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: 2023-B-328-z Empagliflozin

Stand: Dezember 2023

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA

Empagliflozin
zur Behandlung des Diabetes mellitus Typ 2 bei Kindern und Jugendlichen

Kriterien gemäß 5. Kapitel § 6 VerfO	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	Siehe unter *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	- Für Kinder und Jugendliche mit Diabetes mellitus Typ 2 liegen folgende Beschlüsse über die Nutzenbewertung nach § 35a SGB V vor: o Beschluss zu Insulin degludec vom 20. August 2015 o Beschluss zu Dapagliflozin vom 16. Juni 2022 o Beschluss zu Dulaglutid vom 21. September 2023
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:	
Empagliflozin Jardiance	<u>Anwendungsgebiet laut Positive Opinion vom 9. November 2023</u> Jardiance is indicated in adults and **children aged 10 years and above** for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise • as monotherapy when metformin is considered inappropriate due to intolerance • in addition to other medicinal products for the treatment of diabetes
Zugelassene Arzneimittel im Anwendungsgebiet:	
Biguanide	
Metformin A10BA02 generisch	
GLP-(Glucagon-like Peptide)-1-Rezeptor-Agonisten (Inkretinmimetika)	
Exenatid A10BJ01 Bydureon	Bydureon ist indiziert bei Erwachsenen, **Jugendlichen und Kindern im Alter von 10 Jahren** und älter mit Typ-2-Diabetes mellitus zur Verbesserung der Blutzuckerkontrolle in Kombination mit anderen blutzuckersenkenden Arzneimitteln, einschließlich Basalinsulin, wenn die bestehende Therapie den Blutzucker zusammen mit einer Diät und Bewegung nicht ausreichend kontrolliert. Studienergebnisse in Bezug auf Kombinationen, die Wirkung auf die Blutzuckerkontrolle und kardiovaskuläre Ereignisse sowie die untersuchten Populationen siehe Abschnitte 4.4, 4.5 und 5.1.
Liraglutid A10BX07 Victoza	Victoza wird zur Behandlung des unzureichend kontrollierten Diabetes mellitus Typ 2 bei Erwachsenen, **Jugendlichen und Kindern ab dem Alter von 10 Jahren** als Zusatz zu Diät und körperlicher Aktivität angewendet - als Monotherapie, wenn die Anwendung von Metformin aufgrund einer Unverträglichkeit oder Kontraindikation ungeeignet ist - zusätzlich zu anderen Arzneimitteln zur Behandlung des Diabetes mellitus.

II. Zugelassene Arzneimittel im Anwendungsgebiet	
	Für Studienergebnisse hinsichtlich Kombinationen, Auswirkungen auf die glykämische Kontrolle und kardiovaskuläre Ereignisse, sowie untersuchten Populationen, siehe Abschnitte 4.4, 4.5 und 5.1.
Dulaglutid A10BJ05 Trulicity	Typ 2-Diabetes mellitus Trulicity ist angezeigt zur Behandlung von **Patienten ab 10 Jahren** mit unzureichend kontrolliertem Typ 2-Diabetes mellitus unterstützend zu Diät und Bewegung: • als Monotherapie, wenn die Einnahme von Metformin wegen Unverträglichkeit oder Kontraindikationen nicht angezeigt ist. • zusätzlich zu anderen Arzneimitteln zur Behandlung des Diabetes mellitus. Für Studienergebnisse hinsichtlich Kombinationen, Auswirkungen auf die glykämische Kontrolle und kardiovaskuläre Ereignisse, sowie untersuchten Populationen, siehe Abschnitte 4.4, 4.5 und 5.1-
Selektive Natrium-Glucose-Cotransport-Inhibitoren (SGLT-2-Inhibitoren)	
Dapagliflozin A10BK01 Forxiga	Typ-2-Diabetes mellitus Forxiga ist bei Erwachsenen und **Kindern im Alter von 10 Jahren und älter** indiziert zur Behandlung von unzureichend kontrolliertem Typ-2-Diabetes mellitus in Ergänzung zu einer Diät und Bewegung • als Monotherapie, wenn Metformin aufgrund einer Unverträglichkeit als ungeeignet erachtet wird. • zusätzlich zu anderen Arzneimitteln zur Behandlung des Typ-2-Diabetes. Zu Studienergebnissen im Hinblick auf Kombinationen von Behandlungen, die Wirkung auf die Blutzuckerkontrolle, kardiovaskuläre und renale Ereignisse sowie die untersuchten Populationen, siehe Abschnitte 4.4, 4.5 und 5.1.
Humaninsuline	
Insulin human A10AD01 Actraphane	Actraphane wird angewendet zur Behandlung von Diabetes mellitus. ***Kinder und Jugendliche*** *Actraphane kann bei Kindern und Jugendlichen angewendet werden.*
Insulinanaloga	*Verordnungseinschränkung Anlage III – AM-RL*
Insuline schnell wirkend: Insulin lispro, Insulin	NovoRapid wird angewendet zur Behandlung von Diabetes mellitus bei Erwachsenen, **Jugendlichen und Kindern** ab dem Alter von 1 Jahr.

