

# Gabapentin

## Clinical use

Anti-epileptic – adjunctive treatment of partial seizures with or without secondary generalisation  
Neuropathic pain

## Dose in normal renal function

300 mg on day 1, 300 mg twice daily on day 2, 300 mg three times daily on day 3, then increased according to response to 1.2 g daily (in three divided doses). If necessary may be further increased in steps of 300 mg daily to a maximum 2.4 g daily. Usual range 0.9–1.2 g daily; maximum period between doses should not exceed 12 hours

Neuropathic pain: loaded as above but maximum 1.8 g daily

## Pharmacokinetics

Molecular weight (daltons)	171.2
% Protein binding	<3
% Excreted unchanged in urine	≈100
Volume of distribution (L/kg)	1.0
Half-life – normal/ESRF (hrs)	5–7/prolonged

## Dose in renal impairment GFR (mL/min)

60–90	400 mg three times daily
30–60	300 mg twice daily
15–30	300 mg once daily
<15	300 mg on alternate days

## Dose in patients undergoing renal replacement therapies

CAPD	Probably dialysed. Dose as in GFR < 15 mL/min
HD	Dialysed. Loading dose of 300–400 mg in patients who have never received gabapentin. Maintenance dose of 200–300 mg after each HD session
CAV/VVHD	Dialysed. Dose as in GFR = 15–30 mL/min

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- Antacids reduce absorption
- Antidepressants: antagonism of anticonvulsive effect (convulsive threshold lowered)

## Administration

RECONSTITUTION

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ROUTE

- Oral

RATE OF ADMINISTRATION

–

COMMENTS

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## Other information

- Can cause false positive readings with some urinary protein tests
- In patients with moderate to severe renal impairment, start with the lowest possible dose and titrate upwards according to response

# Ganciclovir

## Clinical use

Antiviral agent

- IV: treatment of life- or sight-threatening cytomegalovirus (CMV) in immunocompromised people and for CMV prophylaxis in immunosuppressed patients secondary to organ transplantation
- Oral: maintenance treatment of CMV retinitis in AIDS patients (licensed), prophylaxis and maintenance against CMV infection in immunosuppressed patients (unlicensed use)

## Dose in normal renal function

IV treatment:

Induction/Treatment of active CMV disease:

5 mg/kg 12-hourly for 14–21 days

Maintenance for CMV retinitis: 6 mg/kg per day for 5 days per week or 5 mg/kg per day 7 days per week

Prevention of CMV retinitis: as per treatment except induction length 7–14 days

Oral treatment:

Maintenance for CMV retinitis, or prophylaxis in immunosuppressed patients: 1000 mg three times per day

## Pharmacokinetics

Molecular weight (daltons)	277
% Protein binding	<2
% Excreted unchanged in urine	90–100
Volume of distribution (L/kg)	0.47
Half-life-normal/ESRF (hrs)	2.9/30

## Dose in renal impairment

### GFR (mL/min)

20–50	See 'Other information'
10–20	See 'Other Information'
<10	See 'Other Information'

## Dose in patients undergoing renal replacement therapies

CAPD	Dialysed. Oral and IV: dose as in GFR = <10 mL/min
HD	Dialysed. IV: 1.25 mg/kg every day, given post dialysis on dialysis days. PO: 500 mg three times a week, given post dialysis on dialysis days
CAV/VHHD	Dialysed. IV: 2.5 mg/kg per day. PO: 500 mg once daily

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- Increased risk of myelosuppression with other myelosuppressive drugs
- Profound myelosuppression with zidovudine
- Generalised seizures reported with imipenem-cilastatin

## Administration

RECONSTITUTION

- Reconstitute 1 vial (500 mg) with 10 mL water for injection (50 mg/mL)
- Then transfer dose to 100 mL sodium chloride 0.9%

ROUTE

- IV peripherally in fast-flowing vein or centrally – see below

RATE OF ADMINISTRATION

- Over 1 hour

COMMENTS

- May give 50% dose over 15 minutes after HD in washback (unlicensed)

## Other information

IV dosage:

**Creatinine clearance Dose**

(mL/min)	
>70	5 mg/kg 12-hourly
50–69	2.5 mg/kg 12-hourly
25–49	2.5 mg/kg 24-hourly
10–24	1.25 mg/kg 24-hourly
<10	1.25 mg/kg 24-hourly, given after haemodialysis on dialysis days

Oral dose:

**Creatinine clearance Dose**

(mL/min)	
>70	1000 mg three times a day
50–69	1500 mg daily
25–49	1000 mg daily
10–24	500 mg daily
<10	500 mg three times a week

