to play a role in the pathogenesis of asthma. The drug suppresses both early and late bronchoconstrictor responses to inhaled antigens or irritants, but is not suitable for the management of acute attacks of asthma.

Zafirlukast is used in the management of chronic asthma (see below). It is given orally in doses of 20 mg twice daily, taken at least 1 hour before or 2 hours after meals. For details of doses in children, see below.

◊ General references.

1. García-Marcos L, *et al.* Benefit-risk assessment of antileukotrienes in the management of asthma. *Drug Safety* 2003; **26:** 483–518.
2. Anonymous. Leukotriene receptor antagonists—an update. *Drug Ther Bull* 2005; **43:** 85–8.
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Administration in children. In the management of chronic asthma, US licensed product information recommends a zafirlukast dose of 10 mg twice daily orally in children aged from 5 to 11 years. Children 12 years of age and over may be given the adult dose, see above. In the UK, zafirlukast is unlicensed in children under 12 years of age.

Asthma. Zafirlukast produces modest improvement in mild-to-moderate asthma,[1,2] which was of a similar order to that seen with inhaled sodium cromoglicate in one study,[3] but less than that of inhaled salmeterol in another.[4] It has also been found to be less effective than inhaled fluticasone in persistent asthma.[5-7] Guidelines for the management of asthma (p.1108) permit the use of zafirlukast as an alternative to inhaled corticosteroids in patients with mild persistent asthma, who cannot be managed with inhaled $beta_2$ agonists on an as-needed basis alone. It can also be considered for use in moderate or severe persistent asthma, usually added to standard therapy of inhaled corticosteroids and long-acting inhaled $beta_2$ agonists. Combination of anti-leukotriene drugs with inhaled corticosteroids alone seems, however, to be less effective than a combination of the latter with long-acting inhaled $beta_2$ agonists. In a study in patients presenting to the emergency room with acute severe asthma, adding zafirlukast to standard therapy in hospital and for 28 days after discharge was associated with a reduced rate of relapse, and a reduction in the need for extended care.[8]

1. Suissa S, *et al.* Effectiveness of the leukotriene receptor antagonist zafirlukast for mild-to-moderate asthma: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1997; **126:** 177–83.
2. Fish JE, *et al.* Zafirlukast for symptomatic mild-to-moderate asthma: a 13-week multicenter study. *Clin Ther* 1997; **19:** 675–90.
3. Nathan RA, *et al.* Two first-line therapies in the treatment of mild asthma: use of peak flow variability as a predictor of effectiveness. *Ann Allergy Asthma Immunol* 1999; **82:** 497–503.
4. Busse W, *et al.* Comparison of inhaled salmeterol and oral zafirlukast in patients with asthma. *J Allergy Clin Immunol* 1999; **103:** 1075–80.
5. Busse W, *et al.* Fluticasone propionate compared with zafirlukast in controlling persistent asthma: a randomized double-blind, placebo-controlled trial. *J Fam Pract* 2001; **50:** 595–602.
6. Nathan RA, *et al.* A comparison of short-term treatment with inhaled fluticasone propionate and zafirlukast for patients with persistent asthma. *Am J Med* 2001; **111:** 195–202.
7. Brabson JH, *et al.* Efficacy and safety of low-dose fluticasone propionate compared with zafirlukast in patients with persistent asthma. *Am J Med* 2002; **113:** 15–21.
8. Silverman RA, *et al.* Zafirlukast treatment for acute asthma: evaluation in a randomized, double-blind, multicenter trial. *Chest* 2004; **126:** 1480–9.

