Administration in hepatic impairment. Licensed product information recommends that doses of celecoxib should be reduced by 50% in patients with moderate hepatic impairment (Child-Pugh category B); its use is contra-indicated in those with severe impairment (Child-Pugh category C or a score of 10 or more).

Familial adenomatous polyposis. Celecoxib is used in the treatment of familial adenomatous polyposis, an inherited syndrome known to predispose sufferers to the development of colonic cancer (see p.666). A randomised study[1,2] found that treatment with celecoxib reduced the number of colonic polyps; the authors considered celecoxib to be a useful adjunct to the standard therapy of colectomy.

1. Steinbach G, *et al.* The effect of celecoxib, a cyclooxygenase-2 inhibitor, in familial adenomatous polyposis. *N Engl J Med* 2000; **342:** 1946–52.
2. Phillips RKS, *et al.* A randomised, double blind, placebo controlled study of celecoxib, a selective cyclooxygenase 2 inhibitor, on duodenal polyposis in familial adenomatous polyposis. *Gut* 2002; **50:** 857–60.

Malignant neoplasms. Celecoxib is under investigation as adjuvant therapy in the treatment of cancer;[1-9] preliminary results have been variable. It has also been investigated for chemoprevention of malignancy[10-13] (see also Familial Adenomatous Polyposis, above), but a large study for the prevention of colon cancer was terminated early because of increased cardiovascular risk.[11,12]

1. Dang CT, *et al.* Phase II study of celecoxib and trastuzumab in metastatic breast cancer patients who have progressed after prior trastuzumab-based treatments. *Clin Cancer Res* 2004; **10:** 4062–7.
2. Reardon DA, *et al.* Phase II trial of irinotecan plus celecoxib in adults with recurrent malignant glioma. *Cancer* 2005; **103:** 329–38.
3. Nugent FW, *et al.* Docetaxel and cyclooxygenase-2 inhibition with celecoxib for advanced non-small cell lung cancer progressing after platinum-based chemotherapy: a multicenter phase II trial. *Lung Cancer* 2005; **48:** 267–73.
4. Gasparini G, *et al.* The combination of the selective cyclooxygenase-2 inhibitor celecoxib with weekly paclitaxel is a safe and active second-line therapy for non-small cell lung cancer: a phase II study with biological correlates. *Cancer J* 2005; **11:** 209–16.
5. Prince HM, *et al.* A multicenter phase II trial of thalidomide and celecoxib for patients with relapsed and refractory multiple myeloma. *Clin Cancer Res* 2005; **11:** 5504–14.
6. Pan CX, *et al.* A phase II trial of irinotecan, 5-fluorouracil and leucovorin combined with celecoxib and glutamine as first-line therapy for advanced colorectal cancer. *Oncology* 2005; **69:** 63–70.
7. Ferrari V, *et al.* Gemcitabine plus celecoxib (GECO) in advanced pancreatic cancer: a phase II trial. *Cancer Chemother Pharmacol* 2006; **57:** 185–90.
8. Csiki I, *et al.* Targeting cyclooxygenase-2 in recurrent non-small cell lung cancer: a phase II trial of celecoxib and docetaxel. *Clin Cancer Res* 2005; **11:** 6634–40.
9. Chow LWC, *et al.* Serum lipid profiles in patients receiving endocrine treatment for breast cancer—the results from the Celecoxib Anti-Aromatase Neoadjuvant (CAAN) Trial. *Biomed Pharmacother* 2005; **59** (suppl 2): S302–S305.
10. Limburg PJ, *et al.* Randomized, placebo-controlled, esophageal squamous cell cancer chemoprevention trial of selenomethionine and celecoxib. *Gastroenterology* 2005; **129:** 863–73.
11. Solomon SD, *et al.* Adenoma Prevention with Celecoxib (APC) Study Investigators. Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention. *N Engl J Med* 2005; **352:** 1071–80.
12. Bertagnolli MM, *et al.* Celecoxib for the prevention of sporadic colorectal adenomas. *N Engl J Med* 2006; **355:** 873–84.
13. Arber N, *et al.* Celecoxib for the prevention of colorectal adenomatous polyps. *N Engl J Med* 2006; **355:** 885–95.

