Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

und

Schriftliche Beteiligung der wissenschaftlich-medizinischen Fachgesellschaften und der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2024-B-209 Iptacopan

Stand: Oktober 2024

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA	
Kriterien gemäß 5. Kapitel § 6 VerfO	**Iptacopan [C3-Glomerulopathie]**
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	Siehe Übersicht „II. Zugelassene Arzneimittel im Anwendungsgebiet“.
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	nicht angezeigt
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	Es liegen keine Beschlüsse vor.
Die Vergleichstherapie soll nach dem allgemein anerkannten Stand der medizinischen Erkenntnisse zur zweckmäßigen Therapie im Anwendungsgebiet gehören.	Siehe systematische Literaturrecherche

II. Zugelassene Arzneimittel im Anwendungsgebiet

Wirkstoff **ATC-Code** **Handelsname**	**Anwendungsgebiet** (Text aus Fachinformation)
Zu bewertendes Arzneimittel:	
Iptacopan	Anwendungsgebiet laut Beratungsanforderung: „Iptacopan wird angewendet zur Behandlung von erwachsenen Patienten mit Komplement-3-Glomerulopathie (C3G) in Kombination mit Renin-Angiotensin-System (RAS)-Inhibitoren oder bei Patienten, die intolerant gegen RAS-Inhibitoren sind oder bei denen ein RAS-Inhibitor kontraindiziert ist.“
Explizit zur Behandlung der C3-Glomerulopathie sind keine Arzneimittel zugelassen. Im weiteren Anwendungsgebiet zugelassen sind:	
SGLT2-Inhibitoren	
Empagliflozin A10BK03 Jardiance®	[…] Chronische Niereninsuffizienz Jardiance wird angewendet zur Behandlung von Erwachsenen mit chronischer Niereninsuffizienz. *Stand FI: Dezember 2023*
Dapagliflozin A10BK01 Forxiga®	[…] Chronische Niereninsuffizienz Forxiga ist bei erwachsenen Patienten indiziert zur Behandlung der chronischen Niereninsuffizienz. *Stand FI: August 2024*
Immunsuppressiva	
Ciclosporin L04AD01 (z.B. Sandimmun®)	[…] Nephrotisches Syndrom Steroidabhängiges und steroidresistentes nephrotisches Syndrom in der Folge primärer glomerulärer Krankheiten wie Minimal-Change-Nephropathie, fokale und segmentale Glomerulosklerose oder membranöse Glomerulonephritis. Sandimmun kann zur Induktion und zur Aufrechterhaltung einer Remission eingesetzt werden. Es kann auch zur Aufrechterhaltung einer steroidinduzierten Remission eingesetzt werden und so ein Absetzen von Steroiden ermöglichen.

II. Zugelassene Arzneimittel im Anwendungsgebiet	
	(Stand FI: Juni 2022)
Glucocorticoide	
Prednison H02AB07 (z.B. Prednison acis® Tabletten)	[…] <u>Nephrologie</u> − Minimal Change Glomerulonephritis (DS: a) − Extrakapillär-proliferative Glomerulonephritis (rapid progressive Glomerulonephritis) (DS: hochdosierte Stoßtherapie, in der Regel in Kombination mit Zytostatika), bei Goodpasture-Syndrom Abbau und Beendigung der Behandlung, bei allen anderen Formen langfristige Fortführung der Therapie (DS: d) − idiopathische retroperitoneale Fibrose (DS: b) Stand FI: März 2022
Prednisolon H02AB06 (z.B. Prednisolon acis® Tabletten)	[…] <u>Nephrologie</u> − Minimal Change Glomerulonephritis (DS: a) − Extrakapillär-proliferative Glomerulonephritis (rapid progressive Glomerulonephritis) (DS: hochdosierte Stoßtherapie, in der Regel in Kombination mit Zytostatika), bei Goodpasture-Syndrom Abbau und Beendigung der Behandlung, bei allen anderen Formen langfristige Fortführung der Therapie (DS: d) − idiopathische retroperitoneale Fibrose (DS: b) Stand FI: Juni 2024
Triamcinolon H02AB08 Volon®	[...] <u>Nephrologie</u> − Minimal Change Glomerulonephritis; − Extrakapillär-proliferative Glomerulonephritis (rapid progressive Glomerulonephritis), in der Regel in Kombination mit Zytostatika, bei Goodpasture-Syndrom Abbau und Beendigung der Behandlung, bei allen anderen Formen langfristige Fortführung der Therapie; − idiopathische retroperitoneale Fibrose. Stand FI: März 2022