Rhinitis. Although it was reported to improve symptoms of seasonal allergic rhinitis (p.565) in one study,[1] zafirlukast 20 mg twice daily was not effective when compared with placebo and intranasal beclometasone in another.[2] Some benefits have been reported in perennial allergic rhinitis, in particular an improvement in nasal obstruction.[3,4] A review of the role of leukotrienes in allergic rhinitis concluded that leukotriene receptor antagonists have modest efficacy given alone but can be usefully added to other treatments.[5]

1. Donnelly AL, *et al.* The leukotriene D -receptor antagonist, ICI 204,219, relieves symptoms of acute seasonal allergic rhinitis. *Am J Respir Crit Care Med* 1995; **151:** 1734–9.
2. Pullerits T, *et al.* Randomized placebo-controlled study comparing a leukotriene receptor antagonist and a nasal glucocorticoid in seasonal allergic rhinitis. *Am J Respir Crit Care Med* 1999; **159:** 1814–18.
3. Jiang R-S. Efficacy of a leukotriene receptor antagonist in the treatment of perennial allergic rhinitis. *J Otolaryngol* 2006; **35:** 117–21.
4. Ho C-Y, Tan C-T. Comparison of antileukotrienes and antihistamines in the treatment of allergic rhinitis. *Am J Rhinol* 2007; **21:** 439–43.
5. Peters-Golden M, Henderson WR. The role of leukotrienes in allergic rhinitis. *Ann Allergy Asthma Immunol* 2005; **94:** 609–18.

Urticaria. Leukotriene antagonists, such as zafirlukast, are reported to have some benefit in the management of chronic urticaria (p.1584).

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Accolate; Vanticon†; Zafirasmal†; ***Austral.:*** Accolate; ***Belg.:*** Accolate; Resma; ***Braz.:*** Accolate; ***Canad.:*** Accolate; ***Chile:*** Accolate; ***Cz.:*** Accolate; ***Fin.:*** Accolate; ***Hong Kong:*** Accolate; ***Hung.:*** Accolate; ***India:*** Zuvair; ***Indon.:*** Accolate; ***Irl.:*** Accolate; ***Ital.:*** Accoleit; Zafirst; ***Mex.:*** Accolate; ***Philipp.:*** Accolate; ***Pol.:*** Accolate; ***Port.:*** Accolate; ***Rus.:*** Accolate (Аколат); ***S.Afr.:*** Accolate; ***Singapore:*** Accolate; ***Spain:*** Accolate; Aeronix; Olmoran; ***Switz.:*** Accolate; ***Thai.:*** Accolate†; ***Turk.:*** Accolate; ***UK:*** Accolate; ***USA:*** Accolate; ***Venez.:*** Accolate.

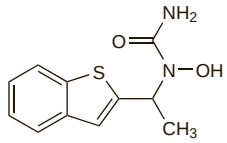
Zileuton *(BAN, USAN, rINN)*

A-64077; Abbott-64077; Zileutón; Zileutonum. (±)-1-(1-Benzo[*b*]thien-2-ylethyl)-*N*-hydroxyurea.

Зилейтон

$C_{11}H_{12}N_2O_2S$ = 236.3.

CAS — 111406-87-2.



Pharmacopoeias. In *US.*

USP 31 (Zileuton). A white to off-white powder. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

The most commonly reported adverse effects associated with zileuton treatment are headache, pain including pharyngolaryngeal pain, gastrointestinal disturbances, myalgia, and sinusitis. Hypersensitivity, urticaria, rash, and leucopenia have been reported in a few patients. Zileuton has also been associated with raised liver enzyme values and severe hepatic injury.

Zileuton is not suitable for the treatment of acute asthma attacks.

Effects on the liver. Cases of severe hepatotoxicity including fatalities, jaundice, hyperbilirubinaemia, and raised liver enzymes have been reported in patients taking zileuton. US licensed product information therefore contraindicates the use of zileuton in patients with active liver disease or liver transaminase elevations greater than or equal to three times the upper limit of normal. Caution is required in patients with a history of liver disease or who consume substantial quantities of alcohol. Alanine aminotransferase (ALT) is considered the most sensitive indicator of liver injury due to zileuton. Most rises in ALT concentrations occurred in the first 3 months of zileuton therapy,[1] and monitoring is therefore recommended before starting zileuton therapy, once a month for the first 3 months of therapy, every 2 to 3 months for the remainder of the first year of therapy, and periodically thereafter.