Musculoskeletal and joint disorders. Celecoxib is used in the treatment of osteoarthritis (p.11) and rheumatoid arthritis (p.11) including juvenile idiopathic arthritis (p.10). However, in the UK it is recommended that the use of celecoxib and other selective cyclo-oxygenase-2 (COX-2) inhibitors be limited to those patients considered to be at high risk of developing serious gastrointestinal problems if given a non-selective NSAID and who do not have pre-existing cardiovascular risk factors (see Adverse Effects, above).

Celecoxib is also used in the treatment of ankylosing spondylitis (see Spondyloarthropathies, p.13).

References.

1. Bensen WG, *et al.* Treatment of osteoarthritis with celecoxib, a cyclooxygenase-2 inhibitor: a randomized controlled trial. *Mayo Clin Proc* 1999; **74:** 1095–1105.
2. Simon LS, *et al.* Anti-inflammatory and upper gastrointestinal effects of celecoxib in rheumatoid arthritis: a randomized controlled trial. *JAMA* 1999; **282:** 1921–28.
3. Emery P, *et al.* Celecoxib versus diclofenac in long-term management of rheumatoid arthritis: randomised double-blind comparison. *Lancet* 1999; **354:** 2106–11.
4. Dougados M, *et al.* Efficacy of celecoxib, a cyclooxygenase 2-specific inhibitor, in the treatment of ankylosing spondylitis: a six-week controlled study with comparison against placebo and against a conventional nonsteroidal antiinflammatory drug. *Arthritis Rheum* 2001; **44:** 180–5.
5. Stengaard-Pedersen K, *et al.* Celecoxib 200 mg qd is efficacious in the management of osteoarthritis of the knee or hip regardless of the time of dosing. *Rheumatology (Oxford)* 2004; **43:** 592–5.
6. Schnitzer TJ, *et al.* VACT-1 and VACT-2 (Protocols 106 and 150) Study Groups. Efficacy of rofecoxib, celecoxib, and acetaminophen in patients with osteoarthritis of the knee: a combined analysis of the VACT studies. *J Rheumatol* 2005; **32:** 1093–1105.
7. Singh G, *et al.* Celecoxib versus naproxen and diclofenac in osteoarthritis patients: SUCCESS-I Study. *Am J Med* 2006; **119:** 255–66.
8. Barkhuizen A, *et al.* Celecoxib is efficacious and well tolerated in treating signs and symptoms of ankylosing spondylitis. *J Rheumatol* 2006; **33:** 1805–12.
9. Luyten FP, *et al.* A prospective randomised multicentre study comparing continuous and intermittent treatment with celecoxib in patients with osteoarthritis of the knee or hip. *Ann Rheum Dis* 2007; **66:** 99–106.

Palmar-plantar erythrodysesthesia syndrome. Celecoxib has been investigated in the treatment of capecitabine-induced hand-foot (palmar-plantar erythrodysesthesia) syndrome; for references, see under Adverse Effects and Precautions of Capecitabine, p.692.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Algybrex; Celebrex; Celemax†; Cloxib†; Coxel†; Coxtenk; Niflam†; Radicacine; Tisorek†; ***Austral.:*** Celebrex; ***Austria:*** Celebrex; Solexa; ***Belg.:*** Celebrex; ***Braz.:*** Celebra; ***Canad.:*** Celebrex; ***Chile:*** Celebra; ***Cz.:*** Celebrex; Onsenal; ***Denm.:*** Celebra; ***Fin.:*** Celebra; ***Fr.:*** Celebrex; Onsenal; ***Ger.:*** Celebrex; ***Gr.:*** Aclarex; Celebrex; ***Hong Kong:*** Celebrex; ***Hung.:*** Celebrex; ***India:*** Celedol; Celib; Cobix; Orthocel; Ultracele†; Zycel; ***Indon.:*** Celebrex; ***Irl.:*** Celebrex; ***Israel:*** Celcox; Celebra; ***Ital.:*** Artilog†; Celebrex; Solexa†; ***Malaysia:*** Celebrex; ***Mex.:*** Celebrex; ***Neth.:*** Celebrex; Onsenal; Solexa; ***Norw.:*** Celebra; Onsenal; ***NZ:*** Celebrex; ***Philipp.:*** Celebrex; Flamar; ***Pol.:*** Celebrex; ***Port.:*** Celebrex; Onsenal; Solexa; ***Rus.:*** Celebrex (Целебрекс); ***S.Afr.:*** Celebrex; ***Singapore:*** Celebrex; ***Spain:*** Celebrex; Onsenal; ***Swed.:*** Celebra; Onsenal; ***Switz.:*** Celebrex; ***Thai.:*** Celebrex; ***UK:*** Celebrex; ***USA:*** Celebrex; ***Venez.:*** Celebrex†; Cexb.

