

Annex III

Amendments to relevant sections of the product information

Note:

These amendments to the relevant sections of the product information are the outcome of the referral procedure.

The product information may be subsequently updated by the Member State competent authorities, in liaison with the reference Member State, as appropriate, in accordance with the procedures laid down in Chapter 4 of Title III of Directive 2001/83/EC.

A - Summary of product characteristics (SmPC)

For quinolones and fluoroquinolones containing medicinal products, the existing product information shall be amended (insertion, replacement or deletion of the text as appropriate) to reflect the agreed wording as provided below (new text **underlined and in bold**, deleted text ~~strike-through~~):

Note: the indications are grouped under headings or cover terms that encompass the same medical entity; all changes apply to both the cover term and sub-headings, as relevant.

1. Section 4.1: therapeutic indications

In addition of the amendments recommended below, the following sentence should be included in all quinolones and fluoroquinolones containing medicinal products at the end of section 4.1:

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

1.1 Deletion of indications

1.1.1 For all quinolones/fluoroquinolones

The indications in the table below should be deleted for all quinolones/ fluoroquinolones containing products

Pharyngitis-Tonsillitis <ul style="list-style-type: none">• Pharyngitis• Tonsillitis
Laryngitis
Acute bronchitis
Prophylaxis of travellers' diarrhoea <ul style="list-style-type: none">• Prophylaxis of infectious gastroenteritis (traveller's diarrhoea)• Prevention of traveller's diarrhoea
Preoperative preparations for chronic cholesteatomatous otitis and chronic otitis spreading to bone
Septicaemia
Selective decontamination of gastrointestinal tract in patients with compromised immune system
Prevention of exacerbations in women with recurring urinary tract infections <ul style="list-style-type: none">• Frequent, recurrent urinary infection prophylaxis• Long term prophylaxis of recurrent urinary infections• Prophylaxis of frequently repeating infections of urinary tract infections• Prevention of systemic urinary tract infections• Prophylaxis of systemic urinary tract infections

Prevention of infection in surgical procedures
<ul style="list-style-type: none"> • Prophylaxis after surgeries or interventions in the urogenital system <ul style="list-style-type: none"> ○ prophylaxis after surgeries or interventions in the urogenital system ○ Prophylaxis of recurrent urinary infections following trans-urethral surgery or trans-rectal prostatic biopsy
Vaginal infections
Meningitis
Infection of cerebrospinal fluid
Endocarditis
Nosocomial pneumonia
External otitis

1.1.2 Additional deletions of indication(s) for specific quinolones/fluoroquinolones

Additionally for the active substance stated below, the following indications should also be deleted:

Pefloxacin

- Acute and chronic prostatitis, including severe forms
- Acute uncomplicated pyelonephritis
- Malignant external otitis
- Exacerbations of broncho-pulmonary infections in cystic fibrosis

Should medicinal products no longer have any authorised indications with a positive benefit-risk balance then the national competent authorities should take the appropriate action in line with the conclusions on this procedure under Article 31 of Directive 2001/83/EC.

1.2 Amendment of indications

1.2.1 For all quinolones/fluoroquinolones

The indications in the table below should be restricted for all quinolones/ fluoroquinolones containing products in order to be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.

Therefore the following text should be added in Section 4.1 as relevant:

“In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.”

<p>Uncomplicated cystitis</p> <ul style="list-style-type: none"> • Simple uncomplicated acute cystitis • Acute cystitis in women • Simple uncomplicated acute cystitis in the premenopausal adult women • Recurrent cystitis in women • Acute uncomplicated infection of lower urinary tract (simple cystitis)
<p>Acute exacerbation of chronic bronchitis and of chronic obstructive pulmonary disease</p> <ul style="list-style-type: none"> • Acute exacerbation of chronic obstructive pulmonary disease including chronic bronchitis • Acute exacerbations of chronic bronchitis • Exacerbation of chronic obstructive pulmonary disease
<p>Acute bacterial rhinosinusitis</p> <ul style="list-style-type: none"> • Acute sinusitis • Acute bacterial sinusitis
<p>Otitis media acute</p>

1.2.2 Additional amendments of indications for specific quinolones/fluoroquinolones

Additionally for the following active substances, the following indications should be amended as recommended below:

Ciprofloxacin

Current indications in product information of ciprofloxacin containing products	Recommended wording
Adults	
<ul style="list-style-type: none"> • Urethritis and cervicitis due to bacteria susceptible to fluoroquinolones 	<ul style="list-style-type: none"> • Gonococcal urethritis and cervicitis due to susceptible <i>Neisseria gonorrhoeae</i>
<ul style="list-style-type: none"> • Bone and joint infections 	<ul style="list-style-type: none"> • Infections of the bones and joints
<ul style="list-style-type: none"> • Treatment of infections in neutropenic patients • Infection in immunocompromised patients 	<ul style="list-style-type: none"> • Ciprofloxacin may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection
<ul style="list-style-type: none"> • Urinary tract infection 	<ul style="list-style-type: none"> • Uncomplicated acute cystitis <i><u>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</u></i> • Acute pyelonephritis • Complicated urinary tract infections • Bacterial prostatitis
Children and adolescents	

