

Urinary Tract Infection (recurrent): antimicrobial prescribing
Consultation on draft guideline - Stakeholder comments table
29 August 2024 - 12 September 2024

ID	Type	Stakeholder	Document	Page No	Line No	Comments	Developer's response
1.	SH	Northern Care Alliance NHS Foundation Trust	Guideline	General	General	We are satisfied that the overall content is suitable, but that a decision aid would be useful	Thank you for your comment. We plan to update the existing decision aids in line with the new recommendations and aim to publish these sometime in first half of 2025
2.	SH	United Kingdom Clinical Pharmacy Association (UKCPA)	Guideline	General	General	UTI prophylaxis is an area with few limited options and for which the evidence base is limited. This leads to a significant unmet need, forcing the use of potentially inappropriate antibiotics, and so it is welcome that methenamine is being recommended as an option in this area	Thank you for your comment
3.	SH	United Kingdom Clinical Pharmacy Association (UKCPA)	Evidence Review	24	1	We are concerned about the lack of guidance either for or against the need for acidic urine to be demonstrated prior to commencing methenamine. Many AMS pharmacists are aware of historical requirements in local guidelines, and it is disappointing that this question was not within scope.	Thank you for this comment. The committee discussed the requirement for acid urine in order for methenamine to be effective, and this discussion is documented in the evidence review. A summary of this discussion has also been added to the rationale and impact section of the guideline. A new recommendation about what to cover when discussing

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							methenamine hippurate includes acknowledgement of the impact of alkalinising agents on effectiveness of methenamine hippurate.
4.	SH	United Kingdom Clinical Pharmacy Association (UKCPA)	Guideline	17	21	<p>The lack of evidence base for requirement of acid urine to be demonstrated prior to methenamine use; and for use of methenamine in recurrent UTI caused by pathogens which raise the urinary pH e.g. <i>Proteus</i> should be considered for addition to this section</p> <p>The committee should also consider whether this section could also recommend the development of evidence base with other non-antimicrobial agents, in line with the UK antimicrobial resistance national action plan Commitment 6.4 - Improvement and adoption “We will drive improvement by assessing and regulating novel technologies and approaches at pace, using evidence to increase timely and appropriate adoption.” https://www.gov.uk/government/publications/uk-5-year-action-plan-for-antimicrobial-resistance-2024-to-2029/confronting-antimicrobial-resistance-2024-to-2029#theme-3---investing-in-innovation-supply-and-access-1</p>	<p>Thank you for this comment. The committee discussed the requirement for acid urine in order for methenamine to be effective, and this discussion is documented in the evidence review. A summary of this discussion has also been added to the rationale and impact section of the guideline. A new recommendation about what to cover when discussing methenamine hippurate includes acknowledgement of the impact of alkalinising agents on effectiveness of methenamine hippurate.</p> <p>Referrals to update or create new guidance are considered by NICE's prioritisation board. For more information, see Prioritising our Guidance Topics https://www.nice.org.uk/about/what-</p>

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							we-do/prioritising-our-guidance-topics
5.	SH	United Kingdom Clinical Pharmacy Association (UKCPA)	Evidence Review	19	8	Whilst it is stated earlier that adverse drug reactions are rare with both antimicrobials and methenamine, there are no stated discussions of any harms with methenamine within the "Benefits and harms" section. We would like to see more clearer statement of any harms that were seen in the evidence base.	<p>Thank you for this comment. We have now added a statement in the 'Benefits and harms' section to highlight that no difference of serious adverse events or adverse events were found in the evidence as follows:</p> <p>Furthermore, the committee also noted that there was no evidence of difference for serious adverse events for methenamine hippurate compared to daily antibiotics, which was further confirmed by the lack of differences for patient satisfaction between methenamine hippurate and antibiotics.</p>
6.	SH	NHS England	Guideline	General	General	The pharmacological management sections which are well evidenced and extremely logical in terms of choice and alternatives. It factors in good antimicrobial stewardship. For people with a learning disability and autistic people, specifically:	Thank you for this comment. Different preparations of other treatments in NG112 are out of scope for this update. However, we understand the need for care to take account of individual needs and preferences. We have added references to NICE's core content on shared decision making and

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						<ol style="list-style-type: none"> 1. Ensure access to liquid preparations where dysphagia and/or sensory preference dictates choice. There are liquid products available for all treatment options apart from Methenamine Hippurate - this can be crushed, if required, and taken in milk or fruit juice. A little concerned by the cost implications of giving nitrofurantoin in liquid form although other options may be available, if necessary. 2. Ensure access to appropriate literature to aid understanding of medication and treatment schedules. This is particularly important in longer term prophylaxis to ensure regular concordance with the medication regime. Good education in accessible format is paramount to driving concordance. 3. Again, accessible information related to the potential for side effects, especially the impact and embarrassment of antibiotic induced diarrhoea 	patient experience in the NHS to emphasise the importance of these aspects (for example, on the information to give about treatments and on how to communicate with people and their families and carers).
7.	SH	NHS England	Guideline	General	General	<ul style="list-style-type: none"> • Consider the need for low threshold trial of topical and systemic HRT for patients 	Thank you for your comment. The guideline is clear that systemic

