18 PRIMARY CARE SUMMARY

18.1 Scope and purpose of this section

18.1.1 This section contains advice and guidance for health professionals in primary care, in the event that the Department of Health has declared UK pandemic alert level 2 (indicating that cases of pandemic influenza have been identified in the UK, against a background of person to person transmission of the pandemic strain in the UK or other countries).

18.1.2 The advice in this section summarises the key elements found in the earlier Sections of this document. It is based on the best evidence available from previous pandemic and interpandemic periods. Thus the guidance may evolve as clinico-pathological information on the eventual pandemic virus emerges. Therefore, once an influenza pandemic is underway, users are strongly urged to ensure that they refer to the most up-to-date version of these guidelines (from web-based access points).

18.1.3 The advice is specific to a pandemic situation and does not apply to the management of seasonal increases in influenza, community acquired pneumonia, lower respiratory tract infections or exacerbations of COPD.

18.2 The impact of an influenza pandemic on primary care (refer to Section 2)

18.2.1 Estimates of case-numbers and excess deaths in a pandemic are based on the average attack rates and case-fatality rates calculated from the documented influenza pandemics which have occurred since 1900. They suggest a likely population attack rate of 25%, with a case-fatality rate of 0.37%, occurring in one, two or three annual waves of cases, with an individual wave lasting around 15 weeks.

18.2.2 This suggests that for a population of 1000 patients, 25 extra GP consultations and up to one excess death would be expected in the pandemic. A population of 100,000 might expect 2500 excess GP consultations, with 90 excess deaths (see Tables 2.2 and 2.3)

18.2.3 The numbers of consultations for influenza may be accompanied by a marked increase in consultations for related problems, including anxiety about symptoms which may or may not be caused by influenza, but reflect the concerns of patients, for their own health, for the health of household members and contacts, and concerning the availability of antiviral medication.

18.2.4 Information for patients will be available through a major campaign to provide public information through the media, and through the use of pre-prepared information algorithms for NHS Direct. Written material will be made available for use by patients and the public. It is hoped that this will reduce the burden of non-clinical work which falls on General Practice staff.

18.2.5 The clinical features of pandemic influenza (refer to Sections 3 and 11)

18.3.1 There is no reliable diagnostic feature of influenza.

18.3.2 The syndrome of influenza-like illness (ILI) described in Box 18.1, is strongly predictive of laboratory-confirmed influenza, especially when influenza is circulating in the community, as would be the case at UK Alert Levels 2 or more (see Appendix 1). The features of ILI are less frequently seen in children and younger adults but are still predictive of influenza, with a lower probability.

Box 18.1: **Clinical Case Definition (October 2005):**

The presence of fever and new (or, in those with chronic lung disease, worsening) cough of acute onset in the context of influenza circulating in the community.

(Important note - This definition may be modified once a pandemic occurs.)

18.3.3 While seasonal cases of influenza tend to present in children and the elderly, the age-range affects by pandemic influenza is likely to be broader, and different from that of seasonal influenza. Infants, small children and otherwise healthy adults may be seriously affected.

18.3.4 The range of clinical features in uncomplicated influenza is given in Section 3.2, Box 3.2. Features in a pandemic may differ from those seen in regular interpandemic (seasonal) influenza cases.

18.3.5 Tests for the diagnosis of influenza are only justified when the proportion of cases of influenza is low (14-20%) compared with other probable viral causes of ILI. (refer to Section 7.1) Therefore, early in a pandemic (UK Alert Levels 1,2 and 3) nasopharyngeal, or nose and throat, swabs in virus transport medium should be collected from all patients, where possible, and submitted to the local laboratory.

18.3.6 Once a pandemic is established (UK Alert Level 4), microbiological investigations are not recommended.

18.4 Severe and complicated influenza (refer to Sections 3.3 and 11.2)

18.4.1 Co-existing conditions such as asthma, COPD, cardiac failure, atrial fibrillation, coronary heart disease, diabetes mellitus, and chronic neurological conditions such as multiple sclerosis and epilepsy may be worsened by influenza infection.