- Monitor patient for myelosuppression, particularly in patients receiving prophylactic co-trimoxazole therapy
- Pre-dialysis therapeutic blood levels in range 5–12 mg/L
- Not to be infused in concentrations over 10 mg/mL peripherally
- Bioavailability of oral ganciclovir is 5%, so this should only be used for maintenance/prophylactic therapy

# Gemcitabine hydrochloride

## Clinical use

Palliative treatment, or first-line treatment with cisplatin, of locally advanced or metastatic non-small-cell lung cancer

Treatment of pancreatic cancer

Treatment of bladder cancer in combination with cisplatin

## Dose in normal renal function

NSLC: 1000 mg/m<sup>2</sup> weekly for 3 weeks, 1 week rest then repeat

Pancreatic: 1000 mg/m<sup>2</sup> weekly for 7 weeks, rest for 1 week then weekly for 3 weeks out of 4

Dose is reduced according to toxicity

## Pharmacokinetics

Molecular weight (daltons)	299.7
% Protein binding	negligible
% Excreted unchanged in urine	<10
Volume of distribution (L/kg)	12.4 L/m <sup>2</sup> (women) 17.5 L/m <sup>2</sup> (men)
Half-life – normal/ESRF (hrs)	42–94 minutes

## Dose in renal impairment

### GFR (mL/min)

20–50	Dose as in normal renal function
10–20	Use with caution. Reduce dose
<10	Avoid

## Dose in patients undergoing renal replacement therapies

CAPD	Likely to be dialysed. Dose as in GFR = 10–20 mL/min
HD	Likely to be dialysed. Dose as in GFR = 10–20 mL/min
CAV/VVHD	Likely to be dialysed. Dose as in GFR = 10–20 mL/min

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- None known

## Administration

RECONSTITUTION

- Reconstitute with sodium chloride 0.9%, 5 mL to 200 mg vial and 25 mL to 1 g vial
- Can be further diluted in sodium chloride 0.9% if required

ROUTE

- IV

RATE OF ADMINISTRATION

- 30 minutes

COMMENTS

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## Other information

- Gemcitabine causes reversible haematuria with or without proteinuria in about 50% of patients
- There is no evidence for cumulative renal toxicity with repeated dosing of gemcitabine
- Haemolytic uraemic syndrome (HUS) has been reported with a crude incidence rate of 0.015%
- A study looking at the use of gemcitabine 500–1000 mg/m<sup>2</sup> administered IV on days 1, 8 and 15 every 28 days in patients with renal dysfunction, concluded that this regimen was well tolerated in patients with a GFR as low as 30 mL/min
- Another study in patients with serum creatinines in the range 130–420 micromol/L at doses of 650–800 mg/m<sup>2</sup> weekly for 3 weeks out of a 4-week cycle, found dose-limiting toxicities, including neutropenia, fever, raised transaminases and increased serum creatinine. It was concluded that a reduced dose of gemcitabine may be appropriate in patients with established renal impairment

# Gemfibrozil

## Clinical use

Hyperlipidaemias of types IIa, IIb, III, IV and V

## Dose in normal renal function

1.2 g daily, usually in two divided doses; range 0.9–1.5 g daily

## Pharmacokinetics

Molecular weight (daltons)	250
% Protein binding	95
% Excreted unchanged in urine	<5
Volume of distribution (L/kg)	–
Half-life – normal/ESRF (hrs)	1.5/1.5–2.4

## Dose in renal impairment GFR (mL/min)

20–50	Initially 900 mg daily
10–20	Initially 900 mg daily. Monitor carefully
<10	Initially 900 mg daily. Monitor carefully

## Dose in patients undergoing renal replacement therapies

CAPD	Not dialysed. Dose as in GFR = <10 mL/min
HD	Not dialysed. Dose as in GFR = <10 mL/min
CAV/VVHD	Not dialysed. Dose as in GFR = 10–20 mL/min

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- Enhanced anticoagulant effect seen with acenocoumarol, phenindione and warfarin
- Ciclosporin: Parke-Davis have one report on file of an interaction with ciclosporin where serum ciclosporin levels were decreased. No effects on muscle were noted
- Statins: increased risk of myopathy

## Administration

RECONSTITUTION

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ROUTE

- Oral

RATE OF ADMINISTRATION

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COMMENTS

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## Other information

- Adverse effects have not been reported in patients with renal disease, but such patients should start treatment at 900 mg daily, which may be increased after careful assessment of response and renal function
- Rare cases of rhabdomyolysis may be increased in those with renal impairment
- Approximately 60–70% is excreted in the urine as both conjugated and unconjugated drug
- Gemfibrozil alone has caused myalgia and myositis, but the effects appear to occur much more frequently and are more severe when an HMG CoA reductase inhibitor is also used. The combination is therefore not recommended