<ul style="list-style-type: none"> Broncho-pulmonary infections in cystic fibrosis caused by <i>Pseudomonas aeruginosa</i> 	<ul style="list-style-type: none"> Broncho-pulmonary infections due to <i>Pseudomonas aeruginosa</i> in patients with cystic fibrosis
<ul style="list-style-type: none"> Complicated urinary tract infections and pyelonephritis 	<ul style="list-style-type: none"> Complicated urinary tract infections and acute pyelonephritis

Levofloxacin

Current category 1 indications in product information of levofloxacin	Recommended wording of category 1 indications
<ul style="list-style-type: none"> Pyelonephritis and complicated urinary tract infections (see section 4.4) 	<ul style="list-style-type: none"> Acute pyelonephritis and complicated urinary tract infections (see section 4.4)
<ul style="list-style-type: none"> Acute exacerbation of chronic bronchitis (last line) 	<ul style="list-style-type: none"> Acute exacerbation of chronic obstructive pulmonary disease including bronchitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i>
<ul style="list-style-type: none"> skin and soft tissue infections skin and soft structure infections 	<p>Complicated skin and soft tissue infections / Complicated skin and skin structure infections</p> <p><i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i></p>

Moxifloxacin

Current category 1 indications in product information of moxifloxacin	Recommended wording of category 1 indications
<ul style="list-style-type: none"> Acute exacerbation of chronic bronchitis (last line) 	<ul style="list-style-type: none"> Acute exacerbation of chronic obstructive pulmonary disease including bronchitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i>

Ofloxacin

Current indications in product information of ofloxacin containing products	Recommended wording
<ul style="list-style-type: none"> • Pyelonephritis and complicated urinary tract infections 	<ul style="list-style-type: none"> • Acute pyelonephritis and complicated urinary tract infections
<ul style="list-style-type: none"> • Prostatitis, epididymo-orchitis <ul style="list-style-type: none"> ○ Chronic bacterial prostatitis (complicated or uncomplicated) ○ Prostatitis by E. coli ○ Prostatitis, epididymo-orchitis ○ Prostatitis, infection of the epididymis and the testicle ○ severe prostatitis 	<ul style="list-style-type: none"> • Bacterial prostatitis, epididymo-orchitis
<ul style="list-style-type: none"> • Pelvic inflammatory disease, in combination treatment <ul style="list-style-type: none"> ○ Acute pelvic inflammatory disease ○ Pelvic inflammatory disease, in combination treatment ○ Pelvic region infection in women (in combination with other antibiotics) ○ Inflammatory pelvic disease, in combinations treatment ○ Upper genital tract infection in women (see 4.4) (complicated or uncomplicated) ○ Upper gynaecological tract infections, including infections due to susceptible strains of Neisseria gonorrhoeae 	<ul style="list-style-type: none"> • Pelvic inflammatory disease, in combination with other antibacterial agents
<ul style="list-style-type: none"> • Sepsis due to above-mentioned genito-urinary infections 	<ul style="list-style-type: none"> • Urosepsis (only applicable for i.v. formulation)

<ul style="list-style-type: none"> • Uncomplicated cystitis (last line) <ul style="list-style-type: none"> ○ Uncomplicated cystitis ○ Uncomplicated cystitis (should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of these infections) ○ Uncomplicated cystitis (XX should only be used if antibacterial treatment considered as first choice of treatment is deemed unfit/inappropriate) 	<ul style="list-style-type: none"> • Uncomplicated cystitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i>
<ul style="list-style-type: none"> • Urethritis (last line) <ul style="list-style-type: none"> ○ Urethritis (should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of these infections) ○ Urethritis (XX should only be used if antibacterial treatment considered as first choice of treatment is deemed unfit/inappropriate) 	<ul style="list-style-type: none"> • Urethritis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i>
<ul style="list-style-type: none"> • Bone and joint infections (last line) <ul style="list-style-type: none"> ○ Bone and joint infections: such as osteomyelitis or septic arthritis. (complicated or uncomplicated) ○ Infections of bones (osteitis, osteomyelitis) ○ Bone and joint infections ○ Gram negative infection of bones and joints ○ Bone infections (such as osteomyelitis and orthopaedic material/implant infection, especially when used in association with other antibiotics like rifampicin) ○ Alternative form of treatment for bones and joints infections 	<ul style="list-style-type: none"> • Bone and joint infections <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i>

