

	ePrescribing Decision Support Components: Dose Range Checking			
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ePrescribing Decision Support Components: Dose Range Checking in Secondary Care

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Glossary of Terms:

List any new terms created in this document. Mail the NPO Quality Manager to have these included in the master glossary above [1].

Term	Acronym	Definition

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1 Main Recommendations

The provision of Dose Range Checking functionality should be prioritised within systems according to age- and weight-based dosing (see section 6). This is mostly relevant for the extremes of age, especially for neonates and infants.

The concept of dosing in renal impairment is also highlighted as a priority. The two main elements related to this – namely renal dosing and renal dose checking – will be the subject of further guidance.

No emphasis is placed on how and where guidance / warnings may be displayed to system users within this document.

2 Summary

This document contains detailed information on one of the decision support components that relates to the electronic prescribing (ePrescribing) of medicines. It provides the background to the specific issue of dose range checking of medicines prescribed within hospital-based ePrescribing systems that will aid clinicians and technicians in understanding the rationale for this component of decision support and the finer detail of particular prescribing circumstances. There is a requirement to specify to what level systems must implement certain elements of the dose range checking functions in order to support decisions made in prescribing. This document therefore provides clarification to previously released functional specification documents around the complexity of such issues, but does not override the basic requirements that have previously been published.

The detail around this decision support component of dose range checking was proposed by the core ePrescribing team, but the relevance of different elements was refined at a national workshop using modified Delphi techniques and subsequently commented on following national consultation to gain a first overall consensus. It is the results of this process that are presented as final recommendations within this document.

The overarching theme in this document is that there are many complex situations where dose range checking can be relevant and that decision support could be used, but few clinicians believe that more than a basic set of rules should be routinely adopted in order to produce safe systems in practice. The most important areas of concern are age- and weight-related dosing. Both of these factors mostly impact on the high-risk situation of prescribing the incorrect dose to children (who clearly usually vary in age and weight from adults), but the other extreme of age is also important. The order of priorities for DRC may alter for different patient groups, for example, in paediatrics weight might be considered first whereas in the elderly renal function may be more important. Whilst there are many other potentially high-risk areas or high-risk drugs, these may be either covered by other decision support components or are not felt to be critical to the successful implementation of ePrescribing systems at present. Over time, however, more comprehensive and complex rules may be incorporated into systems. There is a risk that very complex decision support, as with other areas of checking, may lead to excessive warnings and lead to 'alert fatigue'.

This report will be reviewed in the light of experience as more systems are implemented and expertise developed. Comments, input and lessons learnt are welcomed at any time and can be communicated to the programme via email to eprescribing@nhs.uk

3 About this document

3.1 Purpose

The purpose of this document is outlined below:

To define the background of dose range checking as a component that will be utilised nationally to support hospital-based e-Prescribing

To scope that spectrum of concepts that could be considered in the implementation of dose range checking functionality in ePrescribing systems

To develop a framework for the prioritisation dose range checking elements

3.2 Audience

This document has been written both for software developers, but also third party data suppliers who may be tasked to work with developers to implement effective ePrescribing solutions. It will also be of interest to a wider variety of users including:

Clinicians

NHS Trusts

NHS agencies including NPSA

Other NHS Connecting for Health Programmes

Specialty societies

3.3 Updates

These guidelines incorporate comments received from a wide range of individuals and organisations. They will continue to be updated following user feedback about implementation of this functionality.

4 Introduction

ePrescribing systems have the potential to improve the safety and quality of care in many different ways. One of the major benefits of electronic systems over current methods of prescribing is that information can be provided easily at the point of care and can, if necessary, force practice using built-in rules and functions. Clinical Decision Support is defined as use of information and communication technologies to bring relevant knowledge to bear on the health care and well being of the patientⁱ; one element of this is the provision of drug information at the point of prescribing.

Even in the area of ePrescribing there are various components that will need to be available as part of the process that should be defined nationally. This information may be required to feed in to decision support software and thus needs to be rigorously evaluated to ensure consistency of standards. This guidance document is one of a series of documents that will be published identifying best practice for medicines related decision support. We recognise that such guidance should also be adopted according to local clinical priorities and published research.

