



GLOBAL RESPIRATORY
INFECTION PARTNERSHIP



Module 2: **Diagnosing and defining appropriate antibiotic use in URTIs**

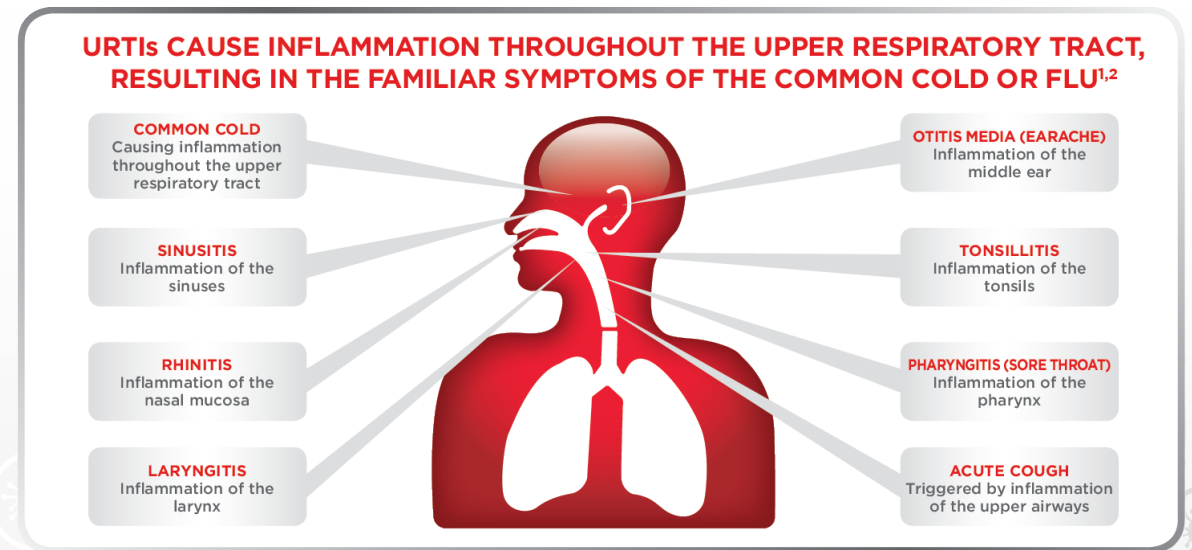
Continuing professional development module from the Global Respiratory Infection Partnership

LEARNING OBJECTIVES

- To **understand** signs and symptoms of an upper respiratory tract infection (URTI)
- To **know** when an antibiotic is appropriate for patients with a URTI
- To **learn** about the appropriate treatment options for a URTI and the benefits of personalised symptomatic relief

WHAT IS A URTI?

- An URTI is an acute infection of the nose, sinuses, throat and/or ears; acute upper respiratory viral infections are the most common type of disease in humans¹
- URTIs can include pharyngitis, sinusitis, common cold, otitis media and influenza.^{1,2} For the vast majority of patients the infection is mild to moderate in severity, self-limiting and complications are rare³
- The **manifestation, symptoms and severity of a URTI can vary between patients**. Patients with a URTI can present with one or more symptoms, depending on the cause, duration and severity of the infection.¹ Symptoms can include a runny or blocked nose, sore throat, cough, headache, sinus pressure or pain, earache, no energy, and/or fever¹



¹. Eccles R. Lancet Infect Dis 2005;5:718-25; ². Baron S. Medical Microbiology 4th edition. Chapter 93. Infections of the Respiratory System. 1996. University of Texas Medical Branch at Galveston, Galveston, Texas; ³. Francis NA, et al. BMJ 2009;339:b2885

WHAT CAUSES URTIs?

- Viruses cause the majority of URTIs, with the remainder caused by bacteria.¹ The **symptoms of a bacterial or a viral throat infection are similar** (see table) and it is hard to differentiate between the two based on symptoms alone²⁻⁴
- Pharyngitis, for example, is the result of an inflammatory response to infection which can be triggered by either a viral or bacterial URTI
- However, distinguishing between bacterial and viral URTIs is not critical for most decisions on antibiotic use, as the majority of bacterial and viral infections can be cleared by a healthy immune system^{5,6}
- URTIs are difficult to prevent due to easy transmission and airborne pathway, through sneezing, coughing or nose blowing.⁷ However, practising good hand hygiene can help prevent the spread of URTIs^{7,8}

