DUODECIM
EBMEDS

User Manual for Duodecim EBMEDS® Clinical Decision Support

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DUODECIM
EBMEDS

Contents

1 Introduction

1.1 Abbreviations

DSO	Diagnosis-specific Overview
EBMEDS	Evidence-Based Medicine Electronic Decision Support
GFR	Glomerular filtration rate
CMR	Comprehensive Medication Review
MDR	Medical Device Regulation
HBA	Health Benefit Analysis

1.2 Text highlighting

Texts appearing in the user interfaces have been highlighted in *italics*. Important sections have been highlighted in **bold**.

2 EBMEDS system in a nutshell

2.1 General introduction to the service

2.1.1 Short description

Duodecim's decision support system EBMEDS® (Evidence-Based Medicine Electronic Decision Support) is a clinical decision support service that combines the information stored in the electronic patient record describing the patient's status with clinical knowledge, producing patient-specifically tailored instructions and links to its user.

2.1.2 Developer of the service and partners

EBMEDS has been developed by Duodecim Publishing Company Ltd owned by the Finnish Medical Society Duodecim. Both the medical society and the limited company cooperate closely together with Finnish and international associations specialised in evidence-based medicine. Known partners include the Cochrane community, which produces systematic literature reviews, the GRADE (Grading of Recommendations Assessment, Development and Evaluation) and the GIN (Guidelines International Network).

2.1.3 Benefits of the service in brief

The operating environment of health care has become more demanding and complex as the amount of information and new forms of treatment have increased rapidly. Finding information in electronic health record systems may be difficult. The most common reasons for patient safety becoming compromised are that an abnormal measurement result has not been taken into account or the result has not been controlled. A common cause of emergency visits and hospitalisation is an adverse effect of medication. Many adverse

drug reactions could be avoided if medication was selected and monitored in accordance with the recommendations, harmful or unnecessary drugs would be discontinued and renal insufficiency would be taken into account in the dosage. In other words, the problems of the information flood are very concrete. EBMEDS includes a wide range of features to improve patient safety. Clinical decision support pays special attention to medication and its correct implementation.

2.1.4 Value promises

The three value promises for EBMEDS are:

- To increase patient safety
- To improve the quality of care and
- To improve the cost-effectiveness of health care.

