# Epirubicin Hydrochloride

*(BANM, USAN, rINNM)*

4′-Epiadriamycin Hydrochloride; 4′-Epidoxorubicin Hydrochloride; Épirubicine, chlorhydrate d'; Epirubicin-hidroklorid; Epirubicin-hydrochlorid; Epirubicinhydroklorid; Epirubicini hydrochloridum; Epirubicino hidrochloridas; Epirubisiinihydrokloridi; Epirubisin Hidroklorür; Hidrocloruro de epirubicina; IMI-28; Pidorubicin Hydrochloride. (8*S*,10*S*)-10-(3-Amino-2,3,6-trideoxy-α-L-*arabino*-hexopyranosyloxy)-8-glycolloyl-7,8,9,10-tetrahydro-6,8,-11-trihydroxy-1-methoxynaphthacene-5,12-dione hydrochloride.

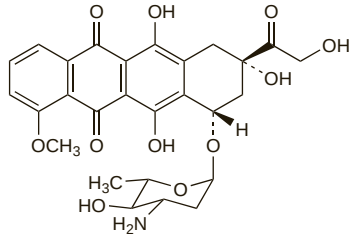
Эпирубицина Гидрохлорид

$C_{27}H_{29}NO_{11}$,HCl = 580.0.

*CAS — 56420-45-2 (epirubicin); 56390-09-1 (epirubicin hydrochloride).*

*ATC — L01DB03.*

*ATC Vet — QL01DB03.*



*(epirubicin)*

**Pharmacopoeias.** In *Eur.* (see p.vii) and *Jpn.*

**Ph. Eur. 6.2** (Epirubicin Hydrochloride). A substance obtained by chemical transformation of a substance produced by certain strains of *Streptomyces peucetius*. An orange-red powder. Soluble in water and in methyl alcohol; slightly soluble in dehydrated alcohol; practically insoluble in acetone. A 0.5% solution in water has a pH of 4.0 to 5.5. Store at 2° to 8° in airtight containers. Protect from light.

**Incompatibility.** Licensed product information states that epirubicin hydrochloride is incompatible with heparin or fluorouracil, resulting in precipitation, and that it is hydrolysed in alkaline solutions.

**Stability.** Epirubicin was not subject to significant photodegradation at clinical concentrations,[1,2] and special precautions to protect solutions from light during use do not appear to be necessary. However, photodegradation may be significant at lower concentrations (below 500 micrograms/mL).[1]

1. Wood MJ, *et al.* Photodegradation of doxorubicin, daunorubicin and epirubicin measured by high-performance liquid chromatography. *J Clin Pharm Ther* 1990; **15:** 291–300.
2. Pujol M, *et al.* Stability study of epirubicin in NaCl 0.9% injection. *Ann Pharmacother* 1997; **31:** 992–5.

## Adverse Effects, Treatment, and Precautions

As for Doxorubicin, p.712. Cardiotoxicity and myelotoxicity may be less than with doxorubicin. Cardiotoxicity is more likely when the cumulative dose exceeds 0.9 to 1 g/m$^2$.

**Effects on the heart.** For further discussion of the cardiotoxicity of anthracyclines, see under Adverse Effects of Doxorubicin, p.713.

## Interactions

As for Doxorubicin, p.713.

**Antineoplastics.** Increased exposure to epirubicin, and a consequent increase in myelotoxicity, has been reported in patients given epirubicin immediately after *paclitaxel*, compared with patients who received epirubicin before paclitaxel.[1] Similar interactions have been seen when paclitaxel was given before other anthracyclines.[2] These and other studies[3,4] have suggested that paclitaxel given in this way is associated with a reduced conversion of epirubicin to the less myelotoxic metabolite, epirubicinol, although the interaction is complex, and may involve both disposition and pharmacodynamics.

1. Venturini M, *et al.* Sequence effect of epirubicin and paclitaxel treatment on pharmacokinetics and toxicity. *J Clin Oncol* 2000; **18:** 2116–25.
2. Danesi R, *et al.* Pharmacokinetic optimisation of treatment schedules for anthracyclines and paclitaxel in patients with cancer. *Clin Pharmacokinet* 1999; **37:** 195–211.
3. Grasselli G, *et al.* Clinical and pharmacologic study of the epirubicin and paclitaxel combination in women with metastatic breast cancer. *J Clin Oncol* 2001; **19:** 2222–31.
4. Danesi R, *et al.* Pharmacokinetics and pharmacodynamics of combination chemotherapy with paclitaxel and epirubicin in breast cancer patients. *Br J Clin Pharmacol* 2002; **53:** 508–18.

**Cimetidine.** Cimetidine increased the formation of the active metabolite of epirubicin in a study in 8 patients; there was also a substantial increase in systemic exposure to unchanged epirubicin.[1] The mechanisms and potential clinical significance of the interaction were unclear.