Each component of decision support will comprise of a number of design elements, and it is clear that technical as well as clinical input is required for a successful solution. The underlying philosophy behind each element should be to guide clinicians rather than to constrain them and/or alert. This paper looks at one particular element of active decision support that might be provided. It assumes that there may also be passive decision support within a system that avoids the need for other checking to take place. Other elements of functionality are identified within the ePrescribing Functional Specification.

This particular review examines the role of dose range checking (DRC) in the prescription process to support the safety and quality of systems. DRC will require both clinical and technical prioritisation in order to implement and deliver ePrescribing in secondary care. Most of the effort will revolve around checking for excessive dosing (i.e. upper limits of the dose range) although in some circumstances minimum dosing or the lower limits of the dose range may also be necessary. This guidance does not cover dose recommendations or dose equivalence for different products.

ⁱ Greenes RA (Ed.) Clinical Decision Support: the road ahead. Academic Press, Burlington MA: 2007.

5 Background and Scope

5.1 Definitions of dose and dose range

The word 'dose' in prescribing relates to the amount of drug that is intended for administration to a patient. The concept of 'dose range' relates to the span of different doses that are given to patients that lies between the minimum effective therapeutic dose and the maximum recommended therapeutic dose. The maximum recommended dose does not always equate to the toxic dose, however the risk of harm clearly increases with doses above this range. Pharmacologically, the concept of the therapeutic index is defined as the ratio between the toxic and the therapeutic dose of the drug. Whilst these concepts are not exactly the same, for electronic prescribing purposes it is easier to refer to the general description of a dose range.

For the majority of drugs the dose range in adults varies by 2 or 3 fold. However, there are some drugs that are used over wide dose ranges (e.g. opiates) – up to 10 fold or more in some cases. Much of the current concern about the need to restrict adult doses given to patients exists for drugs which exhibit dose-dependent toxicity e.g. theophylline, gentamicin (where in some instances blood concentrations of the drugs are taken to prove therapeutic or toxic serum drug concentrations). There are some drugs in which the absolute drug concentration is less important than the body's total drug exposure e.g. some anti-cancer drugs – this requires different dosage calculation based upon cumulative exposure over time.

Dose range checking (DRC) is the functionality that checks the prescribed dose, frequency and/or timing and, in some circumstances, duration against defined ranges in order to alert the prescriber that the dose is outside of that range. This component is usually invoked to reduce the frequency of dose-dependent adverse drug reactions. It may also warn the prescriber when the dose is inappropriate in terms of a number of characteristics relating to a specific patient which could include, for example, the level of renal function, weight, or age. As such, various demographic and clinical characteristics are expected to be available to the DRC module. DRC should be expected to provide an automated method of comparing prescribed medication doses (either individually or over a defined time period), and compare them against pre-established 'safe' ranges for that medication. DRC components do not intend to provide recommended doses for specific patients or conditions.

Medication doses can be appraised against various different criteria related to the patient (as described above) or related to the drug (for example, dose frequency, timing, or route of administration). This functionality should be available for prescriptions in any section of a secondary care prescribing system, including regular scheduled, as required (PRN), one off, or discharge (to take out - TTO) medication and administration. The complex nature of hospital prescribing makes the issues of dose range checking particularly challenging as well as clinically important.

5.2 Dose Range Checking in Secondary Care

There are inherent differences between primary and secondary care prescribing practices. In primary care the process of prescribing results in an order to supply a medication, whereas in secondary care the process results in an order to administer

medicines as well as supply medicines in varying forms e.g. discharge prescriptions. The workflows of primary and secondary care electronic prescribing can therefore be very different. Much of primary care electronic prescribing is done as product-focussed order sentences, i.e. amoxicillin 500mg capsules, 500mg three times a day; whilst secondary care can adopt a similar strategy, it is also possible to construct order sentences from less than the entire set of individual prescription elements (e.g. drug, formulation/strength, dose, route, etc.).