Quellen: AMIce-Datenbank, Fachinformationen

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2024-B-209 (Iptacopan)

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	24. September 2024

Inhaltsverzeichnis

Abkürzungsverzeichnis

AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
ECRI	Emergency Care Research Institute
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HR	Hazard Ratio
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
KI	Konfidenzintervall
LoE	Level of Evidence
NICE	National Institute for Health and Care Excellence
OR	Odds Ratio
RR	Relatives Risiko
SIGN	Scottish Intercollegiate Guidelines Network
TRIP	Turn Research into Practice Database
WHO	World Health Organization

1 Indikation

Komplement-3-Glomerulopathie (C3G)

Hinweis zur Synopse: Informationen hinsichtlich nicht zugelassener Therapieoptionen sind über die vollumfängliche Darstellung der Leitlinienempfehlungen dargestellt.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zur Indikation *Komplement-3-Glomerulopathie* durchgeführt und nach PRISMA-S dokumentiert [A]. Die Recherchestrategie wurde vor der Ausführung anhand der PRESS-Checkliste begutachtet [B]. Es erfolgte eine Datenbankrecherche ohne Sprachrestriktion in: The Cochrane Library (Cochrane Database of Systematic Reviews), PubMed. Die Recherche nach grauer Literatur umfasste eine gezielte, iterative Handsuche auf den Internetseiten von Leitlinienorganisationen. Ergänzend wurde eine freie Internetsuche (*https://www.google.com/*) unter Verwendung des privaten Modus, nach aktuellen deutsch- und englischsprachigen Leitlinien durchgeführt.

Der Suchzeitraum wurde auf die letzten fünf Jahre eingeschränkt und die Recherche am 27.08.2024 abgeschlossen. Die detaillierte Darstellung der Recherchestrategie inkl. verwendeter Suchfilter sowie eine Angabe durchsuchter Leitlinienorganisationen ist am Ende der Synopse aufgeführt. Mit Hilfe von EndNote wurden Dubletten identifiziert und entfernt. Die Recherche ergab 220 Referenzen.

In einem zweistufigen Screening wurden die Ergebnisse der Literaturrecherche bewertet. Im ersten Screening wurden auf Basis von Titel und Abstract nach Population, Intervention, Komparator und Publikationstyp nicht relevante Publikationen ausgeschlossen. Zudem wurde eine Sprachrestriktion auf deutsche und englische Referenzen vorgenommen. Im zweiten Screening wurden die im ersten Screening eingeschlossenen Publikationen als Volltexte gesichtet und auf ihre Relevanz und methodische Qualität geprüft. Dafür wurden dieselben Kriterien wie im ersten Screening sowie Kriterien zur methodischen Qualität der Evidenzquellen verwendet. Basierend darauf, wurde insgesamt 1 Referenz eingeschlossen. Es erfolgte eine synoptische Darstellung wesentlicher Inhalte der identifizierten Referenz.

3 Ergebnisse

3.1 Cochrane Reviews

Es wurden keine relevanten Cochrane Reviews im Anwendungsgebiet identifiziert.

3.2 Systematische Reviews

Es wurden keine relevanten systematischen Reviews im Anwendungsgebiet identifiziert.

3.3 Leitlinien

KDIGO 2021 [1].

Clinical Practice Guideline for the Management of Glomerular Diseases

Zielsetzung/Fragestellung

The Kidney Disease: Improving Global Outcomes (KDIGO) 2021 Clinical Practice Guideline for the Management of Glomerular Diseases is an update to the KDIGO 2012 guideline on the topic. The aim is to assist clinicians caring for individuals with glomerular disease, both adults and children. The scope includes various glomerular diseases, including IgA nephropathy (IgAN) and IgA vasculitis (IgAV), membranous nephropathy, nephrotic syndrome in children, minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), infection-related glomerulonephritis (GN), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, lupus nephritis, and anti-glomerular basement membrane (anti-GBM) antibody GN. In addition, this guideline will be the first to address the subtype of complement-mediated diseases.

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium.
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt.
- Systematische Suche, Auswahl und Bewertung der Evidenz.
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt.
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt.
- Regelmäßige Überprüfung der Aktualität gesichert.

Recherche/Suchzeitraum:

- Searches for RCTs utilized the Cochrane Kidney and Transplant Registry of studies in October 2018 and supplemented until September 2019. An updated search was undertaken in June 2020.

LoE

Grade	Quality of evidence	Meaning
A	High	We are confident that the true effect is close to the estimate of the effect.
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very low	The estimate of the effect is very uncertain, and often it will be far from the true effect.