1. Watkins PB, *et al.* Clinical pattern of zileuton-associated liver injury: results of a 12-month study in patients with chronic asthma. *Drug Safety* 2007; **30:** 805–15.

Interactions

Zileuton has been reported to impair the metabolism of some drugs metabolised via hepatic cytochrome P450 enzymes, including propranolol, terfenadine, theophylline, and warfarin.

Pharmacokinetics

Zileuton is reported to be well absorbed from the gastrointestinal tract after oral dosage, with peak plasma concentrations of immediate-release preparations occurring within about 2 hours of a dose. It is about 93% bound to plasma proteins. It is extensively metabolised in the liver by the cytochrome P450 isoenzymes CYP1A2, CYP2C9, and CYP3A4, and excreted in the urine, largely as glucuronide metabolites. The elimination half-life is reported to be about 2.5 hours for the immediate-release preparation and about 3 hours for the controlled-release preparation.

◊ References.

1. Wong SL, *et al.* The pharmacokinetics of single oral doses of zileuton 200 to 800 mg, its enantiomers, and its metabolites, in normal healthy volunteers. *Clin Pharmacokinet* 1995; **29** (suppl 2): 9–21.
2. Awni WM, *et al.* Pharmacokinetics and pharmacodynamics of zileuton after oral administration of single and multiple dose regimens of zileuton 600 mg in healthy volunteers. *Clin Pharmacokinet* 1995; **29** (suppl 2): 22–33.
3. Braeckman RA, *et al.* The pharmacokinetics of zileuton in healthy young and elderly volunteers. *Clin Pharmacokinet* 1995; **29** (suppl 2): 42–8.
4. Awni WM, *et al.* Population pharmacokinetics of zileuton, a selective 5-lipoxygenase inhibitor, in patients with rheumatoid arthritis. *Eur J Clin Pharmacol* 1995; **48:** 155–60.
5. Awni WM, *et al.* The effect of mild or moderate hepatic impairment (cirrhosis) on the pharmacokinetics of zileuton. *Clin Pharmacokinet* 1995; **29** (suppl 2): 49–61.
6. Awni WM, *et al.* Pharmacokinetics of zileuton and its metabolites in patients with renal impairment. *J Clin Pharmacol* 1997; **37:** 395–404.
7. Dubé LM, *et al.* Zileuton, a leukotriene synthesis inhibitor in the management of chronic asthma: clinical pharmacokinetics and safety. *Clin Rev Allergy Immunol* 1999; **17:** 213–21.

Uses and Administration

Zileuton is an orally active 5-lipoxygenase inhibitor and therefore inhibits leukotriene formation (p.1108). It is used in the management of chronic asthma (see below) but has no bronchodilator properties and is not suitable for the management of acute attacks. Zileuton is given in oral doses of 600 mg 4 times daily as an immediate-release preparation. A controlled-release formulation of zileuton is also available; the usual oral dose is 1.2 g twice daily.

It has also been tried in other disorders including arthritis, allergic rhinitis, and inflammatory bowel disease.

Asthma. Zileuton has been found to be of some benefit in asthma, including that provoked by cold air, exercise, and NSAIDs. US guidelines for the management of asthma (p.1108) permit its use in addition to inhaled corticosteroid therapy in moderate persistent asthma. Combination of anti-leukotriene drugs with inhaled corticosteroids alone seems however to be less effective than a combination of the latter with long-acting inhaled $beta_2$ agonists. Due to a lack of data on efficacy and the need for liver function monitoring, zileuton is also considered a less desirable treatment option for addition to inhaled corticosteroids than the leukotriene receptor antagonists.

An intravenous form of zileuton is under investigation for use in asthma.

References.