2.2 Operating principle and purpose of the service

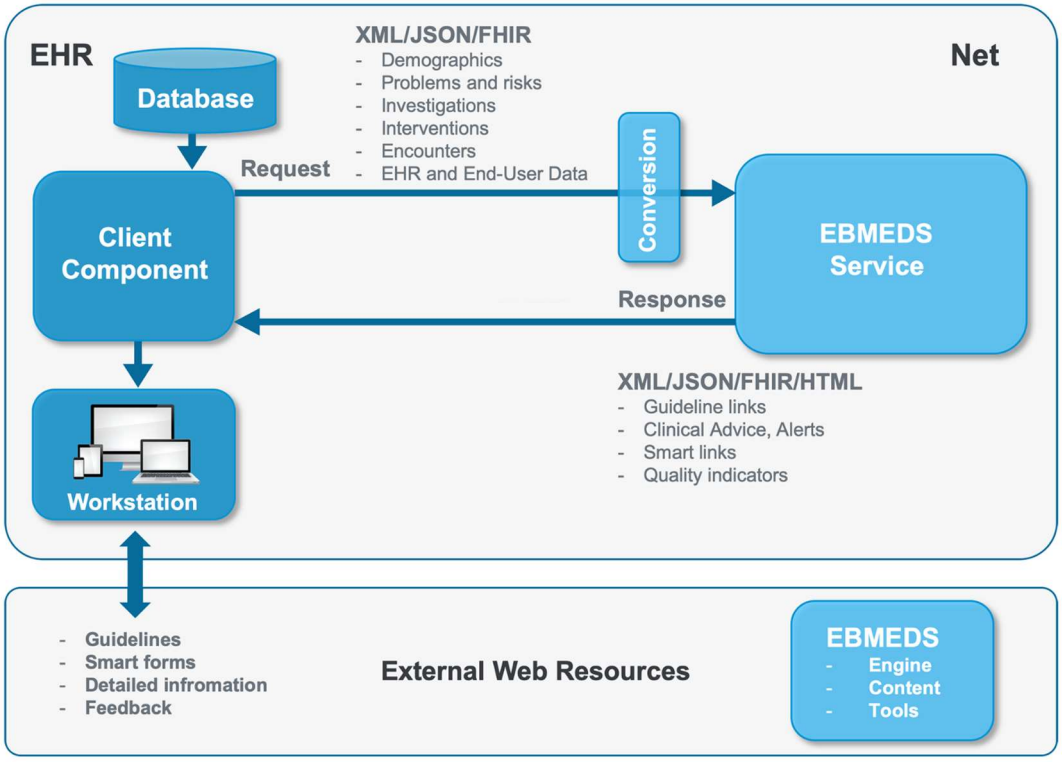
2.2.1 Operating principle

The EBMEDS service receives structured information describing the patient from the patient record or other system containing patient information, and returns to the user reminders, treatment suggestions, warnings, and links to treatment recommendations related to patient diagnoses. It also compiles suitable data in electronic forms and calculators and produces aggregate views of the data, the most important of which are the Comprehensive Medication Review and a Diagnosis-specific Overview. In addition to the real-time clinical decision support intended for the treatment of an individual patient, EBMEDS can be used to produce reports on the health data of population groups, to identify care shortages that should be allocated resources and to measure the quality of the care activities (Health Benefit Analysis = HBA).

The clinical decision support service can be seen as an automated “consultation service” within the electronic health record system. On the electronic health record system side, service integration requires an adaptor application programmed by the electronic health record system developers, which 1) is able to retrieve the patient data needed by the EBMEDS service, 2) send a consultation request to the EBMEDS service, and 3) receive a clinical decision support response and display it appropriately in the electronic health record system user interface. In general, the service is not consulted manually, but certain events in the use of the patient record automatically send a query to the clinical decision support service. In some cases, however, you will go manually through the links to view add-ons (e.g. aggregate views) or move to background material by clicking on the links.

A query from the electronic health record system contains a compact package of patient information, from which irrelevant and outdated information has been filtered. The most important patient data groups are:

- Demographic data (age, gender, etc.)
- Diagnoses (including symptom diagnoses) and risk information (e.g. smoking, pregnancy)
- Current laboratory test results and ordered laboratory tests
- Information on current interventions: Medication and performed and ordered procedures.



If necessary, the clinical decision support service can also filter out irrelevant and outdated information (e.g. temporary diagnoses that can no longer be relevant). EBMEDS analyses the patient data in the query and generates a response consisting of different types of reminders and links to useful items. EBMEDS also uses the patient information that comes in the query to form aggregate views, links to treatment recommendations and background materials, and links to calculators and other platforms that transport and require patient information. The query/response traffic and the quality indicators included in the response (see 3.3.4) are stored in the database, and this information can later be used, for example, in the Health Benefit Analysis.

EBMEDS can be installed either locally or centrally.

2.2.2 Purpose of use

EBMEDS is a medical clinical decision support system that analyses structured patient data related to an individual's health and illnesses. It combines patient data with medical knowledge and practices from multiple sources. The purpose of the clinical decision support is to improve the quality of care and compliance with clinical guidelines, prevent treatment errors, improve patient safety and save the user's time.

EBMEDS is designed to provide clinical decision support such as treatment suggestions and diagnostic assistance for healthcare professionals. Typically, EBMEDS is connected to another information system that can produce the required structured patient information. EBMEDS is designed to be always available to the end user and to generate suggestions both automatically and upon the user's request. The software can be used for all types of patients regardless of age, gender or status of health.

2.3 Integration with electronic health record systems

2.3.1 Duodecim portal services

Duodecim has attempted to respond to the challenge posed by the flood of information by developing electronic databases (Terveysportti, Oppiportti, Terveyskirjasto) as portal services, evidence-based clinical guidelines (EBMG, Evidence-Based Medical Guidelines, Current Care recommendations) and systematic reviews. These solutions are key tools for modern professionals. However, as a solution to the information flood they are not quite sufficient. They require the user to actively search for the information they need.

2.3.2 Clinical decision support as a service for electronic health record systems

Clinical decision support serves as an assistant for a professional within the electronic health record system. It automatically receives a huge amount of patient information, which it analyses in the light of medical knowledge and the latest clinical guidelines, and provides feedback based on the analysis. EBMEDS can generate more than 40,000 evidence-based warnings and reminders and thousands of links.

The EBMEDS service is integrated with most electronic health record systems that contain structured patient information. Electronic health record systems can either use the structured feedback of the clinical decision support system and display it as integrated with the electronic health record system user interface, or use the EBMEDS system's own pre-formatted visualization.

EBMEDS service response times are typically less than one second, but other delays associated with the electronic health record system may increase the response time. The electronic health record system suppliers who have completed the integration provide additional information on the performance of the clinical decision support system and its potential impact on the performance of the electronic health record system in the electronic health record system environment. As a rule, the use of the clinical decision support system does not slow down the use of the electronic health record system.