# Gentamicin

## Clinical use

Antibacterial agent

## Dose in normal renal function

3–7 mg/kg (ideal body weight) daily (divided into 1–4 doses). CAPD peritonitis – see local policy and below

## Pharmacokinetics

Molecular weight (daltons)	1418
% Protein binding	0–20
% Excreted unchanged in urine	95
Volume of distribution (L/kg)	0.23–0.26
Half-life – normal/ESRF (hrs)	2/20–60

## Dose in renal impairment GFR (mL/min)

See 'Other information' for dosage for dialysis and for single daily dosing regimen

30–70	80 mg 12-hourly (60 mg if <60 kg)
10–30	80 mg 24-hourly (60 mg if <60 kg)
5–10	80 mg 48-hourly (60 mg if <60 kg) or post dialysis if on HD

## Dose in patients undergoing renal replacement therapies

CAPD	Dialysed. CAPD clearance is about 3 mL/min. Dose as in GFR = 5–10 mL/min. Monitor levels
HD	Dialysed. Dose as in GFR = 5–10 mL/min. Give after dialysis
CAV/VVHD	Dialysed. Dose in GFR = 10–30 mL/min and measure levels

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- Ciclosporin: increased risk of nephrotoxicity
- Muscle relaxants: effect of tubocurarine enhanced
- Cytotoxics: increased risk of nephrotoxicity with cisplatin

- Cholinergics: antagonism of effect of neostigmine and pyridostigmine
- Botulinum toxin: neuromuscular block enhanced (risk of toxicity)

## Administration

RECONSTITUTION

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ROUTE

- Bolus IV injection or short infusion – maximum 100 mL

RATE OF ADMINISTRATION

- Bolus IV: over not less than 3 minutes. Short infusion: over not more than 20 minutes

COMMENTS

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## Other information

- *Adjustment for renal impairment:* Dialysis patients – 80 mg (or up to 2 mg/kg) post dialysis
- *Single daily dosing regimen:*  
GFR >80: 5.1 mg/kg every 24 hours  
GFR 60–80: 4.0 mg/kg every 24 hours  
GFR 40–60: 3.5 mg/kg every 24 hours  
GFR 30–40: 2.5 mg/kg every 24 hours  
GFR 20–30: 4.0 mg/kg every 48 hours  
GFR 10–20: 3.0 mg/kg every 48 hours  
GFR <10: 2.0 mg/kg every 48 hours
- Concurrent penicillins may result in sub-therapeutic blood levels
- Monitor blood levels. 1 hour post-dose, peak levels must not exceed 10 mg/L. Pre-dose trough levels should be less than 2 mg/L
- Empirical IP therapy for CAPD peritonitis in conjunction with vancomycin. A common regimen used is gentamicin 4–5 mg/L + vancomycin IP at dose of 1–2 g stat on days 1 and 7 of course. Monitoring of blood levels is advisable, as absorption is increased by inflamed peritoneum
- Potential nephrotoxicity of the drug may worsen residual renal function
- Long-term concurrent use of gentamicin with teicoplanin causes additive ototoxicity

# Glibenclamide

## Clinical use

Non-insulin-dependent diabetes mellitus

## Dose in normal renal function

Initially 5 mg daily (elderly patients – 2.5 mg) adjusted according to response; maximum 15 mg daily

## Pharmacokinetics

Molecular weight (daltons)	494
% Protein binding	98–99
% Excreted unchanged in urine	<5
Volume of distribution (L/kg)	0.15–0.2
Half-life – normal/ESRF (hrs)	5–10/–

## Dose in renal impairment GFR (mL/min)

20–50	Initial dose of 1.25–2.5 mg once a day. Monitor closely
10–20	Initial dose of 1.25–2.5 mg once a day. Monitor closely
<10	Initial dose of 1.25–2.5 mg once a day. Use with caution with continuous monitoring

## Dose in patients undergoing renal replacement therapies

CAPD	Not dialysed. Dose as in GFR = <10 mL/min
HD	Low dialysability. Dose as in GFR = <10 mL/min
CAV/VVHD	Unknown dialysability. Dose as in GFR = 10–20 mL/min

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- Analgesics: azapropazone, phenylbutazone and possibly other NSAIDs enhance effect
- Antibacterials: chloramphenicol, co-trimoxazole, 4-quinolones, sulphonamides and trimethoprim enhance effect
- Antifungals: fluconazole and miconazole increase glibenclamide plasma concentration
- Uricosurics: sulfinpyrazone enhances effect of glibenclamide