1. Israel E, *et al.* The effects of a 5-lipoxygenase inhibitor on asthma induced by cold, dry air. *N Engl J Med* 1990; **323:** 1740–4.
2. Israel E, *et al.* The effect of inhibition of 5-lipoxygenase by zileuton in mild-to-moderate asthma. *Ann Intern Med* 1993; **119:** 1059–66.
3. McGill KA, Busse WW. Zileuton. *Lancet* 1996; **348:** 519–24.
4. Israel E, *et al.* Effect of treatment with zileuton, a 5-lipoxygenase inhibitor, in patients with asthma: a randomized controlled trial. *JAMA* 1996; **275:** 931–6.
5. O'Connor BJ, *et al.* Zileuton added to low-dose inhaled beclomethasone for the treatment of moderate to severe persistent asthma. *Respir Med* 2007; **101:** 1088–96.

Inflammatory bowel disease. Despite initial hopes that inhibition of lipoxygenase might prove of benefit in patients with ulcerative colitis,[1] a study in those with mild or moderately active relapsing disease found that the symptomatic benefits of zileuton were confined to those not already receiving sulfasalazine.[2] A subsequent study showed zileuton was not significantly better than placebo in maintaining remission.[3] For a discussion of inflammatory bowel disease and its management, see p.1697.

1. Laursen LS, *et al.* Selective 5-lipoxygenase inhibition in ulcerative colitis. *Lancet* 1990; **335:** 683–5.
2. Laursen LS, *et al.* Selective 5-lipoxygenase inhibition by zileuton in the treatment of relapsing ulcerative colitis: a randomized double-blind placebo-controlled multicentre trial. *Eur J Gastroenterol Hepatol* 1994; **6:** 209–15.
3. Hawkey CJ, *et al.* A trial of zileuton versus mesalazine or placebo in the maintenance of remission of ulcerative colitis. *Gastroenterology* 1997; **112:** 718–24.

Rhinitis. A study in 8 patients with allergic rhinitis (p.565) found that a single dose of zileuton 800 mg reduced the response to a nasal antigen challenge 3 hours later,[1] including reduced sneezing and nasal congestion.

1. Knapp HR. Reduced allergen-induced nasal congestion and leukotriene synthesis with an orally active 5-lipoxygenase inhibitor. *N Engl J Med* 1990; **323:** 1745–8.

Preparations

Proprietary Preparations (details are given in Part 3)

USA: Zyflo.