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						who may struggle to identify and communicate symptoms of recurrent UTI.	<p>HRT should not be offered specifically to reduce the risk of recurrent UTI. See recommendation 1.2.4.</p> <p>Vaginal (topical) oestrogen is included in the guideline and is recommended where personal hygiene measures alone are not effective or not appropriate. We consider that your comment may cover people for whom hygiene measures are not appropriate, and who would therefore be offered topical oestrogen before / instead of hygiene measures - and therefore earlier / with a lower threshold. We have therefore not made changes to this recommendation.</p>
8.	SH	NHS England	Guideline	General	General	<ul style="list-style-type: none"> Have a lower threshold for using a single dose for those who struggle with oral medications/the sensory issues of taking tablets. 	<p>Thank you for this comment. Recommendations about single dose antibiotics are out of scope for this update. However, we understand the need for care to take account of individual needs and preferences. We have added references to NICE's core content</p>

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							on shared decision making and patient experience in the NHS to emphasise the importance of these aspects.
9.	SH	NHS England	Guideline	General	General	Consider the complexities of hygiene measures for those who may have specific anxieties, especially around menstruation and bowels. Additional discussion and possibly desensitisation work may be needed.	Thank you for this comment. The committee agreed not to add more information about which hygiene measures should be taken, or how to amend these for people with specific concerns. They agreed that this would be part of the discussion between the individual and the clinician. However, the committee agreed to add cross-references to the beginning of the recommendations to direct to NICE's core content, which should help to emphasise the importance of supporting people and their individual needs.
10.	SH	NHS England	Guideline	General	General	We suggest reference to making reasonable adjustments: This is a legal requirement as stated in the Equality Act 2010 and is important to help you make the right diagnostic and treatment decisions for an individual. You can ask the person and their carer or family member what reasonable adjustments should be made. Adjustments	Thank you for your feedback. Making reasonable adjustments as required by the Equality Act is a statutory requirement and so this requirement would not be repeated in each individual NICE guideline. However, the committee agreed to add cross-references to the

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						aim to remove barriers, do things in a different way, or to provide something additional to enable a person to receive the assessment and treatment they need. Possible examples include; allocating a clinician by gender, taking blood samples by thumb prick rather than needle, providing a quiet space to see the patient away from excess noise and activity.	beginning of the recommendations to direct to NICE's core guidance on patient experience and shared-decision making, which reference the Equality Act and highlight the importance of individualised care and shared-decision making.
11.	SH	NHS England	Guideline	General	General	We recommend including reference to the importance of Communication: Communicate with and try to understand the person you are caring for. Check with the person themselves, their family member or carer or their hospital or communication passport for the best way to achieve this. Use simple, clear language, avoiding medical terms and 'jargon' wherever possible. Some people may be non-verbal and unable to tell you how they feel. Pictures may be a useful way of communicating with some people, but not all.	Thank you for your feedback. We have not made specific recommendations about communication because this is already covered by other NICE guidance, such as our guidelines on patient experience and shared decision making. The committee has agreed to add some cross-references to these guidelines, and other core content, which highlight many of the areas that you have mentioned (for example, establishing the most effective way of communicating with patients and their families and carers, use of pictures and avoiding jargon)

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12.	SH	NHS England	Guideline	General	General	Be aware of diagnostic overshadowing: This occurs when the symptoms of physical ill health are mistakenly either attributed to a mental health or behavioural problem or considered inherent to the person's learning disability or autism diagnosis. People with a learning disability or autism have the same illnesses as everyone else, but the way they respond to or communicate their symptoms may be different and not obvious. Their presentation with COVID-19 may be different from that for people without a learning disability or autism	Thank you for your comment.
13.	SH	NHS England	Guideline	General	General	Pay attention to healthcare passports: Some people with a learning disability and some autistic people may have a healthcare passport giving information about the person and their health needs, preferred method of communication and other preferences. Ask the person or their accompanying carer if they have one of these	Thank you for your feedback. We have not made specific recommendations about individual preferences for communication because this is already covered by other NICE guidance, such as our guidelines on patient experience and shared decision making. The committee has agreed to add some cross-references to these guidelines, and other core content, which highlight many of the areas that you have mentioned (for example, establishing the most effective way of communicating

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							with patients and their families and carers, use of pictures and avoiding jargon).
14.	SH	NHS England	Guideline	5	2	Please consider adding in oestrogen [vaginal] tablet presentation as an option	Thank you for this comment. The committee acknowledged that recommendations about vaginal oestrogen were out of scope, and that the original evidence from 2018 indicated that vaginal oestrogen administered via a pessary was less effective than oral antibiotic at reducing the risk of recurrent infection in women after the menopause. However, the committee were also aware of the importance of patient preference for different treatment modes, and agreed to align the choice of vaginal oestrogen treatments with NICE's guideline on menopause (updated in November 2024). We have therefore added gel, tablet, pessary and ring to the list of examples as part of this recommendation.
15.	SH	NHS England	Guideline	5	13	Grey text but there is an important omission to recommend that urine is sent for culture before treatment of an acute UTI, to guide selection of	Thank you for your comment. Recommendation 1.1.1 includes a link to NICE's guidelines on UTI

