UK OPERATIONAL FRAMEWORK FOR STOCKPILING, DISTRIBUTING AND USING ANTIVIRAL MEDICINES IN THE EVENT OF PANDEMIC INFLUENZA

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Purpose

1. This framework sets out arrangements for the storage and distribution of antiviral medicines from national stockpiles and provides guidance to support the development of effective local plans for making those medicines available for the treatment of patients. It supplements the guidance contained in UK Health Departments' Influenza Pandemic Contingency Plans and should be read in conjunction with those documents.

Aim

2. The overall aim is to ensure that antiviral medicines are available to treat patients suffering from influenza within 24-48 hours of the onset of symptoms. This framework therefore aims to:
    - arrange the secure storage, maintenance and when necessary distribution of supplies of antiviral medicines to local level
    - make initial supplies available at local access points throughout the UK within 24 hrs of a decision to distribute to those points
    - distribute additional supplies as the pandemic progresses in a way that mirrors its development, optimises clinical benefit and helps maintain availability over its entire period
    - monitor use, ensuring that available stocks are used in clinically effective and equitable ways that conform to nationally agreed clinical protocols and control measures
    - support the development of local arrangements that ensure antiviral medicines are accessible, supplies are used optimally over the whole pandemic and additional burdens on the healthcare system – particularly primary care - are minimised.

Principles

3. The principles guiding the release and use of antiviral medicines support the general principles for managing an influenza pandemic.

Application in the Devolved Administrations (DAs)

4. Health is a devolved responsibility in the UK and each country has its own Chief Medical Officer. Whilst this framework seeks to ensure a consistent and resilient UK wide approach, some differences in operational detail and organisational responsibilities apply in Northern Ireland, Scotland and Wales. All references to health organisations and agencies in England apply to their counterparts in other countries unless otherwise stated.

Organisational Responsibilities and Action Required

5. As an integral part of their influenza pandemic preparations:-

Primary Care Trusts (PCTs) in England should develop, maintain and periodically test multi–agency contingency plans that ensure effective arrangements are in place for:

- supplying information on local antiviral access arrangements to the Department of Health (DH) in the event of a raised pandemic alert level
- nominating one suitable point for the secure receipt and storage of antiviral supplies from national stockpiles and arranging distribution to access points when authorised
- providing public information on antiviral access as an integrated part of a local pandemic communications plan
- making the medicine available at the various access point locations, acute hospitals and other settings determined in plans
- providing suspension for children (see paragraph 19)
- making specific provision for closed communities such as residential homes and prisons
- monitoring availability/use and reporting to SHA daily
- ensuring that supplies are used in accordance with national guidance and in the most clinically effective and equitable way
- consulting and engaging partners – including local authorities/police/voluntary sector at all stages in the process

Strategic Health Authorities in England should:

- compile and forward information on local antiviral arrangements and access points to the DH if the pandemic alert level is raised
- provide communication support and public information advice on antiviral arrangements to PCTs
- link to Regional Directors of Public Health and Regional Resilience mechanisms
- coordinate operational arrangements, forwarding daily reports on stock levels/consumption to DH as the pandemic develops

All NHS Trusts, Primary Care Providers and other supporting health agencies/organisations should review their ability to maintain core services and their capacity to support PCTs in fulfilling the key requirements of this framework by ensuring maximum flexibility in the use of premises, facilities and staff.

DH in England and Health Departments in Devolved Administrations will forward information on access arrangements at the alert stage and provide cross-government advice. For consistency, they will also provide core messages for dissemination in communications plans. Chief Medical Officers (CMOs) will lead and coordinate the NHS and public health response, authorise release of antiviral medicines from national stockpiles, advise on optimal use, monitor availability and decide on priority changes to regulate consumption as a pandemic progresses.

The NHS Purchasing and Supply Agency (PaSA) in England will make and maintain contractual arrangements for the storage of antiviral stockpiles and distribution only when authorised by the CMO. Those arrangements will be the responsibility of Devolved Administrations in respect of their own part of the stockpile.

NHS Direct (NHSx24 in Scotland) will provide access information in their algorithms/pathways for pandemic influenza, including agreed health advice and specific information on when, where and how to access antiviral supplies.