5.3 Dose Range Checking and Safety

The National Patient Safety Agency (NPSA) collects details of medication safety incidents through the National Reporting and Learning System (NRLS). The majority of the reports that are received are from secondary care, and although a large proportion do not result in harm to patients, a small number of errors result in severe harm or death. One of the three most frequently occurring types of medication error reported between January 2005 and June 2006 related to wrong dose errorsⁱⁱ. The report states that a key action is to minimise dosing errors in healthcare systems through the provision of information, training and tools, and having systems that check doses for those prescribing, dispensing and administering medicines. The greatest number of reported incidents of deaths and severe harms related to specific groups of medicines (opioids, anticoagulants and insulin products) and in certain groups of patients (children and older people).

Patient safety is core to NHS CfH implementation. Computerised alerting has the potential to reduce the risks associated with the prescribing process. It is recognised that there is a need for a happy medium, so that users do not suffer from 'alert fatigue', but still receive prompts on dose related issues when appropriate (see below). The prescriber is still responsible for their drug prescribing, and it is also important that DRC is a function that is seen as a 'guide on the side' in order to prevent over-reliance on systems and thoughtless prescribing. This is particularly important if prescribers are moving between institutions which may have adopted some local protocols (where this is possible), as the alerting levels in one institution may not be comparable with another institution. The difference between flexible technical solutions in prescribing must be balanced against the consistency of systems.

5.4 Over-alerting and 'alert fatigue'

With the huge number of medications that are prescribed in secondary care and the complexity of many therapeutic decisions in secondary care, it is important to determine whether DRC alerts should be implemented for every prescription or whether it should be provided for just a subset of drug concepts or in specific circumstances. As DRC is not the only component of decision support there is a real risk within systems of decision support overload through over-alerting. This has been described as an 'overdose' of reminders, alerts and warning messages that are

ⁱⁱ National Patient Safety Agency. Safety in doses: medication safety incidents in the NHS. 2007.

sometimes not even relevant for the user at that momentⁱⁱⁱ and leads to the concept of 'alert fatigue'.

It has been shown for other types of decision support that clinicians tend to override most medication alerts which suggested that the current level of medication-related alerts may be inadequate to protect patient safety^{iv}. As well as leading to neglect of important messages, alert fatigue affects the clinical acceptability of ePrescribing systems. There is a clear balance to be made between relative and critical dosing alerts where low thresholds may lead to messages which could be regarded as false positive warnings and thus reduce the user acceptance of dose alerts in general. This would suggest that there is a need to provide some clarity into the implementation of decision support and to prioritize a subset of high-severity alerts only allowing certain critical warnings interrupt workflow.

There is also the possibility (but no current consensus) that system designs could customize alerts depending on the clinician's specialty or experience, or be configurable to suppress alerts for medications that have previously been received by that patient. This is a level of sophistication that is beyond the scope of this document and also requires human factors consideration (see section on user interface below).

5.5 Other technical considerations

Related to the subject of alert fatigue is the issue of warning when no DRC functionality has been invoked for any particular prescription. A means of identifying the absence of DRC whilst avoiding interruptive alerts is preferable.

Doses calculated on the basis of body weight may well have to be rounded to allow administration to occur safely. The act of rounding may in itself require that a dose sit outside normal ranges. There is currently no guidance as to what acceptable tolerances may be, particularly within the paediatric arena where this is most likely to be prevalent.

5.6 Relationship between decision support components

Clinical Decision Support functions in their entirety have a conceptual architecture that comprises a number of design elements and components. They can be considered to be modular in that different components can exist within the same application environment. This means that there may be overlapping functional components. It is clear that some elements of DRC may be dealt with by other decision support functions, for example a drug-drug interaction warning may alert the prescriber that the dose of a drug is affected when co-prescribed with another medication rather than the DRC component *per se*.

The relationship between decision support components and other functional considerations will need to be borne in mind when implementing DRC concepts in systems. Some of these relate to more strategic decisions about overall baseline

ⁱⁱⁱ Ash JS. *et al.* Some unintended consequences of information technology in health care: The nature of patient care information system-related errors. *Journal of the American Medical Informatics Association* 2004; 11(2): 104-12.