<ul style="list-style-type: none"> • Severe skin and soft-tissue infections (last line) 	<ul style="list-style-type: none"> • Complicated skin and soft-tissue infections <p><i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i></p>
<ul style="list-style-type: none"> • Acute sinusitis (last line) 	<ul style="list-style-type: none"> • Acute bacterial sinusitis <p><i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i></p>
<ul style="list-style-type: none"> • Acute exacerbation of chronic bronchitis (last line) 	<ul style="list-style-type: none"> • Acute exacerbation of chronic obstructive pulmonary disease including bronchitis <p><i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i></p>
<ul style="list-style-type: none"> • Community acquired pneumonia (last line) <ul style="list-style-type: none"> ○ Community acquired pneumonia ○ Community acquired pneumonia (ofloxacin should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of these infections) 	<ul style="list-style-type: none"> • Community acquired pneumonia <p><i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i></p>
<ul style="list-style-type: none"> • Prevention of infections due to ofloxacin susceptible pathogens (prophylaxis of infections, in patients with a significant reduction in resistance to infections (e.g., in neutropenic states) 	<ul style="list-style-type: none"> • Prophylaxis of bacterial infection in neutropenic patients
<ul style="list-style-type: none"> • Non-gonococcal urethritis and cervicitis <ul style="list-style-type: none"> ○ Non-gonococcal urethritis and cervicitis ○ Acute non-gonococcal urethritis and cervicitis caused by <i>Chlamydia</i> 	<ul style="list-style-type: none"> • Non-gonococcal urethritis and cervicitis

<p><i>trachomatis</i></p> <ul style="list-style-type: none"> ○ combination therapy for the treatment of cervical infections 	
<ul style="list-style-type: none"> • Gonorrhoea <ul style="list-style-type: none"> ○ Gonorrhoea ○ Gonococcal and non-gonococcal urethritis and cervicitis (complicated or uncomplicated) ○ Uncomplicated urethral and cervical gonorrhoea. ○ Uncomplicated acute gonococcal urethritis and cervicitis ○ Gonococcal urethritis due to susceptible strains of <i>Neisseria gonorrhoeae</i> and non-gonococcal urethritis 	<ul style="list-style-type: none"> • Gonococcal urethritis and cervicitis due to susceptible <i>Neisseria gonorrhoeae</i>
<ul style="list-style-type: none"> • Chlamydia 	<ul style="list-style-type: none"> • Non-gonococcal urethritis and cervicitis
<ul style="list-style-type: none"> • Tuberculosis 	<ul style="list-style-type: none"> • Tuberculosis, in combination treatment
<ul style="list-style-type: none"> • Chronic sinusitis 	<ul style="list-style-type: none"> • Acute exacerbation of chronic sinusitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i>
<ul style="list-style-type: none"> • Superinfection of chronic otitis (whatever its nature) and cavities after mastoidectomy 	<ul style="list-style-type: none"> • Chronic suppurative otitis media
<ul style="list-style-type: none"> • Bacterial gastroenteritis <ul style="list-style-type: none"> ○ Bacterial gastroenteritis ○ Bacterial enteritis ○ Intestinal infections ○ bacterial diarrhoea, which needs antibacterial treatment 	<ul style="list-style-type: none"> • Infections of the gastrointestinal tract (e.g. travellers' diarrhoea) <u><i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i></u>
<ul style="list-style-type: none"> • Abdominal and hepatobiliary infection <ul style="list-style-type: none"> ○ Abdominal and hepatobiliary infection 	<ul style="list-style-type: none"> • Complicated intra-abdominal infections

<ul style="list-style-type: none"> ○ intra-abdominal infection ○ intra-abdominal and bile-ducts infections ○ Infections of abdominal cavity, including pelvic area ○ Abdominal cavity infections including of the pelvic bone ○ Infections of the abdomen and the lesser pelvis ● Cholangitis 	
<ul style="list-style-type: none"> ● Post-exposure prophylaxis and curative treatment of anthrax. 	<ul style="list-style-type: none"> ● Inhalation anthrax: post-exposure prophylaxis and curative treatment
<ul style="list-style-type: none"> ● Treatment of ofloxacin sensitive prophylaxis of bacterial infections in patients with weakened resistance (for example neutropenic patients) 	<ul style="list-style-type: none"> ● Treatment of bacterial infections in neutropenic patients ● Prophylaxis of bacterial infections in neutropenic patients
<ul style="list-style-type: none"> ● Urinary tract infections <ul style="list-style-type: none"> ○ Urinary tract infection ○ Upper and lower urinary tract infections ○ Upper and lower urinary tract infections, complicated or not ○ Infections of the upper and lower urinary tract ○ Upper and lower, acute and chronic urinary tract infections ○ Complicated and uncomplicated urinary tract infections (cystitis and pyelonephritis) ○ Upper and lower urinary tract infections coming from bacteria such as E. coli, K. pneumoniae, Proteus, P. aeruginosa 	<ul style="list-style-type: none"> ● Uncomplicated acute cystitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i> ● Acute pyelonephritis ● Complicated urinary tract infections
<ul style="list-style-type: none"> ● Lower urinary tract infections <ul style="list-style-type: none"> ○ Acute and chronic lower urinary tract infections 	<ul style="list-style-type: none"> ● Uncomplicated acute cystitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i> ● Complicated urinary tract infections
<ul style="list-style-type: none"> ● Sinusitis <ul style="list-style-type: none"> ○ Sinusitis 	<ul style="list-style-type: none"> ● Acute bacterial sinusitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the</i>