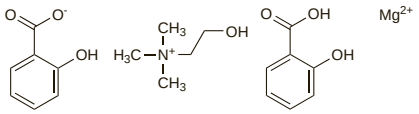
Choline Magnesium Trisalicylate

Trisalicilato de colina y magnesio.

Холин Магнезиум Трисалицилаты

$C_{26}H_{29}O_{10}NMg$ = 539.8.

CAS — 64425-90-7.



Adverse Effects, Treatment, and Precautions

As for Aspirin, p.20.

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

Effects on the liver. References.

1. Cersosimo RJ, Matthews SJ. Hepatotoxicity associated with choline magnesium trisalicylate: case report and review of salicylate-induced hepatotoxicity. *Drug Intell Clin Pharm* 1987; **21:** 621–5.
2. Nadkarni MM, *et al.* Eosinophilic hepatitis after ingestion of choline magnesium trisalicylate. *Am J Gastroenterol* 1992; **87:** 151–3.

Interactions

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

Uses and Administration

Choline magnesium trisalicylate is a combination of the salicylic acid derivatives choline salicylate (p.36) and magnesium salicylate (p.79). It has analgesic, anti-inflammatory, and antipyretic actions similar to those of aspirin (p.23). After oral administration, choline magnesium trisalicylate dissociates and the salicylate moiety is rapidly absorbed. Each unit dose of 500 mg of salicylate is provided by about 293 mg of choline salicylate with 362 mg of magnesium salicylate (anhydrous). Choline magnesium trisalicylate has been used in osteoarthritis, rheumatoid arthritis, and other arthritides in oral doses equivalent to 1 or 1.5 g of salicylate twice daily; doses may also be given as a single daily dose if required. A dose of 750 mg given three times daily may be more suitable for elderly patients. Choline magnesium trisalicylate is also used in similar doses in the general management of other forms of pain and for fever.

Preparations

Proprietary Preparations (details are given in Part 3)

Canad.: Trilisate†; ***USA:*** Trilisate†.

Choline Salicylate *(BAN, USAN, rINN)*

Choline, Salicylate de; Cholini Salicylas; Koliinisalisylaatti; Kolinsalicylat; Salicilato de colina. (2-Hydroxyethyl)trimethylammonium salicylate.

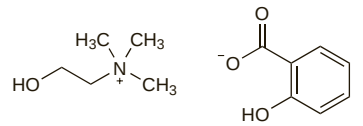
Холина Салицилат

$C_{12}H_{19}NO_4$ = 241.3.

CAS — 2016-36-6.

ATC — N02BA03.

ATC Vet — QN02BA03.



Pharmacopoeias. *Br.* includes a solution.

BP 2008 (Choline Salicylate Solution). An aqueous solution containing 47.5 to 52.5% of choline salicylate. It is a clear colourless liquid. It may contain a suitable antimicrobial preservative.

Profile

Choline salicylate is a salicylic acid derivative (see Aspirin, p.20) used in the treatment of pain and fever, and in the management of rheumatic disorders. In terms of salicylate content, choline salicylate 435 mg is equivalent to about 325 mg of aspirin. Choline salicylate is given orally in doses of 435 to 870 mg every four hours as necessary for pain and fever, and in doses of 4.8 to 7.2 g daily in divided doses for rheumatic disorders.