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						antibiotic for future single-dose prophylaxis. The guidance at the moment only refers to "previous urine culture and susceptibility results" on p 5 line 20 but cultures may not have been taken previously and taking cultures is an important principle that should be inherent in the management of recurrent UTI.	(lower): antimicrobial prescribing and pyelonephritis (acute): antimicrobial prescribing which cover treatment of an acute UTI and sending urine for culture before treatment of an acute UTI. Additionally the choice of antibiotic medicines tables at the end of this guideline include a note about "Choosing antibiotics according to recent culture and susceptibility results where possible, with rotational use based on local policies. Select a different antibiotic for prophylaxis if treating an acute UTI."
16.	SH	NHS England	Guideline	7	16	Grey text but as above (p5, line 13), there is an important omission to recommend that urine is sent for culture and susceptibility results are checked, before selecting the choice of antibiotic for daily prophylaxis.	Thank you for your comment. Recommendation 1.1.1 includes a link to NICE's guidelines on UTI (lower): antimicrobial prescribing and pyelonephritis (acute): antimicrobial prescribing which cover treatment of an acute UTI and sending urine for culture before treatment of an acute UTI. Additionally the choice of antibiotic medicines tables at the end of this guideline include a note about

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							"Choosing antibiotics according to recent culture and susceptibility results where possible, with rotational use based on local policies. Select a different antibiotic for prophylaxis if treating an acute UTI."
17.	SH	NHS England	Guideline	8	13	Rec 1.2.12. Should vaginal oestrogen be added as an option to try, alongside single-dose antibiotic prophylaxis and methenamine hippurate, before progressing to a trial of daily antibiotic prophylaxis?	Thank you for your comment. We have added vaginal oestrogen as an option to this recommendation for consistency.
18.	SH	NHS England	Guideline	11	5	A new randomised controlled trial of D-mannose in UK primary care was published in April 2024 [Hayward G et al, JAMA Internal Medicine 2024; https://pubmed.ncbi.nlm.nih.gov/38587819/]. This trial concluded that D-mannose was not superior to placebo for the primary outcome of proportion contacting ambulatory care with a clinically-suspected UTI. Publication of this trial may warrant reconsideration of the guideline text, to alert clinicians to this new evidence, which contradicts the findings of the RCT considered by the committee in 2018.	Thank you for your comment and we have noted this new study for consideration in future updates of the guideline. This update was confined to the consideration of methenamine hippurate as a new treatment option within the guideline.
19.	SH	NHS England	Guideline	22	Box	Please thank the NICE team for carrying out such a comprehensive review of the latest evidence for methenamine. Please also thank	Thank you for your comment

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						the committee members for their careful and thoughtful consideration of the evidence for methenamine hippurate and for applying their pragmatic, real-world perspective, to reach a recommendation. The risks of resistance associated with long-term trimethoprim prophylaxis and the risks of pulmonary and liver toxicity with long-term nitrofurantoin prophylaxis are significant and methenamine offers a realistic alternative for people who wish to avoid the risks of antibiotics.	
20.	SH	NHS England	Guideline	25	31	The word 'with' or 'for' is missing before the phrase 'antibiotic prophylaxis'.	Thank you for this comment. This correction has been made.
21.	SH	NHS England	Guideline	General	General	Advice to patients/community clinicians to ensure that other clinicians (e.g. hospitals) are aware where prophylaxis is taken and what positive results have previously been noted (ie bacteria and sensitivities) Is there guidance on antibiotic choices for UTI in patients on prophylaxis e.g. avoiding duplication, using alternatives or seeking specialist advice.	Thank you for your comment. We have noted that communication between health care settings about results of prophylactic treatments is important. Guidance about antibiotic choices for UTI in patients on prophylaxis is not within the scope of this guideline. No changes have been made as a result of this comment.
22.	SH	NHS England	Guideline		1.1.4	consider immunosuppression as requiring specialist advice, including those on medications that increase the risk of UTI.	Thank you for your comment. The committee recognised that immunosuppression is an important consideration for a clinician when managing any infection. if profound

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							(e.g. neutropenia) then the patient is very likely to be under the care of a specific specialist anyway. There are several other conditions and medications that produce a less serious degree of immunosuppression, from a history of splenectomy, to diabetes, normal pregnancy, low dose corticosteroid treatment, therefore to have a blanket recommendation to refer everyone in any such category would be impractical and unnecessary.
23.	SH	NHS England	Guideline		1.2.5	define single-dose antibiotic prophylaxis Decisions should be made in conjunction with appropriate specialist input	Thank you for your comments. Changes to recommendations about single-dose antibiotics are not within scope of this update. However we have noted these points for future updates in these areas. More information about single-dose antibiotic prophylaxis is provided in the tables, which should clarify the definition. We would not normally add a definition for a term which we are using in a standard way and