II. Zugelassene Arzneimittel im Anwendungsgebiet	
aspart, Insulin glulisin A10AB01-06 NovoRapid 100 I.E./ml	
Insuline lang wirkend: Insulin detemir, Insulin glargin, Insulin degludec A10AE01-06 Lantus 100 I.E./ml	Insulin glargin: Zur Behandlung von Diabetes mellitus bei Erwachsenen, **Jugendlichen und Kindern im Alter von 2 Jahren und älter**.

Quellen: AMIce-Datenbank, Fachinformationen

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

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

Vorgang: Diabetes mellitus Typ 2 bei Kindern ab 10 Jahren

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	3. Dezember 2021

Inhaltsverzeichnis

Abkürzungsverzeichnis

AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
ECRI	ECRI Guidelines Trust
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
HR	Hazard Ratio
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
KI	Konfidenzintervall
LoE	Level of Evidence
MACE	Major adverse cardiovascular event
mmol/L	Millimol pro Liter
NICE	National Institute for Health and Care Excellence
OR	Odds Ratio
RR	Relatives Risiko
SIGN	Scottish Intercollegiate Guidelines Network
SUE	schweres unerwünschtes Ereignis
TRIP	Turn Research into Practice Database
WHO	World Health Organization

1 Indikation

Diabetes mellitus Typ 2 bei Kindern und Jugendlichen

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zur Indikation *Diabetes Mellitus Typ 2 bei Kindern und Jugendlichen* 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), MEDLINE (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.

Die Erstrecherche wurde am 15.03.2021 durchgeführt, die folgende am 16.11.2021. Die Recherchestrategie der Erstrecherche wurde unverändert übernommen und der Suchzeitraum jeweils auf die letzten fünf Jahre eingeschränkt. Die letzte Suchstrategie inkl. Angabe zu verwendeter Suchfilter ist am Ende der Synopse detailliert dargestellt. Die Recherchen ergaben insgesamt 570 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, wurden insgesamt drei Referenzen eingeschlossen. Es erfolgte eine synoptische Darstellung wesentlicher Inhalte der identifizierten Referenzen.

3 Ergebnisse

3.1 Cochrane Reviews

Es wurden keine relevanten Cochrane Reviews identifiziert.

3.2 Systematische Reviews

Es wurden keine relevanten systematischen Reviews identifiziert.

3.3 Leitlinien

NICE et al., 2015 [2].

National Institute for Health and Care Excellence (NICE)

Diabetes (type 1 and type 2) in children and young people: diagnosis and management; Full guideline (last updated December 2020).

Zielsetzung/Fragestellung

Management of Diabetes in children and young people.

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:

- last updated December 2020

LoE/GoR

Table 6: Levels of evidence

Level	Source of evidence
Ia	Systematic review or meta-analysis of randomised controlled trials
Ib	At least 1 randomised controlled trial
IIa	At least 1 well-designed controlled study without randomisation
IIb	At least 1 well-designed quasi-experimental study, such as a cohort study
III	Well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, case–control studies and case series
IV	Expert committee reports, opinions and/or clinical experience of respected authorities

Table 7: Grading of recommendations

Grade	Basis for recommendation
A	Based directly based on level I evidence
B	Based directly on level II evidence or extrapolated from level I evidence
C	Based directly on level III evidence or extrapolated from level I or level II evidence
D	Based directly on level IV evidence or extrapolated from level I, level II or level III evidence
GPP	Good practice point based on the view of the Guideline Development Group
NICE TA	Recommendation taken from a NICE Technology Appraisal

Recommendations

Management of type 2 diabetes – dietary and weight loss advice and oral drug treatment

Dietary management

1.3.13 At each contact with a child or young person with type 2 diabetes who is overweight or obese, advise them and their families or carers about the benefits of exercise and weight loss, and provide support towards achieving this. See also the NICE guidelines on maintaining a healthy weight and managing obesity. [2015]

1.3.14 Offer children and young people with type 2 diabetes dietetic support to help optimise body weight and blood glucose levels. [2004, amended 2015]

1.3.15 At each contact with a child or young person with type 2 diabetes, explain to them and their families or carers how healthy eating can help to:

- reduce hyperglycaemia
- reduce cardiovascular risk
- promote weight loss (see recommendation 1.3.13). [2015]

1.3.16 Provide dietary advice to children and young people with type 2 diabetes and their families or carers in a sensitive manner. Take into account the difficulties that many people have with losing weight, and how healthy eating can also help with blood glucose levels and avoiding complications. [2015]

1.3.17 Take into account social and cultural considerations when providing dietary advice to children and young people with type 2 diabetes. [2015]

1.3.18 Encourage children and young people with type 2 diabetes to eat at least 5 portions of fruit and vegetables each day. [2015]

1.3.19 At each clinic visit for children and young people with type 2 diabetes:

- measure height and weight and plot on an appropriate growth chart
- calculate BMI.

Check for normal growth or significant changes in weight, because these may reflect changes in blood glucose levels. [2004, amended 2015]

1.3.20 Provide arrangements for weighing children and young people with type 2 diabetes that respect their privacy. [2004, amended 2015]

Metformin

1.3.21 Offer standard-release metformin from diagnosis to children and young people with type 2 diabetes. [2015]

Evidence profile: A single RCT was identified for inclusion for this review question (Jones 2002). This study involved 82 children and young people with type 2 diabetes (age range 10 to 17 years) and compared metformin (dose up to 2000 mg/day) with matching placebo for up to 16 weeks.