Symptoms of a bacterial or viral throat infection^{2,3}

Symptom	Bacterial infection	Viral infection
Swollen tonsils	✓	✓
Swollen neck glands	✓	✓
Discomfort when swallowing	✓	✓
Sore throat	✓	✓
Tonsillar exudates	✓	✓/✗
Absence of cough	✓	✓/✗
Fever	✓	✓/✗

1. Hildreth CJ, et al. JAMA 2009;302:816; 2. Shulman ST, et al. Clin Infect Dis 2012;55:e86-102; 3. Centor RM, et al. Med Decis Making 1981;1:239-46; 4. Altiner A, et al. Scan J Prim Health Care 2009;27:70-3; 5. van Duijn HJ, et al. Br J Gen Pract 2007;57:561-8; 6. Worrall GJ. Can Fam Physician 2007;53:1961-2; 7. Fashner J, et al. Am Fam Physician 2012;86:153-9; 8. Jefferson T, et al. Cochrane Database Syst Rev 2011;1:CD006207

ARE ANTIBIOTICS EFFECTIVE FOR URTIs?

- As antibiotics only affect bacteria, and the majority of URTIs are of viral origin, **antibiotics are not recommended for the treatment of most URTIs**.¹ There are numerous trials reporting only very modest reductions in symptom duration or severity, if present at all, regardless of the infecting organism²
- When considering providing an antibiotics, a **risk vs. benefit** decision-making process should be adopted. For healthy adults, the risks tend to greatly outweigh the benefits:
 - There is only a modest reduction in symptoms and duration when patients are treated with antibiotics and most patients get better without them.¹⁻³ One study of patients with sore throat observed that 90% of both treated and untreated patients were symptom-free within 7 days³
 - The effects of many antibiotics are not immediate. It takes time for antibiotics to reduce symptom severity in respiratory infections⁴
 - Patients may suffer from side effects⁵⁻⁷
 - Antibiotic use can increase antibiotic resistance, reducing their efficacy in the future^{5,6}



21 patients with sore throat need to be treated with antibiotics for 1 patient to benefit from this treatment after 7 days⁶

1. Hildreth CJ, et al. JAMA 2009;302:816; 2. Van Duijn HJ, et al. Br J Gen Pract 2007;57:561-8; 3. Worrall GJ. Can Fam Physician 2007;53:1961-2; 4. Butler CC, et al. J Antimicrob Chemother 2010;65:2472-8; 5. Kenealy T, Arroll B. Cochrane Database Syst Rev 2013;6:CD000247; 6. Spinks A, et al. Cochrane Database Syst Rev 2013;11:CD000023; 7. Wilton L, et al. Drug Saf 2003;26:589-97

URTI MANAGEMENT: MEETING THE PATIENT'S NEEDS

- **Patient views and expectations often influence doctors** to prescribe antibiotics.¹ However, antibiotics do not fulfil the patient's needs:¹⁻⁶
 - Getting better faster – many patients want to get back to normal as soon as possible, however, evidence shows that, compared with placebo, the benefits of antibiotics for patients with sore throat are 'modest'
 - Symptom relief – while the body fights the infection, effective symptomatic relief will help to reduce pain, discomfort and fever; antibiotics do not provide effective symptom relief
 - Kill the source of infection – as most URIs are viral and antibiotics target bacteria, antibiotics are not a suitable treatment option. In addition, the immune system is able to fight most infections on its own, bacterial or viral. Therefore, antibiotics are not needed

Factors that may influence (inappropriate) antibiotic prescribing⁷

Patient/parent factors	Anxiety
	Misconceptions about what antibiotics do
	Belief in healing power of the healthcare professional (HCP)
	Return to work needs
	Day care needs
Healthcare professional factors	Real or perceived patient/parent pressure
	Economic concerns (eg patients missing work, loss of client for HCP)
	Reduced appointment time, allowing little time to educate patient
	Responsiveness to patient satisfaction surveys, that may be salary linked
	Lack of knowledge, or awareness of knowledge that is not implemented

In the majority of cases, **symptomatic relief products are an effective and appropriate way of meeting the patient's needs³**

1. Van Duijn HJ, et al. Br J Gen Pract 2007;57:561-8; 2. Fashner J, et al. Am Fam Physician 2012;86:153-9; 3. Thomas M, et al. Br J Gen Pract 2000;50:817-20; 4. Hildreth CJ, et al. JAMA 2009;302:816; 5. Spinks A, et al. Cochrane Database Syst Rev 2013;11:CD000023; 6. Shephard A, et al. Poster 852 presented at the 23rd European Congress of Clinical Microbiology and Infectious Diseases, 27-30 April 2013, Berlin, Germany; 7. Harrison PF, Lederberg J, eds. antimicrobial resistance: issues and options: Workshop report. 1998

