williamson KA, Curran MP. Lumiracoxib. *Drugs* 2004; **64:** 2237–46.
2. Bannwarth B, Berenbaum F. Clinical pharmacology of lumiracoxib, a second-generation cyclooxygenase 2 selective inhibitor. *Expert Opin Invest Drugs* 2005; **14:** 521–33.
3. Rordorf CM, *et al.* Clinical pharmacology of lumiracoxib: a selective cyclo-oxygenase-2 inhibitor. *Clin Pharmacokinet* 2005; **44:** 1247–66.
4. Schnitzer TJ, *et al.* Lumiracoxib in the treatment of osteoarthritis, rheumatoid arthritis and acute postoperative dental pain: results of three dose-response studies. *Curr Med Res Opin* 2005; **21:** 151–61.
5. Berenbaum F, *et al.* Efficacy of lumiracoxib in osteoarthritis: a review of nine studies. *J Int Med Res* 2005; **33:** 21–41.
6. Sheldon E, *et al.* Efficacy and tolerability of lumiracoxib in the treatment of osteoarthritis of the knee: a 13-week, randomized, double-blind comparison with celecoxib and placebo. *Clin Ther* 2005; **27:** 64–77.
7. Fleischmann R, *et al.* Lumiracoxib is effective in the treatment of osteoarthritis of the knee: a prospective randomized 13-week study versus placebo and celecoxib. *Clin Rheumatol* 2006; **25:** 42–53.

Preparations

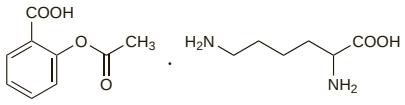
Proprietary Preparations (details are given in Part 3)
Arg.: Prexige; ***Austral.:*** Prexige†; ***Braz.:*** Prexige; ***Chile:*** Prexige; ***Hung.:*** Prexige; ***Indon.:*** Prexige; ***NZ:*** Prexige; ***Port.:*** Frexocel†; Hirzia†; ***UK:*** Prexige†.

Lysine Aspirin

Acetilsalicilato de lisina; Aspirin DL-Lysine; Lysiiniasetyylisalisylaatti; Lysinacetylsalicylat; Lysine Acetylsalicylate; DL-Lysine Acetylsalicylate; Lysinum Acetylsalicylicum.

Лизин-Аспирин

$C_{15}H_{22}N_2O_6$ = 326.3.
CAS — 62952-06-1.



Pharmacopoeias. In *Fr.*

Adverse Effects, Treatment, and Precautions

As for Aspirin, p.20. Anaphylactic shock has been reported in patients given lysine aspirin by injection.

Lysine aspirin, like aspirin, should not generally be given to children because of the risk of Reye's syndrome.

Hypersensitivity. For a suggestion that lysine aspirin might be more suitable than aspirin for the diagnosis of sensitivity to NSAIDs, see under Hypersensitivity on p.21.

Interactions

For interactions associated with aspirin, see p.23.

Uses and Administration

Lysine aspirin has analgesic, anti-inflammatory, and antipyretic actions similar to those of aspirin (see p.23). When given, lysine aspirin dissociates into lysine and aspirin; aspirin is then hydrolysed to salicylic acid. Lysine aspirin 900 mg is equivalent to about 500 mg of aspirin.

Lysine aspirin is used in the treatment of pain, fever, and rheumatic disorders. It is given in oral doses equivalent to 0.5 to 1 g of aspirin, repeated every 4 hours as needed up to a maximum of 3 g of aspirin daily (2 g daily in the elderly) for pain and fever. The dose for rheumatic disorders is equivalent to 3 to 6 g of aspirin daily in 3 or 4 divided doses. Lysine aspirin is also given intramuscularly or intravenously in similar doses; the maximum daily parenteral dose is equivalent to 4 g of aspirin for very severe pain and to 6 g of aspirin for rheumatic disorders.

Lysine aspirin is also used with metoclopramide in the treatment of migraine.

Lysine aspirin has also been used in the management of thromboembolic disorders.

Headache. Some references to the use of lysine aspirin, often with metoclopramide, in the treatment of migraine.

1. Tfelt-Hansen P, *et al.* The effectiveness of combined oral lysine acetylsalicylate and metoclopramide compared with oral sumatriptan for migraine. *Lancet* 1995; **346:** 923–6.
2. Diener HC. Efficacy and safety of intravenous acetylsalicylic acid lysinate compared to subcutaneous sumatriptan and parenteral placebo in the acute treatment of migraine. A double-blind, double-dummy, randomized, multicenter, parallel group study. *Cephalalgia* 1999; **19:** 581–8.
3. Tfelt-Hansen P. The effectiveness of combined oral lysine acetylsalicylate and metoclopramide (Migpriv) in the treatment of migraine attacks: comparison with placebo and oral sumatriptan. *Funct Neurol* 2000; **15** (suppl 3): 196–201.

