For the rapid temporary control of ventricular rate in patients with **supraventricular arrhythmias**, a loading dose of 500 micrograms/kg given over 1 minute is followed by an initial maintenance infusion of 50 micrograms/kg per minute for 4 minutes. If the response is satisfactory this maintenance infusion should be continued at 50 micrograms/kg per minute. If a suitable response is not obtained within the first 5 minutes a further loading dose of 500 micrograms/kg over 1 minute may be given and the maintenance infusion may be increased to 100 micrograms/kg per minute for 4 minutes. If necessary, this procedure may be repeated once or twice more, until a satisfactory response is obtained, increasing the maintenance infusion each time by 50 micrograms/kg per minute to a maximum of 200 micrograms/kg per minute. Little additional benefit is obtained from further increases in maintenance dosage. Once a satisfactory response is obtained infusion may be continued, if necessary, for up to 48 hours.

When transferring a patient to another antiarrhythmic drug, the infusion rate of esmolol hydrochloride is reduced by 50% thirty minutes after starting the alternative drug, and may be stopped one hour after the second dose of that drug.

In the control of perioperative **hypertension** and/or **tachycardia**, esmolol hydrochloride may be given intravenously as follows:

- *during* anaesthesia, a loading dose of 80 mg over 15 to 30 seconds followed by an infusion of 150 micrograms/kg per minute, increased as necessary up to 300 micrograms/kg per minute
- on *waking* from anaesthesia, an infusion of 500 micrograms/kg per minute for 4 minutes, followed by an infusion of 300 micrograms/kg per minute as required
- *postoperatively*, a stepped dosage schedule, as described under control of supraventricular arrhythmias above, although maintenance infusions may be increased up to 300 micrograms/kg per minute as necessary.

◊ References.

1. Wiest D. Esmolol: a review of its therapeutic efficacy and pharmacokinetic characteristics. *Clin Pharmacokinet* 1995; **28:** 190–202.

Tetralogy of Fallot. Beta blockers have been used in the management of tetralogy of Fallot (see under Uses of Propranolol, p.1381). The *BNFC* recommends that neonates may be given esmolol hydrochloride in an initial dose of 600 micrograms/kg by intravenous injection over 1 to 2 minutes; if necessary, this may be followed by an intravenous infusion at a dose of 300 to 900 micrograms/kg per minute.

Preparations

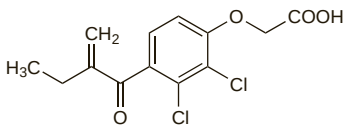
Proprietary Preparations (details are given in Part 3)
Arg.: Brevibloc†; Dublon; ***Austral.:*** Brevibloc; ***Austria:*** Brevibloc; ***Belg.:*** Brevibloc; ***Braz.:*** Brevibloc; ***Canad.:*** Brevibloc; ***Cz.:*** Brevibloc; ***Denm.:*** Brevibloc; ***Fin.:*** Brevibloc; ***Fr.:*** Brevibloc†; ***Ger.:*** Brevibloc; ***Gr.:*** Brevibloc; ***Hong Kong:*** Brevibloc†; ***Hung.:*** Brevibloc; ***India:*** Miniblock; ***Irl.:*** Brevibloc; ***Israel:*** Brevibloc†; ***Ital.:*** Brevibloc; ***Malaysia:*** Brevibloc†; ***Mex.:*** Brevibloc†; ***Neth.:*** Brevibloc; ***NZ:*** Brevibloc; ***Port.:*** Brevibloc; ***S.Afr.:*** Brevibloc; ***Singapore:*** Brevibloc†; ***Spain:*** Brevibloc; ***Swed.:*** Brevibloc; ***Switz.:*** Brevibloc; ***Turk.:*** Brevibloc; ***UK:*** Brevibloc; ***USA:*** Brevibloc.

Etacrynic Acid *(BAN, rINN)* ⊗

Acide étacrynique; Ácido etacrínico; Acidum etacrynicum; Etacrynsäure; Etakrino rūgštis; Etakrinsav; Etakrynsyra; Etakryynihappo; Ethacrynic Acid *(USAN)*; Kwas etakrynowy; Kyselina etakrynová; MK-595; NSC-85791. [2,3-Dichloro-4-(2-ethylacryloyl)phenoxy]acetic acid; [2,3-Dichloro-4-(2-methylene-1-oxobutyl)phenoxy]acetic acid.