WHEN SHOULD ANTIBIOTICS BE CONSIDERED: HIGH-RISK PATIENTS

- Use the **exclusion vs. inclusion** principle – most patients with URTIs will not require an antibiotic (as the majority of URTIs are caused by viruses¹) unless specific inclusion criteria are present. For example, patients with very severe illness or patients considered at high risk, may need an antibiotic to prevent secondary complications. High-risk factors include:^{2,3}



The frail or elderly (>65 years)



Babies and infants under 2 years of age



Pregnant women



Existing co-morbidities including, but not limited to, chronic lung disease, heart disease, kidney disorders, blood disorders, endocrine disorders, liver disorders, metabolic disorders, neurological conditions, diabetes, cystic fibrosis and people with HIV



Immunocompromised (e.g. people receiving chemotherapy and those with HIV)




Morbidly obese (obesity may diminish immune response to infection⁴)



Specific populations (e.g. American Indians, Alaskan Natives, Torres Strait Islanders and Aboriginal populations who are more likely to contract and die from respiratory infections^{5,6})

1. Hildreth CJ, et al. JAMA 2009;302:816; 2. Centers for Disease Control and Prevention. People at high risk of developing flu-related complications. 2013. Available at: http://www.cdc.gov/flu/about/disease/high_risk.htm (accessed April 2019); 3. Influenza Specialist Group. Who is at risk. 2014. Available at: <http://www.isg.org.au/index.php/clinical-information/who-is-at-risk/> (accessed April 2019); 4. Mancuso P. Pulm Pharmacol Ther 2013;26:412-9; Moberley SA, et al. Communicable diseases intelligence quarterly report 2016;40:E340-6; Groom, A, et al. Am J Public Health 2014;104:S460-9

WHEN TO REFER FROM THE PHARMACY TO A GENERAL PRACTITIONER OR PHYSICIAN: RED FLAGS

 **Red flag** signs, or serious alarm symptoms, may indicate a more serious illness and further medical help is required.^{1,2} This may include treatment with antibiotics. Red flags for URTIs are listed below:¹⁻³



Shortness of breath



Great difficulty swallowing



Coughing up blood



Neck swelling on one side, unrelated to lymph nodes



Very high temperature or night sweats



Drooling or muffled voice



Wheezing sounds when breathing

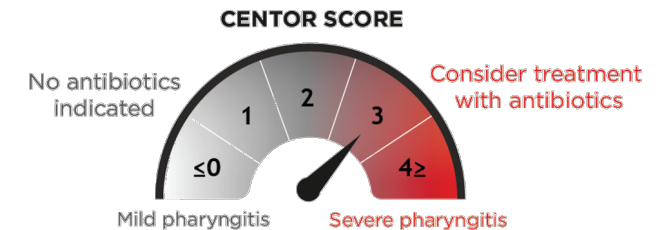
1. van Duijn HJ, et al. Br J Gen Pract 2007;57:561-8; 2. Centor RM, Samlowski R. AAFP 2011;83:26-8; 3. Merck Manual. Sore throat. 2013. Available at: http://www.merckmanuals.com/professional/ear_nose_and_throat_disorders/approach_to_the_patient_with_nasal_and_pharyngeal_symptoms/sore_throat.html (accessed April 2019)

THE ROLE OF PREDICTIVE TOOLS: SORE THROAT EXAMPLE

- Although sore throat is often caused by a viral infection,¹ antibiotics may be prescribed for confirmed bacterial infections as they could reduce illness duration and the risk of possible complications²
- Symptoms of a bacterial or a viral throat infection can be similar, and it is hard to differentiate between the two based on symptoms alone³
- Point-of-care testing is useful to help identify the cause of sore throat, particularly in high-risk groups and the modified Centor criteria are used widely to predict if the throat infection is a bacterial infection, caused by group A Streptococcus (Strep A)^{2,4,5}
- The modified Centor criteria has been shown to reduce unnecessary antibiotic prescriptions by up to 88% in a study of 441 adult patients, comparing physician judgement against the Centor score recommendation²

THE LIKELIHOOD OF STREP THROAT CAN BE ESTIMATED USING MODIFIED CENTOR CRITERIA,⁵⁻⁷ WITH ANTIBIOTICS CONSIDERED FOR PATIENTS WITH THREE OR MORE CENTOR CRITERIA