The Health Protection Agency (HPA) will support the operational health response and has a major role in checking for antiviral resistance, monitoring the virus' susceptibility and assessing effectiveness in reducing complications/deaths.

Background and key planning assumptions for use of antiviral supplies

6. An influenza pandemic might consist of one or more waves, perhaps weeks or months apart, the first lasting up to 17 weeks. For planning purposes, the most likely scenario is a cumulative attack rate affecting 25% of the total population over the entire pandemic period. A suitable vaccine is unlikely to be available at the start of a pandemic and development could take 4-6 months.

7. Used primarily for patient treatment in the absence of - or as an adjunct to – vaccination, antiviral medicines may lessen the severity and duration of illness, reduce the need for antibiotics and lower demand for hospital care. Making best use of antiviral medicines over the entire pandemic period is therefore critical to the provision of effective patient care.

8. The stock levels of antiviral medicines normally available would be inadequate in a pandemic scenario and high international demand would make rapid post-event supply unlikely. UK Health Departments are therefore building stockpiles of the antiviral medicine osteltamivir phosphate (Tamiflu), comprising 14.6 million treatment courses – including powder for children - when completed.

9. Although stockpiles are intended to provide treatment for all influenza patients who might benefit at a cumulative clinical attack rate of 25%, small amounts may be devoted to controlling or limiting the spread of a pandemic in the initial stage. All plans must assume severe pressure on stocks. Measures to avoid waste and ensure that supplies are used only in accordance with national clinical guidelines must form an important element.

10. A pandemic is likely to affect all localities. To ensure equity, each PCT should assume that its maximum cumulative allocation of antivirals will be no more than needed for 25% of its total resident population. Until adult and child stock levels are fully established – and/or if the attack rate proves higher - it may be necessary to determine clinical priorities nationally and cascade to PCTs and clinicians if alert levels increase.

11. To inform and assist contingency planning an *'as fast as is reasonable'* temporal profile of the likely health impact and spread of a pandemic has been derived from historical data on previous pandemics. (Annex A). This provides working estimates of the additional workload expected over time as the pandemic develops. If a pandemic starts abroad better information on the attack rate, speed of spread and patient impact may be available before it reaches the UK.

12. Arrangements for antivirals must allow for initial uncertainties in these key areas and be flexible enough to adapt approaches as definitive data become available. Plans must also recognise that the response needs sustaining over a significant period and adjusting to match expected variation in additional workload as the pandemic develops.

Who should receive antiviral treatment?

13. Although a pandemic virus is likely to affect some groups more severely than others, it will be impossible to identify them until the virus starts circulating. National decisions on treatment priorities will be taken if consumption threatens to exceed available supplies but plans should assume that antiviral treatment will initially be available for all patients – including non residents and other nationals – who have:
    - an acute influenza-like illness ***and***
    - fever(>38^0C) ***and***
    - have been symptomatic for no more than 2 days.

14. The patients considered most at clinical risk from influenza related respiratory complications in seasonal outbreaks are listed in Annex B. If necessary - and subject to the advice of the UK National Influenza Pandemic Committee – that list will provide the basis for setting national treatment priorities. CMOs will monitor antiviral use and provide regular information and advice to health professionals on priorities and use as the pandemic develops.

Prescribing information, cautions and side effects

15. Oseltamivir is an orally administered neuraminidase inhibitor excreted mainly through the kidneys. It is licensed for the treatment of influenza A and B within 48 hours of the onset of symptoms in those aged above 1 year and post exposure prevention in those aged 13 and over when influenza is circulating in the community. Although not currently licensed for children under one, clinicians may need to consider treatment on a named patient basis in those under that age in a pandemic scenario if the child is so ill as to alter the risk-benefit argument in favour of doing so.

16. Caution is also necessary if recipients are suffering renal impairment, in breast-feeding or pregnant women, or if there is a history of a previous hypersensitivity reaction to the drug. It may also produce adverse reactions such as gastro intestinal symptoms, skin/hypersensitivity reactions and hepatic function disorders.

