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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that platelet counts should be monitored before and 2 hours after starting abciximab, and that the drug should be withdrawn if thrombocytopenia occurs.[3] However, pseudothrombocytopenia also occurs in some patients and should be excluded before withdrawing therapy.[5,6] Although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.

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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.

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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.

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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-

dures, p.1181), use of abciximab as an adjunct to heparin and aspirin improves short-term[1-3] and long-term[4,5] outcomes in various groups of patients, including those receiving coronary stents.[6-8] Most benefit has been seen in patients given abciximab as a bolus injection immediately before intervention followed by intravenous infusion for 12 hours,[1,2] and in a study[9] in which abciximab was given for 18 to 24 hours before angioplasty and for 1 hour after, the initial benefit was not maintained at 6 months.

For patients undergoing PCI who are pretreated with both aspirin and clopidogrel, the role of abciximab is less clear. In stable patients undergoing elective PCI, no benefit was found at 30 days,[10] or at 1 year.[11] A study[12] in diabetic patients also found no effect on mortality or risk of myocardial infarction at 1 year, despite their higher risk, although restenosis was reduced. However, in patients undergoing PCI for non-ST elevation acute coronary syndromes, use of abciximab in addition to aspirin and clopidogrel pretreatment improved clinical outcomes at 30 days, although this effect was restricted to patients with raised troponins.[13] Positive results have also been reported[14,15] with abciximab given as a single bolus injection without subsequent infusion in patients undergoing coronary stenting.

In *acute ST-elevation myocardial infarction* (p.1175), abciximab has been used as an adjunct to primary PCI, including coronary stenting, and has been shown to reduce reinfarction rates and mortality,[16] with benefit persisting long-term.[17] There is some evidence that starting treatment as soon as possible rather than immediately before the procedure may provide additional benefit.[18,19] Abciximab has also been used as an adjunct to thrombolysis and some benefit has been shown,[20] but this appears to be offset by an increased bleeding rate, even when reduced doses of thrombolytics are used.[21,22] In patients with *unstable angina* (p.1157) receiving noninterventional treatment, a large study[23] with abciximab failed to show any benefit over placebo, although other glycoprotein IIb/IIIa inhibitors have a role in such patients.

Some promising results have been reported with intracoronary abciximab in patients with acute coronary syndromes,[24] and with abciximab-coated stents in patients with acute myocardial infarction.[25]

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Preparations

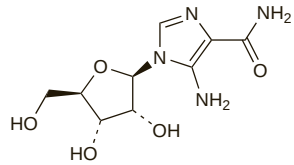
Proprietary Preparations (details are given in Part 3)
Arg.: ReoPro†; ***Austral.:*** ReoPro; ***Austria:*** ReoPro; ***Belg.:*** ReoPro; ***Braz.:*** ReoPro; ***Canad.:*** ReoPro; ***Chile:*** ReoPro; ***Cz.:*** ReoPro; ***Denm.:*** ReoPro; ***Fin.:*** ReoPro; ***Fr.:*** ReoPro; ***Ger.:*** ReoPro; ***Gr.:*** ReoPro; ***Hong Kong:*** ReoPro; ***India:*** ReoPro; ***Irl.:*** ReoPro; ***Israel:*** ReoPro; ***Ital.:*** ReoPro; ***Malaysia:*** ReoPro; ***Mex.:*** ReoPro; ***Neth.:*** ReoPro; ***Norw.:*** ReoPro; ***NZ:*** ReoPro; ***Pol.:*** ReoPro; ***Port.:*** ReoPro; ***Rus.:*** ReoPro (Реопро); ***S.Afr.:*** ReoPro; ***Singapore:*** ReoPro; ***Spain:*** ReoPro; ***Swed.:*** ReoPro; ***Switz.:*** ReoPro; ***Thai.:*** ReoPro; ***UK:*** ReoPro; ***USA:*** ReoPro.