18.4.2 The most common specific complications associated with influenza infection in adults are respiratory complications - acute bronchitis or influenza-related pneumonia. Other complications are listed in Table 3.1. Otitis media is the most common bacterial superinfection of influenza in children (see Table 11.2).

18.4.3 Influenza-related pneumonia can be caused primarily by influenza virus alone or by secondary bacterial infection. In addition to the usual well-recognised respiratory pathogens (predominantly *Streptococcus pneumoniae* and *Haemophilus influenzae)*, *Staphylococcus aureus* is a common cause of influenza-related pneumonia which can be severe. *Staph aureus* does not respond to treatment with amoxicillin and also has a significant rate of resistance to macrolide antibiotics (eg. erythromycin and clarithromycin).

18.5 Management of suspected pandemic influenza cases: early preparations and general measures (refer to Sections 2.7, 4 and 12)

18.5.1 **Triage.** A significantly increased demand for advice and consultation should be anticipated. Practices may make a number of arrangements to deal with this, including:

- Telephone triage and advice, which may be nurse-led
- Triage and advice immediately after reception at the practice
- Nurse-led prescribing of antiviral medication or antibiotics, according to patient group directives (PGDs)
- Making arrangements to provide domiciliary services for some patients who are unwell at home, but who may be able to avoid hospital admission
- Possibly making arrangements for patient care in intermediate-level community facilities, again to avoid hospital admission

18.5.2 Patients with non-ILIs who would normally self-medicate should be advised not to seek medical care where possible. PCTs and practices should formulate triage arrangements in advance of a pandemic to allow GPs to predominantly assess high risk patients and those developing complications.

18.5.3 **Patients at increased risk of severe disease or hospital admission.** These will be broadly the same patients as those who should receive routine annual influenza vaccination (see Appendix 2). Similarly, children with underlying respiratory or cardiac disease, immune compromise or who are non-ambulant are more likely to be severely affected. These patients should be promptly reassessed if the illness is getting worse to consider antibiotic treatment or hospital referral.

18.5.2 Pneumococcal vaccine. Patients over 65 years of age should already have been offered vaccination against *Streptococcus pneumoniae*, those who have not been vaccinated should be encouraged to have the vaccine before an influenza pandemic becomes established.

18.5.3 General advice to patients. Whether or not a patient has been prescribed antiviral drugs or antibiotics, they should be advised to self-manage their condition in the following ways:

- Stay at home and avoid contact with others until the feverish symptoms or elevated temperature have resolved
- Treat feverish symptoms, headache and myalgia with paracetamol, ibuprofen or (for patients over 16 years) aspirin
- Rest as much as possible while acute symptoms persist
- Drink plenty of fluids
- Avoid smoking
- Consider steam inhalation, short course of topical decongestants, throat lozenges.

18.5.4 The management of children in the community is summarised in Appendix 5.

18.6 Antiviral treatment (refer to Sections 9 &16)

18.6.1 The antiviral treatment of choice is oseltamivir (Tamiflu ™). This is given as a five-day course of oral tablets; 75mg twice daily for adults. Liquid suspension is available for children from the age of one year upwards.

Table 18.1: **Adult and child dosages of oseltamivir.**

Child aged >1yr; body weight 15kg or lower	30mg 12-hourly
15-23kg	45mg 12-hourly
24-40kg	60mg 12-hourly
Adult and child >40kg	75mg 12-hourly

(Dose to be reduced by 50% if creatinine clearance is less than 30ml/minute)

From clinical trial data accrued to date and based on seasonal, interpandemic influenza, the *anticipated* positive effect of antivirals in a pandemic will be:

(a) reduction of illness duration by 24 hours, and therefore more rapid mobilisation of affected individuals including essential workers
(b) a possible reduction in hospitalisation of infected individuals
(c) a reduction of subsequent antibiotic use by infected individuals

The evidence accrued to date does not suggest there will be a reduction of overall mortality.

18.6.2 Who should receive antiviral drugs? Ideally, antiviral treatment should be offered to every patient over the age of one year who

a) has an acute influenza-like illness
b) fever (38° C in adults, or 38.5 °C in children) *and*
c) presents within 48 hours of the onset of symptoms.