63. Büller HR, *et al.* Fondaparinux or enoxaparin for the initial treatment of symptomatic deep venous thrombosis: a randomized trial. *Ann Intern Med* 2004; **140:** 867–73.
64. British Society for Haematology: British Committee for Standards in Haematology—Haemostasis and Thrombosis Task Force. Guidelines on oral anticoagulation: third edition. *Br J Haematol* 1998; **101:** 374–87. Also available at: http://www.bcshguidelines.com/pdf/bjh715.pdf (accessed 10/02/06) Updated 2005 guidelines. *Br J Haematol* 2006; **132:** 277–85. Also available at: http://www.bcshguidelines.com/pdf/oralanticoagulation.pdf (accessed 10/02/06)
65. Hutten BA, Prins MH. Duration of treatment with vitamin K antagonists in symptomatic venous thromboembolism. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2006 (accessed 10/02/06).
66. Ost D, *et al.* Duration of anticoagulation following venous thromboembolism: a meta-analysis. *JAMA* 2005; **294:** 706–15.
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68. Kyrle PA, *et al.* The risk of recurrent venous thromboembolism in men and women. *N Engl J Med* 2004; **350:** 2558–63.
69. Research Committee of the British Thoracic Society. Optimum duration of anticoagulation for deep-vein thrombosis and pulmonary embolism. *Lancet* 1992; **340:** 873–6.
70. Kearon C, *et al.* Comparison of 1 month with 3 months of anticoagulation for a first episode of venous thromboembolism associated with a transient risk factor. *J Thromb Haemost* 2004; **2:** 743–9.
71. Iorio A, *et al.* Low-molecular-weight heparin for the long-term treatment of symptomatic venous thromboembolism: meta-analysis of the randomized comparisons with oral anticoagulants. *J Thromb Haemost* 2003; **1:** 1906–13.
72. Luk C, *et al.* Extended outpatient therapy with low molecular weight heparin for the treatment of recurrent venous thromboembolism despite warfarin therapy. *Am J Med* 2001; **111:** 270–3.
73. Lee AYY, *et al.* Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. *N Engl J Med* 2003; **349:** 146–53.
74. Ridker PM, *et al.* Long-term, low-intensity warfarin therapy for the prevention of recurrent venous thromboembolism. *N Engl J Med* 2003; **348:** 1425–34.
75. Kearon C, *et al.* Comparison of low-intensity warfarin therapy with conventional-intensity warfarin therapy for long-term prevention of recurrent venous thromboembolism. *N Engl J Med* 2003; **349:** 631–9.
76. Buller HR, *et al.* van Gogh Investigators. Idraparinux versus standard therapy for venous thromboembolic disease. *N Engl J Med* 2007; **357:** 1094–1104.
77. Buller HR, *et al.* van Gogh Investigators. Extended prophylaxis of venous thromboembolism with idraparinux. *N Engl J Med* 2007; **357:** 1105–12.
78. Decousus H, *et al.* A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. *N Engl J Med* 1998; **338:** 409–15.
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82. Robinson GV. Pulmonary embolism in hospital practice. *BMJ* 2006; **332:** 156–60.
83. Piazza G, Goldhaber SZ. Acute pulmonary embolism. Part II: treatment and prophylaxis. *Circulation* 2006; **114:** e42–e47.
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85. Konstantinides SV. Acute pulmonary embolism revisited. *Heart* 2008; **94:** 795–802.
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90. Wan S, *et al.* Thrombolysis compared with heparin for the initial treatment of pulmonary embolism: a meta-analysis of the randomized controlled trials. *Circulation* 2004; **110:** 744–9.
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92. Parasuraman S, Goldhaber SZ. Venous thromboembolism in children. *Circulation* 2006; **113:** e12–e16.
93. Monagle P, *et al.* Antithrombotic therapy in neonates and children: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest* 2008; **133** (suppl): 887S–968S.
94. Sanson B-J, *et al.* Safety of low-molecular-weight heparin in pregnancy: a systematic review. *Thromb Haemost* 1999; **81:** 668–72.
95. Bates SM, *et al.* Venous thromboembolism, thrombophilia, antithrombotic therapy, and pregnancy: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). *Chest* 2008; **133** (suppl): 884S–886S.
96. Toglia MR, Weg JG. Venous thromboembolism during pregnancy. *N Engl J Med* 1996; **335:** 108–14.
97. Greer IA. Thrombosis in pregnancy: maternal and fetal issues. *Lancet* 1999; **353:** 1258–65.
98. Drife J. Thromboembolism. *Br Med Bull* 2003; **67:** 177–90.
99. James AH. Prevention and management of venous thromboembolism in pregnancy. *Am J Med* 2007; **120** (issue 10 suppl 2): S26–S34.
100. Lim W, *et al.* Inherited thrombophilia and pregnancy associated venous thromboembolism. *BMJ* 2007; **334:** 1318–21.
101. Royal College of Obstetricians and Gynaecologists. Thromboembolic disease in pregnancy and the puerperium: acute management (February 2007). Available at: http://www.rcog.org.uk/resources/Public/pdf/green_top_28_thromboembolic_minorrevision.pdf (accessed 27/02/08)
102. Royal College of Obstetricians and Gynaecologists. Thromboprophylaxis during pregnancy, labour and after vaginal delivery (January 2004). Available at: http://www.rcog.org.uk/resources/Public/pdf/Thromboprophylaxis_no037.pdf (accessed 27/08/08)
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Abciximab *(BAN, USAN, rINN)*

Abciximabum; Absiksimab; Absiksimabi; Absiximab; c7E3; c7E3 Fab; 7E3. Immunoglobulin G (human-mouse monoclonal c7E3 clone p7E3V_HhC 4 Fab fragment anti-human platelet glycoprotein IIb/IIIa complex), disulphide with human-mouse monoclonal c7E3 clone p7E3V hC light chain.