1. Murray LS, *et al.* The effect of cimetidine on the pharmacokinetics of epirubicin in patients with advanced breast cancer: preliminary evidence of a potentially common drug interaction. *Clin Oncol* 1998; **10:** 35–8.

## Pharmacokinetics

After intravenous doses epirubicin is rapidly and extensively distributed into body tissues, and undergoes metabolism in the liver, with the formation of epirubicinol (13-hydroxyepirubicin) and appreciable amounts of glucuronide derivatives. Epirubicin is eliminated mainly in bile, with a terminal plasma elimination half-life of about 30 to 40 hours. About 10% of a dose is recovered in urine within 48 hours. Epirubicin does not cross the blood-brain barrier.

◊ References.

1. Morris RG, *et al.* Disposition of epirubicin and metabolites with repeated courses to cancer patients. *Eur J Clin Pharmacol* 1991; **40:** 481–7.
2. Robert J. Clinical pharmacokinetics of epirubicin. *Clin Pharmacokinet* 1994; **26:** 428–38.

## Uses and Administration

Epirubicin is an anthracycline antibiotic with antineoplastic actions similar to those of doxorubicin (p.714). It is used, alone or with other antineoplastics, in acute leukaemias, lymphomas, multiple myeloma, and in solid tumours including Wilms' tumour (p.667), cancer of the bladder (p.659), breast (p.661), and stomach (p.664).

Epirubicin hydrochloride is given by intravenous injection of a solution in sodium chloride 0.9% or Water for Injections into a fast-running infusion of sodium chloride 0.9% or glucose 5% over 3 to 5 minutes, or by infusion over up to 30 minutes. It is given as a single agent in usual doses of 60 to 90 mg/m$^2$ as a single dose every 3 weeks; this dose may be divided over 2 or 3 days if desired. A regimen of 12.5 to 25 mg/m$^2$ once a week has also been tried in palliative care. High-dose regimens, of 120 mg/m$^2$ or more every 3 weeks, or 45 mg/m$^2$ for 3 consecutive days every 3 weeks have been used.

Doses may need to be reduced if epirubicin is given with other antineoplastics. Doses should also be reduced in patients with liver impairment (see below) and in those whose bone-marrow function is impaired by age or previous chemotherapy or radiotherapy.

A total cumulative dose of 0.9 to 1 g/m$^2$ should not generally be exceeded, because of the risk of cardiotoxicity.

Epirubicin has also been given by intravesical instillation in the local treatment of bladder cancer. Instillation of 50 mg weekly as a 0.1% solution (in sodium chloride 0.9% or sterile water) for 8 weeks has been suggested, reduced to 30 mg in 50 mL weekly if chemical cystitis develops; for carcinoma *in-situ*, the dose may be increased, if tolerated, to 80 mg in 50 mL weekly. For the prophylaxis of recurrence in patients who have undergone transurethral resection, 50 mg weekly for 4 weeks, followed by 50 mg instilled once a month for 11 months is the suggested regimen. The solution should be retained in the bladder for 1 hour.

Blood counts should be made routinely during treatment with epirubicin (see also Bone-marrow Depression, p.639) and cardiac function should be carefully monitored. Liver function should be assessed before and if possible during therapy.

◊ References.

1. Plosker GL, Faulds D. Epirubicin: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in cancer chemotherapy. *Drugs* 1993; **45:** 788–856.
2. Coukell AJ, Faulds D. Epirubicin: an updated review of its pharmacodynamic and pharmacokinetic properties and therapeutic efficacy in the management of breast cancer. *Drugs* 1997; **53:** 453–82.
3. Onrust SV, *et al.* Epirubicin: a review of its intravesical use in superficial bladder cancer. *Drugs Aging* 1999; **15:** 307–33.
4. Ormrod D, *et al.* Epirubicin: a review of its efficacy as adjuvant therapy and in the treatment of metastatic disease in breast cancer. *Drugs Aging* 1999; **15:** 389–416.
5. Earl H, Iddawela M. Epirubicin as adjuvant therapy in breast cancer. *Expert Rev Anticancer Ther* 2004; **4:** 189–95.

**Administration in hepatic impairment.** Doses of epirubicin should be halved in patients with moderate liver dysfunction (serum bilirubin concentrations of 12 to 30 micrograms/mL), while those with severe liver impairment (serum bilirubin greater than 30 micrograms/mL) should be given a quarter of the usual dose.

**Amyloidosis.** For reference to a regimen including epirubicin used to control disease in a patient with amyloidosis, see p.743.