GoR

	Implications		
Grade	Patients	Clinicians	Policy
Level 1 'Strong' "We recommend"	Most people in your situation would want the recommended course of action, and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure.
Level 2 'Weak' "We suggest"	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.

Empfehlungen

8.2.2 C3 glomerulopathy

An optimal treatment strategy for C3G using currently available therapeutics has not been established. Expert opinion has encouraged the usual supportive measures (Chapter 1), as well as the use of immunosuppression in the setting of moderate to- severe disease, defined as moderate-to-marked proliferation on biopsy and proteinuria (>2 g/d).543 This opinion is based primarily on 4 retrospective cohorts and on an extrapolation of data from other non-related proliferative glomerulonephritides. Well-controlled data are unavailable.

Practice Point 8.2.2.1: In the absence of a monoclonal gammopathy, C3G in patients with moderate-to-severe disease should be treated initially with MMF plus glucocorticoids, and if this fails, eculizumab should be considered.

Consider treating patients with C3G who have proteinuria >1 g/d and hematuria or have had declining kidney function for at least 6 months. The reported effectiveness of immunosuppressive treatment in C3G has been variable. Medjeral-Thomas et al. reported 32 patients with C3G who received immunosuppressive treatment (glucocorticoids alone or combined with other drugs). Immunosuppression did not seem to reduce progression to kidney failure as compared to no treatment.544 Similar results were obtained by Servais et al. in a cohort of 85 patients with C3G.537

More recent data showed encouraging results with MMF. Rabasco et al. reported a relative treatment advantage with MMF in a cohort of 60 patients with C3G.545 In a mean follow-up of 47 months, the 22 patients who received MMF plus glucocorticoids showed lower rates of ESKD (0%vs. 16.6%) and doubling of SCr (0% vs. 39%) as compared to patients exposed to other immunosuppression. In addition, the rates of remission in the MMF group were significantly higher (19 of 22 patients vs. 9 of 18 patients; $P < 0.05$). The response to immunosuppression seen in this retrospective cohort provided the support for the current expert opinion on treatment approach for C3G.543

Similarly, Avasare et al. reported the kidney outcomes for 30 patients with C3G after MMF.546 After a mean follow-up of 3 years, two-thirds had an either stabilized or reduced SCr level and reduced proteinuria. Ravindran et al. reported the kidney outcomes on a subcohort of 144 patients with C3G.533 Of 24 patients given MMF (median follow-up 9.6 months), 3 had improved kidney outcome measures, and 4 had stable disease. Fifteen patients worsened. Finally, Bomback et al. reported the results of a subcohort of their 111 patients with C3G.532 Of the 42 patients exposed to MMF, 19 achieved either a complete or partial remission.

The benefits of terminal complement blockade with the anti- C5 monoclonal antibody eculizumab remain unestablished. A trial involved 3 patients with DDD (including 1 kidney transplant recipient) and 3 patients with C3GN (including 2 kidney transplant recipients), all of whom had proteinuria >1 g/d and/ orAKI at enrollment. Complement testing identified pathogenic variants in Complement Factor H (CFH) and CD46 in one patient each and C3 nephritic factors in 3 patients. After 12 months of twice-weekly eculizumab, 3 patients had a renal response (decrease in SCr levels and/or proteinuria), and 1 patient with stable laboratory parameters had histopathologic evidence of improvement. Eculizumab normalized soluble C5b-9 level in all patients with elevated levels of this biomarker of terminal pathway activity at baseline, suggesting it may represent a potentially useful marker of response.

In a recent retrospective study, 26 patients with C3G were treated with eculizumab for a median duration of 14 months. Of these, 6 patients (23%) had a global clinical response, 6 (23%) had a partial clinical response, and 14 (54%) had no response. As compared to those with partial response or no response, responders had lower eGFRs, more rapidly progressive disease, and more extra-capillary proliferation on kidney biopsy samples. Age, extent of kidney fibrosis, frequency of NS, and features of alternative pathway activation did not differ. These results are consistent with the fact that eculizumab mainly targets glomerular inflammation and has no effect or limited effect on the complement dysregulation that governs C3G.547

In the absence of clear evidence, the use of eculizumab can be considered in patients with progressive disease who fail to respond to other therapies.

Practice Point 8.2.2.2: Patients who fail to respond to the treatment approaches discussed in 8.2.2.1 should be considered for a clinical trial where available.