Table 56: Evidence profile for effectiveness of metformin in improving glycaemic control in children and young people with type 2 diabetes when compared with placebo

Number of studies	Number of children and young people		Effect		Quality
	Metformin	Placebo	Relative (95% confidence interval)	Absolute (95% confidence interval)	
HbA1c value (% at endpoint)					
1 (Jones 2002)	36	36	NA	MD between the groups at endpoint 1.1 lower (1.19 lower to 1.01 lower)[a]	High
Number needing rescue medication					
1 (Jones 2002)	4/42 (9.5%)	26/40 (65%)	RR 0.15 (0.06 to 0.4)	552 fewer per 1000 (from 390 fewer to 611 fewer)	High
Number reporting any adverse event (including number with DKA)					
1 (Jones 2002)	29/42 (69%)	24/40 (60%)	RR 1.15 (0.83 to 1.59)	90 more per 1000 (from 102 fewer to 354 more)	High
Number of dropouts					
1 (Jones 2002)	6/42 (14.3%)	4/40 (10%)	RR 1.43 (0.42 to 3.91)	43 more per 1000 (from 58 fewer to 291 more)	High
FPG concentration (change from baseline, mmol/l)					
1 (Jones 2002)	36	36	NA	MD between the groups 3.6 lower (3.83 lower to 3.37 lower)[b]	High

DKA diabetic ketoacidosis, FPG fasting plasma glucose, MD mean difference, NA not applicable, RR relative risk
a. Adjusted mean HbA1c at baseline (%), metformin 7.2±1.2, placebo 8.6±0.2
b. No apparent risk of bias in the included study

The quality of the evidence for all of the following was high.

One study (total 72 participants) showed a reduction in HbA1c was associated with the use of metformin monotherapy in children and young people with type 2 diabetes.

One study (total 82 participants) showed a smaller proportion of participants needing rescue medication following the use of metformin in children and young people with type 2 diabetes.

One study (total 72 participants) showed a reduction in FPG was associated with the use of metformin in children and young people with type 2 diabetes.

One study (total 82 participants) showed that the numbers of participants for whom adverse events (including DKA) were reported was similar for both treatment groups.

One study (total 82 participants) showed that the number of dropouts was similar for both treatment groups.

There was no evidence for outcomes relating to changes in BMI or patient satisfaction with treatment.

HbA1c targets and monitoring:

1.3.22 Measure HbA1c using methods that have been calibrated according to International Federation of Clinical Chemistry (IFCC) standardisation. [2015]

1.3.23 Explain to children and young people with type 2 diabetes and their families or carers that an HbA1c target level of 48 mmol/mol (6.5%) or lower will minimise their risk of long-term complications. [2015]

1.3.24 Explain to children and young people with type 2 diabetes who have an HbA1c level above 48 mmol/mol (6.5%) that any reduction in HbA1c level reduces their risk of long-term complications. [2015]

1.3.25 Explain the benefits of safely achieving and maintaining the lowest attainable HbA1c to children and young people with type 2 diabetes and their families or carers. [2015]

1.3.26 Agree an individualised lowest achievable HbA1c target with each child or young person with type 2 diabetes and their families or carers. Take into account factors such as their daily activities, individual life goals, complications and comorbidities. [2015]

1.3.27 Measure HbA1c levels every 3 months in children and young people with type 2 diabetes. [2015]

1.3.28 Support children and young people with type 2 diabetes and their families or carers to safely achieve and maintain their individual agreed HbA1c target level. [2015]

1.3.29 Diabetes services should document the proportion of children and young people with type 2 diabetes who achieve an HbA1c level of 53 mmol/mol (7%) or lower. [2015]

References:
Jones,K.L., Arslanian,S., Peterokova,V.A., Park,J.S., Tomlinson,M.J., Effect of metformin in pediatric patients with type 2 diabetes: a randomized controlled trial, Diabetes Care, 25, 89-94, 2002

Peña AS et al., 2020 [3].

Screening, assessment and management of type 2 diabetes mellitus in children and adolescents: Australasian Paediatric Endocrine Group guidelines.

Zielsetzung/Fragestellung

Assessment and management of paediatric type 2 diabetes at all levels of care (eg, general practitioners, paediatricians, paediatric endocrinologists, allied health care professionals).

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium (Patientenbeteiligung unklar / wird nicht berichtet)
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt;
- Systematische Suche, Auswahl und Bewertung der Evidenz;
- Konsensusprozess nicht beschrieben; externes Begutachtungsverfahren dargelegt;
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt;
- keine Angaben zur Überprüfung der Aktualität

Recherche/Suchzeitraum:

- Searches were done until February 2019 except the pharmacotherapy one that was done until May 2019

LoE/GoR

1 National Health and Medical Research Council (NHMRC) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) levels of evidence