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							which has a standard definition. No definition has been added.
24.	SH	NHS England	Guideline		1.2.11	advice to seek optimal management of any underlying chronic illnesses to reduce the incidence and severity of future infections.	Thank you for your comments. Changes to recommendations about antibiotic prophylaxis are not within scope of this update. However we have noted these points for future updates in these areas.
25.	NICE	NICE GP Reference Panel	Guideline		General	The GP Reference panel received 7 responses to this consultation despite a short window of opportunity which is an average level of response for the panel. 3 respondents made generally positive comments on the value of the updates and overall presentation of the guideline. No overall negative comments were received.	Thank you for your comments.
26.	NICE	NICE GP Reference Panel	1.2.2	4	9	Addressing Patient Concerns Around Vaginal Oestrogen: Many patients are hesitant about using vaginal oestrogen due to perceived cancer risks. Including concise, patient-friendly resources or decision aids within the guideline could help GPs reassure patients about its safety, especially in post-menopausal women with recurrent UTIs. This would likely improve patient acceptance and adherence.	Thank you for your comment. We plan to update the existing decision aids in line with the new recommendations and aim to publish these sometime in first half of 2025. We have aligned the recommendations about vaginal oestrogen, including the low cancer risk, with the recommendations in

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						A specific statement about an absence of cancer risk with vaginal oestrogen would also be valuable and provide more clarity. Current statements "serious side effects are very rare" and "unlikely to have a significant effect throughout the body" are a little ambiguous.	the NICE menopause guideline (updated November 2024)
27.	NICE	NICE GP Reference Panel	Rec 1.2.8	6	10	One respondent asked for more clarity on the relative benefits of methenamine compared to prophylactic antibiotics. My interpretation [JT] of their response is that they may have mistaken "single-dose antibiotic prophylaxis" to mean <i>ongoing</i> antibiotic prophylaxis. Is there a better term than "single-dose prophylaxis" such as "one-off dose when needed"?	Thank you for your comment. We have added the term "one-off dose" which we hope makes this clearer.
28.	NICE	NICE GP Reference Panel	Rec 1.2.8	6	10	Two respondents suggested including contraindications as per the BNF (gout, metabolic acidosis, severe dehydration) in the recommendation. As a new drug to GP practice, many will not be aware of these. Should methenamine be withheld if a patient is at risk of dehydration e.g. vomiting and diarrhoea?	Thank you for this comment. The committee agreed that there were factors to discuss before deciding on methenamine hippurate for preventing recurrent UTIs. They agreed that dehydration severe enough to be a contraindication for methenamine hippurate was a rare occurrence and not something that would need discussing with most patients, especially as many people with recurrent UTIs are

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							<p>hyperhydrating to alleviate symptoms. They did agree that people should be aware of the impact of alkalinising agents (e.g. over the counter sachets) on the effectiveness of methenamine hippurate, as these agents are commonly used.</p> <p>The committee agreed that important information about contra-indications was available from the BNF which is linked to in the medicines tables and so chose not to replicate that information in the recommendations.</p>
29.	NICE	NICE GP Reference Panel	Rec 1.2.8	6	10	“Implementation: Providing clearer guidance on patient selection criteria and practical monitoring strategies may help GPs implement this option more effectively in primary care, particularly in patients who have exhausted other prophylactic measures.”	Thank you for your comment. We will consider this as part of implementation of the guideline, but it was not part of the scope of these recommendations.
30.	NICE	NICE GP Reference Panel	Rec 1.2.8	6	10	“It may be useful to include a reference to the brand name Hiprex as this is widely known.”	Thank you for your comment. We only use generic names, as opposed to brand names, in guidelines. We would only do this

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							in exceptional circumstances, for example, if there was no clear generic name. Adding this here would introduce an inconsistency and may leave us open to requests from drug manufacturers for other topics.
31.	NICE	NICE GP Reference Panel	Rec 1.2.8	6	10	“Should 1.2.8 be followed by a shared decision making rec e.g. as with vaginal oestrogen and antibiotics? Eg, “When considering a trial of methenamine for preventing recurrent UTI, explain that it may reduce the number of UTIs less than an antibiotic, and it may reduce the number of antibiotic resistant bugs but the evidence is uncertain.” Personally I would find this very helpful. “	Thank you for this comment. The committee agreed that there were factors to discuss before deciding on methenamine hippurate for preventing recurrent UTIs. The uncertainty of the evidence is intended to be communicated in the strength of this recommendation, which is weak as denoted by the recommendation to "consider" methenamine hippurate. There is also further information to consider in the summary of committee discussion which will be linked to this recommendation. The committee considered that antibiotic resistance was an important contextual factor, so it is detailed in the evidence reviews, but was not a priority to discuss with individuals, as people are not