## Preparations

**Proprietary Preparations** (details are given in Part 3)
***Arg.:*** Crisabon; Cuatroepi; Epidoxo; Epifil; Epikebir; EPR†; Farmorubicin; Robanul; Rubifarm†; ***Austral.:*** Pharmorubicin; ***Austria:*** Epi-Cell; Farmorubicin; ***Belg.:*** Farmorubicine; ***Braz.:*** Farmorubicina; Nuovodox; Rubina; Tecnomax; ***Canad.:*** Pharmorubicin; ***Chile:*** Farmorrubicina; ***Cz.:*** Farmorubicin; ***Denm.:*** Farmorubicin; ***Fin.:*** Farmorubicin; ***Fr.:*** Farmorubicine; ***Ger.:*** Epi-Cell; Epi-NC; Farmorubicin; Riboepi; ***Gr.:*** Ciazil; Epirub; Farmorubicin; Megarubicin; ***Hong Kong:*** Pharmorubicin; ***Hung.:*** Farmorubicin; ***Irl.:*** Pharmorubicin; ***Israel:*** Farmorubicin; ***Ital.:*** Farmorubicina; ***Jpn:*** Farmorubicin; ***Malaysia:*** Pharmorubicin; ***Mex.:*** Binarin; Epilem; Farmorubicin; ***Neth.:*** Farmorubicine; ***Norw.:*** Farmorubicin; ***NZ:*** Pharmorubicin; ***Philipp.:*** Pharmorubicin; ***Pol.:*** Bioepicyna; Farmorubicin; ***Port.:*** Epi-cell; Farmorubicina; ***Rus.:*** Epilem (Эпилем)†; Farmorubicin (Фарморубицин); ***S.Afr.:*** Farmorubicin; ***Singapore:*** Pharmorubicin; ***Spain:*** Farmorubicina; ***Swed.:*** Farmorubicin; ***Switz.:*** Farmorubicin; ***Thai.:*** Anthracin; E.P.Mycin; Epilem; Pharmorubicin; ***Turk.:*** Farmorubicin; ***UK:*** Pharmorubicin; ***USA:*** Ellence; ***Venez.:*** Farmorubicin.

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# Epratuzumab *(rINN)*

Épratuzumab; Epratuzumabum. Immunoglobulin G (human-mouse monoclonal IMMU-hLL2 γ-chain anti-human antigen CD22), disulfide with human-mouse monoclonal IMMU-hLL2 κ-chain, dimer.

Эпратузумаб

*CAS — 205923-57-5.*

## Profile

Epratuzumab is a humanised anti-CD22 monoclonal antibody under investigation, alone or conjugated with yttrium-90, for the treatment of non-Hodgkin's lymphoma. It is also under investigation for the treatment of moderate to severe SLE.

◊ References.

1. Davies SL, Martin L. Epratuzumab. *Drugs Of The Future* 2005; **30:** 683–7.
2. Leonard JP, *et al.* Combination antibody therapy with epratuzumab and rituximab in relapsed or refractory non-Hodgkin's lymphoma. *J Clin Oncol* 2005; **23:** 5044–51.
3. Lindén O, *et al.* Dose-fractionated radioimmunotherapy in non-Hodgkin's lymphoma using DOTA-conjugated, Y-radiolabeled, humanized anti-CD22 monoclonal antibody, epratuzumab. *Clin Cancer Res* 2005; **11:** 5215–22.
4. Goldenberg DM. Epratuzumab in the therapy of oncological and immunological diseases. *Expert Rev Anticancer Ther* 2006; **6:** 1341–53.
5. Leonard JP, Goldenberg DM. Preclinical and clinical evaluation of epratuzumab (anti-CD22 IgG) in B-cell malignancies. *Oncogene* 2007; **26:** 3704–13.

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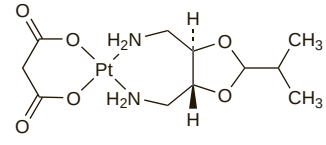
# Eptaplatin *(rINN)*

Eptaplatine; Eptaplatino; Eptaplatinum; Heptaplatin; SKI-2053R. *cis*-[(4*R*,5*R*)-2-Isopropyl-1,3-dioxolane-4,5-bis(methylamine)-*N*,*N*′][malonato(2–)-*O*,*O*′]platinum.

Эптаплатин

$C_{11}H_{20}N_2O_6Pt$ = 471.4.

*CAS — 146665-77-2.*



## Profile

Eptaplatin is a platinum derivative that is used as an antineoplastic in the treatment of gastric cancer. Nephrotoxicity is the main adverse effect.

◊ References.

1. Ahn JH, *et al.* Nephrotoxicity of heptaplatin: a randomized comparison with cisplatin in advanced gastric cancer. *Cancer Chemother Pharmacol* 2002; **50:** 104–10.
2. Min YJ, *et al.* Combination chemotherapy with 5-fluorouracil and heptaplatin as first-line treatment in patients with advanced gastric cancer. *J Korean Med Sci* 2004; **19:** 369–73.

## Preparations

**Proprietary Preparations** (details are given in Part 3)
***Kor.:*** Sunpla.