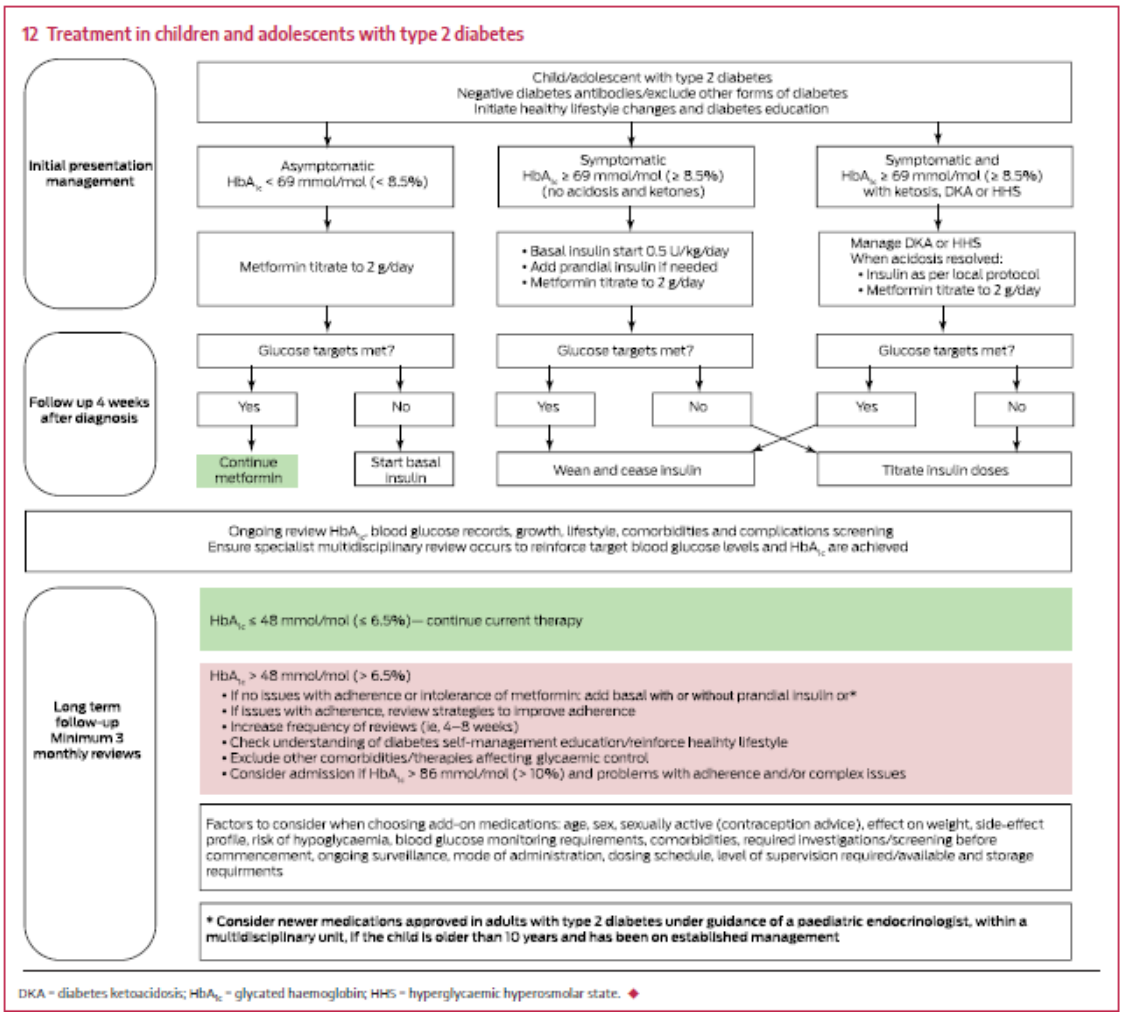
GRADE definition and NHMRC levels of evidence	A Excellent	B Good	C Satisfactory	D Poor
Definition	Body of evidence can be trusted to guide practice	Body of evidence can be trusted to guide practice in most situations	Body of evidence provides some support for recommendations but care should be taken in its application	Body of evidence is weak and recommendation should be applied with caution
Evidence base	Several level I or II studies with low risk of bias	One or more level II studies with low risk of bias	Level III studies with low risk of bias, or level II studies with moderate risk of bias	Level IV studies or level I to III with high risk of bias
Consistency	All studies consistent	Most studies consistent and inconsistencies may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Populations studied in body of evidence are the same as the target population for the guideline	Populations studied in body of evidence are similar to the target population for the guideline	Populations studied in body of evidence differ to target population for guideline but it is clinically sensible to apply this evidence to target population	Populations studied in body of evidence differ from target population and it is hard to judge whether it is sensible to generalise to target population
Applicability	Directly applicable to Australian health care context	Applicable to Australian health care context with few caveats	Probably applicable to Australian health care context with some caveats	Not applicable to Australia health care context
GRADE quality of evidence and definition	High quality. Further research is unlikely to change our confidence in the estimate of effect	Moderate quality. Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	Low quality. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	Very low quality. Any estimate of effect is very uncertain