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							likely to be choosing between antibiotics and methenamine hippurate at this point.
32.	NICE	NICE GP Reference Panel	Rec 1.2.8	6	10	"I understand that if this rec goes forward , discussions with BNF will take place to remove the 'less suitable for prescribing section" [although on inspection, it looks like this section would just need amending slightly JT]	Thank you for this comment. That is correct, the BNF page for methenamine hippurate will be updated with the publication of this guideline.
33.	NICE	NICE GP Reference Panel	Rec 1.2.8	6	10	One respondent requested guidance on monitoring in primary care. How often? 6-monthly? When should a trial of withdrawal be considered?	Thank you for this comment. The committee agreed that monitoring for methenamine hippurate was important, and they have made a new recommendation to cover this as follows: "1.2.11: Review treatment with methenamine hippurate within 6 months, and then every 12 months, or earlier if agreed with the person."
34.	NICE	NICE GP Reference Panel	Evidence summary Methenamine	20	11	There seems to be a contradiction. Line 11 (page 20) states: "Evidence on antibiotic resistance in E. coli during prophylactic treatment found fewer antimicrobial categories and fewer antibiotics to which E. coli from perineal swabs was resistant for women taking methenamine hippurate	Thank you for your comment. We have amended the text to make this clearer that one outcome was during the prophylactic treatment (fewer antibiotics and antimicrobial categories) and the other one was at the end of follow-up (higher antibiotics).

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						<p>compared with antibiotics (low quality evidence).</p> <p>The top of page 21 states:</p> <p>"There was a higher number of antibiotics to which E. coli from perineal swabs was resistant at the end of the follow-up period for women taking methenamine hippurate compared with antibiotics (low quality evidence)."</p> <p>Is this stating there is evidence (albeit low quality) demonstrating both improvement and deterioration of antimicrobial resistance patterns with methenamine vs antibiotics? It could be more clear, if this is the case</p>	
35.	NICE	NICE GP Reference Panel	Changes to language recs 1.1.4, 1.2.2, 1.2.4	3,4,5		<p>3 respondents commented on these in general terms:</p> <p>"Support for Inclusive Language: This is important to ensure that all patients, including trans and non-binary individuals, feel adequately represented and understood in clinical practice."</p>	<p>Thank you for your feedback. Where we can, we use gender inclusive language to ensure we reflect the experiences of all patients. For this guideline, we introduced several changes to make the recommendations more inclusive – it is good to hear that you think this has added some clarity and will help ensure that all</p>

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						<p>"I support changes to make the language more inclusive but find the current phrasing makes the guideline more complicated and thus harder to understand."</p> <p>"Changes re. inclusivity look great and brings clarity to management of different patient populations."</p>	<p>people feel adequately represented. However, we do also know that being more specific about population groups means using more words. And that it is sometimes hard to find the right balance between being specific and being concise. We will review the wording in these recommendations to see if we can make them easier to read and to understand.</p>
36.	SH	Frimley Health NHS Foundation Trust, Microbiology department	Guideline	3	4-18	Referral and seeking specialist advice 1.1.4 : From this list, it would make more sense to say when not to refer. This might make it clearer who should or should not be offered this.	Thank you for this comment. Reasons for naming these subgroups specifically are given in the evidence and discussion section on antibiotic prophylaxis, (section titled Antibiotic Prophylaxis (2018)), linked to from rec 1.1.4. No change has been made to this recommendation.

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37.	SH	Frimley Health NHS Foundation Trust, Microbiology department	Guideline	6	11	Methenamine hippurate 1.2.8 : For single and daily antibiotic prophylaxis it states to ensure that any current UTI has been adequately treated first, so presumably this also applies to methenamine Hippurate. If this is the case, then this should be included here.	Thank you for this comment. The committee agreed that any current UTI should be treated before starting prophylaxis with methenamine hippurate, in line with single-dose and daily antibiotic prophylaxis recommendations. They therefore decided to amend recommendation 1.2.8 to reflect this.
38.	SH	Frimley Health NHS Foundation Trust, Microbiology department	Guideline	6	11-19	The overview outcome of the committee review p22-23 suggests methenamine hippurate should be considered as an alternative to antibiotic prophylaxis (there was no comment on whether this was single or daily antibiotics). In the recommendation 1.2.8 line 11 it suggests methenamine hippurate as an alternative to daily antibiotic prophylaxis and on 1.2.8 line 18 it also states single dose antibiotic prophylaxis should have been trialled before considering methenamine hippurate. However, in recommendation 1.2.12 it suggests that daily antibiotic prophylaxis should be tried if there has been no improvement after single-dose antibiotic prophylaxis OR methenamine Hippurate; which implies methenamine	Thank you for your comment. The evidence review undertaken for this update compared methenamine hippurate with daily antibiotic prophylaxis. Methenamine hippurate was not compared with single-dose antibiotic prophylaxis. We have edited the text in the evidence review and in the guideline where evidence is discussed to clarify that methenamine hippurate should be considered as an alternative to daily antibiotic prophylaxis, not single-dose antibiotic prophylaxis.