	<p><i>treatment of these infections.</i></p> <ul style="list-style-type: none"> • Chronic bacterial sinusitis
<ul style="list-style-type: none"> • Respiratory infections <ul style="list-style-type: none"> ○ Acute, chronic or recurrent respiratory tract infections; superior – acute otitis media, otitis externa, sinusitis, pharyngitis and laryngitis ○ Acute, chronic or recurrent respiratory tract infections caused by Haemophilus influenzae or other Gram-negative or multi-resistant pathogens, as well as by Staphylococcus aureus ○ Respiratory tract infections (with the exception, if infection is of pneumococcal origin or is suspected) ○ Severe respiratory infections caused by gram-negative bacilli and susceptible staphylococci ○ Lower respiratory tract infections 	<ul style="list-style-type: none"> • Acute exacerbations of chronic obstructive pulmonary disease including chronic bronchitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i> • Community-acquired pneumonia <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i>
<ul style="list-style-type: none"> • Pulmonary infections <ul style="list-style-type: none"> ○ Pulmonary infections [such as: acute exacerbation of chronic bronchitis, exacerbation of cystic fibrosis, nosocomial pneumonia, pulmonary tuberculosis by resistant mycobacteria, especially in immunocompromised patients (minor anti-tuberculosis medicine)] 	<ul style="list-style-type: none"> • Acute exacerbations of chronic obstructive pulmonary disease including chronic bronchitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i> • Community-acquired pneumonia <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i> • Pulmonary tuberculosis by resistant mycobacteria, especially in immunocompromised patients (minor anti-tuberculosis medicine)
<ul style="list-style-type: none"> • Pneumonia <ul style="list-style-type: none"> ○ Pneumonia, especially when caused by so-called "problematic" germs such as: E. coli, Klebsiella, Enterobacter, Proteus, Pseudomonas, Legionella or Staphylococcus ○ Pneumonia, above all if it's caused by bacteria such as Escherichia coli, Klebsiella, Enterobacter, Proteus, Pseudomonas, Legionella or Staphylococcus 	<p>Community-acquired pneumonia. In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</p>

<ul style="list-style-type: none"> • Bronchial suppurations, in the absence of any parenchymal lesion <ul style="list-style-type: none"> ▪ In chronic bronchitis during recurrent exacerbations • Bronchial suppurations, in the absence of any parenchymal lesion: <ul style="list-style-type: none"> ▪ In subjects at risk (chronic alcoholism, smoking, subjects over 65 years) 	<p>Acute exacerbations of chronic obstructive pulmonary disease including chronic bronchitis. In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</p>
<ul style="list-style-type: none"> • Ear, nose and throat infections <ul style="list-style-type: none"> ○ Ear, nose and throat infections (with the exception of acute tonsillitis) 	<ul style="list-style-type: none"> • Acute bacterial sinusitis <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i> • Chronic bacterial sinusitis • Acute otitis media <i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i> • Chronic suppurative otitis media
<ul style="list-style-type: none"> • Chronic ear, nose and throat infections <ul style="list-style-type: none"> ○ Severe chronic ENT infections caused by gram-negative bacilli and susceptible staphylococci ○ Chronic and recurrent infections of the nose, throat and ear, only when caused by Gram-negative pathogens, including Pseudomonas, or by Staphylococci ○ Chronic and recurrent infections of ears, nose and throat, above all if they are caused by gram-negative bacteria including Pseudomonas, or if they are caused by Staphylococcus ○ Ear, nose and throat (ENT) infections (such as: chronic sinusitis, superinfection in chronic otitis, prophylaxis of infections following inner ear surgery) ○ Chronic and recurrent 	<ul style="list-style-type: none"> • Chronic bacterial sinusitis • Chronic suppurative otitis media

otorhinolaryngological infections	
<ul style="list-style-type: none"> • Genital tract infections <ul style="list-style-type: none"> ○ Infections of genital organs ○ Infections of genitals ○ Severe genital tract infections caused by gram-negative bacilli and susceptible staphylococci 	<ul style="list-style-type: none"> • Bacterial prostatitis, epididymo-orchitis including cases due to susceptible Neisseria gonorrhoeae • Urethritis and cervicitis including cases due to susceptible Neisseria gonorrhoeae
<ul style="list-style-type: none"> • Gynaecological infections <ul style="list-style-type: none"> ○ Gynaecological infections 	<ul style="list-style-type: none"> • Urethritis and cervicitis including cases due to susceptible Neisseria gonorrhoeae • Pelvic inflammatory disease including cases due to susceptible Neisseria gonorrhoeae
<ul style="list-style-type: none"> • Skin and soft tissue infections <ul style="list-style-type: none"> ○ Skin and soft tissue infections ○ Gram negative infection of skin and soft tissue ○ Skin and soft tissues infections or infections of traumas from microbes such as E. coli, K. pneumoniae, Enterobacter, P. mirabilis and P. vulgaris, Providencia, Citrobacter, P. aeruginosa, S. aureus 	<ul style="list-style-type: none"> • Complicated skin and soft tissue infections <p><i>In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.</i></p>

