Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

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

Vorgang: 2018-B-128-Fidaxomicin

Stand: August 2018

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

Fidaxomicin (2018-B-128)
[zur Behandlung von *Clostridium-difficile*-Infektionen bei Patienten unter 18 Jahren]

Kriterien gemäß 5. Kapitel § 6 VerfO	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	Arzneimittel zur Behandlung einer *Clostridium-difficile*-Infektion: 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.	Stuhltransplantation („Applikation einer Spenderstuhlsuspension“)
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	Beschluss des Gemeinsamen Bundesausschusses über eine Änderung der Arzneimittel-Richtlinie (AM-RL) Anlage XII: Fidaxomicin vom 04.07.2013
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:	
Fidaxomicin A07AA12 Dificlir®	zur Behandlung von *Clostridium-difficile*-Infektionen (CDI), auch bekannt unter der Bezeichnung *Clostridium-difficile*-assoziierte Diarrhö (CDAD) bei Patienten unter 18 Jahren (bereits zugelassen: DIFICLIR ist indiziert bei Erwachsenen zur Behandlung von *Clostridium-difficile*-Infektionen (CDI), auch bekannt unter der Bezeichnung *Clostridium-difficile*-assoziierte Diarrhö (CDAD) (siehe Abschnitt 5.1). Offizielle Leitlinien zum angemessenen Gebrauch von Antibiotika sollten berücksichtigt werden.)
Metronidazol P01AB01 Arilin®	Arilin 500 mg wird angewendet bei Erwachsenen und Kindern über 6 Jahren. Arilin 500 mg ist angezeigt zur Behandlung von: […] - Infektionen mit Beteiligung von Anaerobiern, besonders Infektionen, die vom weiblichen Genitale, Magen-Darm-Trakt, Hals-Nasen-Ohren- und Zahn-Mund-Kiefer-Bereich ausgehen […] Die offiziellen Richtlinien für den angemessenen Gebrauch von antimikrobiellen Wirkstoffen sind bei der Anwendung von Metronidazol zu berücksichtigen. 5.1 Pharmakodynamische Eigenschaften (Ausschnitt):

Üblicherweise empfindliche Spezies
Anaerobe Mikroorganismen
Bacteroides fragilis
Clostridium difficile
Clostridium perfringens°Δ
Fusobacterium spp.°
Peptoniphilus spp.°
Peptostreptococcus spp.°
Porphyromonas spp.°
Prevotella spp.°
Veillonella spp.°

II. Zugelassene Arzneimittel im Anwendungsgebiet

<table>
<tr><td>Metronidazol
Infusionslösung
J01XD01</td><td>Metronidazol ist bei Erwachsenen und Kindern für die folgenden Indikationen angezeigt: […]
- Infektionen des Gastrointestinaltraktes (z. B. Peritonitis, Leberabszes, Infektionen nach Kolo-Rektaloperationen, eitrige Erkrankungen des Bauch- und Beckenraumes)
[…] Die offiziellen Richtlinien für den angemessenen Gebrauch von antimikrobiellen Wirkstoffen sind bei der Anwendung von Metronidazol zu berücksichtigen.
5.1 Pharmakodynamische Eigenschaften (Ausschnitt):
<table><tr><th>Üblicherweise empfindliche Spezies</th></tr><tr><td>Anaerobe Mikroorganismen</td></tr><tr><td>Bacteroides fragilis</td></tr><tr><td>Clostridium difficile</td></tr><tr><td>Clostridium perfringens°Δ</td></tr><tr><td>Fusobacterium spp.°</td></tr><tr><td>Peptoniphilus spp.°</td></tr><tr><td>Peptostreptococcus spp.°</td></tr><tr><td>Porphyromonas spp.°</td></tr><tr><td>Prevotella spp.°</td></tr><tr><td>Veillonella spp.°</td></tr></table></td></tr>
<tr><td>Teicoplanin
J01XA02
Targocid®</td><td>[…] Targocid ist auch angezeigt zur oralen Anwendung als Alternativbehandlung von durch Infektion mit Clostridium difficile verursachter Diarrhö und Kolitis.
Targocid sollte falls erforderlich in Kombination mit anderen antibakteriellen Arzneimitteln eingesetzt werden. Offizielle Empfehlungen zum angemessenen Gebrauch von Antibiotika sollten berücksichtigt werden.</td></tr>
<tr><td>Vancomycin
A07AA09
Vanco-saar®</td><td>Bei oraler Anwendung: Vancomycin-Pulver kann nach Auflösen eingenommen werden zur Behandlung bestimmter Darmentzündungen:
- antibiotikabedingter pseudomembranöser Enterokolitis (z. B. durch Clostridium difficile) […]
Parenteral angewandt ist Vancomycin bei diesen Erkrankungen nicht wirksam. […]</td></tr>
</table>

Quellen: AMIS-Datenbank, Fachinformationen. Stand August 2018.