17. Reported side effects include gastrointestinal symptoms, headache, fatigue, insomnia, dizziness, conjunctivitis, epistaxis, rash, hypersensitivity reactions and - very rarely - hepatitis and Stevens Johnson syndrome.

18. Tamiflu is pre-packed in adult treatment courses – 75mg twice daily for five days. The recommended dose for children between 24 and 40kg bodyweight is 60mg twice daily. Although the use of adult dose capsules in those children is outside the license, there is no evidence to suggest that these slightly higher doses are harmful. Children over 23 kg (usually at or over 5 years of age) can therefore be given adult dose capsules for treatment in a pandemic scenario.

19. Children 23 kg body weight or below must be referred to a clinician for treatment. In order to treat children below 24kg but over one year old, PCTs will receive an allocation of their antiviral supply as oseltamivir phosphate powder based on 4.5% of their total resident population. Instructions for its preparation by hospital pharmacies will be included

20. Local plans must include arrangement for producing suspension for children to meet prescribed demand. They should also allow for the identification and treatment of contraindicated patients and providing advice on recognising and dealing with side effects.

Initial alert and stockpile release arrangements

21. Surveillance and alert systems for pandemic influenza are already in place. Release of antiviral stocks will require specific authorisation and CMOs may decide to provide initial supplies to PCTs if alert levels increase (UK levels 1+). They should not be distributed further unless authorised. At alert level 2+ an initial supply will be delivered within 24 hours for immediate distribution to access points.

22. Initial supplies - based on anticipated consumption over the first two weeks at an attack rate of 25% – will be supplemented by further deliveries that may become more frequent as the pandemic reaches its peak (See Annex C). To conserve supplies and ensure equitable distribution, subsequent releases will take account of expert advice, the pandemic's progress and reported usage.

Developing local plans for making antivirals available to patients

23. Providing safe storage and rapid access to antiviral medicines - without adding to pressures on health systems, encouraging spread of infection or allowing multiple doses to be obtained against one case – must form key elements of response plans.

24. PCTs should identify a location for the receipt and storage of antivirals and plan for onward distribution. Secure facilities are essential, preferably using hospital pharmacies with a qualified pharmacist in attendance. Police and other local partners must be involved in developing plans and appropriate security and control arrangements included at all stages.

25. Plans should determine the optimal numbers and locations of access points from which antiviral medicines will be available and how those locations will be publicised. Numbers should be restricted to balance ease of access with the need to maintain rigorous stock control and distribute. Arrangements are also required for supplying acute care facilities, residential accommodation and other closed establishments.

26. In planning the optimal numbers and locations of access points, PCTs will need to take account of population density, public transport links and similar factors. PCTs have the flexibility to use locally derived service specifications and any agreements with general practices or community pharmacies should be based on level of provision. DH will provide guidance on specifying service levels. Plans should also provide for daily monitoring and reporting consumption.

27. NHS Direct (NHSD) is likely to be the first point of contact for many and its advanced telephone system allows pressure sharing across all its sites. DH will therefore compile and forward information on local antiviral access arrangements in the event of any increased alert level.

28. Antiviral medicines are normally available only on prescription and patients – or others seeking medication on their behalf - are likely to present at surgeries, hospital emergency departments, walk in centres, community pharmacies and other health care establishments, risking serious detraction from their normal functions.

29. Whilst health care facilities might provide sufficient surge capacity to cope with the initial additional workload, response needs to be sustained and acute pressure is likely over a 6-8 week period. Many patients are unlikely to be well enough to attend health care facilities, GP capacity to undertake home visits will be severely limited, thresholds for hospital admission will be raised and pressure will be acute on all aspects of health and social care,

30. Supplementary arrangements will be necessary to ensure that patients have 24x7 access to antiviral medicines whilst allowing hospitals and GPs focus on greatest clinical need. As an integral part of their plans PCTs should consider alternative mechanisms for providing access to antiviral medicines that suit the geography, topography and requirements of their areas. Locally determined options might include:

- telephone diagnosis and remote prescribing
- pharmacists and other health professionals supplying antiviral medicines following a clinical protocol and authorised by a Patient Group Direction (PGD)
- utilising minor injuries units and walk in centres
- home visiting teams, utilising a range of health professionals and following agreed algorithms to assess and supply by PGD
- designating Influenza Centres - where patients able to attend can be assessed and supplied with the medicine if indicated.