CRITERIA	POINTS
Absence of cough	1
Swollen and tender anterior cervical nodes	1
Temperature >38°C	1
Tonsillar exudates or swelling	1
Age	
3-14 years	1
15-44 years	0
45 years and older	-1
Cumulative score	—



¹. Ebell MH, et al. JAMA 2000;284:2912-8; ². McIsaac WJ, et al. CMAJ 2000;163:811-5; ³. Shulman ST, et al. Clin Infect Dis 2012;55:e86-102; ⁴. Fine AM, et al. Arch Intern Med 2012;172:847-52; ⁵. McIsaac WJ, et al. JAMA 2004;291:1587-95; ⁶. Centor RM, Samlowski R. Am Fam Physician 2011;83:26-8; ⁷. Centor RM, et al. Med Decis Making 1981;1:239-46

THE ROLE OF PREDICTIVE TOOLS: SORE THROAT EXAMPLE

Note: Centor criteria identifies the risk of Strep A infection only
It doesn't identify other bacterial causes of sore throat

- Assessing patients with a physical examination and identifying Centor variables has value above the actual Centor score
- Patients can feel reassured following a thorough examination of the throat and neck where permitted
- Further reassurance that the infection is not serious is one of the primary reasons patients consult their physician with sore throat¹
- GRIP recommends a simple 1,2,3-step approach to responsibly address the needs of individuals with sore throat in the pharmacy setting

1,2,3 APPROACH FOR SORE THROAT

1

ADDRESS PATIENT'S
CONCERNS

2

BE VIGILANT -
ADDRESS SEVERITY

3

COUNSEL ON EFFECTIVE
SELF-MANAGEMENT

1. van Driel ML, et al. Ann Fam Med 2006;4:494-9

THE GRIP 1,2,3-STEP APPROACH

		DOCTOR	PHARMACIST
1	ADDRESS PATIENT'S CONCERNS	<ul style="list-style-type: none"> + Identify the main symptoms, their duration and impact + Ask about treatments taken so far 	<ul style="list-style-type: none"> + Identify the main symptoms, their duration and impact + Ask about treatments taken so far
2	BE VIGILANT - ASSESS SEVERITY	<ul style="list-style-type: none"> + Identify risk factors and co-morbidities + Ask about red flag symptoms + Reassure patient with a thorough examination of the throat and neck 	<ul style="list-style-type: none"> + Identify risk factors and co-morbidities + Ask about red flag symptoms + Determine whether referral to a doctor is needed and address any objections
3	COUNSEL ON EFFECTIVE SELF-MANAGEMENT	<ul style="list-style-type: none"> + Reassure the patient regarding the non-serious nature of the infection, duration of symptoms and symptomatic treatment advice + Recommend appropriate symptomatic relief products, taking into account individual preferences + Advise on when to return to the clinic if symptoms have not improved 	<ul style="list-style-type: none"> + Reassure the patient regarding the non-serious nature of the infection, duration of symptoms and symptomatic treatment advice + Recommend appropriate symptomatic relief products, taking into account individual preferences + Advise on when a doctor's visit might be needed if symptoms don't improve

WHAT IS THE ROLE OF SYMPTOMATIC RELIEF?

- All symptoms of URTIs can be addressed by a selection of symptomatic relief products. **Different active agents and formulations offer a range of benefits**, so treatment can be tailored to individual patients¹
- Efficacy is important and the **speed and duration of action can vary between products**. Formulation and dose format may also have a role in patients' treatment decisions and experience¹
- Multiple active ingredients may be required for the treatment of differing symptoms



Solubles



Drops



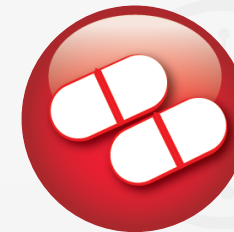
Syrups



Gargles



Lozenges



Tablets



Sprays

¹ Oxford JS, Leuwer M. J Clin Pract 2011;65:524-30

SYMPTOMATIC RELIEF OPTIONS

- The following symptomatic treatments can be recommended to patients to help relieve their URTI symptoms