Абциксимаб

$C_{2101}H_{3229}N_{551}O_{673}S_{15}$ = 47455.4.

CAS — 143653-53-6.

ATC — B01AC13.

ATC Vet — QB01AC13.

Adverse Effects

Bleeding during the first 36 hours after a dose is the most common adverse effect of abciximab. Other adverse effects include hypotension, nausea and vomiting, back pain, chest pain, headache, haematoma, bradycardia, fever, cardiac tamponade, and thrombocytopenia. Hypersensitivity reactions (see Precautions, below) have occurred on repeated use.

Effects on the blood. In clinical studies increased bleeding has been the most common adverse effect of abciximab, and this has also been reported[1] during clinical use. Thrombocytopenia is also a well documented adverse effect of abciximab therapy. In a review[2] of the major clinical studies of abciximab, mild thrombocytopenia was reported in 4.2% of patients and severe thrombocytopenia in 1.0%; patients also received heparin. There have also been a number of case reports of patients developing severe thrombocytopenia.[3,4] It is recommended that platelet counts should be monitored before and 2 hours after starting abciximab, and that the drug should be withdrawn if thrombocytopenia occurs.[3] However, pseudothrombocytopenia also occurs in some patients and should be excluded before withdrawing therapy.[5,6] Although there have been case reports, the incidence of thrombocytopenia does not appear to be increased with other glycoprotein IIb/IIIa receptor inhibitors,[2] and there have been reports of the successful use of eptifibatide[7] and tirofiban[8] in patients who developed thrombocytopenia with abciximab.

1. Cote AV, *et al.* Hemorrhagic and vascular complications after percutaneous coronary intervention with adjunctive abciximab. *Mayo Clin Proc* 2001; **76:** 890–6.
2. Dasgupta H, *et al.* Thrombocytopenia complicating treatment with intravenous glycoprotein IIb/IIIa receptor inhibitors: a pooled analysis. *Am Heart J* 2000; **140:** 206–11.
3. Bishara AI, Hagmeyer KO. Acute profound thrombocytopenia following abciximab therapy. *Ann Pharmacother* 2000; **34:** 924–30.
4. Lown JAG, *et al.* Prolonged profound abciximab associated immune thrombocytopenia complicated by transient multispecific platelet antibodies. Abstract: *Heart* 2004; **90:** e55. Full text: http://heart.bmj.com/cgi/reprint/90/9/e55 (accessed 19/03/08)
5. Sane DC, *et al.* Occurrence and clinical significance of pseudothrombocytopenia during abciximab therapy. *J Am Coll Cardiol* 2000; **36:** 75–83.
6. Wool RL, *et al.* Abciximab-associated pseudothrombocytopenia. *Am J Med* 2002; **113:** 697–8.
7. Rao J, Mascarenhas DAN. Successful use of eptifibatide as an adjunct to coronary stenting in a patient with abciximab-associated acute profound thrombocytopenia. *J Invasive Cardiol* 2001; **13:** 471–3.
8. Desai M, Lucore CL. Uneventful use of tirofiban as an adjunct to coronary stenting in a patient with a history of abciximab-associated thrombocytopenia 10 months earlier. *J Invasive Cardiol* 2000; **12:** 109–12.

Precautions

Abciximab should not be given to patients who are actively bleeding or to patients at increased risk of haemorrhage. Such patients include: those with haemorrhagic disorders, including thrombocytopenia; those with cerebrovascular disorders, including intracerebral neoplasms, aneurysms, or arteriovenous malformation, and those with a history of stroke; those with uncontrolled hypertension; or those who have recently undergone major surgery or severe trauma. Other patients in whom caution is required include those with severe renal impairment, vasculitis, haemorrhagic retinopathy, acute pericarditis, or aortic dissection. Abciximab should be stopped if serious uncontrolled bleeding occurs or emergency surgery is required. Abciximab should not be given to patients with severe renal impairment requiring haemodialysis, or to those with severe hepatic impairment, in whom coagulation may be affected. Platelet counts should be monitored before and after giving abciximab.