Note: Patients who are unable to mount an adequate febrile response eg. the immunocompromised or very elderly, make still be eligible for antiviral treatment despite the lack of documented fever.

18.6.3 There is no evidence of benefit for antiviral therapy commenced more than 48 hours after the onset of ILI in otherwise healthy patients. Immunosuppressed patients, including those on long-term corticosteroid therapy, may suffer more prolonged viraemia, and could possibly benefit from antiviral therapy commenced later than 48 hours after the onset of ILI. However, there is no evidence to support this hypothetical situation.

18.6.4 **Delivery of antivirals.** The drug will be delivered to PCTs via specific National distribution arrangements, and will be available through these arrangements to pharmacies or GP surgeries. PCTs are encouraged to plan for the delivery of antivirals to the large numbers of previously healthy persons with an ILI via community health professionals, while GPs should focus on those persons at high risk of complications (Appendix 2).

18.6.5 In the event of a shortage of antiviral drugs, the Department of Health will issue advice on the priority groups who should receive treatment. This will depend on evidence from previous pandemics, the epidemiological behaviour of the current pandemic and the real-time modelling of the effectiveness of antiviral treatment for various population groups. Information will be available through NHS websites, fax cascades and public information systems, including NHS Direct.

18.6.6 **Adverse effects of antiviral drugs.** The commonest adverse effect of oseltamivir is nausea. This can be managed with mild anti-emetic medication. Other side-effects are listed in Table 9.4.

18.7 Antibiotic treatment (refer to Sections 10.4 & 17)

18.7.1 Who should receive antibiotic treatment?

a) Patients in recognised high risk groups for severe and complicated influenza are at high risk of secondary bacterial infection (see Appendix 2). To reduce the burden on primary care of repeat consultations and potentially minimise influenza-related complications, it is recommended that these patients are offered prescriptions for 'prophylactic' antibiotics at their first consultation with clear instructions that the antibiotics should be used if the illness is not starting to settle after 24 hours or if there is worsening of symptoms.

b) **Patients who develop influenza-related pneumonia and acute bacterial otitis media.**

c) **Patients with significant worsening of symptoms** particularly recrudescent fever or increasing breathlessness.

18.7.2 Previously well adults with uncomplicated influenza or acute bronchitis complicating influenza, in the absence of pneumonia, do not routinely require antibiotics.

18.7.3 **Co-amoxiclav** is the preferred antibiotic for all ages. (Adult dose: 625 mg tds) In patients over 12 years of age, doxycycline is an alternative (Adult dose 200mg stat then 100mg po). See Appendix 7 for paediatric doses. (This empirical antibiotic regimen provides cover for *Staph aureus* in addition to the 'usual' respiratory pathogens.)

18.7.4 Most patients can de adequately treated with a week's course of antibiotic.

18.8 When to refer patients to hospital care (refer to Sections 5 & 12.4)

18.8.1 Patients with uncomplicated influenza infection usually do not require hospital referral.

18.8.2 Adults who experience a clinical deterioration of pre-existing medical problems (eg COPD) due to influenza infection should be managed according to recommended best practice for the medical condition in question.

18.8.3 In adults with influenza-related pneumonia clinically, hospital referral and assessment should be considered for patients with CRB-65 score of 1 *or 2.(*see Box 18.2)

18.8.4 Urgent hospital referral is recommended for adults with influenza-related pneumona and either a) bilateral chest signs of pneumonia or b) CRB-65 score of 3 or more.

Box 18.2: CRB-65 score - Severity assessment used to determine the management of influenza-related pneumonia in the community

Score 1 point for each feature present:
- **C**onfusion (Mental Test Score of ≤ 8, or new disorientation in person, place or time.)
- **R**espiratory rate ≥ 30/min
- **B**lood pressure (SBP < 90mmHg or DBP ≤ 60mmHg)
- Age ≥ **65** years

CRB-65 score	Recommended action
0	Likely suitable for home treatment
1 or 2	Consider hospital referral
3 or 4	Urgent hospital referral

18.8.5 Children who are severely ill, as indicated by signs of respiratory distress, cyanosis, severe dehydration, altered conscious level, complicated or prolonged seizure or sepsis, should be referred for assessment for admission (see Appendix 5).