Recommendations

Guidelines sections and subsections	Recommendations	GRADE category
Pharmacotherapy	Metformin up to 2 g per day should be used as the first line medication in patients presenting with mild symptoms or in those who are diagnosed after screening	A
	Insulin should be the first line treatment for patients who present with diabetes ketoacidosis, hyperglycaemic hyperosmolar state or ketosis, and should be added to metformin where glycaemic targets have not been achieved or maintained with metformin monotherapy	B
	If glycaemic targets are not achieved with metformin (with or without insulin), other glucose-lowering medications approved for adults should be considered. Such medications should only be prescribed under the guidance of a paediatric endocrinologist, given limited evidence for safety and efficacy in children and adolescents	D
Complications and comorbidities	Screen for all complications and comorbidities soon after diagnosis of type 2 diabetes to establish prompt management and ongoing assessment and management†	A
Retinopathy	Assess retina using dilated pupil exam or retinal photography by an optometrist or ophthalmologist at diagnosis and yearly unless abnormal†	A
Nephropathy	Assess early morning urine albumin to creatinine ratio at diagnosis and yearly unless abnormal†	A
Neuropathy	Foot examination at diagnosis and yearly unless abnormal†	C
Overweight/obesity	Optimise weight management as well as glycaemia to reduce risk of comorbidities and complications†	B
	Consider bariatric surgery for selected post-pubertal adolescents with type 2 diabetes with severe obesity, taking into account special considerations in relation to consent, procedure, family support and availability of adequate services†	C
Psychosocial	Quick screening tools for psychosocial comorbidities and diabetes distress should be used regularly after diagnosis†	B
	Consider screening for disordered eating behaviour†	D
Reproductive health	For adolescent girls, a review of menstrual cycle regularity, symptoms and signs of hyperandrogenism, and need of contraception should be done at every visit, especially if the HbA_{1c} level is above target or the patient is using teratogenic medications†	B
Liver disease	Assess liver function test (aspartate aminotransferase and alanine aminotransferase) at diagnosis and yearly unless abnormal†	B
Obstructive sleep apnoea	Evaluate symptoms of obstructive sleep apnoea in children and adolescents with obesity†	C
Hypertension	Assess blood pressure using appropriate cuff at every visit†	A
Lipids	Assess lipid profile when glycaemic targets have been achieved after diagnosis and yearly unless abnormal†	B
Transition	Transition to adult endocrinologist within a multidisciplinary team due to the severity of disease progression and higher risk of diabetes complications	C

BMI = body mass index; GRADE = Grading of Recommendations Assessment, Development and Evaluation; HbA_{1c} = glycated haemoglobin. * This will also apply to non-Indigenous adolescents. † Refer to Box 13. ◆

Healthy lifestyle	Weight management and multicomponent approach to lifestyle modification is required at diagnosis and ongoing	C
Weight management	Optimise weight management	B
Diet	Aim for healthy eating: eliminate sugar-sweetened beverages, reduce calorie-dense and nutrient-poor foods, provide education regarding carbohydrates (role, sources, portion control and, if appropriate, counting of carbohydrates) and ensure adequate intake of nutrient-dense and low glycaemic index foods	B
	Reduce total energy intake to achieve ≥ 7% decrease in excess weight	B
Physical activity	Aim for at least 60 min/day of moderate to vigorous physical activity to improve body composition, glucose management and insulin sensitivity	B
	Exercise programs should include resistance activities to increase muscle mass, contributing to improved blood glucose management	B
Sedentary behaviour	Recreational screen time should be limited to ≤ 2 hours a day	C
Sleep	Encourage quality sleep of 8–11 hours duration according to age, with consistent bed and wake-up times and reduction of electronic media use in the evening	C



ADA, 2021 [1].

American Diabetes Association (ADA)

Standards of Medical Care in Diabetes 2021.

Zielsetzung/Fragestellung

Management of Diabetes.

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 im Hintergrundtextbeschrieben;
- Regelmäßige Überprüfung der Aktualität gesichert.

Recherche/Suchzeitraum:

- Through july 1th 2020. Critical updates through 1 September 2020.

LoE/GoR

Table 1—ADA evidence-grading system for "Standards of Medical Care in Diabetes"

Level of evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including • Evidence from a well-conducted multicenter trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis Compelling nonexperimental evidence, i.e., "all or none" rule developed by the Centre for Evidence-Based Medicine at the University of Oxford Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including • Evidence from a well-conducted trial at one or more institutions • Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Supportive evidence from well-conducted cohort studies • Evidence from a well-conducted prospective cohort study or registry • Evidence from a well-conducted meta-analysis of cohort studies Supportive evidence from a well-conducted case-control study
C	Supportive evidence from poorly controlled or uncontrolled studies • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • Evidence from case series or case reports Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience

Recommendations

13. Children and Adolescents: Standards of Medical Care in Diabetes -2021 / Type 2 Diabetes

- Glycemic Targets
  - 13.60 Home self-monitoring of blood glucose regimens should be individualized, taking into consideration the pharmacologic treatment of the patient. E
  - 13.61 Glycemic status should be assessed every 3 months. E
  - 13.62 A reasonable A1C target for most children and adolescents with type 2 diabetes treated with oral agents alone is ,7% (53mmol/mol).More stringent A1C targets (such as ,6.5% [48 mmol/mol]) may be appropriate for selected individual patients if they can be achieved without significant hypoglycemia or other adverse effects of treatment. Appropriate patients might include those with short duration of diabetes

and lesser degrees of b-cell dysfunction and patients treated with lifestyle or metformin only who achieve significant weight improvement. E