## Administration

RECONSTITUTION

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ROUTE

- Oral

RATE OF ADMINISTRATION

–

COMMENTS

- Take with breakfast

## Other information

- The metabolites of glibenclamide are only weakly hypoglycaemic, this is not clinically relevant where renal and hepatic functions are normal. If  $CL_{CR} < 10$  mL/min, accumulation of metabolite and unchanged drug in plasma may cause prolonged hyperglycaemia
- Company information states that use is contra-indicated in severe renal impairment
- Compensatory excretion via bile in faeces occurs in renal impairment

# Gliclazide

## Clinical use

Non-insulin-dependent diabetes mellitus

## Dose in normal renal function

Initially: 40–80 mg daily, adjusted according to response up to 160 mg as a single dose, with breakfast; higher doses divided. Maximum 320 mg daily

## Pharmacokinetics

Molecular weight (daltons)	323
% Protein binding	85–95
% Excreted unchanged in urine	<5
Volume of distribution (L/kg)	0.24
Half-life – normal/ESRF (hrs)	8–11/prolonged

## Dose in renal impairment

### GFR (mL/min)

20–50	Initially 20–40 mg daily. Use with caution and monitor
10–20	Initially 20–40 mg daily. Use with caution and monitor
<10	Initially 20–40 mg daily. Use with great caution and monitor closely

## Dose in patients undergoing renal replacement therapies

CAPD	Unlikely dialysability. Dose as in GFR = <10 mL/min
HD	Unlikely dialysability. Dose as in GFR = <10 mL/min
CAV/VVHD	Unknown dialysability. Dose as in GFR = 10–20 mL/min

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- Analgesics: azapropazone, phenylbutazone and possibly other NSAIDs enhance effect
- Antibacterials: chloramphenicol, co-trimoxazole, 4-quinolones, sulphonamides and trimethoprim enhance effect
- Antifungals: fluconazole and miconazole increase gliclazide plasma concentration
- Uricosurics: sulfipyrazone enhances effect

## Administration

RECONSTITUTION

–

ROUTE

- Oral

RATE OF ADMINISTRATION

–

COMMENTS

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## Other information

- Care should be exercised in patients with hepatic and/or renal impairment and a small starting dose should be used with careful patient monitoring
- Company contra-indicates prescribing of Diamicon in severe renal impairment which they define as  $CL_{CR}$  below 40 mL/min

# Glimepiride

## Clinical use

Non-insulin-dependent diabetes mellitus

## Dose in normal renal function

1–4 mg daily. Maximum 6 mg daily taken shortly before or with first main meal

## Pharmacokinetics

Molecular weight (daltons)	490.6
% Protein binding	>99
% Excreted unchanged in urine	58–60 (as metabolites)
Volume of distribution (L/kg)	8.8
Half-life – normal/ESRF (hrs)	5–9/prolonged

## Dose in renal impairment GFR (mL/min)

20–50	Dose as in normal renal function
10–20	Dose as in normal renal function
<10	Contra-indicated

## Dose in patients undergoing renal replacement therapies

CAPD	Unlikely dialysability. Dose as in GFR = <10 mL/min
HD	Unlikely dialysability. Dose as in GFR = <10 mL/min
CAV/VVHD	Unlikely dialysability. Dose as in GFR = 10–20 mL/min

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- Azapropazone, phenylbutazone and possibly other NSAIDs enhance effect of sulphonylureas
- Antibacterials: chloramphenicol, co-trimoxazole, 4-quinolones, sulphonamides and trimethoprim enhance effect
- Antifungals: fluconazole and miconazole increase sulphonylurea plasma concentration
- Sulfinpyrazone enhances effect

## Administration

RECONSTITUTION

–

ROUTE

- Oral

RATE OF ADMINISTRATION

–

COMMENTS

–

## Other information

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# Glipizide

## Clinical use

Non-insulin-dependent diabetes mellitus

## Dose in normal renal function

Initially 2.5–5 mg daily, adjusted according to response; maximum 20 mg daily; up to 15 mg may be given as a single dose before breakfast; higher doses divided

## Pharmacokinetics

Molecular weight (daltons)	445
% Protein binding	97
% Excreted unchanged in urine	4.5–7
Volume of distribution (L/kg)	0.13–0.16
Half-life – normal/ESRF (hrs)	3–7/–

## Dose in renal impairment GFR (mL/min)

20–50	Initially 2.5 mg daily. Use with caution
10–20	Initially 2.5 mg daily. Use with caution
<10	Contra-indicated