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						Hippurate is an alternative to single-dose antibiotic. A simple flow chart may help practical implementation of this guidance and clarify when to consider Methenamine Hippurate.	A visual summary of the treatment pathway for recurrent UTIs will be produced alongside the guideline. This will reinforce where in the pathway methenamine hippurate should be considered.
39.	SH	Frimley Health NHS Foundation Trust, Microbiology department	Guideline	16	25	Recommendations for research: Suggest including strengthening research in methenamine hippurate vs no antibiotics and vs single dose antibiotic prophylaxis to see if benefit as option to try before both forms of antibiotic prescription.	Thank you for this comment. Methenamine hippurate compared with no antibiotics or compared with single dose antibiotic prophylaxis was outside of the scope of this update. However we have noted these points for future updates in these areas.
40.	SH	Frimley Health NHS Foundation Trust, Microbiology department	Guideline	21	11-21	Contradicts other bullet points of evidence	Thank you for your comment. We have amended the bullet points to make it clearer that we are talking about other measures of antibiotic resistance and other measures of antibiotic use than the measures already discussed earlier in the evidence section, by adding "other measures of" before the bullet points.

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41.	SH	Frimley Health NHS Foundation Trust, Microbiology department	Evidence review B	21	6-10	Again, here the committee state that methenamine Hippurate should be considered if behavioural, hygiene and oestrogen options have not been effective, but don't state that any antibiotics need to have been trialled previously as they do in the guideline pg 6 1.2.8 line18 and in evidence review B pg24 line 4. It is unclear if this is a change based on the cost analysis or not.	Thank you for your comment. We have added single-dose antibiotic prophylaxis to the list in evidence review B of what has been trialled previously so that it is clear where in the pathway methenamine sits.
42.		UK Health Security Agency	Guideline	General	General	The use of the terms for gender (“mainly women, and trans men and non-binary people with a female urinary system”) become repetitive and make the guidance difficult to read. Could you use <i>people with a female urinary system</i> or <i>people with a male urinary system</i> throughout and then provide information on which gender categories are covered under each at the beginning of the guidance? Especially as those with re-assignment surgery will be referred.	Thank you for your feedback. We have updated the language in the guideline to ensure that, where possible, we are being inclusive. The terminology we are using aligns with our current style guide, which states that we need to be specific about groups of people if it would otherwise be unclear, unsafe or inaccurate. We do appreciate that it is difficult to balance the need to be specific with being concise, especially in a guideline which has specific recommendations for specific populations. We will however review the guideline to see if we can make further changes to help with clarity or readability. We will

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							also pass this feedback on to NICE's style guide group, so it is taken into account when we update the relevant section of the style guide.
43.		UK Health Security Agency	Guideline	19		The statement on page 19 <i>“The committee agreed that, based on their experience, vaginal oestrogen is also effective in reducing the risk of recurrent UTI in women, and trans men and non-binary people with a female urinary system, during the perimenopausal period.”</i> Can you clarify if the expert consensus covers the menopausal period as well as I do not see it discussed elsewhere in the evidence review, but it is included in the recommendations?	Thank you for this comment. In the 2018 guideline, recommendations for vaginal oestrogen were restricted to the menopausal period. However, the committee for the 2024 update agreed to extend these recommendations to the perimenopausal period as well. Please see evidence review A section 1.5.2 for full explanation of this. Please see also the "committee discussion on oestrogens", which is linked to from the recommendations on oestrogen (recommendations 1.2.1 to 1.2.4).
44.		UK Health Security Agency	Guideline	16		In the section defining recurrent UTI on page 16, can you clarify if, when you tally the number of UTIs to be considered under the recurrent UTI diagnosis (2 in the last 6 months etc...), the clinician should include the current episode.	Thank you for this comment. The committee confirmed that the current episode would be included in the number of UTIs to consider under the recurrent UTI diagnosis definition. They also noted that the person with recurrent UTIs might not be experiencing a current

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							episode at the time that these recommendations are relevant, but would still be classed as having recurrent UTIs if they otherwise met the definition. No change has been made to the definition as a result of this comment.
45.		UK Health Security Agency	Guidelines			Regarding choice of antibiotic for prophylaxis – 2 nd choice amoxicillin. Many laboratories may not perform amoxicillin susceptibility as the rates of resistance are so high- and instead test co-amoxiclav. Amoxicillin and trimethoprim should not be prescribed empirically due the very high rates of resistance. This may be better placed explicitly in the table as opposed to text.	Thank you for your comment. This has been noted for future updates
46.		UK Health Security Agency	Guidelines			Future updates should review the role of immune agents and intra vesical antibiotics and delivery devices.	Thank you for your comment. This has been noted for future updates.
47.		British Society for Antimicrobial Chemotherapy	Guideline	General	General	We welcome the inclusion of non-antibiotic (particularly methenamine) and self-care measures to prevent UTI, however we feel it would be valuable to provide a bolder statement about the importance of efforts to reduce overuse of antibiotics to limit AMR given the high prevalences of UTI-related antibiotic prescribing in the UK and its relationship with AMR.	Thank you for this comment. We understand the very serious concerns about antimicrobial stewardship. The new recommendations on methenamine hippurate aim to support this by offering an alternative to daily antibiotic prophylaxis.