INFECTION	RECOMMENDED TREATMENTS
Sore throat/tonsillitis	Anti-inflammatory lozenge (flurbiprofen, benzydamine) Medicated lozenge (local anaesthetic, antiseptic) Pain relief (paracetamol or ibuprofen tablets)
Common cold	Pain relief (paracetamol or ibuprofen tablets) Tablets containing decongestant or antihistamine Decongestant nasal spray
Flu	Pain relief (paracetamol or ibuprofen tablets) Tablets containing a decongestant or antihistamine Decongestant nasal spray
Runny nose/blocked nose	Decongestant nasal spray Tablets containing a decongestant or antihistamine
Sinusitis	Corticosteroid nasal spray Pain relief (paracetamol or ibuprofen tablets) Tablets containing a decongestant or antihistamine
Earache	Pain relief (paracetamol or ibuprofen tablets) Medicated ear drops (local anaesthetic)
Dry, tickly cough	Cough suppressant (dextromethorphan)

SYMPTOMATIC RELIEF OPTIONS: SORE THROAT EXAMPLE

- For sore throat, as well as relieving pain, products can differ in their speed of onset¹ (i.e. products with local delivery are faster acting than systemic treatments and may also provide sensorial benefits like demulcency), duration, mode of action, delivery method and product-related side effects

Examples of formulations and active ingredients	Local delivery	Relieves pain	Anti-inflammatory effect	Demulcent effect	Low dose, low risk of adverse effect	Notes
Local non-steroidal anti-inflammatory drug (NSAID) lozenge (e.g. flurbiprofen)	✓	✓ ^{1-4,6}	✓ ⁵	✓ ⁴	✓ ^{1-4,6}	Locally inhibits prostaglandin production ⁵ to target inflammation. Local anti-inflammatory ⁵ and pain relieving ^{1-4,6} action in the throat
Local NSAID throat spray (e.g. flurbiprofen)	✓	✓ ^{7,8}	✓ ⁵	✗	✓ ^{7,8}	Locally inhibits prostaglandin production ⁵ to target inflammation. Directly targets the throat ⁹ to provide local anti-inflammatory ⁵ and pain relieving ^{7,8} action
Medicated lozenge containing antiseptics/anaesthetics (e.g. amylmetacresol [AMC], 2,4-dichlorobenzyl alcohol [DCBA], hexylresorcinol, lidocaine)	✓	✓ ¹⁰⁻¹³	✗	✓ ¹⁰	✓ ^{10, 13}	Lozenge dissolves slowly to release active ingredients. ¹⁴ AMC/DCBA and hexylresorcinol have antiseptic/antibacterial/antiviral actions and block voltage-gated Na ⁺ channels in a local anaesthetic-like manner ^{11,14} Lidocaine is a local anaesthetic, blocks voltage-gated Na channels ^{11,14}
Oral NSAID tablet (e.g. ibuprofen)	✗	✓ ¹⁵⁻¹⁷	✓ ¹⁶	✗	✗	NSAIDs inhibit prostaglandin production throughout the body and in the central nervous system ¹⁵ to relieve pain, inflammation and fever. ¹⁶ Slower acting ¹⁷ than local treatments ^{4,7}
Oral analgesic tablet (e.g. paracetamol)	✗	✓ ^{15,16}	✗	✗	✗	Paracetamol is thought to act on prostaglandins in the central nervous system ¹⁸ to relieve pain ¹⁸ and fever ¹⁶ but has only low-level anti-inflammatory activity ¹⁸

1. Oxford JS, Leuwer M. J Clin Pract 2011;65:524-30; 2. Blagden M, et al. Int J Clin Pract 2002;56:95-100; 3. Watson N, et al. Int J Clin Pract 2000;54:490-6; 4. Benrimoj SI, et al. Clin Drug Invest 2001;21:183-93; 5. Schachtel B, et al. Pain 2014;155:422-8; 6. Sefia E, et al. Poster presented at the annual scientific meeting of the British Pain Society, 24-27 April 2007, Glasgow, UK; 7. Schachtel B, et al. Pain Pract 2016;16:6-176 [abstract]; 8. Bychkova V, et al. Int J Clin Pharm 2017;39:208-341 [abstract]; 9. de Looze F, et al. Eur J Gen Pract 2016;22:111-8; 10. Veale D, et al. Curr Drug Deliv 2017;14:725-33; 11. Wade AG, et al. BMC Fam Pract 2011;12:6; 12. Buchholz V, et al. Naunyn Schmiedebergs Arch Pharmacol 2009;380:161-8; 13. McNally, D et al. Int J Clin Pract 2010;64:194-207; 14. McNally, D et al. J Pharm Pharm Sci 2012;15:281-94; 15. Burian M, Geisslinger G. Pharmacol Ther 2005;107:139-54; 16. Rainsford KD. Inflammopharmacology 2009;17:275-342; 17. Schachtel BP, et al. Clin Pharmacol Ther 1994;55:464-70; 18. Graham GG, et al. Inflammopharmacology 2013;21:201-32