Lomefloxacin

Current indications in product information for lomefloxacin containing products	Recommended wording
<ul style="list-style-type: none"> • Acute prostatitis 	<ul style="list-style-type: none"> • Acute bacterial prostatitis
<ul style="list-style-type: none"> • Acute pyelonephritis • Uncomplicated acute pyelonephritis 	<ul style="list-style-type: none"> • Uncomplicated acute pyelonephritis
<ul style="list-style-type: none"> • Urinary tract infections 	<ul style="list-style-type: none"> • Simple uncomplicated cystitis. <p><i>In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections</i></p> <ul style="list-style-type: none"> • Acute uncomplicated pyelonephritis
<ul style="list-style-type: none"> • Lower respiratory tract infections 	<ul style="list-style-type: none"> • Acute exacerbations of chronic obstructive

Current indications in product information for lomefloxacin containing products	Recommended wording
	<p>pulmonary disease including chronic bronchitis</p> <p><i>In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections.</i></p>

Norfloxacin

Current indications included in product information for norfloxacin containing products	Recommended wording
<ul style="list-style-type: none"> • Acute urinary tract infections in men <ul style="list-style-type: none"> ○ acute urinary tract infections in men ○ acute infection of lower urinary tract infections in men 	<ul style="list-style-type: none"> • Acute urinary tract infection in men
<ul style="list-style-type: none"> • Uncomplicated pyelonephritis <ul style="list-style-type: none"> ○ uncomplicated pyelonephritis ○ acute uncomplicated pyelonephritis in women 	<ul style="list-style-type: none"> • Uncomplicated acute pyelonephritis
<ul style="list-style-type: none"> • Complicated cystitis <ul style="list-style-type: none"> ○ chronic cystitis in women 	<ul style="list-style-type: none"> • Complicated acute cystitis
<ul style="list-style-type: none"> • Prostatitis <ul style="list-style-type: none"> ○ prostatitis ○ chronic bacterial prostatitis ○ Acute prostatitis caused by Escherichia coli 	<ul style="list-style-type: none"> • Bacterial prostatitis
<ul style="list-style-type: none"> • Gonorrhoea <ul style="list-style-type: none"> ○ gonorrhoea ○ uncomplicated gonorrhoea ○ Gonococcal urethritis, pharyngitis, proctitis or cervicitis from Neisseria gonorrhoeae irrespective of the production of penicillinase. ○ gonococcal urethritis without signs of pelvic dissemination, in men ○ cervical gonorrhoea without signs of pelvic 	<ul style="list-style-type: none"> • Gonococcal urethritis and cervicitis due to susceptible Neisseria gonorrhoeae

Current indications included in product information for norfloxacin containing products	Recommended wording
<p>dissemination</p> <ul style="list-style-type: none"> ○ urethral and cervical gonorrhoea ○ Gonorrhoea (urethritis and cervicitis) 	
<ul style="list-style-type: none"> • Gastroenteritis <ul style="list-style-type: none"> ○ bacterial gastroenteritis ○ Gastroenteritis ○ Acute bacterial gastroenteritis ○ bacterial enteritis ○ Acute bacterial gastroenteritis after stool culture and laboratory confirmation of the susceptibility of the causative organism to NOROCIN 	<ul style="list-style-type: none"> • Infections of the gastrointestinal tract (e.g. travellers' diarrhoea)
<ul style="list-style-type: none"> • Immunocompromised patients: <ul style="list-style-type: none"> ○ Infections in neutropenic patients (as prophylaxis). 	<ul style="list-style-type: none"> • Prophylaxis of bacterial infections in neutropenic patients
<ul style="list-style-type: none"> • Cystitis <ul style="list-style-type: none"> ○ Cystitis ○ Acute and chronic cystitis in women 	<ul style="list-style-type: none"> • Uncomplicated acute cystitis. In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections. • Complicated acute cystitis
<ul style="list-style-type: none"> • Lower urinary tract infections <ul style="list-style-type: none"> ○ Lower urinary tract infections 	<ul style="list-style-type: none"> • Uncomplicated acute cystitis. In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections. • Urethritis including cases due to susceptible Neisseria gonorrhoeae