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							<p>The section of the guideline on general principles for prescribing antibiotics is outside of the scope of this update, but other NICE content addresses this:</p> <ul style="list-style-type: none"> - Guidance on recurrent UTI (link), lower UTI (link) and upper UTI (link) all document committee discussion about minimising the risk of antibiotic resistance. For example, in lower UTI delaying antibiotic treatment with a back-up prescription to see if symptoms will resolve without antibiotic treatment is an option. -NICE also has guidance on antimicrobial stewardship: NG15 and NG63.
48.		British Society for Antimicrobial Chemotherapy	Guideline	006	011	Methenamine could be more strongly promoted as an equivalent option to single dose or regular antibiotic prophylaxis rather than as an alternative. Ordering methenamine above antibiotic prophylaxis in the guideline would achieve this and emphasise the importance of the antimicrobial stewardship principle of minimising antibiotic exposure. The guideline notes that the cost may be higher in the short	Thank you for your comment. We have ordered methenamine prophylaxis above daily antibiotic prophylaxis in the guideline. We have also added methenamine prophylaxis to the medicines tables as an alternative to antibiotics at the end of the guideline and this will also be included in the visual

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						term but will be insubstantial when compared to the future costs of antimicrobial resistance.	summary. We hope this helps promote the use of methenamine as an alternative to antibiotic prophylaxis. We have also produced a resource impact tool which we hope will help with local implementation and decision making and includes more detail about cost comparisons.
49.		British Society for Antimicrobial Chemotherapy	Guideline	040	006	We note that the evidence summary for D-mannose does not include a recent randomised control trial published in April of this year by Hayward et al – doi:10.1001/jamainternmed.2024.0264 - which found D-mannose was not effective at preventing recurrent UTI in women presenting to UK primary care. This is important evidence that should be reflected in the guideline.	Thank you for your comment and we have noted this new study for consideration in future updates of the guideline. This update was confined to the consideration of methenamine hippurate as a new treatment option within the guideline.
50.		British Society for Antimicrobial Chemotherapy	Guideline	General	General	We note that Uromune has not been included in the evidence review or draft guideline despite increasing use within secondary care and the private sector. The use of immunoactive prophylaxis has been recommended by the European Association of Urology since 2019, continuing to feature in their guidelines. We feel that NICE guidelines have an important role in increasing the awareness and promoting the use of effective vaccines and non-antibiotic	Thank you for this comment. Referrals to update or create new guidance are considered by NICE's prioritisation board. For more information, see Prioritising our Guidance Topics. (link: https://www.nice.org.uk/about/what-we-do/prioritising-our-guidance-topics)

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						options, supported by clinical evidence, to reduce overall antibiotic exposure to help slow the development and spread of antibiotic resistance.	
51.		British Society for Antimicrobial Chemotherapy	Guideline	007	013	The section on general principles for prescribing antibiotics should include a clear statement on antibiotics that must be reserved or avoided unless other options, including self-care and non-antibiotic management, have failed and there are no alternative antibiotic options. Examples include fosfomycin and pivmecillinam, which should be reserved for the treatment of infection with ESBL-producing <i>Enterobacterales</i> , and ciprofloxacin in light of the MHRA warning released earlier this year. It should be highlighted that in such cases, the advice of a specialist must be sought. This section of the guideline provides an excellent opportunity to reinforces the principles and importance of antibiotic stewardship.	<p>Thank you for this comment. We understand the very serious concerns about antimicrobial stewardship. The new recommendations on methenamine hippurate aim to support this by slowing the emergence of resistance to antibiotics used for recurrent UTIs.</p> <p>The section of the guideline on general principles for prescribing antibiotics is outside of the scope of this update, but other NICE content addresses this:</p> <p>- Guidance on recurrent UTI (link), lower UTI (link) and upper UTI (link) all document committee discussion about minimising the risk of antibiotic resistance. For example, in lower UTI delaying antibiotic treatment with a back-up prescription to see if symptoms will</p>

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							<p>resolve without antibiotic treatment is an option.</p> <p>-NG111 (link) was updated in September 2024. Table 1 was updated to reflect new safety advice on fluoroquinolones. The table now recommends that ciprofloxacin is used only if other first-choice antibiotics are unsuitable. The box also links to MHRA advice from January 2024 on restrictions and precautions for using fluoroquinolone antibiotics.</p> <p>-NICE also has guidance on antimicrobial stewardship: NG15 and NG63.</p>
52.		Royal College of General Practitioners	Guideline	006	011	<p>Rec 1.2.8 The recommendation for using methenamine hippurate as an alternative to daily antibiotic prophylaxis is a positive step toward antimicrobial stewardship. However, the document could benefit from clearer guidance on monitoring protocols.</p> <p>Whilst promising, the evidence is open to bias, it isn't suitable for anyone with undiagnosed urinary tract abnormalities, and the prospect of increased resistance after treatment is surprising and unexplained. It would, however,</p>	<p>Thank you for this comment. We hope the below addresses your points:</p> <p>Monitoring: The committee agreed that monitoring for methenamine hippurate was important, and they have made a new recommendation to cover this as follows:</p> <p>"1.2.11: Review treatment with methenamine hippurate within 6</p>