Nasal polyps. Two long-term controlled studies[1] suggested that topical (endonasal) lysine aspirin may be effective in preventing the recurrence of nasal polyps after surgical removal (see p.1508) in both aspirin-tolerant and aspirin-sensitive patients. This effect may be attributed to the non-specific anti-inflammatory properties of lysine aspirin. Although no adverse effects were reported in this study, hypersensitivity reactions have been seen after use of salicylates in the presence of nasal polyps (see Hypersensitivity under Adverse Effects of Aspirin, p.21).

In another study[2] intranasal lysine aspirin did not show significant clinical benefit in preventing the recurrence of nasal polyps when compared with placebo. However, significant improvement at a microscopic level was noted.

1. Nucera E, *et al.* Effects of lysine-acetylsalicylate (LAS) treatment in nasal polyposis: two controlled long term prospective follow up studies. *Thorax* 2000; **55** (suppl 2): S75–78.
2. Parikh AA, Scadding GK. Intranasal lysine-aspirin in aspirin-sensitive nasal polyposis: a controlled trial. *Laryngoscope* 2005; **115:** 1385–90.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Aspirina; Corplus†; Decitriol; Yectaspirin; ***Belg.:*** Aspegic; Cardegic; ***Cz.:*** Aspegic†; Dolorosan†; Kardegic; ***Fr.:*** Aspegic; Cardiosolupsan; Kardegic; ***Ger.:*** Aspisol†; ***Gr.:*** Aspicalm; Egicalm; Egicalm Cardio; ***Hung.:*** Aspegic; Kardegic; Kardiren†; ***Israel:*** Lysoprin†; ***Ital.:*** Aspegic; Aspidol†; Cardirene; Flectadol; ***Malaysia:*** Aspegic†; ***Mex.:*** Coraspir; Kardegic; ***Neth.:*** Aspegic; Cardegic; ***Pol.:*** Laspal; ***Port.:*** Aspegic; Inesprin; Intraspir; Kardegic; Lisaspin; Tiplac†; ***Span:*** ASL; Inyesprin; Lysinotol†; Solusprin†; ***Switz.:*** Alcacyl instantanee; Aspegic; Kardegic; ***Venez.:*** Asalis†.

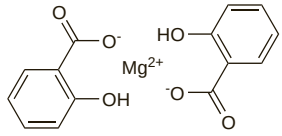
Multi-ingredient: ***Belg.:*** Migpriv; ***Chile:*** Dolotol 12; ***Cz.:*** Migpriv†; ***Denm.:*** Migpriv†; ***Fin.:*** Migpriv; ***Fr.:*** Aspegic Codeine†; Migpriv; ***Gr.:*** Premig; ***Hung.:*** Migpriv; ***Ital.:*** Migpriv; Migraprim; ***Mex.:*** Antigram; ***Neth.:*** Migrafin; ***Norw.:*** Migpriv†; ***Pol.:*** Migpriv; ***Spain:*** Fluxal†; ***Swed.:*** Migpriv; ***Switz.:*** Migpriv; ***UK:*** Migramax.

Magnesium Salicylate

Salicilato magnésico.

Магния Салицилат

$C_{14}H_{10}MgO_6.4H_2O$ = 370.6.
CAS — 18917-89-0 (anhydrous magnesium salicylate); 18917-95-8 (magnesium salicylate tetrahydrate).



Pharmacopoeias. In *Chin.* and *US.*
USP 31 (Magnesium Salicylate). A white, odourless, efflorescent, crystalline powder. Soluble in water and in alcohol; slightly soluble in ether; freely soluble in methyl alcohol. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Aspirin, p.20. Magnesium salicylate should also be used with caution in renal impairment because of the risk of hypermagnesaemia.

The use of aspirin and other acetylated salicylates is generally not recommended for children because of the risk of Reye's syndrome, unless specifically indicated. Some licensed drug information extends this precaution to magnesium salicylate.

Interactions

For interactions associated with salicylates, see Aspirin, p.23.

Uses and Administration

Magnesium salicylate has analgesic, anti-inflammatory, and antipyretic actions similar to those of aspirin (see p.23). Anhydrous magnesium salicylate 1 g is equivalent to about 1.2 g of aspirin. It is used in the treatment of pain and fever and has been used in the management of inflammatory conditions such as osteoarthritis, rheumatoid arthritis, and other arthritides. Usual oral doses of magnesium salicylate, expressed in terms of anhydrous magnesium salicylate, are about 300 to 600 mg every 4 hours for pain or fever.