31. To allow for remote prescribing and supply/administration within defined clinical protocols by pharmacists, nurses and other suitably qualified/trained health professionals in a pandemic scenario model Patient Group Directions (PGD) and Patient Specific Directives (PSD) are being developed and will be made available on each Health Department website for adoption by NHS organisations.

32. DH intends exploring options to use web based real time information systems to register and manage the distribution of antivirals but it is likely to prove difficult to eliminate misuse entirely in a pandemic scenario. Supplementary mechanisms for providing antiviral medicines must include a requirement for clear patient identification and make provision for basic documentation. PCTs should also consider additional precautionary measures such as compiling/sharing lists and checking against electoral registers.

Conclusion

33. Strategies for the rapid delivery and effective use of antiviral medicines are crucial to a successful health response to any influenza pandemic. Expert opinion suggests that they can lessen the severity of illness and may reduce demand for acute hospital beds by up to 50%. Local influenza pandemic arrangements must include provision for making them available to those patients who will benefit whilst conserving stock and ensuring their best use over the entire pandemic period.

34. As clinical knowledge is constantly advancing and vaccine development on-going, guidance on arrangements for the delivery and use of antiviral medicines will be subject to continuing review. Revisions or updated information will be published on Health Department websites as new information emerges.

Annex A

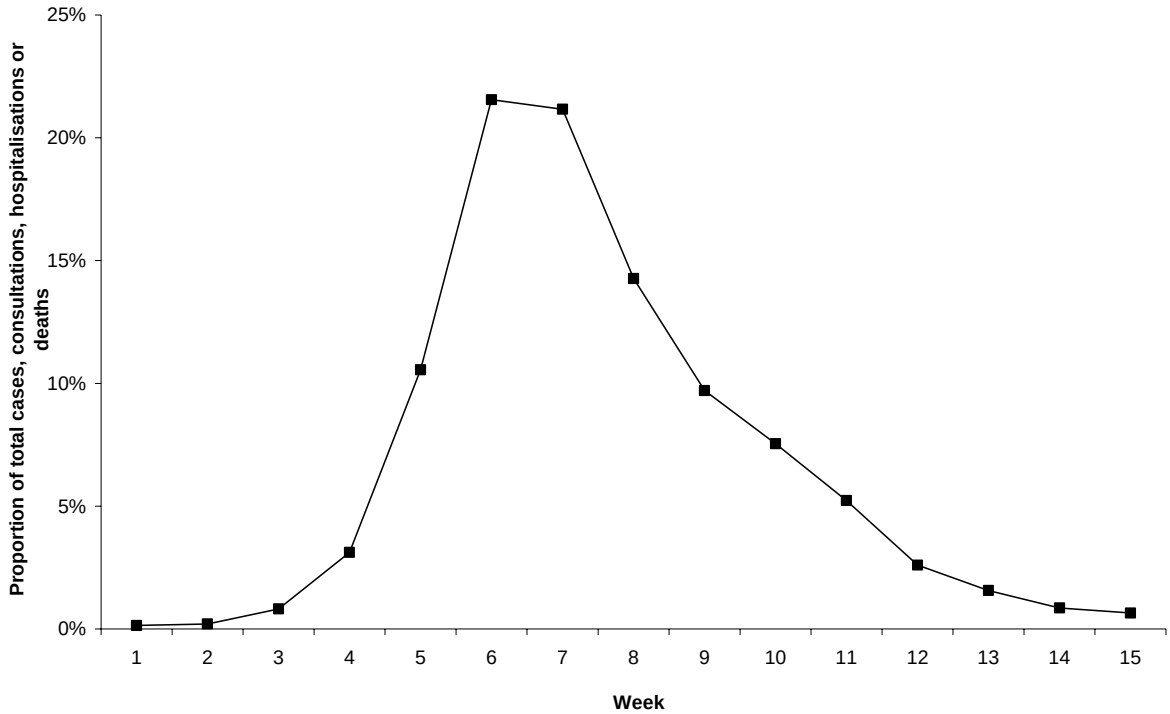
"AS FAST AS IS REASONABLE" TEMPORAL PROFILE FOR PANDEMIC FLU

i) Weekly percentages summarising the temporal component of UK data from the three 20th century pandemics

wk 1	wk 2	wk 3	wk 4	wk 5	wk 6	wk 7	wk 8	wk 9	wk 10	wk 11	wk 12	wk 13	wk 14	wk 15
0.1%	0.2%	0.8%	3.1%	10.6%	21.6%	21.2%	14.3%	9.7%	7.5%	5.2%	2.6%	1.6%	0.9%	0.7%