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						<p>be helpful for NICE to voice the clinically relevant reasons for its placement in the guideline to facilitate informed discussion with patients and medicines management teams.</p> <p>If methenamine is not recommended in pregnancy [BNF] then we would suggest that this recommendation should say “consider methenamine ... in non-pregnant women ...” rather than including them in rec 1.2.9. It will be very hard to get an evidence base for safety in pregnancy.</p> <p>We believe this recommendation should be followed by a shared decision making recommendation e.g. as with vaginal oestrogen and antibiotics? Eg, “When considering a trial of methenamine for preventing recurrent UTI, explain that it may reduce the number of UTIs less than an antibiotic, and it may reduce the number of antibiotic-resistant bugs but the evidence is uncertain.”</p>	<p>months, and then every 12 months, or earlier if agreed with the person.”</p> <p>Pregnancy: No changes have been made as the committee considered the existing wording, which includes a bullet point to clarify that methenamine hippurate is for people "who are not pregnant", to be sufficiently clear. The committee agreed that seeking specialist advice for people who are pregnant was appropriate.</p> <p>Shared decision making: The committee agreed that there were factors to discuss before deciding on methenamine hippurate for preventing recurrent UTIs. The uncertainty of the evidence is intended to be communicated in the strength of this recommendation, which is weak as denoted by the recommendation to "consider" methenamine hippurate. There is also further information to consider in the summary of committee discussion which will be</p>

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							linked to this recommendation. The committee considered that antibiotic resistance was an important contextual factor, so it is detailed in the evidence reviews, but was not a priority to discuss with individuals, as people are not likely to be choosing between antibiotics and methenamine hippurate at this point.
53.		Royal College of General Practitioners	Guideline	011	009/018	Whilst the evidence for treatment with lactobacilli isn't of the highest quality, this is easily available and present in foodstuffs. In NICE's evidence review, cranberry seems no longer thought to be effective whereas, certain strains of lactobacilli might be. Surely, therefore the emphasis in these two paragraphs might reflect this finding/ comparison.	Thank you for your comments. Changes to recommendations about probiotics and cranberry products are not within scope of this update. We have not made changes to this content as a result of this comment.
54.		Royal College of General Practitioners	Guideline	General	General	We recommend including practical checklists, decision trees, or flowcharts to help GPs quickly determine the appropriate course of action for different patient demographics.	Thank you for your feedback. We published a visual summary (which includes a flowchart) and a patient decision aid alongside the 2018 guideline to help aid implementation of the more complex areas of this guideline. We are updating these as part of the 2024 update.

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55.		Royal College of General Practitioners	Equality and Health Inequalities Assessment	General	General	We welcome the identification of several groups at risk of inequality (e.g., people from lower socioeconomic backgrounds, ethnic minorities, and people with disabilities). However, more actionable recommendations are needed to address barriers these groups may face, such as targeted outreach programs or access to culturally sensitive healthcare services	Thank you for your comment. We have noted your concerns about these groups however the effectiveness of interventions to address barriers to primary care that these groups face was outside of the scope of this evidence review. We will note these concerns for future updates.
56.		Royal College of General Practitioners	Evidence review	General	General	<p>The evidence reviews provide detailed analysis of methenamine hippurate and topical oestrogen, but we believe these could be summarised into key points relevant for GPs, such as indications, contraindications, and specific scenarios where one treatment might be preferred over another.</p> <p>We would value some consideration for reviewing methenamine as it will require some monitoring at least yearly to ensure that the person isn't getting lots of UTIs.</p> <p>Methenamine could end up on repeats forever. We question whether a review 6 months after initiation should be encouraged.</p> <p>Methenamine will be new to many GPs and therefore, we believe, providing information</p>	<p>Thank you for this comment. We hope the below addresses your points:</p> <p>Summary of key points for GPs: the committee have added a recommendation about factors that should be discussed with someone who is considering methenamine hippurate, which includes considerations about the impact of taking alkalinising agents at the same time. Information about contra-indications would not usually be included in NICE guidance, and the BNF should be referred to for this information.</p>

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						<p>may be helpful. BNF states that methenamine is contraindicated in severe dehydration. It would be good to understand what the risk is. Presumably, methenamine should be withheld if a patient has a risk of dehydration such as vomiting or severe diarrhoea. We understand that if this recommendation goes forward, discussions with BNF will take place to remove the 'less suitable for prescribing'</p>	<p>Monitoring: The committee agreed that monitoring for methenamine hippurate was important, and they have made a new recommendation to cover this as follows:</p> <p>"Review treatment with methenamine hippurate within 6 months, and then every 12 months, or earlier if agreed with the person."</p> <p>Dehydration: The committee discussed this and agreed that dehydration severe enough to be a contra-indication for methenamine hippurate was a rare occurrence and not something that would need discussing with most patients, especially as many people with recurrent UTIs are hyperhydrating to alleviate symptoms.</p> <p>BNF: That is correct, the BNF page for methenamine hippurate will be updated with the publication of this guideline.</p>

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**None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry.*

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