SORE THROAT CASE STUDY: MEET PRIYA

PRIYA HAS VISITED HER LOCAL PHARMACY COMPLAINING OF A SORE THROAT

“My throat is so scratchy... I can’t talk and it hurts to swallow. I just want it to go away... I’ve had enough”



CASE DETAILS

AGE: 27 years

BACKGROUND: Works as a public relations executive, which requires her to be talking to her team/clients all day

SYMPTOMS: Sore, scratchy and painful throat for 3 days, with an unproductive, dry cough

IMPACT: Symptoms are affecting her speech and ability to swallow, and she is feeling unwell at work

OTHER CONCERNS: She would like some analgesics and thinks antibiotics are the best option to stop her from passing symptoms on to others

HEALTH STATUS: Otherwise healthy

OTHER MEDICATIONS: Antihistamines for seasonal allergies

SEE HOW 1,2,3 CAN BE USED TO HELP PRIYA

ADDRESS PATIENT'S CONCERNS

1 ADDRESS PATIENT'S CONCERNS

- Identify the main symptoms, their duration and impact
- Ask about treatments taken so far



The pharmacist sympathises with Priya and acknowledges her frustrations

It sounds really frustrating... tell me what symptoms bother you most, and how long you've been having them, and we can work out what to do"



Priya confirms that her throat has been sore and scratchy for the past 3 days and she has been drinking hot lemon drinks to soothe her throat

"What bothers me most is the scratchy pain, which gets worse when I try to talk or swallow"

BE VIGILANT - ASSESS SEVERITY

2 BE VIGILANT - ASSESS SEVERITY

- Identify risk factors and co-morbidities
- Ask about red flag symptoms
- Determine whether a referral is needed and address any objections



The pharmacist tells Priya that her sore throat sounds painful and will likely benefit from symptomatic relief. Some more details on her health are requested to understand what treatment would be best for her

“Although it’s really frustrating, most sore throats clear up by themselves in less than 1 week”



Priya confirms that she doesn’t have any other health issues and is not taking any medications except antihistamines. She doesn’t have any worrying symptoms, but is concerned that she ought to get antibiotics

“I’ve had antibiotics for my sore throat in the past”



The pharmacist explains to Priya that it is unlikely she will benefit from antibiotics as they don’t act on the painful symptoms, but there are some treatments that can provide relief for her pain and difficulty swallowing

“Sore throats are almost always caused by viruses, so antibiotics won’t work. There are treatments that can rapidly address the sore throat pain and difficulty swallowing”

COUNSEL ON EFFECTIVE SELF-MANAGEMENT

3 COUNSEL ON EFFECTIVE SELF-MANAGEMENT

- Determine what the patient needs from symptomatic relief
- Recommend appropriate symptomatic relief products, taking into account individual preferences
- Advise on when a doctor's visit might be needed



The pharmacist asks Priya about what sort of treatment she might prefer. Priya would ideally like something that acts rapidly, that can help her when she needs to talk, and that will relieve her pain and difficulty swallowing

“I want something that acts fast, and I need to be able to talk and swallow without pain”

The pharmacist recommends anti-inflammatory lozenges to quickly relieve the pain and for help with swallowing. Priya also decides that she will use an anti-inflammatory spray for extra relief when needed

Before completing the consultation, the pharmacist reminds Priya to look out for any red flag symptoms and advises her what to do next



“If you get any of those worrying symptoms we discussed, or if you're still feeling unwell after 1 week, you might need to visit your doctor, or you can always come back here for some more advice”

ASSESSMENT

Question 1: Which of these definitions describes a URTI?

- A. Infection of the main airway and lungs
- B. Infection of the urinary tract
- C. Infection of the sinuses, nose, throat and/or ears

Question 2: In which of these scenarios should an antibiotic be considered?

- A. 6 year old with runny nose and cough for 2 days - otherwise fit and healthy
- B. 75 year old with diabetes, experiencing flu-like symptoms for 10 days
- C. 35 year old lady with sinus pain and blocked nose for 5 days. No cough or fever

Question 3: Which of these symptoms is a red flag?

- A. Difficulty breathing
- B. Earache
- C. Blocked nose

ANSWERS: 1=C, 2=B, 3=A.