2.3.3 Operating environment

Operating environment

EBMEDS is used in connection with patient care or planning treatment in the healthcare environment. The same computers that use the patient systems are used as tools. No specific hardware or operating system requirements have been set for the EBMEDS end-user, EBMEDS operates in the same environment where the electronic health record system does.

Data security and data protection

The data security of the operating environments is typically at a good level, as sensitive data is already processed in them. The user organisation is responsible for ensuring that EBMEDS can be used securely.

The end user should note that data protection requirements may also apply to content produced by EBMEDS because it uses patient data as a basis for reasoning. Thus, the content may contain information from which the patient's identity may, in rare cases, be indirectly inferred.

Browser requirements

The features of clinical decision support are browser-based, with the exception of any reminders embedded directly in the electronic health record system. The browser is embedded to the electronic health record system. In some cases, links may also be opened in the default browser of the operating system.

EBMEDS can be used with the latest versions of the most common browsers. The following browsers are used for design and testing, and we recommend changing to them in case of problems

- Chrome and Firefox (Windows, MacOS, Linux)
- Edge (Windows 10 +)

2.3.4 Structured recording in electronic health record systems

Clinical decision support cannot understand the free text in the patient's medical record; it needs structured information. Structured information differs from the free text so that it has its own place in the electronic health record system where the information in question is stored in a standardised manner (e.g. smoking status). Structured information is often associated with a code (e.g. diagnosis or procedure code). Drugs and laboratory tests are also backed by their own codes, even though the end user often does not see them.

Because clinical decision support depends on the structured information it receives, clinical decision support may give incomplete or unjustified messages to the user if the structured information is incomplete or incorrect. In other words, it is always essential to record the information in a structured and careful manner[1]. However, not all data used in clinical decision support can be recorded in a structured manner in all electronic health record systems - an example of this is breastfeeding. This constraint must be taken into account when interpreting feedback from clinical decision support[2].

It is important that the records of the patient's diagnoses are up to date and that no working diagnoses that have proven to be incorrect remain in the electronic health record system[3]. It is also important that temporary drugs are not marked as permanent.

2.3.5 Patient information available

In general, the electronic health record system can only send data stored in the local system in question to clinical decision support. Thus, clinical decision support may remind of missing examination results in primary health care, even if the results can be found in specialised medical care. In some cases, when a regional patient information solution is used, clinical decision support may also receive information from other organisations, such as specialised medical care. The supplier of the electronic health record system is able to describe this in more detail.[4]

For performance and information security reasons, clinical decision support does not currently receive national-level information, for example from the Finnish Prescription Centre or the Finnish Kanta archive.

2.4 Qualitative aspects

2.4.1 Certification as a medical device

EBMEDS clinical decision support is a class IIa medical device in accordance with the EU Medical Device Regulation MDR 2017/745, manufactured by Duodecim Publishing Company Ltd. The quality system is certified in accordance with the requirements of ISO 13485:2016.

2.4.2 Limitation of liability[5]

Clinical decision support makes use of the latest and best available medical information collected from clinical guidelines, systematic reviews and high-quality original studies. The content of the clinical decision support system will be developed with great care and using the best editorial methods.

However, clinical decision support may also show unjustified reminders, for example, because it is dependent on the quality of the structured patient information it receives. Decisions related to treatment and the responsibility for them are without exception the responsibility of the responsible physician or other health care professional responsible for the patient. Clinical decision support is one source of information related to care and it does not replace the professional skills and discretion of a doctor or other health care professional.

Clinical decision support is usually updated twice a year at agreed publication dates. The aim is to update pharmaceutical databases more often than this. However, due to installation delays, it is possible that the content of the clinical decision support installation is lagging behind the content of the source materials. The user should always check the version of the current clinical decision support and the date it was updated and take into account any shortcomings. [8]

2.4.3 Notifying of serious incidents related to the use of clinical decision support

Duodecim Publishing Company Ltd and the supervisory authority (Finnish Medicines Agency Fimea) must be notified of serious incidents related to clinical decision support.

2.5 More information on EBMEDS service

2.5.1 Clinical decision support online courses

There are two online courses on EBMEDS clinical decision support in Oppiportti by Duodecim:

- Basics of clinical decision support
    - The course answers the questions:
        - What is clinical decision support?
        - Can I utilise it in my own work?