Chapter 1: General principles for the management of glomerular disease

1.4 Management of complications of glomerular disease

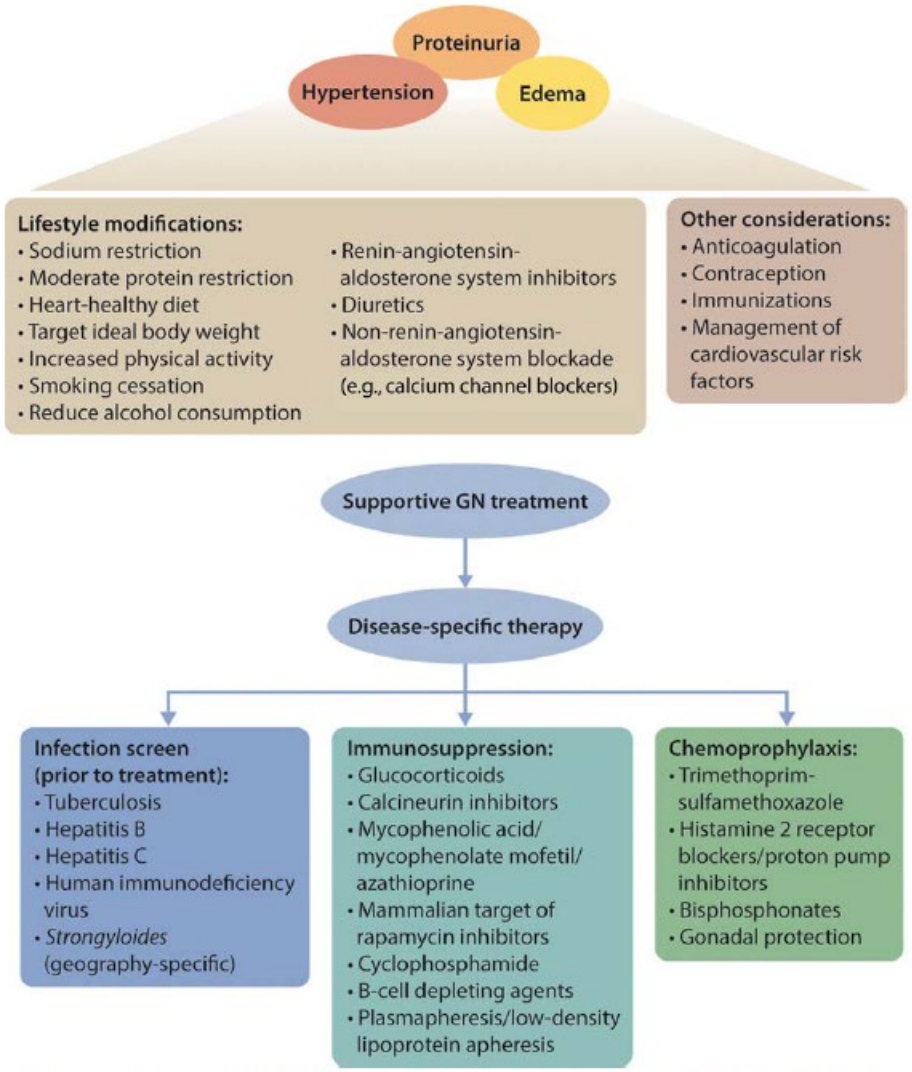

Figure 6 | Summary of supportive management of glomerular disease. Note: Prednisone and prednisolone are equivalent, used in the same dosage, and have both been used in RCTs, depending on the country of origin. All later usages of "prednisone" in this guideline refer to prednisone or prednisolone. All later usages of "glucocorticoids" refer to prednisone or prednisolone, unless otherwise specified. GN, glomerulonephritis; RCT, randomized controlled trial.