^{iv} Isaac T. *et al.* Overrides of medication alerts in ambulatory care. *Archives of Internal Medicine* 2009; 169(3): 305-11.

functionality, rather than relating to specific prescribing concepts. Some of these are addressed in the baseline ePrescribing functional specification for NHS Trusts [NPFIT-EP-DB-0010.08], but due to a better understanding of the wider detail and availability of data, the focus of effort has changed over time.

5.7 User Interface

It is now understood that user interface design plays a big role in how users interpret and utilise the information provided. It is clear when reviewing existing systems that there are a variety of different approaches to highlighting warnings and alerts. It is not clear which of these, if any, are the most likely to be utilised and understood by system users (although there is ongoing research about alert philosophy being undertaken by NHS CFH). Alerts relating to DRC should follow guidance given in the literature and current best practice. We recognise that the text used in warnings may be more relevant than other features such as number of alerts or interruptive nature. Further work from the Common User Interface (CUI) programme and related patient safety research will inform the user interface design issues. Details of work underway and current guidelines can be found at www.cui.nhs.uk.

5.8 National / Regional / Local restrictions and recommendations

Some decisions regarding DRC may relate to national guidance from organisations such as the National Patient Safety Authority (NPSA), for example their dosing guidance on methotrexate. There are also some high profile safety concerns that related to medication prescription and administration identified as 'Never Events'. These were identified in the Darzi report "High Quality Care for All" as serious and largely preventable errors in the Health Service^v. There are other potential regional and local restrictions that will have implications on dose ranges for use in specified settings. It is recognised that a degree of local configuration will be important in determining to what extent the functionality is utilised in specific clinical areas. It will be important in the longer term for local organisations, system vendors and third party providers to all be able to react accordingly to safety critical dosing warnings and implement warnings appropriately in systems in an appropriate time-scale.

5.9 Sources of information about dose range checking

It is common for the drug catalogue and active decision support to be provided by a third party vendor. The complexity of the file structures required and the ongoing maintenance and quality assurance (QA) are beyond the scope of many organisations. The limited number of such suppliers also means that given the right input it should be easier to standardise delivery approach and output in conjunction with system functionality. The source(s) and validity of information has implications on the data availability for system integration. Once dose limits are in place, maintenance of DRC requires an up to date information source to remain credible in order to keep current with regulatory and/or drug safety updates.

There are currently no specific standards that third parties are required to work to in relation to the content provided. However, there are quality standards that many

^v Department of Health. High Quality Care for All – NHS Next Stage Review Final Report. London: Stationary Office, 2008.

adhere to as regards the processes used for the identification and incorporation of information and around clinical safety. Further work is underway to identify standards that might be used.

Published research suggests that the choice of an appropriate database for DRC decision support is an important factor for successful system implementation and that the differences between the available information sources may be considerable^{vi}.

5.10 Approaches to limited dose range information

For some drugs, such as new therapeutic entities, trial drugs and special / unlicensed drugs, there may be limited or non-existent information about dose ranges on which to based DRC decision support. A systematic way to identify which drugs this affects may be necessary.

5.11 Areas out of scope

As well as elements of DRC that were seen as low priority, there are some areas of prescribing that are likely to remain out of the scope of the majority of third-party decision support information sources. These include:

Doses for topical creams, ointments and gels

Doses for drugs given into the eye, ear, nose or oropharynx.

Doses for immunological products and vaccines

Doses for inhaled and intravenous anaesthetics

Dosing of treatments as defined within elements of the Mental Health Act

Antipsychotic maximum doses within BNF dose ranges

Dosing of drugs within clinical trials

^{vi} Seidling HM. *et al.* Detection and prevention of prescriptions with excessive doses in electronic prescribing systems. *European Journal of Clinical Pharmacology* 2007; 63: 1185-92.