Current indications included in product information for norfloxacin containing products	Recommended wording
	<ul style="list-style-type: none"> • Complicated acute cystitis
<ul style="list-style-type: none"> • Urinary tract infections <ul style="list-style-type: none"> ○ Urinary tract infections ○ Complicated and uncomplicated upper and lower urinary tract infections: cystitis, pyelitis, cystopyelitis ○ Upper and lower urinary tract infections, including cystitis, pyelitis and cystopyelitis caused by norfloxacin susceptible bacteria ○ Complicated and uncomplicated urinary tract infections ○ Acute urinary tract infections in men ○ Other lower urinary tract infections, including prostatic infections, and upper urinary tract infections with susceptible bacteria, in adults (i.e. other than uncomplicated acute cystitis) ○ Acute (except acute pyelonephritis) and chronic (except chronic complicated pyelonephritis) infections of urinary tract caused by sensitive microorganisms ○ Acute and chronic urinary tract infections, uncomplicated (cystitis, pyelitis) and complicated, excluding complicated pyelonephritis, acute or chronic ○ Acute infection of lower urinary tract infections in men ○ Acute lower urinary tract infection in men 	<ul style="list-style-type: none"> • Uncomplicated acute cystitis. In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections. • Urethritis including cases due to susceptible Neisseria gonorrhoeae • Complicated urinary tract infections (except complicated pyelonephritis) • Complicated acute cystitis
<ul style="list-style-type: none"> • Urinary tract and related infections <ul style="list-style-type: none"> ○ Complicated and uncomplicated, acute and chronic, upper and lower urinary tract infections. These infections include: cystitis, pyelitis, chronic prostatitis and infections related to urological surgical procedures, neurogenic bladder or nephrolithiasis (except acute and chronic complicated pyelonephritis) caused by bacteria sensitive to norfloxacin ○ Upper and lower, complicated and uncomplicated, acute and chronic urinary tract infections. These infections include cystitis, pyelitis, chronic prostatitis and those urinary infections associated with urological surgery, neurogenic bladder or nephrolithiasis caused by bacteria susceptible to [name of product] ○ Upper and lower, complicated and uncomplicated, acute and chronic urinary tract infections. These infections include cystitis, pyelitis, pyelocystitis, 	<ul style="list-style-type: none"> • Uncomplicated acute cystitis. In [indication] [name of product] should be used only when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections. • Bacterial prostatitis • Epididymo-orchitis including cases due to susceptible Neisseria gonorrhoeae • Urethritis including cases due to susceptible Neisseria gonorrhoeae • Complicated urinary tract infections (except complicated pyelonephritis) • Complicated acute cystitis

Current indications included in product information for norfloxacin containing products	Recommended wording
pyelonephritis, chronic prostatitis, epididymitis and those urinary tract infections associated with urological surgery, neurogenic bladder or nephrolithiasis caused by bacteria susceptible to [name of product]	
Medically incorrect indications	
<ul style="list-style-type: none"> • Prophylaxis of systemic urinary tract infections • Prevention of systemic urinary tract infections 	<ul style="list-style-type: none"> • Perioperative prophylaxis in invasive urological surgery

Pefloxacin

Current indications included in product information for pefloxacin containing products	Recommended wording
<ul style="list-style-type: none"> • Chronic sinusitis 	<ul style="list-style-type: none"> • Acute exacerbation of chronic bacterial sinusitis <p><i>In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections</i></p>
<ul style="list-style-type: none"> • Gonorrhoea • Gonococcal urethritis in humans 	<ul style="list-style-type: none"> • Gonococcal urethritis and cervicitis due to susceptible <i>Neisseria gonorrhoea</i>
<ul style="list-style-type: none"> • Severe/Serious gastro-intestinal bacterial infections 	<ul style="list-style-type: none"> • Serious gastro-intestinal bacterial infections
<ul style="list-style-type: none"> • Salmonella infections (carrier) • Germ carrying of salmonellosis 	<ul style="list-style-type: none"> • Salmonella infections (carrier)
<ul style="list-style-type: none"> • Bone and joint infections • Bone and joint infections (gram negative osteomyelitis) • Alternative form of treatment for bone and joint infections • Infections of bone and joints (osteomyelitis caused by gram-negative microorganisms) 	<ul style="list-style-type: none"> • Bone and joint infections
<ul style="list-style-type: none"> • Respiratory tract infections <ul style="list-style-type: none"> ○ Respiratory infections ○ Respiratory infection - severe 	<ul style="list-style-type: none"> • Acute bacterial sinusitis. <p><i>In [indication] [name of product] should</i></p>