Practice Point 1.4.1. Use loop diuretics as first-line therapy for treatment of edema in the nephrotic syndrome	• Twice daily dosing preferred over once daily dosing; daily dosing may be acceptable for reduced GFR • Increase dose of loop diuretic to cause clinically significant diuresis or until maximally effective dose has been reached • Switch to longer acting loop diuretic such as bumetanide or torsemide/torasemide if concerned about treatment failure with furosemide, or if concerned about oral drug bioavailability
Practice Point 1.4.2. Restrict dietary sodium intake	• Restrict dietary sodium to <2.0 g/d (<90 mmol/d)
Practice Point 1.4.3. Use loop diuretics with other mechanistically different diuretics as synergistic treatment of resistant edema in the nephrotic syndrome	• All thiazide-like diuretics in high doses are equally effective. None is preferred. • Thiazide diuretics, administered with an oral or i.v. loop diuretic, will impair distal sodium reabsorption and improve diuretic response • Amiloride may provide improvement in edema/hypertension, and counter hypokalemia from loop or thiazide diuretics • Acetazolamide may be helpful for the metabolic alkalosis of diuresis • Spironolactone may provide improvement in edema/hypertension, and counter hypokalemia from loop or thiazide diuretics
Practice Point 1.4.4. Monitor for adverse effects of diuretics	• Hyponatremia with thiazide diuretics • Hypokalemia with thiazide and loop diuretics • Impaired GFR • Volume depletion, especially in pediatric/elderly patients • Hyperkalemia with spironolactone and eplerenone especially if combined with RAS blockade
Practice Point 1.4.5. Strategies for diuretic-resistant patient	• Amiloride • Acetazolamide • i.v. loop diuretics (bolus or infusion) alone • i.v. loop diuretics in combination with i.v. albumin • Ultrafiltration • Hemodialysis • Amiloride may reduce potassium loss and improve diuresis. Acetazolamide may help to treat metabolic alkalosis but is a weak diuretic

gure 7 | Edema management in NS. GFR, glomerular filtration rate; i.v., intravenous; NS, nephrotic syndrome; RAS, renin–angiotensin system.

Practice Point 1.5.1.	Use an ACEi or ARB to maximally tolerated or allowed dose as first-line therapy in treating patients with both hypertension and proteinuria	• Do not stop ACEi or ARB with modest and stable increase in serum creatinine (up to 30%) • Stop ACEi or ARB if kidney function continues to worsen, and/or refractory hyperkalemia • Combinations of ACEi and ARB may be used in young adults without diabetes or cardiovascular disease, but benefits and safety are uncertain Caveat: do not start ACEi/ARB in patients who present with abrupt onset of NS. These drugs can cause AKI especially in patients with MCD
Practice Point 1.5.2.	Target systolic blood pressure in most adult patients is <120 mm Hg using standardized office BP measurement. Target 24 h mean arterial pressure in children is ≤50th percentile for age, sex, and height by ambulatory blood pressure monitoring	• Refer to KDIGO BP Guideline (https://kdigo.org/guidelines/blood-pressure-in-ckd/) • Formally speaking, SBP <120 mm Hg has not been validated in GN. In practicality, we are able to achieve an SBP of 120–130 mm Hg in most patients with glomerular disease
Practice Point 1.5.3.	Uptitrate an ACEi or ARB to maximally tolerated or allowed daily dose as first-line therapy in treating patients with GN and proteinuria alone	• Indicated for persistent proteinuria despite treatment of primary GN with immunosuppression (where indicated) • Avoid use of an ACEi or ARB if kidney function is rapidly changing
Practice Point 1.5.4.	Proteinuria goal is variable depending on primary disease process; typically, <1 g/d	• It may be reasonable to delay initiation of ACEi or ARB for patients without hypertension with podocytopathy (MCD, SSNS, or primary FSGS) expected to be rapidly responsive to immunosuppression • Proteinuria goal is disease-specific in adults with GN
Practice Point 1.5.5.	Monitor labs frequently if on ACEi or ARB	• Titration of ACEi or ARB may cause acute kidney injury or hyperkalemia
Practice Point 1.5.6.	Counsel patients to hold ACEi or ARB and diuretics when at risk for volume depletion	• Increased risk for acute kidney injury and hyperkalemia • Counsel patients according to level of education in a culturally sensitive manner • Consider transiently stopping RASi during sick days
Practice Point 1.5.7.	Use potassium-wasting diuretics and/or potassium-binding agents to reduce serum potassium to normal, in order to use RAS blocking medications for BP control and proteinuria reduction Treat metabolic acidosis (serum bicarbonate <22 mmol/l)	• Loop diuretics • Thiazide diuretics • Patiromer • Sodium zirconium cyclosilicate (each 10 g of sodium zirconium cyclosilicate contains 800 mg of sodium) • Supplement with oral sodium bicarbonate
Practice Point 1.5.8.	Employ lifestyle modifications in all GN patients as synergistic means for improving control of hypertension and proteinuria	• Restrict dietary sodium to <2.0 g/d (<90 mmol/d) • Normalize weight • Exercise regularly • Stop smoking
Practice Point 1.5.9.	Intensify dietary sodium restriction in those patients who fail to achieve proteinuria reductions, and who are on maximally tolerated medical therapy	• Restrict dietary sodium to <2.0 g/d (<90 mmol/d). Consider using mineralocorticoid receptor antagonists in refractory cases (monitor for hyperkalemia)

ɟure 8 | Management of hypertension and proteinuria in glomerular disease. ACEi, angiotensin-converting enzyme inhibitor; ARB, giotensin II receptor blocker; BP, blood pressure; FSGS, focal segmental glomerulosclerosis; GN, glomerulonephritis; KDIGO, Kidney sease: Improving Global Outcomes; MCD, minimal change disease; NS, nephrotic syndrome; RAS, renin–angiotensin system; RASi, nin–angiotensin system inhibitors; SBP, systolic blood pressure; SSNS, steroid-sensitive nephrotic syndrome.