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        - How does it work?
- Clinical decision support in practical work
    - The course answers the questions:
        - How do I use clinical decision support?
        - What is the Comprehensive Medication Review included in clinical decision support?
        - And how do I use Diagnosis-specific Overview or calculators?
    - The course contains instructions for clinical decision support and screen captures from most electronic health record systems used in Finland.

Both courses are free and do not require login. The courses take 20-30 minutes to complete per course.

2.5.2 Website

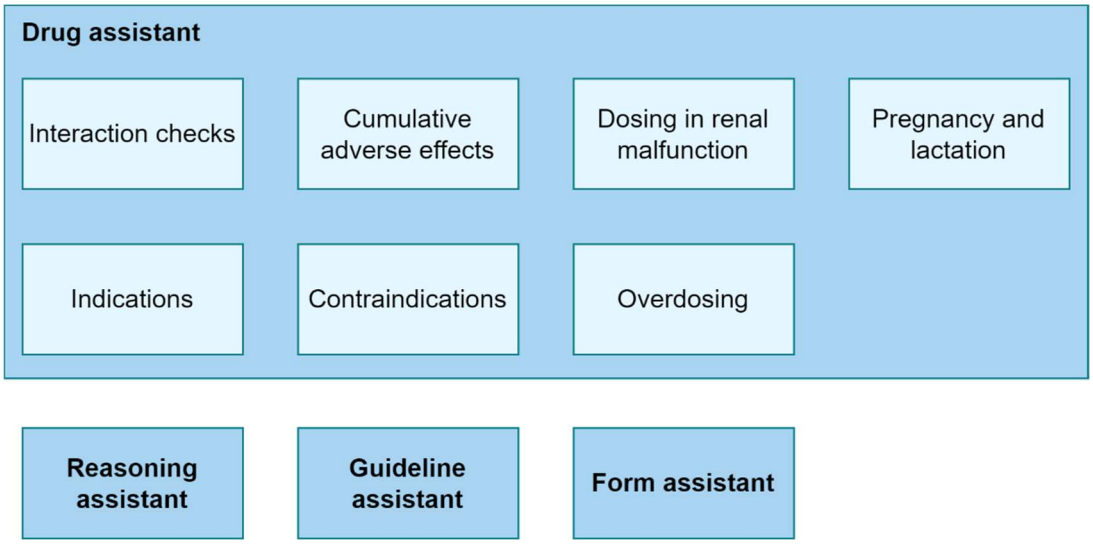
The EBMEDS clinical decision support website can be found at www.ebmeds.org. You can find more information on the content of clinical decision support rules, scientific evidence of the benefits of clinical decision support and the technology used by EBMEDS clinical decision support on the website.

3 System structure and knowledge content

3.1 Structure

The EBMEDS system consists of four modules called assistants:

- Drug Assistant
- Reasoning Assistant
- Form Assistant
- Treatment Recommendation Assistant



The content and functionality of the assistants are described in more detail below.

3.2 Drug Assistant

3.2.1 Drug databases

The Drug Assistant uses the same drug databases that are also available through Terveysportti. However, clinical decision support is able to automatically utilise pharmaceutical and other information from the electronic health record system, which significantly speeds up the use of databases, especially in patients who use numerous drugs.

Some drug databases are produced by Medbase Ltd. in Turku, Finland.

3.2.2 Indication database

The indication database contains information on indications for drugs. In practice, it consists of drug-diagnosis pairs. The database does not contain indications other than diagnoses (e.g. no anaesthetics or other medication support drugs).

The indication database is used in the patient's drug indication check (see 4.3.2). In addition, the database can be used to display pharmacotherapy recommendations after a new diagnosis has been added (see 4.2.3.6).

3.2.3 Contraindication database

The contraindication database contains information on drug contraindications. A contraindication reminder is generated when a drug with a contraindication on the diagnosis list is found on the patient's list of drugs. Contraindications are divided into particularly important and important contraindications. Particularly important are often absolute contraindications (the drug should not be used). In the case of relative contraindications, the drug should be avoided or at least prescribed with caution.

3.2.4 Interaction database

Medbase Ltd's interaction database (Inxbase®; previous name SFINX) contains information on drug interactions. Inxbase interactions are divided into severity levels A through D, of which only clinically significant (C and D) interactions are utilised in clinical decision support:

- C = Clinically significant interaction that can be alleviated, for example, by dose changes.
- D = Clinically significant interaction that is best avoided.

The analysis takes into account the routes of medication administration. For example, there are usually no interaction warnings for topical medications.