Choline salicylate is also used as a local analgesic. Solutions containing up to about 20% choline salicylate are used in ear disorders such as the relief of pain in otitis media and externa but are considered to be of doubtful value; they are also used to soften ear wax as an aid to removal (see p.1725). An 8.7% gel is used for lesions of the mouth (p.1700). Choline salicylate has also been applied topically in a rubefacient preparation for the relief of muscular and rheumatic pain.

Choline salicylate is also given in the form of choline magnesium trisalicylate (see above).

Adverse effects. A 21-month-old boy developed salicylate poisoning after his mother had rubbed the contents of 3 tubes of *Bonjela* teething ointment (containing a total of 2.61 g of choline salicylate) on his gums over 48 hours.[1]

In another case, an 8-year-old boy with G6PD deficiency developed an oral mucosal burn a few hours after application of about half a tube of *Teejel* oral gel.[2] He developed mouth ulcers and displayed signs of apathy, lethargy, and nasal congestion 3 days after exposure. His condition improved after a week. The authors felt that G6PD deficiency may have been a contributing factor in the occurrence of adverse effects.

1. Paynter AS, Alexander FW. Salicylate intoxication caused by teething ointment. *Lancet* 1979; **ii:** 1132.
2. Sapir S, Bimstein E. Cholinsalicylate gel induced oral lesion: report of case. *J Clin Pediatr Dent* 2000; **24:** 103–6.

REYE'S SYNDROME. The link between aspirin use in children and the development of Reye's syndrome is established although the evidence for other salicylates could not be adequately evaluated (see p.22). However, a 20-month-old boy who had received a teething gel containing choline salicylate (applied in doses of 1.31 g daily, equivalent to acetylsalicylate 100 mg/kg daily, which exceeds the recommended dose) developed Reye's syndrome following a viral illness.[1] The authors noted that the MHRA in the UK were aware of two earlier reports suggesting an association between choline salicylate and Reye's syndrome.

1. Oman TK, *et al.* Topical choline salicylates implicated in Reye's syndrome. *BMJ* 2008; **336:** 1376.

Preparations

BP 2008: Choline Salicylate Ear Drops; Choline Salicylate Oromucosal Gel.

Proprietary Preparations (details are given in Part 3)

Arg.: Dercolina; ***Austral.:*** Applicaine; Herron Baby Teething Gel; Ora-Sed Jel; ***Belg.:*** Teejel; ***Ger.:*** Audax†; ***Hong Kong:*** Ora-Sed; ***India:*** Gelora; Zytee; ***Irl.:*** Audax; Teejel; ***Israel:*** Teejel; ***NZ:*** Ora-Sed; ***Pol.:*** Cholinex; Otinum; ***Port.:*** Bucagel; ***Rus.:*** Otinum (Отинум); ***Singapore:*** Ora-Sed; ***UK:*** Audax†; Dinnefords Teejel†; ***USA:*** Arthropan†.

Multi-ingredient: ***Arg.:*** Pansoral; ***Austral.:*** Bonjela; Seda-Gel; ***Austria:*** Mundisal; ***Belg.:*** Givalex; ***Cz.:*** Mundisal; ***Fr.:*** Givalex; Pansoral; ***Ger.:*** Givalex†; Mundisal†; ***Gr.:*** Mundisal; ***Hong Kong:*** Bonjela; Dermojela; ***Hung.:*** Mundisal; ***Irl.:*** Bonjela; ***Israel:*** Baby Gum; Bonjela; ***Malaysia:*** Bonjela; Orregel; ***NZ:*** Bonjela; ***Pol.:*** Sachol zel Stomatologiczny; ***Rus.:*** Cholisal (Холисал); Pansoral (Пансорал); ***S.Afr.:*** Bonjela; ***Singapore:*** Bonjela; Soragel; ***Spain:*** Aldo Otico†; ***Switz.:*** Mundisal; Pansoral; Tenderdol; ***Thai.:*** Bonjela; ***UK:*** Bonjela; Earex Plus.