*Figures are percentages of the total for the outbreak as a whole. They may represent percentages of the total number of clinical cases, GP consultations, hospitalisations or deaths.

ii) Illustration of the "as fast as is reasonable profile" showing proportion of new clinical cases, consultations, hospitalisations or deaths by week.



*These percentages are derived from historical data on previous pandemics. The temporal profile they represent is considerably "faster" than the theoretical profile that has been used for health impact modelling. Antiviral treatment reduces the infectious period, thus slowing the spread of disease -and shifting the temporal profile to a slower one, with a relatively low peak and a relatively long base. This profile is therefore as "fast" as might reasonably be expected for a UK outbreak of pandemic flu and is particularly useful for operational planning where timescales are important. Plans designed with this fast profile in mind should perform well if, as seems likely, the actual profile proves to be somewhat slower.

Annex B

PATIENTS AT HIGH-RISK OF INFLUENZA-RELATED RESPIRATORY COMPLICATIONS

(adapted from Green Book, updated Influenza chapter August 2005)

Clinical risk category	Examples
Chronic respiratory disease, including asthma	This includes chronic obstructive pulmonary disease (COPD) including chronic bronchitis and emphysema, and such conditions as bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and bronchopulmonary dysplasia (BPD). Asthma requiring continuous or repeated use of inhaled or systemic steroids or with previous exacerbations requiring hospital admission. Children who have previously been admitted to hospital for lower respiratory tract disease.
Chronic heart disease	This includes congenital heart disease, hypertension with cardiac complications, chronic heart failure.and individuals requiring regular medication and/or follow-up for ischaemic heart disease.
Chronic renal disease	Including nephrotic syndrome, chronic renal failure, renal transplantation.
Chronic liver disease.	Including cirrhosis
Diabetes	Diabetes mellitus requiring insulin or oral hypoglycaemic drugs.
Immunosuppression	Due to disease or treatment. Including asplenia or splenic dysfunction, HIV infection at all stages. Patients undergoing chemotherapy leading to immunosuppression. Individuals on or likely to be on systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day (any age) or for children under 20kg a dose of 1mg or more per kg per day. *However, some immunocompromised patients may have a suboptimal immunological response to the vaccine.*
Long-stay residential care homes residents	This does *not* include prisons, young offender institutions, university halls of residence.
Aged 65 years or older	

Annex C

Estimated weekly totals for the amount of antivirals required to treat all cases given a 25% clinical attack rate.

Period	% of total clinical cases	Requirements per 100,000 population	
		Adult treatment courses[1]	Treatment courses for children under 23 kg[2]
Week 1	0.1%	34	2
Week 2	0.2%	49	2
Week 3	0.8%	196	9
Week 4	3.1%	745	35
Week 5	10.6%	2,519	119
Week 6	21.6%	5,146	242
Week 7	21.2%	5,052	238
Week 8	14.3%	3,407	161
Week 9	9.7%	2,319	109
Week 10	7.5%	1,801	85
Week 11	5.2%	1,249	59
Week 12	2.6%	622	29
Week 13	1.6%	374	18
Week 14	0.9%	206	10
Week 15	0.7%	156	7
All weeks	**100%**	**23,875**	**1,125**

[1] The adult treatment course is 10 pre-packed Tamiflu capsules.

[2] For children over 1 year old and under 23 kg, Tamiflu will be supplied as bulk powder, which will then need to be made into suspension. In the table above, each treatment course for children under 23 kg represents the maximum dose (0.66 grams of powder) Prescribed dose will be weight adjusted.