- 13.63 Less stringent A1C goals (such as 7.5% [58mmol/mol]) maybe appropriate if there is increased risk of hypoglycemia. E
- 13.64 A1C targets for patients on insulin should be individualized, taking into account the relatively low rates of hypoglycemia in youth-onset type 2 diabetes. E

- Pharmacologic Management
  - 13.65 Initiate pharmacologic therapy, in addition to behavioral counseling for healthful nutrition and physical activity changes, at diagnosis of type 2 diabetes. A
  - 13.66 In incidentally diagnosed or metabolically stable patients (A1C, <8.5% [69 mmol/mol] and asymptomatic), metformin is the initial pharmacologic treatment of choice if renal function is normal. A
  - 13.67 Youth with marked hyperglycemia (blood glucose >250 mg/dL [13.9 mmol/L], A1C ≥8.5% [69 mmol/mol]) without acidosis at diagnosis who are symptomatic with polyuria, polydipsia, nocturia, and/or weight loss should be treated initially with basal insulin while metformin is initiated and titrated. B
  - 13.68 In patients with ketosis/ ketoacidosis, treatment with subcutaneous or intravenous insulin should be initiated to rapidly correct the hyperglycemia and the metabolic derangement. Once acidosis is resolved, metformin should be initiated while subcutaneous insulin therapy is continued. A
  - 13.69 In individuals presenting with severe hyperglycemia (blood glucose ≥600 mg/dL [33.3 mmol/L]), consider assessment for hyperglycemic hyperosmolar nonketotic syndrome. A
  - 13.70 If glycemic targets are no longer met with metformin (with or without basal insulin), liraglutide (a glucagon-like peptide 1 receptor agonist) therapy should be considered in children 10 years of age or older if they have no past medical history or family history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2. A
  - 13.71 Patients treated with basal insulin who do not meet glycemic target should be moved to multiple daily injections with basal and premeal bolus insulins. E
  - 13.72 In patients initially treated with insulin and metformin who are meeting glucose targets based on home blood glucose monitoring, insulin can be tapered over 2–6 weeks by decreasing the insulin dose 10–30% every few days. B
  - 13.73 Use of medications not approved by the U.S. Food and Drug Administration for youth with type 2 diabetes is not recommended outside of research trials. B

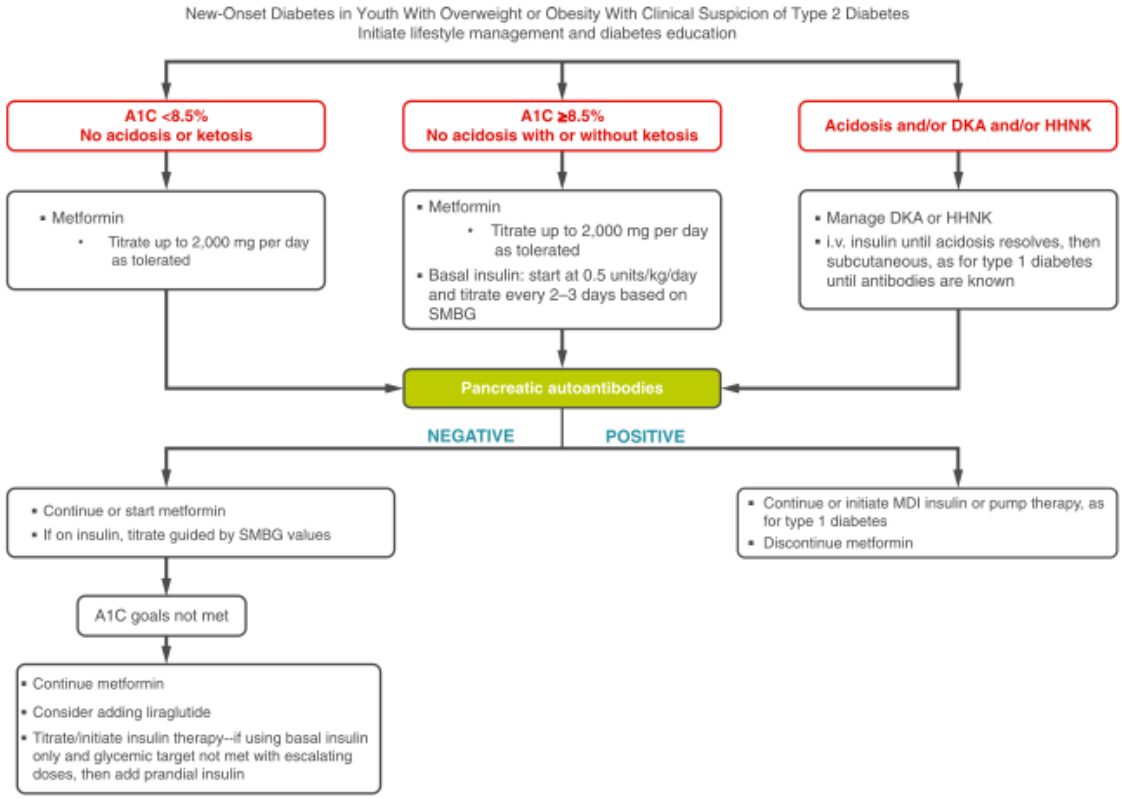


Figure 13.1—Management of new-onset diabetes in youth with overweight or obesity with clinical suspicion of type 2 diabetes. A1C 8.5% = 69 mmol/mol. Adapted from the ADA position statement "Evaluation and Management of Youth-Onset Type 2 Diabetes" (2). DKA, diabetic ketoacidosis; HHNK, hyperosmolar hyperglycemic nonketotic syndrome; MDI, multiple daily injections; SMBG; self-monitoring of blood glucose.