19 MANAGEMENT OF ADULTS IN HOSPITALS- SYNOPSIS OF RECOMMENDATIONS

19.1 Scope and Purpose

19.1.1 This document is intended for use in the UK in event that the World Health Organisation declares that an influenza pandemic has started,[1] and the Department of Health in England (UK-wide lead agency on pandemic influenza, including the devolved administrations) has declared UK Pandemic Alert Level 2 (cases of pandemic influenza identified within the UK).

19.1.2 **These guidelines are not relevant for the management of patients affected by seasonal/ interpandemic influenza, lower respiratory tract infections, community acquired pneumonia or exacerbations of chronic obstructive pulmonary disease (COPD).**

19.1.3 Once an influenza pandemic is underway, users are strongly urged to ensure that they refer to the most up-to-date version of these guidelines (from web-based access points).

19.2 Severity assessment in hospital (see Appendix 4)

19.2.1 Patients with uncomplicated influenza infection would be expected to make a full recovery and do not require hospital care.

19.2.2 In uncomplicated infection, the illness usually resolves in 7 days although cough, malaise and lassitude may persist for weeks.

19.2.3 Patients with worsening of pre-existing comorbid medical conditions should be managed according to best practice for that condition with reference to published disease-specific guidelines, if available eg. COPD NICE guidelines.

(A) Influenza-related pneumonia

19.2.4 In hospital, patients with influenza-related pneumonia and who have a CURB-65 score of 3, 4 or 5 (see BOX 19.1) are at high risk of death and should be managed as having severe pneumonia.

19.2.5 Patients with bilateral lung infiltrates on chest radiography consistent with primary viral pneumonia should be managed as having severe pneumonia regardless of CURB-65 score.

19.2.6 Patients who have a CURB-65 score of 2 are at increased risk of death. They should be considered for short stay inpatient treatment or hospital supervised outpatient treatment. This decision is a matter of clinical judgment.

19.2.7 Patients who have a CURB-65 score of 0 or 1 are at low risk of death. They can be treated as having non-severe pneumonia and may be suitable for home treatment.

BOX 19.1: CURB-65 score

Score 1 point for each feature present:
- **C**onfusion (Mental Test Score of ≤ 8, or new disorientation in person, place or time)
- **U**rea > 7 mmol/l
- **R**espiratory rate ≥ 30/min
- **B**lood pressure (SBP < 90mmHg or DBP ≤ 60mmHg)
- Age ≥ **65** years

(B) High Dependency or Intensive Care Unit transfer

19.2.7 Patients with primary viral pneumonia *or* a CURB-65 score of 4 or 5 should be considered for HDU/ICU transfer.

19.2.8 General indications for HDU/ICU transfer include:
- persisting hypoxia with PaO_2 <8Kpa despite maximal oxygen administration
- progressive hypercarbia
- severe acidosis (pH<7.26)
- septic shock

19.2.9 Patients with influenza admitted to Intensive Care Unit should be managed by specialists with appropriate training in Intensive Care, Respiratory Medicine and Infectious Diseases.

19.3 General Investigations (see Appendix 3)

19.3.1 The following investigations are recommended in patients referred to hospital:

Test	Who this applies to
Full blood count	All patients
Urea and electrolytes	All patients
Liver function tests	All patients
Chest x-ray	All patients
Pulse oximetry	All patients. If <92% on air, then arterial blood gases.
ECG	Patients with cardiac and respiratory complications or comorbid illnesses.
C-reactive protein	If influenza-related pneumonia is suspected

19.3.2 In those patients who are subsequently followed up in a hospital outpatient clinic or by a general practitioner a repeat chest X-ray should be obtained at around 6 weeks if respiratory symptoms or signs persist or where there is a higher risk of underlying malignancy (especially smokers and those over 50 years of age).

19.3.3 Further investigations including a CT thoracic scan and bronchoscopy should be considered if the chest X-ray remains abnormal at follow up.

19.4 Microbiological investigations (see Appendix 3)

(A) Early in a pandemic (UK Alert Levels 1, 2 and 3)

19.4.1 ALL PATIENTS should have virological tests:

- **Nose and throat swabs** in virus transport medium.
- If presentation is more than 7 days after onset of illness, an 'acute' serum (5-10mLs clotted blood) should be collected and a 'convalescent' sample (5-10mLs clotted blood) obtained after an interval of not less than 7days.