Current indications included in product information for pefloxacin containing products	Recommended wording
<p>infections caused by gram-negative bacilli and susceptible staphylococci</p> <ul style="list-style-type: none"> ○ Infection of respiratory tract (acute exacerbation of chronic bronchitis, exacerbation in cystic fibrosis, nosocomial pneumonia) 	<p><i>be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections</i></p> <ul style="list-style-type: none"> • Acute exacerbation of chronic bacterial sinusitis. In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections. • Acute exacerbations of chronic obstructive pulmonary disease including chronic bronchitis. In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections.
<ul style="list-style-type: none"> • Pulmonary infections <ul style="list-style-type: none"> ○ Pulmonary infections (acute exacerbation of chronic bronchitis, exacerbation of cystic fibrosis, nosocomial pneumonia) 	<ul style="list-style-type: none"> • Acute exacerbations of chronic obstructive pulmonary disease including chronic bronchitis. In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections.
<ul style="list-style-type: none"> • Ear, nose and throat infections <ul style="list-style-type: none"> ○ Ear, nose and throat infections ○ Ear, nose and throat infection - severe infections caused by gram-negative bacilli and susceptible staphylococci ○ Ear, nose and throat (ENT) infections (such as: chronic sinusitis, external otitis) ○ Ear nose and throat infections (such as chronic sinusitis, malignant otitis externa) 	<ul style="list-style-type: none"> • Acute bacterial sinusitis. In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections. • Acute exacerbation of chronic bacterial sinusitis. In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections.
<ul style="list-style-type: none"> • Urinary infections <ul style="list-style-type: none"> ○ Urinary tract infections ○ Urinary infection - severe infections caused by gram-negative bacilli and susceptible staphylococci ○ Urinary tract infections (including prostatitis) ○ Infections of urinary tract (inclusive of prostatitis) 	<ul style="list-style-type: none"> • Acute uncomplicated cystitis. In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections

Current indications included in product information for pefloxacin containing products	Recommended wording
<ul style="list-style-type: none"> ○ Urinary tract infections (acute or recurrent cystitis, acute uncomplicated pyelonephritis) 	
<ul style="list-style-type: none"> • Genital tract infections <ul style="list-style-type: none"> ○ Genital infections (chronic prostatitis) ○ Genital tract infection - severe infections caused by gram-negative bacilli and susceptible staphylococci 	<ul style="list-style-type: none"> • Gonococcal urethritis and cervicitis including cases due to susceptible <i>Neisseria gonorrhoeae</i>
<ul style="list-style-type: none"> • Abdominal and hepato-biliary infections <ul style="list-style-type: none"> ○ Abdominal infections ○ Abdominal infections - severe infections caused by gram-negative bacilli and susceptible staphylococci ○ Hepatobiliary infections ○ Hepatobiliary infection - severe infections caused by gram-negative bacilli and susceptible staphylococci ○ Infections of bile ducts 	<ul style="list-style-type: none"> • Hepato-biliary infections • <i>Complicated intra-abdominal infections.</i> <i>In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections</i>
<ul style="list-style-type: none"> • Skin and soft tissue infections <ul style="list-style-type: none"> ○ Skin infections ○ Skin infection - severe infections caused by gram-negative bacilli and susceptible staphylococci ○ Skin and soft tissue infections by penicillin resistant <i>Staphylococcus</i> ○ Infections of skin and soft tissue caused by <i>staphylococcus</i> resistant to penicillin 	<ul style="list-style-type: none"> • Complicated skin and soft tissue infections. In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections

Prulifloxacin

Current indications included in product information for prulifloxacin containing products	Recommended wording
<ul style="list-style-type: none"> • Complicated infections of lower urinary tract 	<ul style="list-style-type: none"> • Complicated urinary tract infections

Rufloxacin

Current category indications included in product information for rufloxacin containing products	Recommended wording
Lower respiratory tract infections	<ul style="list-style-type: none"> • Acute exacerbations of chronic obstructive pulmonary disease including chronic

Current category indications included in product information for rifloxacin containing products	Recommended wording
	<p>bronchitis. <i>In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections</i></p>
Urinary tract infections	<ul style="list-style-type: none"> • Uncomplicated acute cystitis. <i>In [indication] [name of product] should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the treatment of these infections</i>

2. Section 4.4: special warnings and precautions for use

For quinolones and fluoroquinolones containing medicinal products, the existing product information shall be amended (insertion, replacement or deletion of the text as appropriate) to reflect the agreed wording as provided below (new text **underlined and in bold**, deleted text ~~strike-through~~):

The following new warning should be included at the beginning of the warning statements on **safety issues**:

The use of [INN] should be avoided in patients who have experienced serious adverse reactions in the past when using quinolone or fluoroquinolone containing products (see section 4.8). Treatment of these patients with [INN] should only be initiated in the absence of alternative treatment options and after careful benefit/risk assessment (see also section 4.3).

[...]

The following warning should be included:

Prolonged, disabling and potentially irreversible serious adverse drug reactions

Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses) have been reported in patients receiving quinolones and fluoroquinolones irrespective of their age and pre-existing risk factors. [INN] should be discontinued immediately at the first signs or symptoms of any serious adverse reaction and patients should be advised to contact their prescriber for advice.