- TRANSITION FROM PEDIATRIC TO ADULT CARE
  - 13.110 Pediatric diabetes providers should begin to prepare youth for transition to adult health care in early adolescence and, at the latest, at least 1 year before the transition. E
  - 13.111 Both pediatric and adult diabetes care providers should provide support and resources for transitioning young adults. E
  - 13.112 Youth with type 2 diabetes should be transferred to an adult-oriented diabetes specialist when deemed appropriate by the patient and provider. E

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 11 of 12, November 2021) am 16.11.2021

#	Suchfrage
1	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees
2	(t2dm OR dmt2 OR niddm OR mody):ti
3	(diabetes OR dm):ti
4	("adult onset" OR "maturity onset" OR young OR (non NEXT insulin NEXT dependan*) OR (noninsulin NEXT dependan*) OR "slow onset" OR (ketosis NEXT resistan*) OR "type 2" OR "type II" OR t2 OR tII OR ("t 2") OR ("t II")):ti
5	#3 AND #4
6	#1 OR #2 OR #5
7	#6 with Cochrane Library publication date Between Nov 2016 and Nov 2021

Systematic Reviews in Medline (PubMed) am 15.11.2021

verwendete Suchfilter:

Konsentierter Standardfilter für Systematische Reviews (SR), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 02.01.2020.

The Cochrane Childhood Cancer search strategy for identifying studies including Children [C]

#	Suchfrage
1	"diabetes mellitus, type 2"[MeSH Terms]
2	(T2DM[Title/Abstract] OR DMT2[Title/Abstract] OR NIDDM[Title/Abstract] OR MODY[Title/Abstract])
3	(Diabetes[Title/Abstract] OR dm[Title/Abstract])
4	"adult onset"[Title/Abstract] OR "maturity onset"[Title/Abstract] OR young[Title/Abstract] OR (non-insulin dependan*[Title/Abstract]) OR noninsulin dependan*[Title/Abstract] OR "slow onset"[Title/Abstract] OR ketosis resistan*[Title/Abstract] OR "type 2"[Title/Abstract] OR "type II"[Title/Abstract] OR "T 2"[Title/Abstract] OR T2[Title/Abstract] OR TII[Title/Abstract] OR "T II"[Title/Abstract]
5	(#3 AND #4)
6	(#1 OR #2 OR #5)
7	(metformin[MeSH Terms]) OR metformin[Title/Abstract] OR Dimethylbiguanidine[Title/Abstract] OR Dimethylguanylguanidine[Title/Abstract] OR Glucophage[Title/Abstract]
8	insulins[MeSH Terms] OR insulin*[Title/Abstract]

#	Suchfrage
9	(Sulfonylurea Compounds[MeSH Terms]) OR (Sulfonylurea*[Title/Abstract] OR Sulphonylurea*[Title/Abstract])
10	Liraglutide[MeSH Terms] OR Liraglutid*[tiab] OR Lira[tiab] OR NN-2211[tiab] OR NN2211[tiab] OR Saxenda[tiab] OR Victoza[tiab]
11	Hypoglycemic Agents[MeSH Terms] OR Antidiabetics[Title] OR Anti-diabetics[Title] OR Antihyperglycemics[Title] OR Antihyperglycaemics[Title] OR Hypoglycemics[Title] OR Hypoglycaemics[Title]
12	(Antidiabetic*[Title] OR Anti-diabetic*[Title] OR Antihyperglycemic*[Title] OR Antihyperglycaemic*[Title] OR Hypoglycemic*[Title] OR Hypoglycaemic*[Title]) AND (Agent*[Title] OR drug*[Title] OR effect*[Title])
13	#7 OR #8 OR #9 OR #10 OR #11 OR #12
14	infan* OR newborn* OR new-born* OR perinat* OR neonat* OR baby OR baby* OR babies OR toddler* OR minors OR minors* OR boy OR boys OR boyfriend OR boyhood OR girl* OR kid OR kids OR child OR children* OR schoolchild* OR schoolchild OR "school child"[tiab] OR school child*[tiab] OR adolescen* OR juvenil* OR youth* OR teen* OR under*age* OR pubescen* OR pediatrics[mh] OR pediatric* OR paediatric* OR peadiatric* OR school[tiab] OR school*[tiab] OR prematur* OR preterm* OR infant[mh] OR child[mh] OR adolescent[mh]
15	#5 AND #13 AND #14
16	(#15) AND (((Meta-Analysis[ptyp] OR systematic[sb] OR ((systematic review [ti] OR meta-analysis[pt] OR meta-analysis[ti] OR systematic literature review[ti] OR this systematic review[tw] OR pooling project[tw] OR (systematic review[tiab] AND review[pt]) OR meta synthesis[ti] OR meta-analy*[ti] OR integrative review[tw] OR integrative research review[tw] OR rapid review[tw] OR umbrella review[tw] OR consensus development conference[pt] OR practice guideline[pt] OR drug class reviews[ti] OR cochrane database syst rev[ta] OR acp journal club[ta] OR health technol assess[ta] OR evid rep technol assess summ[ta] OR jbi database system rev implement rep[ta]) OR (clinical guideline[tw] AND management[tw]) OR ((evidence based[ti] OR evidence-based medicine[mh] OR best practice*[ti] OR evidence synthesis[tiab]) AND (review[pt] OR diseases category[mh] OR behavior and behavior mechanisms[mh] OR therapeutics[mh] OR evaluation study[pt] OR validation study[pt] OR guideline[pt] OR pmcbook)) OR ((systematic[tw] OR systematically[tw] OR critical[tiab] OR (study selection[tw]) OR (predetermined[tw] OR inclusion[tw] AND criteri* [tw]) OR exclusion criteri*[tw] OR main outcome measures[tw] OR standard of care[tw] OR standards of care[tw]) AND (survey[tiab] OR surveys[tiab] OR overview*[tw] OR review[tiab] OR reviews[tiab] OR search*[tw] OR handsearch[tw] OR analysis[ti] OR critique[tiab] OR appraisal[tw] OR (reduction[tw] AND (risk[mh] OR risk[tw]) AND (death OR recurrence))) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR publication [tiab] OR bibliography[tiab] OR bibliographies[tiab] OR published[tiab] OR pooled data[tw] OR unpublished[tw] OR citation[tw] OR citations[tw] OR database[tiab] OR internet[tiab] OR textbooks[tiab] OR references[tw] OR scales[tw] OR papers[tw] OR datasets[tw] OR trials[tiab] OR meta-analy*[tw] OR (clinical[tiab] AND studies[tiab]) OR treatment outcome[mh] OR treatment outcome[tw] OR pmcbook)) NOT (letter[pt] OR newspaper article[pt])) OR Technical Report[ptyp]) OR (((((trials[tiab] OR studies[tiab] OR database*[tiab] OR