19.4.2 PATIENTS WITH INFLUENZA-RELATED PNEUMONIA should also have the following bacteriological tests:

- **Blood culture** (preferably before antibiotic treatment is commenced)
- **Pneumococcal urine antigen** (20 mls urine sample)
- **Legionella urine antigen** (20 mls urine sample)
- **Sputum Gram stain, culture** and antimicrobial susceptibility tests on samples obtained from patients who:
  - i. are able to expectorate purulent samples, *and*
  - ii. have not received prior antibiotic treatment.
- **Paired serological examination for influenza/other agents**. Acute serum should be collected and a 'convalescent' sample obtained after an interval not less than 7days (both 5-10mLs clotted blood).

(B) Once a pandemic is established (UK Alert Level 4)

19.4.3 Virological tests are not routinely recommended.

19.4.4 PATIENTS WITH INFLUENZA-RELATED PNEUMONIA should have bacteriological tests in accordance to the severity of illness.

a. Non-severe pneumonia (CURB-65 Score 0, 1 or 2)

- No routine testing.
- In patients who do not respond to empirical antibiotic therapy, sputum samples should be sent for Gram stain culture and antimicrobial susceptibility tests.

b. Severe pneumonia (CURB-65 Score 3, 4 or 5, or bilateral CXR changes)

- **Blood culture**, preferably before antibiotic treatment is commenced
- **Pneumococcal urine antigen** (20mls urine)
- **Sputum Gram stain, culture** and antimicrobial susceptibility tests on samples obtained from patients who are able to expectorate purulent samples, *and* have not received prior antibiotic treatment.
- **Paired serological examination** for influenza/other agents. 'Acute' serum should be collected and a 'convalescent' sample obtained after an interval not less than 7 days (both 5-10mLs clotted blood).
- **Tracheal or endotracheal aspirate samples**, if available, should be sent for Gram stain, culture and antimicrobial susceptibility testing.

19.5 General Management (refer to Section 6)

(A) Initial management

19.5.1 Hypoxic patients should receive appropriate oxygen therapy with monitoring of oxygen saturations and inspired oxygen concentration with the aim to maintain $PaO_2 \geq 8$ Kpa and $SaO_2 \geq 92\%$. High concentrations of oxygen can safely be given in uncomplicated pneumonia.

19.5.2 Oxygen therapy in patients with pre-existing chronic obstructive pulmonary disease complicated by ventilatory failure should be guided by repeated arterial blood gas measurements. Non invasive ventilation may be helpful.

19.5.3 Patients should be assessed for cardiac complications and also volume depletion and their need for additional intravenous fluids.

19.5.4 Nutritional support should be given in severe or prolonged illness.

(B) Monitoring in hospital

19.5.5 Temperature, respiratory rate, pulse, blood pressure, mental status, oxygen saturation and inspired oxygen concentration should be monitored and recorded initially at least twice daily and more frequently in those with severe illness or requiring regular oxygen therapy. An Early Warning Score system is a convenient way to perform this.

19.5.6 In patients who are not progressing satisfactorily a full clinical reassessment and a repeat chest radiograph are recommended.

(C) Discharge and follow up

19.5.7 Patients should be reviewed 24 hours prior to discharge home. Those with more than 2 of the following unstable clinical factors should consider remaining in hospital:

- temperature > 37.8^{o}C
- heart rate > 100/min
- respiratory rate > 24/min
- systolic blood pressure <90mmHg
- oxygen saturation < 90%
- inability to maintain oral intake and abnormal mental status.

19.5.8 Follow up clinical review should be considered for all patients who suffered significant complications or who had significant worsening of their underlying disease, either with their general practitioner or in a hospital clinic.

19.5.9 At discharge or at follow up, patients should be offered access to information about their illness, take home medication and any follow up arrangements.

19.5.10 It is the responsibility of the hospital team to arrange the follow up plan with the patient and the general practitioner.