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

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

Vorgang: 2018-B-128 (Fidaxomicin)

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	20. Juli 2018

Inhaltsverzeichnis

Abkürzungsverzeichnis

AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
CDAD	Clostridium-difficile-assoziierte Diarrhö
CDI	Clostridium-difficile-Infektion
DAHTA	DAHTA Datenbank
FMT	Fecal microbiota transplantation (Stuhltransplantation)
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
NGC	National Guideline Clearinghouse
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

Zur Behandlung von Clostridium-difficile-Infektionen (CDI), auch bekannt unter der Bezeichnung Clostridium-diffizile-assoziierte Diarrhö (CDAD) bei Patienten unter 18 Jahren.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen, HTA-Berichten und evidenzbasierten systematischen Leitlinien zur Indikation *Clostridium difficile* durchgeführt. Der Suchzeitraum wurde auf die letzten 5 Jahre eingeschränkt und die Recherche am 15.06.2018 abgeschlossen. Die Suche erfolgte in den aufgeführten Datenbanken bzw. Internetseiten folgender Organisationen: The Cochrane Library (Cochrane Database of Systematic Reviews, Health Technology Assessment Database), MEDLINE (PubMed), AWMF, DAHTA, G-BA, GIN, IQWiG, NGC, NICE, TRIP, SIGN, WHO. Ergänzend erfolgte eine freie Internetsuche nach aktuellen deutschen und europäischen Leitlinien. Die detaillierte Darstellung der Suchstrategie ist am Ende der Synopse aufgeführt.

Die Recherche ergab 411 Quellen, die anschließend in einem zweistufigen Screening-Verfahren nach Themenrelevanz und methodischer Qualität gesichtet wurden. Zudem wurde eine Sprachrestriktion auf deutsche und englische Quellen vorgenommen. Insgesamt ergab dies 4 Quellen, die in die synoptische Evidenz-Übersicht aufgenommen wurden.

3 Ergebnisse

3.1 IQWiG Berichte/G-BA Beschlüsse

G-BA, 2013 [1].

Titel des Beschlusses

Beschluss des Gemeinsamen Bundesausschusses über eine Änderung der Arzneimittel-Richtlinie (AM-RL): Anlage XII - Beschlüsse über die Nutzenbewertung von Arzneimitteln mit neuen Wirkstoffen nach § 35a SGB V – Fidaxomicin

Siehe auch IQWiG, 2013 [3] und IQWiG, 2013 [2].

Anwendungsgebiet

DIFICLIR® ist indiziert bei Erwachsenen zur Behandlung von Clostridium-difficile-Infektionen (CDI), auch bekannt unter der Bezeichnung Clostridium-difficile-assoziierte Diarrhö (CDAD). Offizielle Leitlinien zum angemessenen Gebrauch von Antibiotika sollten berücksichtigt werden.

a) Patienten mit milden behandlungspflichtigen Krankheitsverläufen von Clostridium-difficile-assoziierten Diarrhöen

Zweckmäßige Vergleichstherapie

Metronidazol

Fazit / Ausmaß des Zusatznutzens / Ergebnis

Ein Zusatznutzen ist nicht belegt.

b) Patienten mit schweren und/ oder rekurrenten Krankheitsverläufen von Clostridium-difficile-assoziierten Diarrhöen

Zweckmäßige Vergleichstherapie

Vancomycin

Fazit / Ausmaß des Zusatznutzens / Ergebnis

Beleg für einen beträchtlichen Zusatznutzen

3.2 Cochrane Reviews

Es wurden keine relevanten Quellen identifiziert.

3.3 Systematische Reviews

Es wurden keine relevanten Quellen identifiziert.

3.4 Leitlinien

McDonald LC et al., 2018 [4].

Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

Fragestellung

"Clinical practice guidelines are statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options"

Methodik

Grundlage der Leitlinie

Panel Composition

- 14 multidisciplinary experts
- A systematic evidence-based approach was adopted for the guideline questions and population, intervention,
- comparator, outcome (PICO) formulations, the selection of patient-important outcomes, as well as the literature searches and screening of the uncovered citations and articles.
- The rating of the quality of evidence and strength of recommendation was supported by a Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodologist.