Этакриновая Кислота

$C_{13}H_{12}Cl_2O_4$ = 303.1.
CAS — 58-54-8.
ATC — C03CC01.
ATC Vet — QC03CC01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Etacrynic Acid). A white or almost white, crystalline powder. Very slightly soluble in water; freely soluble in alcohol. It dissolves in ammonia and in dilute solutions of alkali hydroxides and carbonates.
USP 31 (Ethacrynic Acid). A white or practically white, odourless or practically odourless, crystalline powder. Very slightly soluble in water; soluble 1 in 1.6 of alcohol, 1 in 6 of chloroform, and 1 in 3.5 of ether. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Sodium Etacrynate *(BANM, rINNM)* ⊗

Etacrinato sódico; Étacrynate de Sodium; Etacrynate Sodium; Ethacrynate Sodium *(USAN)*; Natrii Etacrynas; Sodium Ethacrynate.

Натрий Этакринат

$C_{13}H_{11}Cl_2NaO_4$ = 325.1.
CAS — 6500-81-8.
ATC — C03CC01.
ATC Vet — QC03CC01.

Pharmacopoeias. In *Chin.*
Pol. and *US* include sodium etacrynate for injection.

Stability. Solutions in water of sodium etacrynate containing the equivalent of etacrynic acid 0.1% have a pH of 6.3 to 7.7. Solutions are relatively stable at about pH 7 at room temperatures for short periods and less stable at higher pH values and temperatures. They are incompatible with solutions with a pH below 5. The injection should be protected from light.

Adverse Effects

As for Furosemide, p.1292. Gastrointestinal disturbances may be more common and severe with etacrynic acid; profuse watery diarrhoea is an indication for stopping therapy. Gastrointestinal bleeding has been associated with etacrynic acid. Tinnitus and deafness, particularly after high parenteral doses, may also be more common. Other adverse effects include confusion, fatigue, nervousness, and apprehension. Haematuria has been reported rarely.

Local irritation and pain may follow intravenous injection.

Effects on carbohydrate metabolism. Although etacrynic acid is generally considered to have less pronounced effects on carbohydrate metabolism than furosemide or the thiazide diuretics, adverse effects have been reported. Reductions in glucose tolerance[1] after etacrynic acid 200 mg daily for 6 weeks were similar to those produced by hydrochlorothiazide 200 mg daily. The effect was most pronounced in diabetic patients. Hyperosmolar hyperglycaemic coma[2] and symptomatic hypoglycaemia with convulsions[3] have been reported in patients receiving high doses of etacrynic acid.

1. Russell RP, *et al.* Metabolic and hypotensive effects of ethacrynic acid: comparative study with hydrochlorothiazide. *JAMA* 1968; **205:** 11–16.
2. Cowley AJ, Elkeles RS. Diabetes and therapy with potent diuretics. *Lancet* 1978; **i:** 154.
3. Maher JF, Schreiner GE. Studies on ethacrynic acid in patients with refractory edema. *Ann Intern Med* 1965; **62:** 15–29.

Effects on the ears. Drug-induced deafness occurred in 2 of 184 patients given etacrynic acid intravenously.[1,2] Deafness accompanied by nystagmus was reported in a patient[3] after an intravenous infusion of etacrynic acid. Symptoms resolved within 1 hour. He had previously been taking furosemide and etacrynic acid orally.

1. Boston Collaborative Drug Surveillance Program. Drug-induced deafness: a cooperative study. *JAMA* 1973; **224:** 515–16.
2. Porter J, Jick H. Drug-induced anaphylaxis, convulsions, deafness, and extrapyramidal symptoms. *Lancet* 1977; **i:** 587–8.
3. Gomolin IH, Garshick E. Ethacrynic acid-induced deafness accompanied by nystagmus. *N Engl J Med* 1980; **303:** 702.

Precautions

Etacrynic acid's precautions and contra-indications are generally dependent on its effects on fluid and electrolyte balance and are similar to those of the thiazide diuretics (see Hydrochlorothiazide, p.1309). Etacrynic acid, especially in the form of dust, is irritating to the skin, eyes, and mucous membranes.