Antibodies may develop 2 to 4 weeks after a dose of abciximab and hypersensitivity reactions could occur when other monoclonal antibodies are used or after re-administration of abciximab (see below). Hypersensitivity reactions have not been noted after a single dose but the possibility should be considered.

Readministration. Antibodies to abciximab develop in about 5.8% of patients after use and could lead to hypersensitivity reactions or to reduced efficacy if use of abciximab is repeated. In a retrospective study[1] in 164 patients given a second course of therapy with abciximab, efficacy was not affected and no allergic or anaphylactic reactions occurred. However, severe thrombocytopenia was noted in 4% of patients, and the incidence was highest in those receiving abciximab within 2 weeks of the first course. Similar results were reported from a larger registry study;[2] the patients included had received abciximab at least 7 days previously without developing thrombocytopenia, suggesting that platelet counts need to be monitored in patients receiving a first or repeated course of abciximab.

1. Madan M, *et al.* Efficacy of abciximab readministration in coronary intervention. *Am J Cardiol* 2000; **85:** 435–40.
2. Tcheng JE, *et al.* Abciximab readministration: results of the ReoPro Readministration Registry. *Circulation* 2001; **104:** 870–5.

Interactions

There may be an increased risk of bleeding if abciximab is given with other drugs that affect bleeding, including anticoagulants, other antiplatelet drugs, or thrombolytics.

Pharmacokinetics

After intravenous doses of abciximab free plasma concentrations fall rapidly due to binding to platelet receptors. Platelet function recovers over about 48 hours although abciximab may remain in the circulation for 15 days or more in a platelet-bound state.

Uses and Administration

Abciximab is the Fab fragment of the chimeric monoclonal antibody 7E3. It binds to the glycoprotein IIb/IIIa receptor on the surface of platelets. This prevents binding of fibrinogen, von Willebrand factor, and other adhesive molecules to the receptor sites and inhibits platelet aggregation. It is used as an adjunct to heparin and aspirin therapy for the prevention of acute ischaemic complications in patients undergoing percutaneous transluminal coronary procedures including angioplasty, atherectomy, and stenting. It is also used in patients with unstable angina who are candidates for such procedures. It has been investigated in acute ischaemic stroke.

Abciximab is given intravenously as a bolus injection over 1 minute in a dose of 250 micrograms/kg followed immediately by an infusion of 0.125 micrograms/kg per minute (to a maximum dose of 10 micrograms/minute). For stabilisation in patients with unstable angina the bolus dose followed by the infusion should be started up to 24 hours before the possible intervention and continued for 12 hours after; for other patients the bolus should be given 10 to 60 minutes before the intervention followed by the infusion for 12 hours.

◊ General references.

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2. Kleiman NS. A risk-benefit assessment of abciximab in angioplasty. *Drug Safety* 1999; **20:** 43–57.
3. Ibbotson T, *et al.* Abciximab: an updated review of its therapeutic use in patients with ischaemic heart disease undergoing percutaneous coronary revascularisation. *Drugs* 2003; **63:** 1121–63.
4. Kandzari DE, *et al.* Improved clinical outcomes with abciximab therapy in acute myocardial infarction: a systematic overview of randomized clinical trials. *Am Heart J* 2004; **147:** 457–62.
5. Gabriel HM, Oliveira EI. Role of abciximab in the treatment of coronary artery disease. *Expert Opin Biol Ther* 2006; **6:** 935–42.
6. Romagnoli E, *et al.* Rationale for intracoronary administration of abciximab. *J Thromb Thrombolysis* 2007; **23:** 57–63.

Ischaemic heart disease. Antiplatelet drugs have an established role as adjuncts to medical or interventional treatment in patients with ischaemic heart disease (stable angina, unstable angina, or myocardial infarction) and abciximab has been used to provide additional antiplatelet effects during interventional procedures and in patients with acute myocardial infarction.

In patients undergoing acute or elective *percutaneous coronary intervention* (PCI; see Reperfusion and Revascularisation Proce-