Literature Review and Analysis:

- search strategies, in collaboration with the guideline panel members, were developed and built by independent health sciences librarians
- In addition, the strategies focused on articles published in English or in any language with available English abstracts. The Ovid platform was used to search 5 electronic evidence databases: Medline, Embase, Cochrane Central Registry of Controlled Trials, Health Technology Assessment, and the Database of Abstracts of Reviews of Effects.
- Additionally hand-searched relevant journals, conference proceedings, reference lists from manuscripts retained from electronic searches, and regulatory agency web sites for relevant articles.

Process Overview

- The process for evaluating the evidence was based on the IDSA Handbook on Clinical Practice Guideline Development and involved a systematic weighting of the quality of the evidence and the grade of recommendation using the GRADE system
- Each author was asked to review the literature (based on screening examination of titles and abstracts and manuscript full-text examination, as well as abstraction of relevant variables/data from eligible studies/reports), evaluate the evidence, and determine the strength of the recommendations along with an evidence summary supporting each recommendation.

- The panel reviewed all recommendations, their strength, and quality of evidence. For recommendations in the category of good practice statements that should not be graded, we followed published principles by the GRADE working group on how to identify such recommendations and use appropriate wording choices.
- Discrepancies were discussed and resolved, and all panel members are in agreement with the final recommendations.

Consensus Development Based on Evidence

- The panel met face-to-face on 3 occasions and conducted numerous monthly subgroup and full panel conference calls to complete the work of the guideline.
- The panel as a whole reviewed all individual sections.
- The guideline was reviewed and approved by the IDSA Standards and Practice Guidelines Committee (SPGC) and SHEA Guidelines Committee as well as both organizations' respective Board of Directors (BOD).
- The guideline was endorsed by ASHP, SIDP, and PIDS.

Conflicts of Interest: reported for each member of the guideline group

<u>Recherche/Suchzeitraum:</u>

- 4 December 2012, updated on 3 March 2014, and further extended to 31 December 2016

<u>LoE/GoR</u>

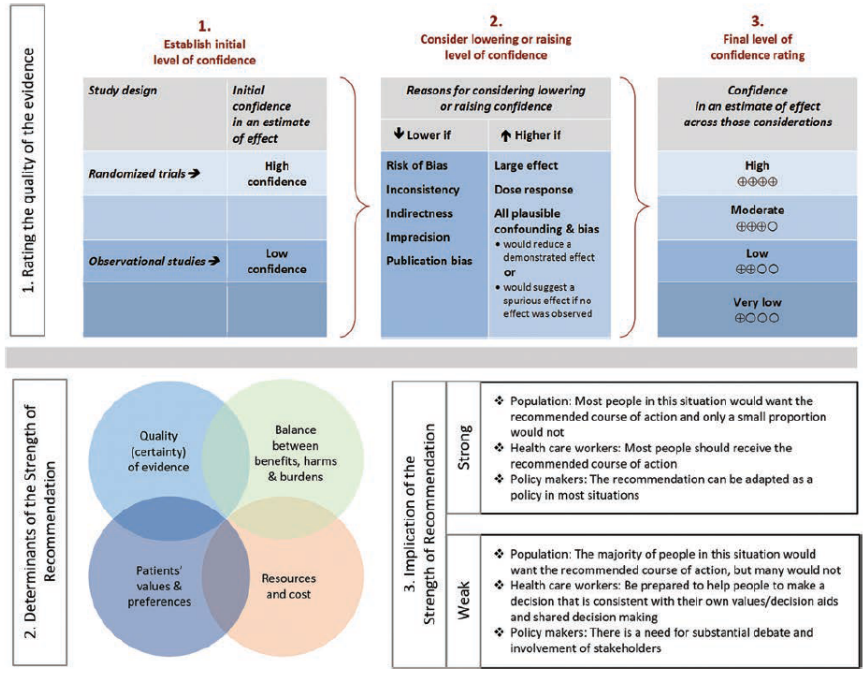

Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using the *Grading* of Recommendations, Assessment, Development and Evaluation (GRADE) methodology (unrestricted use of this figure granted by the US GRADE Network) [1–4].

TREATMENT (PEDIATRIC CONSIDERATIONS)

Empfehlung XXXII. What is the best treatment of an initial episode or first recurrence of nonsevere CDI in children?