Interactions

As for Furosemide, p.1293. The risks of gastrointestinal bleeding may be enhanced by use of etacrynic acid with other gastric irritants or with anticoagulants.

Anticoagulants. For reference to the interaction between *warfarin* and etacrynic acid, see p.1430.

Pharmacokinetics

Etacrynic acid is fairly rapidly absorbed from the gastrointestinal tract. The plasma half-life is 30 to 60 minutes. It is excreted both in the bile and the urine, partly unchanged and partly in the form of metabolites. It is extensively bound to plasma proteins.

Uses and Administration

Although chemically unrelated, etacrynic acid is a loop diuretic with actions and uses similar to those of furosemide (p.1294). Etacrynic acid is used in the treatment of oedema associated with heart failure (p.1165) and with renal and hepatic disorders.

Diuresis begins within about 30 minutes after an oral dose, and lasts for about 6 to 8 hours; after intravenous injection of its sodium salt, the effects are evident within a few minutes and last for about 2 hours.

In the treatment of **oedema**, the usual initial oral dose is 50 mg in the morning. The dose may be increased, if necessary, by 25- to 50-mg increments daily to the minimum effective dose. Severe cases have required gradual titration of the dose up to a maximum of 400 mg daily, but the effective range is usually between 50 and 150 mg daily. Dosage of more than 50 mg daily should be given in divided doses. All doses should be taken with food. Maintenance doses may be taken daily or intermittently.

In emergencies, such as acute pulmonary oedema, or when oral therapy cannot be given, etacrynic acid may be given intravenously. It is given as its salt, sodium etacrynate, but doses are expressed in terms of the acid. 10.7 mg of sodium etacrynate is equivalent to about 10 mg of etacrynic acid. The usual dose is 50 mg, or 0.5 to 1 mg/kg, as a 1 mg/mL solution in glucose 5% (provided the pH is above 5) or sodium chloride 0.9%, given by slow intravenous injection either directly or into the tubing of a running infusion. Should a subsequent injection be required the site should be changed to avoid thrombophlebitis. Single doses of 100 mg have been given intravenously in critical situations. It is not suitable for subcutaneous or intramuscular injection.

For children over 2 years of age an initial dose of etacrynic acid is 25 mg daily by mouth, cautiously increased as necessary by 25 mg daily.

If very high doses of etacrynic acid are used careful laboratory control is essential as described for furosemide (p.1294; high-dose therapy).

Preparations

BP 2008: Sodium Etacrynate Injection;
USP 31: Ethacrynate Sodium for Injection; Ethacrynic Acid Tablets.

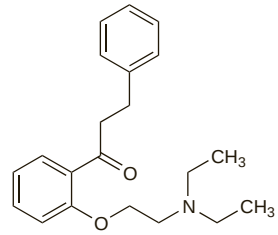
Proprietary Preparations (details are given in Part 3)
Austral.: Edecrin; ***Austria:*** Edecrin; ***Canad.:*** Edecrin; ***Cz.:*** Uregyt†; ***Ger.:*** Hydromedin†; ***Hung.:*** Uregyt; ***Ital.:*** Reomax; ***Rus.:*** Uregyt (Урегит); ***Swed.:*** Edecrina†; ***USA:*** Edecrin.

Etafenone Hydrochloride *(rINNM)*

Étafénone, Chlorhydrate d'; Etafenoni Hydrochloridum; Hidrocloruro de etafenona; LG-11457. 2′-(2-Diethylaminoethoxy)-3-phenylpropiophenone hydrochloride.

Этафенона Гидрохлорид

$C_{21}H_{27}NO_2$,HCl = 361.9.
CAS — 90-54-0 (etafenone); 2192-21-4 (etafenone hydrochloride).
ATC — C01DX07.
ATC Vet — QC01DX07.



(etafenone)

Profile

Etafenone hydrochloride is a vasodilator that has been used in ischaemic heart disease.

Ethacizine

Aethacizin; Etacizin; Ethacizin; Ethacyzin; EZ-55; NIK-244. Ethyl 10-[3-(diethylamino)propionyl]phenothiazine-2-carbamate.

Этацизин

$C_{22}H_{27}N_3O_3S$ = 413.5.
CAS — 33414-33-4 (ethacizine); 57530-40-2 (ethacizine hydrochloride).