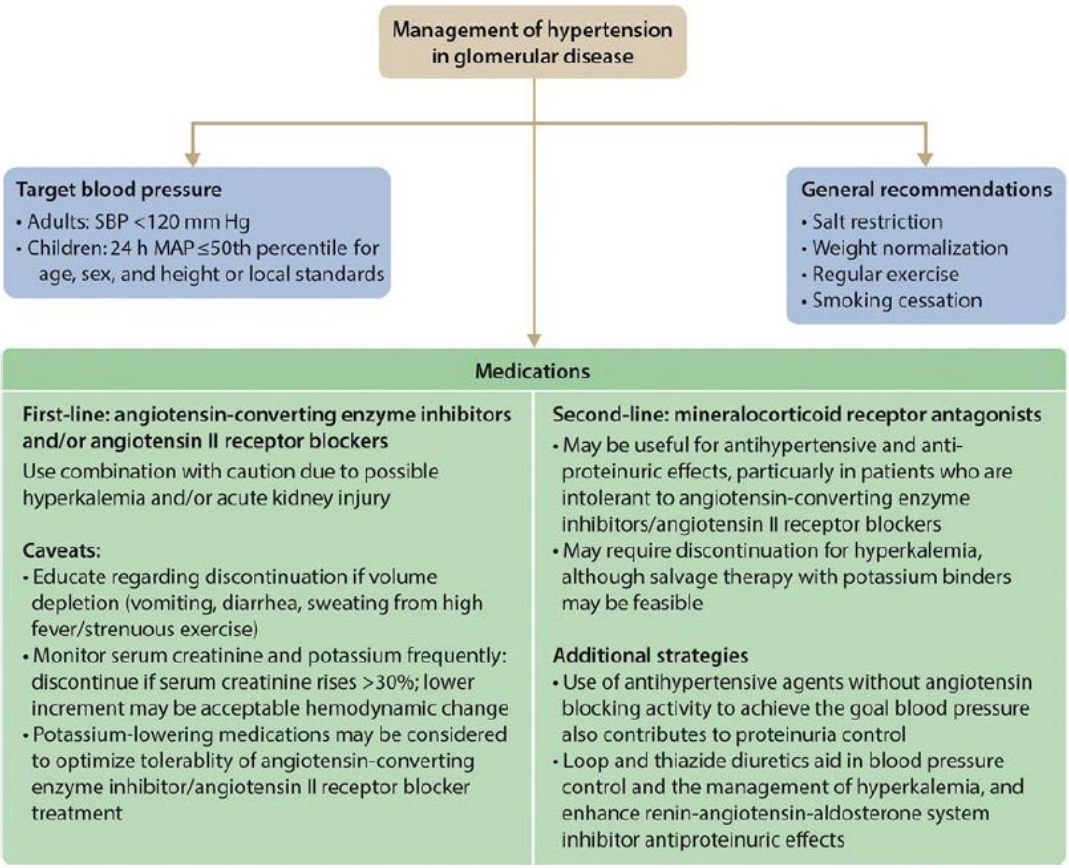

Figure 9 | Management of hypertension in glomerular disease. MAP, mean arterial pressure; SBP, systolic blood pressure.