Either metronidazole or vancomycin is recommended for the treatment of children with an initial episode or first recurrence of nonsevere CDI (see Pediatric treatment section for dosing) (weak recommendation, low quality of evidence) (Table 2).

Summary of the Evidence:

Robust data assessing the optimal approach for treating an initial episode of CDI in children are limited, and evidence of the comparative effectiveness of metronidazole and vancomycin for treating pediatric CDI is lacking. There are no RCTs comparing the use of these agents in children. A few recent studies suggest that failure rates with metronidazole may be higher than traditionally reported, but these data have limitations. Kim et al [165] prospectively studied 82 children with CDI, of whom 56 received metronidazole; 6 (11%) of them had treatment failure, but half of these were children with severe disease. Khanna et al [125] performed a population-based cohort study of CDI epidemiology in children 0–18 years of age. Among 69 patients with community-acquired CDI, treatment failure rate was 18% for metronidazole and 0% for vancomycin, but these rates were not statistically different. In a survey of pediatric infectious diseases physicians by Sammons et al [382], 100% of respondents reported using metronidazole for initial therapy in healthy children with mild CDI, but the proportion fell to 41%–79% for treating mild CDI in children with underlying comorbidities. Schwenk et al [383] used a national administrative database to study vancomycin use for pediatric CDI and found that vancomycin use for initial therapy increased significantly between 2006 and 2011, with substantial variability between children's hospitals. Complications and mortality from CDI in children are uncommon, regardless of severity of disease or choice of antibiotic for treatment [125, 126, 158, 345]. Treatment recommendations for pediatric CDI should balance the accumulated experience of good outcomes with metronidazole for initial mild disease and emerging data in both adults and children, suggesting a possible difference in favor of vancomycin. At the current time there are insufficient pediatric data to recommend vancomycin over metronidazole as preferred treatment, so either metronidazole or vancomycin should be used for an initial episode or first recurrence of nonsevere CDI in children (Table 2). However, because oral vancomycin is not absorbed, the risk of side effects is lower than for metronidazole. Nonetheless, studies have demonstrated that vancomycin exposure promotes carriage of vancomycin-resistant enterococci in the intestinal flora of treated patients, although available data suggest that metronidazole use is also associated with this outcome [307, 384].

Referenzen aus Leitlinien
125. Khanna S, Baddour LM, Huskins WC, et_al. The epidemiology of Clostridium difficile infection in children: a population-based study. Clin Infect Dis 2013; 56:1401–6.
126. Kim J, Smathers SA, Prasad P, Leckerman KH, Coffin S, Zaoutis T. Epidemiological features of Clostridium difficile-associated disease among inpatients at children's hospitals in the United States, 2001–2006. Pediatrics 2008; 122:1266–70.
158. Sandora TJ, Fung M, Flaherty K, et_ al. Epidemiology and risk factors for Clostridium difficile infection in children. Pediatr Infect Dis J 2011; 30:580–4.
165. Kim J, Shaklee JF, Smathers S, et_al. Risk factors and outcomes associated with severe Clostridium difficile infection in children. Pediatr Infect Dis J 2012; 31:134–8.
307. Al-Nassir WN, Sethi AK, Li Y, Pultz MJ, Riggs MM, Donskey CJ. Both oral metronidazole and oral vancomycin promote persistent overgrowth of vancomycin-resistant enterococci during treatment of Clostridium difficile-associated disease. Antimicrob Agents Chemother 2008; 52:2403–6.
345. Kim YG, Graham DY, Jang BI. Proton pump inhibitor use and recurrent Clostridium difficile-associated disease: a case-control analysis matched by propensity score. J Clin Gastroenterol 2012; 46:397–400.
382. Sammons JS, Gerber JS, Tamma PD, et_ al. Diagnosis and management of Clostridium difficile infection by pediatric infectious diseases physicians. J Pediatric Infect Dis Soc 2014; 3:43–8.

383. Schwenk HT, Graham DA, Sharma TS, Sandora TJ. Vancomycin use for pediatric Clostridium difficile infection is increasing and associated with specific patient characteristics. Antimicrob Agents Chemother 2013; 57:4307–13.
384. Gerding DN. Is there a relationship between vancomycin-resistant enterococcal infection and Clostridium difficile infection? Clin Infect Dis 1997; 25(Suppl 2):S206–10.

Empfehlung XXXIII. What is the best treatment of an initial episode of severe CDI in children?

For children with an initial episode of severe CDI, oral vancomycin is recommended over metronidazole (strong recommendation, moderate quality of evidence).