The warning on tendinopathies / tendon disorders should be included/ amended as follows:

Tendinitis and tendon rupture

Tendinitis and tendon rupture (especially but not limited to Achilles tendon), sometimes bilateral, may occur as early as within 48 hours of starting treatment with quinolones and fluoroquinolones and have been reported to occur even up to several months after discontinuation of treatment. The risk of tendinitis and tendon rupture is increased in older patients, patients with renal impairment, patients with solid organ transplants, and those treated concurrently with corticosteroids. Therefore, concomitant use of corticosteroids should be avoided.

At the first sign of tendinitis (e.g. painful swelling, inflammation) the treatment with [INN] should be discontinued and alternative treatment should be considered. The affected limb(s) should be appropriately treated (e.g. immobilisation). Corticosteroids should not be used if signs of tendinopathy occur.

For systemically administered levofloxacin containing products the listing of risk factors within the first above mentioned sentence should additionally include "in patients receiving daily doses of 1000 mg levofloxacin".

The warning about peripheral neuropathies should be included/amended as follows:

Peripheral neuropathy

Cases of sensory or sensorimotor polyneuropathy resulting in paraesthesia, hypaesthesia, dysesthesia, or weakness have been reported in patients receiving quinolones and fluoroquinolones. Patients under treatment with [INN] should be advised to inform their doctor prior to continuing treatment if symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness develop in order to prevent the development of potentially irreversible condition. (see section 4.8)

3. Section 4.8: undesirable effects

An asterisk should be added to the title of selected SOCs as follows:

Musculoskeletal and connective tissue disorders*

Nervous system disorders*

General disorders and administrative site conditions*

Psychiatric disorders*

Eye disorders*

Ear and labyrinth disorders*

*Very rare cases of prolonged (up to months or years), disabling and potentially irreversible serious drug reactions affecting several, sometimes multiple, system organ classes and senses (including reactions such as tendonitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, depression, fatigue, memory impairment, sleep disorders, and impairment of hearing, vision, taste and smell) have been reported in association with the use of quinolones and fluoroquinolones in some cases irrespective of pre-existing risk factors (see Section 4.4).

B. Package leaflet: Information for the patient

For quinolones and fluoroquinolones containing medicinal products, the existing package leaflet shall be amended (insertion, replacement or deletion of the text as appropriate) to reflect the agreed wording as provided below (new text **underlined and in bold**, deleted text ~~strike through~~):

Section 2 Warnings and precautions

The following new warning should be included:

Before taking this medicine

You should not take fluoroquinolone/quinolone antibacterial medicines, including [product name], if you have experienced any serious adverse reaction in the past when taking a quinolone or fluoroquinolone. In this situation, you should inform your doctor as soon as possible.

The current warning statement on tendinopathies/tendon disorders should be amended with regard to risk factors, time to onset and need for monitoring of patients and should include at least the following information (or added as new statement if missing):

When taking this medicine

Pain and swelling in the joints and inflammation or rupture of tendons may occur rarely. Your risk is increased if you are elderly (above 60 years of age), have received an organ transplant, have kidney problems or if you are being treated with corticosteroids. Inflammation and ruptures of tendons may occur within the first 48 hours of treatment and even up to several months after stopping of <product name> therapy. At the first sign of pain or inflammation of a tendon (for example in your ankle, wrist, elbow, shoulder or knee), stop taking <product name>, contact your doctor and rest the painful area. Avoid any unnecessary exercise as this might increase the risk of a tendon rupture.

A new or current warning statement on peripheral neuropathies should include at least the following information:

You may rarely experience symptoms of nerve damage (neuropathy) such as pain, burning, tingling, numbness and/or weakness especially in the feet and legs or hands and arms. If this happens, stop taking <product name> and inform your doctor immediately in order to prevent the development of potentially irreversible condition.

The following new warning should be included:

Prolonged, disabling and potentially irreversible serious side effects

Fluoroquinolone/quinolone antibacterial medicines, including [product name], have been associated with very rare but serious side effects, some of them being long lasting (continuing months or years), disabling or potentially irreversible. This includes tendon, muscle and joint pain of the upper and lower limbs, difficulty in walking, abnormal sensations such as pins and needles, tingling, tickling, numbness or burning (paraesthesia), sensory disorders including impairment of vision, taste and smell, and hearing, depression, memory impairment, severe fatigue, and severe sleep disorders.

If you experience any of these side effects after taking [Name of product], contact your doctor immediately prior to continuing treatment. You and your doctor will decide on continuing the treatment considering also an antibiotic from another class.

Section 4. Possible side effects

The following new wording should be included after listing of side effects:

Very rare cases of long lasting (up to months or years) or permanent adverse drug reactions, such as tendon inflammations, tendon rupture, joint pain, pain in the limbs, difficulty in walking, abnormal sensations such as pins and needles, tingling, tickling, burning, numbness or pain (neuropathy), depression, fatigue, sleep disorders, memory impairment, as well as impairment of hearing, vision, and taste and smell have been associated with administration of quinolone and fluoroquinolone antibiotics, in some cases irrespective of pre-existing risk factors.