Preparations

USP 31: Magnesium Salicylate Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Rati Salil E†; ***Canad.:*** Herbogesic; ***USA:*** Backache Maximum Strength Relief; Bayer Select Maximum Strength Backache; Doans; Magan; Mobidin; Momentum Muscular Backache Formula; MST; Novasal; Nuprin Backache†.

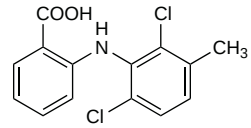
Multi-ingredient: ***Cz.:*** Cholagol; ***Hung.:*** Cholagol; ***Rus.:*** Cholagol (Холагол); ***USA:*** Cafgesic Forte; Combiflex ES; Durabac Forte; Extra Strength Doans PM; Mobigesic; Painaid BRF Back Relief Formula; Tetra-Mag.

Meclofenamic Acid *(BAN, USAN, rINN)*

Acide Méclofénamique; Ácido meclofenámico; Acidum Meclofenamicum; CI-583; INF-4668. *N*-(2,6-Dichloro-*m*-tolyl)anthranilic acid.

Меклофенамовая Кислота

$C_{14}H_{11}Cl_2NO_2$ = 296.1.
CAS — 644-62-2.
ATC — M01AG04; M02AA18.
ATC Vet — QM01AG04; QM02AA18.



Pharmacopoeias. In *BP(Vet).*
BP(Vet) 2008 (Meclofenamic Acid). A white or almost white, crystalline powder. Practically insoluble in water; slightly soluble in alcohol and in chloroform; sparingly soluble in ether; soluble in dimethylformamide and in 1M sodium hydroxide.

Meclofenamate Sodium *(BANM, USAN, rINNM)*

Méclofénamate de Sodium; Meclofenamato sódico; Natrii Meclofenamas.

Натрий Меклофенамат

$C_{14}H_{10}Cl_2NNaO_2.H_2O$ = 336.1.
CAS — 6385-02-0.

Pharmacopoeias. In *US.*
USP 31 (Meclofenamate Sodium). A white to creamy white, odourless to almost odourless, crystalline powder. Freely soluble in water, the solution sometimes being somewhat turbid due to partial hydrolysis and absorption of carbon dioxide; the solution is clear above pH 15. Slightly soluble in chloroform; practically insoluble in ether; soluble in methyl alcohol. Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

Incidence of adverse effects. The commonest adverse effect in 2500 patients given meclofenamate sodium was gastrointestinal disturbance.[1] Diarrhoea occurred in 11.2% of patients in double-blind studies and 32.8% of patients in long-term studies (up to 3 years). Ulcers were detected in 22 patients during therapy and skin rashes occurred in 4% of patients. Transient increases in serum aminotransferases and BUN occurred in some patients.

1. Preston SN. Safety of sodium meclofenamate (Meclomen™). *Curr Ther Res* 1978; **23** (suppl 4S): S107–12.

Effects on the blood. Case reports of agranulocytosis[1] and thrombocytopenia[2] associated with meclofenamate therapy.

1. Wishner AJ, Milburn PB. Meclofenamate sodium-induced agranulocytosis and suppression of erythropoiesis. *J Am Acad Dermatol* 1985; **13:** 1052–3.
2. Rodriguez J. Thrombocytopenia associated with meclofenamate. *Drug Intell Clin Pharm* 1981; **15:** 999.

Interactions

For interactions associated with NSAIDs, see p.99.

Pharmacokinetics

Meclofenamate sodium is readily absorbed when given orally. Peak plasma concentrations occur about 0.5 to 2 hours after ingestion. Meclofenamate is over 99% bound to plasma proteins. The plasma elimination half-life of meclofenamate sodium is about 2 to 4 hours. It is metabolised by oxidation, hydroxylation, dehalogenation, and conjugation with glucuronic acid and excreted in urine mainly as glucuronide conjugates of the metabolites. About 20 to 30% is recovered in the faeces. One of the metabolites, a 3-hydroxymethyl compound, is reported to be active although to a lesser extent than the parent drug.

◊ References.

1. Koup JR, *et al.* A single and multiple dose pharmacokinetic and metabolism study of meclofenamate sodium. *Biopharm Drug Dispos* 1990; **11:** 1–15.

Uses and Administration

Meclofenamic acid, an anthranilic acid derivative similar to mefenamic acid (below), is an NSAID (p.99). It is given orally as the sodium salt in musculoskeletal and joint disorders such as