6 Recommendations for Dose Range Checking Functions

During initial consultation about ePrescribing functionality the list of requirements for decision support were wide-ranging. DRC is a key component of decision support, but the specific elements that should be aspired to for successful implementation of a system has a much narrower scope. The workshop attendees were insistent that only two areas of DRC functionality were essential baseline functionality in ePrescribing systems. Comments received support this but suggest that the priority order for DRC alters according to the patient group (e.g. paediatrics compared to the elderly). The other considerations for DRC elements are provided in the detailed guidance below.

The following elements of DRC decision support are felt to be critical to the successful implementation of ePrescribing systems and should achieve maximum benefit if efforts are made to get the clinical and technical specifications correct. As a minimum, system providers should aim to provide technical solutions to be able to implement these elements of DRC and there should be a consistency of approach in different systems.

6.1 Age related

Where patients have different dose ranges depending on their age (e.g. infants compared to elder patients) this needs to be considered but not as a priority except in paediatrics.

Many different drugs have specific dosing recommendations based upon age – especially with respect to children and the elderly. Paediatric dose ranges, in particular, may be either based on age or other parameters such as weight or surface area (see other detailed considerations).

Within this category there are more subtle issues such as anatomical versus physical age which may be relevant both for very young children as well as the very old. There are sometimes issues related to overlapping or non-overlapping age ranges which are difficult to rectify in systems unless pre-built order sentences are used. There is also some overlap between this category and weight-related dose ranges – as sometimes both age and weight are taken together in a dose-range checking algorithm.

6.2 Weight related

For some drugs the correct dose is dependent upon the patient's weight (or weight range); DRC functionality will need to consider weight for some prescriptions. This is likely to be mainly relevant for patients at the extremes of age. Other weight based measures may be utilised for example body surface area.

For some drugs the maximum recommended therapeutic dosing is expressed as daily dose per kilogram of body weight. As mentioned above the specifications of certain drugs in paediatrics may also have combinations of age and weight ranges. There is an additional issue which is often not well specified in drug information, relating to bariatric dosing (morbidly obese patients), where dose per body weight /mass has a theoretically upper limit of weight (e.g. acetylcysteine) above which the relationship of dose range and weight no longer holds true. Attempts are also

sometimes made to dose based on ideal body weight or estimated lean body mass. There may be circumstances for all types of patients where a maximum dose overrides a weight calculated dose.

Some nuances exist within weight-related dose ranges. In clinical practice it may be necessary to use estimated weights (which are often not always accurate) – which depending on the toxicity of the drug may come with risk. Weight is not always static over short-term or medium-term especially, for example, in young children who are growing. Provision for regular update of recorded weights should also be evident and may include rules for clinically relevant weight changes which require dose adjustment. Weight may not be steady in the short-term even in adults in certain situations, for example end stage renal failure on haemodialysis, where dry weight and body weight can vary between dialysis sessions and patients with accumulating ascites. Whilst for many drugs such short-term variations or variance in estimates may be irrelevant, for toxic drugs these differences may be clinically relevant.

7 Detailed Background Considerations for Dose Range Checking

The concepts below are all relevant for the DRC component of decision support, and form the framework for the supporting functions of DRC within ePrescribing systems. For each of the elements the overview of the concept, clinical examples where appropriate, and relevant comments from the expert workshop (see Appendix 1 for more details), are presented.

7.1 Wide dose ranges

Some drugs are used appropriately over very wide dose ranges. Restrictions or alerts relating to the dose range may be relevant for some patients, but lead to over-alerting if used in all patients or in patients who are known to tolerate high doses.

There are some drugs for which the minimum effective therapeutic dose and maximum recommended therapeutic dose are widely different; this is sometimes true amongst different patient groups, e.g. warfarin. The implication is that there may be relative and absolute dose limits for such drugs – the relative dose limits being relevant to the ‘average’ population group. It may be appropriate that there is a mechanism by which the dose range for a specific patient can be set or systems can recall the usual dose for the patient (so that for example excessive but appropriate doses do not alert the prescriber every time they are re-used for a specific patient).

For example, a patient who normally takes a dose of warfarin of 40mg may alert the prescriber every time a single dose is prescribed, and whilst it is a high dose compared to the whole population, it may be appropriate for that patient. Warnings could prove counter-productive either by adding to the burden of over-alerting or encouraging a sub-therapeutic dose to be prescribed. The absence of warnings may however allow prescribers to replicate medication errors where the concept of suppressing an alert exists.