## Dose in patients undergoing renal replacement therapies

CAPD	Dialysability insignificant, however contra-indicated if GFR <10 mL/min
HD	Dialysability insignificant, however contra-indicated if GFR <10 mL/min
CAV/VVHD	Dialysability insignificant. Dose as in GFR = 10–20 mL/min

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- Azapropazone, phenylbutazone and possibly other NSAIDs enhance effect of sulphonylureas
- Antibacterials: chloramphenicol, co-trimoxazole, 4-quinolones, sulphonamides and trimethoprim enhance effect
- Antifungals: fluconazole and miconazole increase glipizide plasma concentration
- Sulfinpyrazone enhances effect

## Administration

RECONSTITUTION

–

ROUTE

- Oral

RATE OF ADMINISTRATION

–

COMMENTS

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## Other information

- Company does not recommend the use of Glibenese in patients with renal insufficiency
- Renal or hepatic insufficiency may cause elevated blood levels of glipizide (increased risk of serious hypoglycaemic reactions)

# Granisetron

## Clinical use

Prevention or treatment of nausea and vomiting induced by cytotoxic chemotherapy, radiotherapy or post-operative nausea and vomiting

## Dose in normal renal function

Cytotoxic chemotherapy or radiotherapy:  
PO: 1–2 mg within 1 hour before start of treatment, then 2 mg daily in 1–2 divided doses during treatment

IV: 3 mg before start of cytotoxic therapy, up to two additional 3 mg doses can be given within 24 hours no less than 10 minutes apart

Operative procedures: IV: 1 mg before induction of anaesthesia; treatment 1 mg (maximum 2 mg in one day)

## Pharmacokinetics

Molecular weight (daltons)	312.4 (348.9 as hydrochloride)
% Protein binding	≈65
% Excreted unchanged in urine	<20
Volume of distribution (L/kg)	3
Half-life – normal/ESRF (hrs)	3.0–4.0/ unchanged

## Dose in renal impairment

### GFR (mL/min)

20–50	Dose as in normal renal function
10–20	Dose as in normal renal function
<10	Dose as in normal renal function

## Dose in patients undergoing renal replacement therapies

CAPD	Unknown dialysability. Dose as in normal renal function
HD	Unknown dialysability. Dose as in normal renal function. Company recommend timing HD for greater than 2 hours after granisetron dose
CAV/VVHD	Unknown dialysability. Dose as in normal renal function

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- None known

## Administration

RECONSTITUTION

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ROUTE

- Oral, IV bolus, IV infusion

RATE OF ADMINISTRATION

- IV bolus: diluted in 5 mL sodium chloride 0.9% over not less than 30 seconds
- IV infusion: 20–50 mL over 5 minutes

COMMENTS

- Compatible with sodium chloride 0.9%, sodium chloride 0.18% and glucose 4% solution, glucose 5%, Hartmann's solution, compound sodium lactate, 10% mannitol
- Maximum administered dose over 24 hours should not exceed 9 mg

## Other information

- No special dosing adjustments necessary in patients with renal or hepatic failure

# Griseofulvin

## Clinical use

Antifungal agent: dermatophyte infections of the skin, scalp, hair and nails

## Dose in normal renal function

500 mg daily, in divided doses or as a single dose  
In severe infection dose may be doubled

## Pharmacokinetics

Molecular weight (daltons)	353
% Protein binding	84
% Excreted unchanged in urine	1
Volume of distribution (L/kg)	1.6
Half-life – normal/ESRF (hrs)	9.5–21/20

## Dose in renal impairment

### GFR (mL/min)

20–50	Dose as in normal renal function
10–20	Dose as in normal renal function
<10	Dose as in normal renal function

## Dose in patients undergoing renal replacement therapies

CAPD	Not dialysed. Dose as in normal renal function
HD	Not dialysed. Dose as in normal renal function
CAV/VVHD	Not dialysed. Dose as in normal renal function

## Important drug interactions

POTENTIALLY HAZARDOUS INTERACTIONS WITH OTHER DRUGS

- Anticoagulants: metabolism of acenocoumarol and warfarin accelerated (reduced anticoagulant effect)
- Metabolism of oral contraceptives accelerated (reduced contraceptive effect)
- Ciclosporin: griseofulvin possibly reduces plasma – ciclosporin concentration. (Two reports of such an interaction in literature.)

## Administration

RECONSTITUTION

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ROUTE

- Oral

RATE OF ADMINISTRATION

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COMMENTS

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## Other information

- Use with extreme caution in patients with SLE