Practice Point 1.6.1.	Treatment of hyperlipidemia may be considered in patients with the nephrotic syndrome, particularly for patients with other cardiovascular risk factors, including hypertension and diabetes	High quality data are lacking to guide treatment in these patients
Practice Point 1.6.2.	Use lifestyle modifications in all patients with persistent hyperlipidemia and glomerular disease: • Heart-healthy diet • Increased physical activity • Weight reduction • Smoking cessation	• Not well studied as primary means of reducing lipids in nephrotic syndrome • Can be used as primary therapy in low-risk individuals with mild to moderate hyperlipidemia • Additive to pharmacologic treatment of hyperlipidemia • Considered first-line treatment of hyperlipidemia in children • Consider a plant-based diet • Avoid red meat
Practice Point 1.6.3.	Consider starting a statin drug as first-line therapy for persistent hyperlipidemia in patients with glomerular disease: • Assess ASCVD risk based on LDL-C, Apo B, triglyceride and Lp (a) levels, age group, and ASCVD 'risk enhancers' • Align statin dosage intensity to ASCVD risk • Statins can be initiated in children aged > 8 years with concerning family history, extremely elevated LDL-C or Lp(a), in the context of informed shared decision-making and counselling with patient and family	• Reduced eGFR (<60 ml/min/1.73 m^2 not on dialysis) and albuminuria (ACR >30 mg/g) are independently associated with an elevated risk of ASCVD • ASCVD risk enhancers include chronic inflammatory conditions such as systemic lupus erythematosus, rheumatoid arthritis, history of preeclampsia, early menopause, South Asian ancestry, chronic kidney disease and human immunodeficiency virus/AIDS (accuracy of ASCVD risk estimators have not been well validated for adults with chronic inflammatory disorders or human immunodeficiency virus) • Adherence to changes in lifestyle and effects of LDL-C lowering medication should be assessed by measurement of fasting lipids and appropriate safety indicators 4–12 weeks after statin initiation/dose adjustment or inflammatory disease-modifying therapy/antiretroviral therapy, and every 3–12 months thereafter based on need to assess adherence or safety
Practice Point 1.6.4.	Consider initiation of non-statin therapy in those individuals who cannot tolerate a statin, or who are at high ASCVD risk and fail to achieve LDL-C or triglyceride goals despite maximally tolerated statin dose: • Bile acid sequestrants • Fibrates • Nicotinic acid • Ezetimibe • PCSK9 inhibitor • Lipid apheresis	• Bile acid sequestrants have a high rate of gastrointestinal side effects limiting their use • Bile acid sequestrants and fibrates have been shown in small studies to reduce serum cholesterol in nephrotic syndrome • Fibrates will increase serum creatinine level due to direct action on the kidney • Ezetimibe has limited vascular and clinical benefits, but is used in statin-intolerant patients as salvage therapy • Nicotinic acid and ezetimibe have not been studied in patients with nephrotic syndrome • PCSK9 inhibitors may be beneficial in nephrotic syndrome; trials ongoing

Figure 10 | Management of hyperlipidemia in glomerular disease. ACR, albumin–creatinine ratio; AIDS, acquired immunodeficiency syndrome; Apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein cholesterol; Lp, lipoprotein; PCSK9, proprotein convertase subtilisin/kexin type 9.

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 08 of 12, August 2024) am 26.08.2024

#	Suchfrage
1	MeSH descriptor: [Glomerulonephritis] this term only
2	MeSH descriptor: [Glomerulonephritis, Membranoproliferative] explode all trees
3	(glomerulopath* OR c3g OR c3gn):ti,ab,kw OR glomerul*:ti
4	(glomerul* OR nephrit* OR nephropath* OR (Bright* AND Disease) OR (Kidney* AND Scar*)):ti,ab,kw
5	(C3 OR "C 3" OR "Complement 3" OR "PRO C3"):ti,ab,kw
6	#4 AND #5
7	#1 OR #2 OR #3 OR #6
8	#7 with Cochrane Library publication date from Aug 2019 to present

Systematic Reviews in PubMed am 26.08.2024

verwendete Suchfilter:
Konsentierter Standardfilter für Systematische Reviews (SR), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 14.02.2023.

#	Suchfrage
1	Glomerulonephritis[mh:noexp] OR Glomerulonephritis, Membranoproliferative[mh]
2	glomerulopath*[tiab] OR glomerul*[ti] OR c3g[tiab] OR c3gn[tiab]
3	glomerul*[tiab] OR nephrit*[tiab] OR nephropath*[tiab] OR (Bright*[tiab] AND Disease[tiab]) OR (Kidney*[tiab] AND Scar*[tiab])
4	C3[tiab] OR "C 3"[tiab] OR "Complement 3"[tiab] OR "PRO C3"[tiab]
5	#3 AND #4
6	#1 OR #2 OR #5
7	(#6) AND (systematic review[ptyp] OR meta-analysis[ptyp] OR network meta-analysis[mh] OR (systematic*[tiab] AND (review*[tiab] OR overview*[tiab])) OR metareview*[tiab] OR umbrella review*[tiab] OR "overview of reviews"[tiab] OR meta-analy*[tiab] OR metaanaly*[tiab] OR metanaly*[tiab] OR meta-synthes*[tiab] OR metasynthes*[tiab] OR meta-study[tiab] OR metastudy[tiab] OR integrative review[tiab] OR integrative literature review[tiab] OR evidence review[tiab] OR ((evidence-based medicine[mh] OR evidence synthes*[tiab]) AND review[pt]) OR ((("evidence based" [tiab:~3]) OR evidence base[tiab]) AND (review*[tiab] OR overview*[tiab])) OR (review[ti] AND (comprehensive[ti] OR studies[ti] OR trials[ti])) OR ((critical appraisal*[tiab] OR critically appraise*[tiab] OR study selection[tiab] OR ((predetermined[tiab] OR inclusion[tiab] OR selection[tiab] OR eligibility[tiab]) AND criteri*[tiab]) OR exclusion criteri*[tiab] OR screening criteri*[tiab] OR systematic*[tiab] OR data extraction*[tiab] OR data synthes*[tiab] OR prisma*[tiab] OR moose[tiab] OR entreq[tiab] OR mecir[tiab] OR stard[tiab] OR strobe[tiab] OR "risk of bias"[tiab]) AND