Summary of the Evidence:

There are no well-designed trials that examine the comparative effectiveness of metronidazole and oral vancomycin for the initial treatment of children with severe CDI. As noted above, observational studies of hospitalized children with CDI suggest that the rate of treatment failure may be greater among children with severe disease as compared to those with nonsevere disease [345]. Although pediatric studies have not demonstrated conclusively that the therapeutic agent used to treat a child with severe CDI is associated with different outcomes, evidence from adult RCTs has demonstrated improved outcomes in adult patients with severe CDI who are treated with oral vancomycin compared with those treated with oral metronidazole. Therefore, clinicians should use vancomycin in children who present with severe or fulminant CDI (Table 2). […]

Referenzen aus Leitlinien

345. Kim YG, Graham DY, Jang BI. Proton pump inhibitor use and recurrent Clostridium difficile-associated disease: a case-control analysis matched by propensity score. J Clin Gastroenterol 2012; 46:397–400.

Empfehlung XXXIV. What are the best treatments for a second or greater episode of recurrent CDI in children?

For children with a second or greater episode of recurrent CDI, oral vancomycin is recommended over metronidazole (weak recommendation, low quality of evidence).

Summary of the Evidence:

There are no well-designed trials that examine the effectiveness of various treatment regimens in children with multiply recurrent CDI. In addition, pediatric studies have not demonstrated conclusively that there is a difference in the risk of recurrence related to the therapeutic agent used to treat an initial episode [125, 165]. Thus, recommendations about the therapeutic approach to children with multiply recurrent CDI must be guided by evidence drawn from the studies performed in adults and an assessment of the theoretical benefits and harms associated with various treatment regimens. As described above, evidence from adult studies supports the use of an extended course of oral vancomycin (tapered or pulse regimen), oral vancomycin followed by rifaximin, or fidaxomicin in patients with multiply recurrent CDI. For children with a second recurrence of CDI who have been treated exclusively with metronidazole, a conventional course of oral vancomycin should be considered. For children with multiple recurrences of CDI despite conventional courses of metronidazole and oral vancomycin, an alternate therapeutic regimen should be used (Table 2).

Vancomycin, fidaxomicin, and rifaximin are not absorbed when orally administered; thus, there are few systemic adverse events associated with these drugs. […]

Referenzen aus Leitlinien

125. Khanna S, Baddour LM, Huskins WC, et_al. The epidemiology of Clostridium difficile infection in children: a population-based study. Clin Infect Dis 2013; 56:1401–6.
165. Kim J, Shaklee JF, Smathers S, et_al. Risk factors and outcomes associated with severe Clostridium difficile infection in children. Pediatr Infect Dis J 2012; 31:134–8.

Empfehlung XXXV. Is there a role for fecal microbiota transplantation in children with recurrent CDI?

Consider fecal microbiota transplantation for pediatric patients with multiple recurrences of CDI following standard antibiotic treatments (weak recommendation, very low quality of evidence).

Summary of the Evidence:

[…] Good clinical response has been shown in adults with refractory or recurrent CDI with few reports of adverse events. At present, robust data examining the effectiveness of FMT for pediatric patients are lacking. Thus, recommendations regarding the therapeutic approach to multiply recurrent CDI in children should be guided primarily by evidence from adult studies. Limited evidence from case reports and case series in pediatric patients suggests that FMT via nasogastric tube or colonoscopy can be effective in children with multiply recurrent CDI who have failed standard antibiotic therapy, with follow-up periods up to 16 months [387, 388]. In most reported cases, fecal sample donation was from the child's mother or father [388]. Despite limited pediatric data, a survey of pediatric infectious diseases physicians revealed that 18% of respondents who reported using alternative therapies for CDI had recommended FMT, most commonly for the treatment of a third or later recurrence [382]. Finally, the potential benefits of FMT must be balanced against theoretical risks. As described above, instillation of donor stool typically requires use of nasogastric tube or colonoscopy, which may carry procedure-related risks. In addition, use of donor stool introduces the potential for transmission of resistant organisms and blood-borne pathogens, necessitating donor-screening protocols. There is a general concern that FMT might ultimately lead to unexpected adverse events such as metabolic or immune-based disorders [359].