7.2 Off label use outside usual dose limits

Use of drugs outside their product license is considered ‘off-label’, and some instances of off-label use relate to unusual but appropriately high doses.

Many of the dose ranges relate to the licensed use of a particular drug, and use outside the product license is considered to be off-label. A significant proportion of prescribing takes place off-label (estimated up to 20% of inpatient adult prescriptions and higher percentages in paediatric practice). A fraction of these off-label uses will be because of appropriate prescription outside the recommended dose ranges.

DRC protocols may be required to take account of off label use outside normal limits. In hospitalised patients, who may be considered to be in a well-controlled setting, the dose ranges used are often different from ‘normal’ doses. Examples of drugs that are used outside licensed doses include metoclopramide (five times normal amounts given as one off doses for post-operative nausea and vomiting), and diazepam (which may be given in daily doses of 10 to 100-fold the normal daily dose limits in

severe agitation related to alcohol withdrawal). These considerations are equally applicable to the outpatient setting.

7.3 Mixed route administration

Where drugs are given via different routes close together, there are issues about the calculation of excessive frequency of administration or excessive daily doses.

A specific feature of hospital-based electronic prescribing is the wide variety of routes of drug administration that are used in comparison to the mostly oral preparations used in primary care or the outpatient setting. To reduce the risk of excessive doses in hospitalised patients will require different maximum recommended therapeutic doses relating to parenteral administration (e.g. intravenous or intramuscular injections).

Further issues are raised when the same drug is given by different routes during the course of therapy. In some cases (e.g. cyclizine as an antiemetic) the oral and parenteral doses are equivalent, so that the total daily dose will be fixed regardless of the routes by which the drug is administered. For other drugs, oral and parenteral (or other combinations of route) are not equivalent (e.g. prochlorperazine). The total daily dose calculation of such mixed routes of administration therefore becomes computationally complicated. This category has implications not just for DRC at the time of prescribing, but also DRC at the time of administration.

7.4 Different routes at the same time

On some occasions the same drug is given at the same time by two separate routes of administration. This creates computational difficulties in systems which are required to 'add the doses up'.

Following from the issues of mixed routes of drug administration in hospitalised patients at different times, there is the additional issue that on occasion there is a requirement for the same drug to be given at the same time by two different routes.

An example might be the concurrent therapy with oral and intravenous vancomycin, or the concurrent use of intrathecal and intravenous chemotherapeutic agents. DRC functionality may need to take account of such issues as these may be legitimate therapy, whilst complicating computerised dose checking protocols. There may be times when DRC is critical to prevent overdosage when the same drug is being given by different routes. This area of DRC functionality has some overlap with other areas of decision support such as drug interaction and therapeutic duplication checking.

7.5 Drug interaction effects

In some cases the presence of an interacting drug may affect the recommended doses (and therefore dose range) of a current drug that a patient is taking.

DRC functionality in relation to the concurrent prescribing of an interacting drug should not replace the overall concept of drug-drug interaction checking. However, there are some concepts related to dose range in which drug-drug interactions play an important part. For example the dose range limits of some drugs change markedly when another drug is used concurrently (e.g. when allopurinol is used in patients

taking azathioprine, it is recommended that the dose of the latter is reduced to one quarter of the usual dose). Whether systems should be able to cope with the complexity of these issues, where this functionality is available in interaction checking, for example as warnings to the prescriber, is unclear. Whilst drug-drug interactions are very common, the situations of drug interactions requiring dose adjustment may be so comparatively rare that systems should have checks in place to warn the prescriber of these facts.

7.6 Renal and Liver functional impairment

Where different aged patients have different dose ranges depending on underlying disease states (e.g. liver or renal disease) this needs to be considered.

Drugs which are renally excreted or which undergo hepatic metabolism may have additional instructions based upon levels of renal or liver impairment. Real time monitoring of laboratory tests has been shown to be effective in using logic to alert when excessive dosing based on most recent tests is discovered. Again this may be dealt with in drug-lab interaction functionalities, but has implications for any DRC protocols.