#	Suchfrage
	(survey*[tiab] OR overview*[tiab] OR review*[tiab] OR search*[tiab] OR analysis[ti] OR apprais*[tiab] OR research*[tiab] OR synthes*[tiab]) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR bibliographies[tiab] OR published[tiab] OR citations[tiab] OR database*[tiab] OR references[tiab] OR reference-list*[tiab] OR papers[tiab] OR trials[tiab] OR studies[tiab] OR medline[tiab] OR embase[tiab] OR cochrane[tiab] OR pubmed[tiab] OR "web of science" [tiab] OR cinahl[tiab] OR cinhal[tiab] OR scisearch[tiab] OR ovid[tiab] OR ebsco[tiab] OR scopus[tiab] OR epistemonikos[tiab] OR prospero[tiab] OR proquest[tiab] OR lilacs[tiab] OR biosis[tiab])) OR technical report[ptyp] OR HTA[tiab] OR technology assessment*[tiab] OR technology report*[tiab])
8	(#7) AND ("2019/08/01"[PDAT] : "3000"[PDAT])
9	(#8) NOT "The Cochrane database of systematic reviews"[Journal]
10	(#9) NOT (retracted publication [pt] OR retraction of publication [pt] OR preprint[pt])

Leitlinien in PubMed am 26.08.2024

verwendete Suchfilter:
Konsentierter Standardfilter für Leitlinien (LL), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 21.06.2017.

#	Suchfrage
1	Glomerulonephritis[mh:noexp] OR Glomerulonephritis, Membranoproliferative[mh]
2	glomerulopath*[tiab] OR glomerul*[ti] OR c3g[tiab] OR c3gn[tiab]
3	glomerul*[tiab] OR nephrit*[tiab] OR nephropath*[tiab] OR (Bright*[tiab] AND Disease[tiab]) OR (Kidney*[tiab] AND Scar*[tiab])
4	C3[tiab] OR "C 3"[tiab] OR "Complement 3"[tiab] OR "PRO C3"[tiab]
5	#3 AND #4
6	#1 OR #2 OR #5
7	(#6) AND (Guideline[ptyp] OR Practice Guideline[ptyp] OR guideline*[Title] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] *OR recommendation*[ti])*
8	(#7) AND ("2019/08/01"[PDAT] : "3000"[PDAT])
9	(#8) NOT (retracted publication [pt] OR retraction of publication [pt] OR preprint[pt])

Iterative Handsuche nach grauer Literatur, abgeschlossen am 27.08.2024

- Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)
- Nationale VersorgungsLeitlinien (NVL)

- National Institute for Health and Care Excellence (NICE)
- Scottish Intercollegiate Guideline Network (SIGN)

- World Health Organization (WHO)

- ECRI Guidelines Trust (ECRI)
- Dynamed / EBSCO
- Guidelines International Network (GIN)
- Trip Medical Database

Referenzen

1. **Kidney Disease: Improving Global Outcomes (KDIGO).** KDIGO 2021 clinical practice guideline for the management of glomerular diseases. Kidney Int 2021;100(4s):S1-S276.

[A] **Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, et al.** PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev 2021;10(1):39. https://doi.org/10.1186/s13643-020-01542-z

[B] **McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C.** PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin Epidemiol 2016;75:40-46. https://doi.org/10.1016/j.jclinepi.2016.01.021

Gemeinsamer Bundesausschuss

Schriftliche Beteiligung der wissenschaftlich-medizinischen Fachgesellschaften und der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

- keine eingegangenen schriftlichen Rückmeldungen gem. § 7 Absatz 6 VerfO