Referenzen aus Leitlinien

359. Bakken JS. Fecal bacteriotherapy for recurrent Clostridium difficile infection. Anaerobe 2009; 15:285–9.
387. Russell G, Kaplan J, Ferraro M, Michelow IC. Fecal bacteriotherapy for relapsing Clostridium difficile infection in a child: a proposed treatment protocol. Pediatrics 2010; 126:e239–42.
388. Walia R, Garg S, Song Y, et al. Efficacy of fecal microbiota transplantation in 2 children with recurrent Clostridium difficile infection and its impact on their growth and gut microbiome. J Ped Gastroenterol Nutr 2014; 59:565–70.

Table 2. Recommendations for the Treatment of *Clostridium difficile* Infection in Children

Clinical Definition	Recommended Treatment	Pediatric Dose	Maximum Dose	Strength of Recommendation/ Quality of Evidence
Initial episode, non-severe	• Metronidazole × 10 days (PO), OR • Vancomycin × 10 days (PO)	• 7.5 mg/kg/dose tid or qid • 10 mg/kg/dose qid	• 500 mg tid or qid • 125 mg qid	Weak/Low Weak/Low
Initial episode, severe/ fulminant	• Vancomycin × 10 days (PO or PR) with or without metronidazole × 10 days (IV)[a]	• 10 mg/kg/dose qid • 10 mg/kg/dose tid	• 500 mg qid • 500 mg tid	Strong/Moderate Weak/Low
First recurrence, non-severe	• Metronidazole × 10 days (PO), OR • Vancomycin × 10 days (PO)	• 7.5 mg/kg/dose tid or qid • 10 mg/kg/dose qid	• 500 mg tid or qid • 125 mg qid	Weak/Low
Second or subsequent recurrence	• Vancomycin in a tapered and pulsed regimen[b], OR • Vancomycin for 10 days followed by rifaximin[c] for 20 days, OR • Fecal microbiota transplantation	• 10 mg/kg/dose qid • Vancomycin: 10 mg/kg/dose qid; rifaximin: no pediatric dosing • …	• 125 mg qid • Vancomycin: 500 mg qid; rifaximin: 400 mg tid • …	Weak/Low Weak/Low Weak/Very low

Abbreviations: IV, intravenous; PO, oral; PR, rectal; qid, 4 times daily; tid, 3 times daily.

[a]In cases of severe or fulminant *Clostridium difficile* infection associated with critical illness, consider addition of intravenous metronidazole to oral vancomycin.

[b]Tapered and pulsed regimen: vancomycin 10 mg/kg with max of 125 mg 4 times per day for 10–14 days, then 10 mg/kg with max of 125 mg 2 times per day for a week, then 10 mg/kg with max of 125 mg once per day for a week, and then 10 mg/kg with max of 125 mg every 2 or 3 days for 2–8 weeks.

[c]No pediatric dosing for rifaximin; not approved by the US Food and Drug Administration for use in children <12 years of age.

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library (Cochrane Database of Systematic Reviews, Health Technology Assessment Database) am 14.06.2018

#	Suchfrage
#1	MeSH descriptor: [Clostridium Infections] explode all trees
#2	MeSH descriptor: [Clostridium difficile] explode all trees
#3	(Clostridium and (infection* or difficile)):ti,ab,kw
#4	#1 or #2 or #3
#5	#4 Publication Year from 2013 to 2018

SR, HTAs in Medline (PubMed) am 15.06.2018

#	Suchfrage
1	(Clostridium Infections[mh:noexp]) OR Clostridium difficile[mh]
2	Clostridium[tiab] AND (Infection*[tiab] OR difficile*[tiab])
3	(#1 OR #2)
4	(#3) AND (Meta-Analysis[ptyp] OR systematic[sb] OR Technical Report[ptyp])
5	(#3) AND (((((trials[tiab] OR studies[tiab] OR database*[tiab] OR 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]))))
6	(#4 OR #5)
7	(#6) AND ("2013/06/01"[PDAT] : "3000"[PDAT])
8	(#7) NOT "The Cochrane database of systematic reviews"[Journal]
9	(#8) NOT retracted publication[ptyp]

Leitlinien in Medline (PubMed) am 14.06.2018

#	Suchfrage
1	(Clostridium Infections[mh:noexp]) OR Clostridium difficile[mh]
2	Clostridium[tiab] AND (Infection*[tiab] OR difficile*[tiab])
3	(#1 OR #2)
4	(#3) AND (Guideline[ptyp] OR Practice Guideline[ptyp] OR guideline*[Title] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] OR recommendation*[ti])
5	(#4) AND ("2013/06/01"[PDAT] : "3000"[PDAT])
6	(#5) NOT retracted publication[ptyp]

Referenzen

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