Renal dosing is without doubt a priority within electronic systems. There are many issues for consideration including which renal function measurement to use for support. It is the intention to address prescribing and renal disease as a decision support function in its own right followed by a review of how and whether DRC should support this.

7.7 Cumulative dose checking

Drugs may have a toxicity related to the total body exposure over time (often in haematology and oncology prescribing) and for these drugs cumulative dose checking may be necessary.

Drugs which provide cumulative toxicity over time may have dose ranges over longer periods than the single day. Some drugs may require cumulative dose checking over weeks, months or years. This is complicated by the fact that the doses may be given over different episodes of care. There therefore needs to be clear linkage of prescribing and previous administration records. Nevertheless, due consideration of cumulative dose checking should be given for drugs such as cytotoxics (e.g. doxorubicin) which have serious, potentially fatal, adverse toxic effects. There is no current list of drugs to which this issue applies, but the programme will seek to clarify this.

7.8 Daily dose limits

Some drugs have specified daily dose limits which override any frequency dose limits imposed on the drug. There are also potentially slightly longer cumulative dose limits – for example weekly or 48 hourly (see below).

Dose checking of administration over the period of 24 hours is a common approach, and many drugs have maximal daily therapeutic dose limits. Specific examples such as paracetamol have already been mentioned above. The checking of daily dose limits is particularly important where the individual dose limits multiplied by the minimum dose frequency is not equal to the daily dose limits or where a mixture of

PRN and regular doses are given. For example loperamide orally has a dose of 4mg initially and then 2mg according to symptoms which may be required every few hours, however, the maximum dose in 24 hours is 16mg which could easily be exceeded if daily limits were not set. Special consideration therefore needs to be given to daily dose limit warnings.

7.9 Dosing by indication

For drugs which are used for more than one disease or indication, the dose range limits may be very different.

Dosing by indication relates to the concept of different doses based upon the condition for which that drug is being used. Functionality relating to dosing by indication relies on health care professionals indicating in one of the prescription fields what that drug is being used for, or programmatically checking for active conditions in DRC protocols. However, workflow may not easily support such functionality as for existing systems the diagnosis or indication is often one of the last pieces of information to be added to prescribing systems unless there is the concept of indication-driven dose selection or order sentences. Difficulties exist because there are some drugs which have entirely different dose ranges depending on indication (e.g. clonidine), and also some drugs where the same drug has different dose ranges/frequencies based upon the indications (e.g. aciclovir).

7.10 Dosing by specified drug brand

Some drugs are required to be prescribed according to their brand as the apparently 'same drug' may contain very different doses of active ingredient depending on the preparation administered.

There are some drugs where it is important to prescribe the drug as a specified brand (proprietary preparation) instead of a generic title. This is usually related to differences in bioavailability whereby the patient should always receive the same brand. There is a similar issue when drug doses vary according to the salt or ester used in different products. An example is Lithium treatment where drugs are prescribable by brands, especially as lithium citrate 200mg is equivalent to lithium carbonate 509mg. This issue may need to be considered in DRC protocols.

7.11 Minimal dose checking

There are circumstances where there is considered to be a minimum effective dose and therefore the lower limit of dosing may need to be considered in dose range checking protocols for some drugs.

Many of the issues regarding dose range checking refer to the upper limit of normal for dosing; however, a consideration may be made for minimal dose checking. Dose range should relate to both minimum and maximum range of a dose of medicine. For many oral preparations the minimal dose is restricted by the formulation that is available and this may be specified in the prescription order entry catalogue. For liquid and parenteral preparations, catalogue entries will usually not be restrictive with respects to minimal doses. Other functionality may need to be invoked if minimal dose checking is included into DRC.

8 Other DRC elements considered

The concepts below have also been considered for the DRC component of decision support, but they are low priority supporting functions within ePrescribing systems.

8.1 Drug forms with difficult dosing

Some drugs such as creams are difficult to accurately measure in terms of doses administered which makes their dose checking concepts more difficult.