Acadesine *(BAN, USAN, rINN)*

Acadesina; Acadésine; Acadesinum; AICA Riboside; GP-1-110; GP-1-110-0. 5-Amino-1-(β-D-ribofuranosyl)imidazole-4-carboxamide.

Акадезин

$C_9H_{14}N_4O_5$ = 258.2.
CAS — 2627-69-2.
ATC — C01EB13.
ATC Vet — QC01EB13.



Profile

Acadesine is a purine nucleoside analogue reported to have cardioprotective effects. It is being investigated in the management of myocardial ischaemia, particularly in patients undergoing coronary artery bypass graft surgery. Acadesine may protect against further ischaemia by influencing metabolism in ischaemic cells, enhancing the release of adenosine in preference to inosine after the breakdown of adenosine monophosphate.

Acadesine is also under investigation for chronic lymphocytic leukaemia.

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3. Mangano DT. Effects of acadesine on myocardial infarction, stroke, and death following surgery: a meta-analysis of the 5 international randomized trials. *JAMA* 1997; **277:** 325–32.
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ACE Inhibitors

Angiotensin-converting Enzyme Inhibitors; Inhibidores de la ECA.

There appear to be few significant differences between ACE inhibitors. They may be distinguished from each other by the presence or absence of a sulfhydryl group, whether they are prodrugs or not, their route of elimination, and their affinity for angiotensin-converting enzyme in vascular and other tissue, although whether these characteristics modify pharmacodynamics and therefore clinical efficacy is uncertain. Differences in these characteristics do however influence onset and duration of action of ACE inhibitors.

Adverse Effects and Treatment

Many of the adverse effects of ACE inhibitors relate to their pharmacological action and all therefore have a similar spectrum of adverse effects. Some effects, such as taste disturbances and skin reactions, were at one time attributed to the presence of a sulfhydryl group (as in captopril) but have now also been reported with other ACE inhibitors; however, they may be more common with captopril.

The most common adverse effects are due to the vascular effects of ACE inhibitors and include hypotension, dizziness, fatigue, headache, and nausea and other gastrointestinal disturbances.

Pronounced hypotension may occur at the start of therapy with ACE inhibitors, particularly in patients with heart failure and in sodium- or volume-depleted patients (for example, those given previous diuretic therapy). Myocardial infarction and stroke have been reported and may relate to severe falls in blood pressure in patients with ischaemic heart disease or cerebrovascular disease. Other cardiovascular effects that have occurred include tachycardia, palpitations, and chest pain.

Deterioration in renal function, including increasing blood concentrations of urea and creatinine, may occur, and reversible acute renal failure has been reported. Renal effects are most common in patients with existing renal or renovascular dysfunction or heart failure, in whom vasodilatation reduces renal perfusion pressure; it may be aggravated by hypovolaemia. Proteinuria has also occurred and in some patients has progressed to nephrotic syndrome. Hyperkalaemia and hyponatraemia may develop due to decreased aldosterone secretion.

Other adverse effects include persistent dry cough and other upper respiratory tract symptoms, and angioedema; these may be related to effects on bradykinin or prostaglandin metabolism. Skin rashes (including erythema multiforme and toxic epidermal necrolysis) may occur; photosensitivity, alopecia, and other hypersensitivity reactions have also been reported.

Blood disorders have been reported with ACE inhibitors and include neutropenia and agranulocytosis (especially in patients with renal failure and in those with collagen vascular disorders such as systemic lupus erythematosus and scleroderma), thrombocytopenia, and anaemias.

Other less common adverse effects reported with ACE inhibitors include stomatitis, abdominal pain, pancreatitis, hepatocellular injury or cholestatic jaundice, muscle cramps, paraesthesias, mood and sleep disturbances, and impotence.

ACE inhibitors have been associated with fetal toxicity (see Pregnancy under Precautions, below).

Most of the adverse effects of ACE inhibitors are reversible on withdrawing therapy. Symptomatic hypotension, including that after overdosage, generally responds to volume expansion with an intravenous infusion of sodium chloride 0.9%.

◊ General reviews.

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