19.6 Use of antivirals (see Appendix 4)

19.6.1 Individuals should only be considered for treatment with antivirals (neuraminidase inhibitors) if they have all of the following:

- an acute influenza-like illness
- fever (>38^{0}C) *and*
- been symptomatic for 2 days or less.

19.6.2 Treatment Schedule: Adults - Oseltamivir 75mg every 12 hours for 5 days.
(Dose to be reduced by 50% if creatinine clearance is less than 30ml/minute)

19.6.3 Patients who are unable to mount an adequate febrile response eg. the immunocompromised or very elderly, may still be eligible for antiviral treatment despite lack of documented fever.

19.6.4 Hospitalised patients who are severely ill, particularly if also immunocompromised, may benefit from antiviral treatment started more than 48 hours from disease onset, although there is no evidence to demonstrate benefit, or lack of, in such circumstances.

19.7 Antibiotic Management (see Appendix 4)

(A) Bronchial complications without influenza-related pneumonia

19.7.1 Previously well adults with acute bronchitis complicating influenza, in the absence of pneumonia, do not routinely require antibiotics.

19.7.2 Antibiotics should be considered in those previously well adults who develop worsening symptoms (recrudescent fever or increasing dyspnoea) and have persisting purulent sputum.

19.7.3 Patients at risk of complications or superinfection should be considered for antibiotics in the presence of lower respiratory features. These include patients who are within the group currently recommended for influenza vaccination (see Appendix 2).

19.7.4 Patients with chronic lung disease, including COPD, should receive antibiotics in the presence of increased purulent sputum.

19.7.5 Most patients can be adequately treated with oral antibiotics.

19.7.6 The preferred choice includes co-amoxiclav or a tetracycline.

19.7.7 A macrolide such as clarithromycin (or erythromycin) or a fluoroquinolone active against *S pneumoniae and S aureus is* an alternative choice in certain circumstances.

(B) Non-severe influenza-related pneumonia

19.7.8 Most patients can be adequately treated with oral antibiotics.

19.7.9 Oral therapy with co-amoxiclav or a tetracycline is preferred.

19.7.10 When oral therapy is contra-indicated, recommended parenteral choices include intravenous co-amoxiclav, or a second or third generation cephalosporin (cefuroxime or cefotaxime).

19.7.11 A macrolide (erythromycin or clarithromycin) or a fluoroquinolone active against *S pneumoniae and Staphylococcus aureus* is an alternative regimen for those intolerant of penicillins or where there are local concerns over *C difficile* associated diarrhoea. Currently levofloxacin and moxifloxacin are the only recommended fluoroquinolones licenced in the UK.

(C) Severe influenza-related pneumonia

19.7.12 Patients with severe pneumonia should be treated immediately after diagnosis with parenteral antibiotics.

19.7.13 An intravenous combination of a broad spectrum beta-lactamase stable antibiotic such co-amoxiclav or a second (eg cefuroxime) or third (eg cefotaxime) generation cephalosporin together with a macrolide (clarithromycin or erythromycin) is preferred.

19.7.14 An alternative regimen includes a fluoroquinolone with enhanced activity against pneumococci together with a broad spectrum β-lactamase stable antibiotic or a macrolide. Currently levofloxacin is the only such fluoroquinolone licenced in the UK.

(D) Route and duration of antibiotic

19.7.15 Patients treated initially with parenteral antibiotics should be transferred to an oral regimen as soon as clinical improvement occurs and the temperature has been normal for 24 hours, providing there is no contra-indication to the oral route.

19.7.16 For most patients admitted to hospital with non severe and uncomplicated pneumonia, 7 days of appropriate antibiotics is recommended.

19.7.17 For those with severe, microbiologically undefined pneumonia, 10 days treatment is proposed. This should be extended to 14 to 21 days where *Staph aureus* or Gram negative enteric bacilli pneumonia is suspected or confirmed.

(E) Failure of empirical antibiotics

19.7.18 For those with non-severe pneumonia in hospital on combination therapy, changing to a fluoroquinolone with effective pneumococcal and staphylococcal cover is an option.

19.7.19 Adding further antibiotics effective against MRSA is an option for those with severe pneumonia not responding to combination antibiotic therapy.