For certain dose forms, e.g. topical treatments/creams, the prescribed dose for administration cannot easily be defined. Therefore a factor relating strength and prescribed unit cannot be defined, which means that it is not possible to calculate the dosage unless the prescribed unit and the intended amount of active ingredient can be indicated quantitatively. For these forms the safe dosing may depend on other functionality such as administration messages (e.g. apply sparingly).

8.2 Sequence within a schedule

This is used when it is necessary to work through two or more different dose regimens as part of a single dose type. For example, a decreasing regimen may comprise a series of separate decreasing doses that need to be followed in a particular order (e.g. dimercaprol). It is not necessary to specify a dose sequence when a single maintenance dose follows a single starting dose because the sequence is implicit in the dose type. But when a single starting dose precedes a sequence of increasing or decreasing doses, the starting dose itself is considered the first component of the sequence. Any sequenced changes in doses will make DRC functionality computationally complicated and may be impossible to easily implement.

8.3 Severity as a determinant of dose or duration or both

DRC is primarily a safety checking feature rather than a clinical suggestion procedure. Whilst it is acknowledged that the dose of medicines will vary according to the specific condition and also the severity of the condition, this is not a key component of this functionality. It is recognised that sophisticated systems which contain dosing by indication may also contain information about the severity of conditions and therefore be able to cope with such nuances in DRC. For example, clarithromycin is recommended to be given at a dose of 250 mg twice daily for 7–14 days, but this dose is doubled in severe infections. In order to avoid inappropriate alerting and possible cancellation of important therapy, DRC should only alert for the dose limits of the most severe infection unless severity of condition is captured in the prescription stage prior to the DRC triggering.

8.4 Stopping medicines

Most DRC is done at the point of adding a prescription, but as there are sometimes interactions between medicines which require dose alteration (as noted in section 7.5 above), it may be relevant to identify when stopping drugs requires that other drugs need to have doses altered. This is potentially complicated by the fact that some

drugs will have a residual effect and therefore dose alteration may need to be delayed for a period of time.

8.5 Dosing equivalence checking when moving between different forms

The maximum recommended therapeutic doses of medicines may vary between brands and this may create issues in ePrescribing systems if medicines are prescribed at Actual Medicinal Product (AMP) level rather than as a Virtual Medicinal Product (VMP). Examples of drugs where there may be important differences between brands are phenytoin and theophylline preparations.

8.6 Variance in dose intervals and effect on DRC

DRC concepts may need to take account of dosing intervals of longer than one day. Such dosing will be more complicated than daily dose limit warnings. For example calculating dose limits of thrice weekly drugs such as co-trimoxazole or alternate day dosing. Consideration may also be required for the 'permissible' delays between doses and the effect that this may have on DRC functionality within systems. Specific examples would include delays between injections of depot anti-psychotics.

9 Appendix 1 - Summary of Expert Workshop Discussions and Output

A workshop took place on Wednesday 5th November 2008 at the Royal College of Surgeons of England in London. The workshop was mainly clinically focused although technical experts were invited to contribute to this expert review. People who have already contributed in various CfH engagement events were invited to attend this workshop, although other clinicians or technicians that have knowledge and expertise in related areas to electronic prescribing and medicines management also contributed. Attendees to the workshop were given an initial proposal document that outlined some of the basic elements within DRC to consider in advance of the event. The intent was to gauge priority for DRC functionality within e-Prescribing solutions and ensure that all issues had been considered. The structure of this document has been written to match the priorities that were identified by the workshop and are subject for ratification during the external consultation phase.

Prior to the workshop individual views on the different elements were taken and attendees were asked to record their views on the safety risks of the specific elements, the feasibility of implementation and the relevance to prescribers. A key view was also sought on whether a system would be used if it did not contain this decision support component in one form or another.

Attendees were grouped together and through facilitated sessions were asked to consider each of the elements of DRC functions. Detailed notes were taken and a summary of the information can be found within the file below.



Summary of the
Output from the Expe

10 Appendix 2 - List of Contributors

Workshop Attendees	
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