#	Suchfrage
	literature[tiab] OR publication*[tiab] OR Medline[tiab] OR Embase[tiab] OR Cochrane[tiab] OR Pubmed[tiab])) AND systematic*[tiab] AND (search*[tiab] OR research*[tiab]))) OR ((((((((((HTA[tiab]) OR technology assessment*[tiab]) OR technology report*[tiab]) OR (systematic*[tiab] AND review*[tiab])) OR (systematic*[tiab] AND overview*[tiab])) OR meta-analy*[tiab]) OR (meta[tiab] AND analyz*[tiab])) OR (meta[tiab] AND analys*[tiab])) OR (meta[tiab] AND analyt*[tiab]))) OR (((review*[tiab]) OR overview*[tiab]) AND ((evidence[tiab]) AND based[tiab]))))))
17	(#16) AND ("2016/11/01"[PDAT] : "3000"[PDAT])
18	(#17) NOT "The Cochrane database of systematic reviews"[Journal]
19	(#18) NOT (retracted publication [pt] OR retraction of publication [pt])

Leitlinien in Medline (PubMed) am 16.11.2021

verwendete Suchfilter:

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

The Cochrane Childhood Cancer search strategy for identifying studies including Children [C]

#	Suchfrage
1	"diabetes mellitus, type 2"[MeSH Terms]
2	(T2DM[Title/Abstract] OR DMT2[Title/Abstract] OR NIDDM[Title/Abstract] OR MODY[Title/Abstract])
3	(Diabetes[Title/Abstract] OR dm[Title/Abstract])
4	"adult onset"[Title/Abstract] OR "maturity onset"[Title/Abstract] OR young[Title/Abstract] OR (non insulin dependan*[Title/Abstract]) OR noninsulin dependan*[Title/Abstract] OR "slow onset"[Title/Abstract] OR ketosis resistan*[Title/Abstract] OR "type 2"[Title/Abstract] OR "type II"[Title/Abstract] OR "T 2"[Title/Abstract] OR T2[Title/Abstract] OR TII[Title/Abstract] OR "T II"[Title/Abstract]
5	(#3 AND #4)
6	(#1 OR #2 OR #5)
7	infan* OR newborn* OR new-born* OR perinat* OR neonat* OR baby OR baby* OR babies OR toddler* OR minors OR minors* OR boy OR boys OR boyfriend OR boyhood OR girl* OR kid OR kids OR child OR children* OR schoolchild* OR schoolchild OR "school child"[tiab] OR school child*[tiab] OR adolescen* OR juvenil* OR youth* OR teen* OR under*age* OR pubescen* OR pediatrics[mh] OR pediatric* OR paediatric* OR peadiatric* OR school[tiab] OR school*[tiab] OR prematur* OR preterm* OR infant[mh] OR child[mh] OR adolescent[mh]

#	Suchfrage
8	(Guideline[ptyp] OR Practice Guideline[ptyp] OR guideline*[Title] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] OR recommendation*[ti])
9	#6 AND #7 AND #8
10	(#9) AND ("2016/11/01"[PDAT] : "3000"[PDAT])
11	(#10) NOT (retracted publication [pt] OR retraction of publication [pt])

Referenzen

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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 fristgerecht eingegangenen schriftlichen Rückmeldungen gem. § 7 Absatz 6 VerfO