3.2.5 Cumulative adverse drug reactions database

The cumulative adverse drug reactions estimate is based on the Riskbase® database (formerly PHARAO) produced by Medbase Oy. The database can be used to assess the risks associated with the patient's medication for the occurrence of the following adverse effects:

- Anticholinergic effect
- Constipation
- Sedation
- Orthostatism
- Risk of bleeding

- Serotonergic effect
- Risk of seizures
- QT-prolongation
- Renal toxicity (nephrotoxicity).

The database contains information on the risk of adverse effects to individual medicinal substances on a scale of zero (no effect) to three (high effect). The overall risks of adverse effects are assessed on the basis of either the highest risk score (seizure risk) or the sum of scores (all other adverse effects) on a scale of A (no increased risk) to D (significantly increased risk).

The database also contains adverse effect-specific instructions on how to avoid these adverse effects.

Topical medications are excluded from the cumulative adverse drug reactions analysis.

3.2.6 Use of drugs in renal failure (Renbase database)

This assessment is based on the Renbase® database produced by Medbase Oy. The database contains information on drug dosing restrictions in renal failure. The degree of renal failure is defined in four categories based on the glomerular filtration rate (GFR):

- 90 to 60 ml/min: Mild renal failure
- 60 to 30 ml/min: Moderate renal failure
- 30 to 15 ml/min: Severe renal failure
- <15 ml/min: End-stage renal failure

In adults, GFR is calculated based on the patient's age, gender and creatinine value using the CKD-EPI formula. For 15-18-year-olds, the Bedside-Schwartz formula is used, which also requires a fresh height of the patient. GFR value is not calculated for those under 15 and Renbase is not used in this age group.

The most common medication recommendations for renal failure are:

- Decreasing single doses of drugs
- Extending the dosage intervals of drugs
- Avoiding drugs.

The database also contains information on the direct adverse effect of drugs on the kidneys (nephrotoxicity).

The recommendations in the Renbase database are categorised on the basis of the severity of the potential problem and the available scientific evidence (Group B):

- A: No dose or dosage interval modification required
- B: Information missing or assessed based on pharmacokinetic properties of the substance
- C: Modification of dose or dosage interval is required
- D: The use should be avoided.

The analysis takes into account the routes of medication administration. For example, the doses of topical medication do not, as a rule, need to be changed in renal failure.

3.2.7 Use of drugs during pregnancy and breastfeeding (Gravbase, Lactbase)

This estimate uses Medbase Ltd's Gravbase® and Lactbase® databases, which contain information on restrictions on the use of drugs during pregnancy and breastfeeding.

The recommendations of these databases are categorised on the basis of the severity of the potential problem and the available scientific evidence.

Classification of Gravbase reminders:

- A: Controlled studies or large patient materials have failed to demonstrate an increased risk for malformations or for direct or indirect fetal adverse effects after the drug has been used during the 1st trimester. Also, there is no evidence of increased risk after use during the 2nd or 3rd trimester.
- B: There is only a limited amount information on the use during pregnancy and there are no controlled studies in pregnant women. No increase in the incidence of malformations or direct or indirect fetal adverse effects has been observed in humans or in animal tests.
- C1: There is only a limited amount information on the use of the drug during pregnancy and there are no controlled studies, or the results of the studies are conflicting Animal tests have shown congenital malformations or direct or indirect fetal adverse effects or no animal tests have been performed.
- C2: Animal tests or human data indicate no evidence of increased risk of malformations, but (late) pregnancy use may pose a risk of adverse effects during the neonatal period or during childhood.
- D: The drug is suspected or shown to cause malformations or irreversible direct or indirect fetal adverse effects. As a rule, pregnancy is a contraindication for using the drug. In some cases the benefit may overweigh the potential harm.

Classification of Lactbase reminders:

- A: The drug is not excreted into breast milk in clinically significant amounts or its use during breastfeeding is not expected to cause adverse effects in the infant, when the mother uses the drug in therapeutic doses.
- B: No studies are available on the excretion of the drug into breast milk. Only limited or no data is available on the safety of human use during breastfeeding.
- C: Based on the available information, clinically significant amounts of the drug are excreted into breast milk. Use of the drug during breastfeeding may cause adverse effects in the infant at maternal therapeutic doses. The decision on breastfeeding must be based on an assessment of the benefits of breastfeeding in relation to the possible adverse effects of the use of the drug.
- D: Breastfeeding is contraindicated while using the drug. Use of the drug during breastfeeding may cause serious adverse effects in the infant.

The analysis takes into account the routes of medication administration. For example, topical medication can often be used normally during pregnancy and breastfeeding.

3.2.8 Overdosage

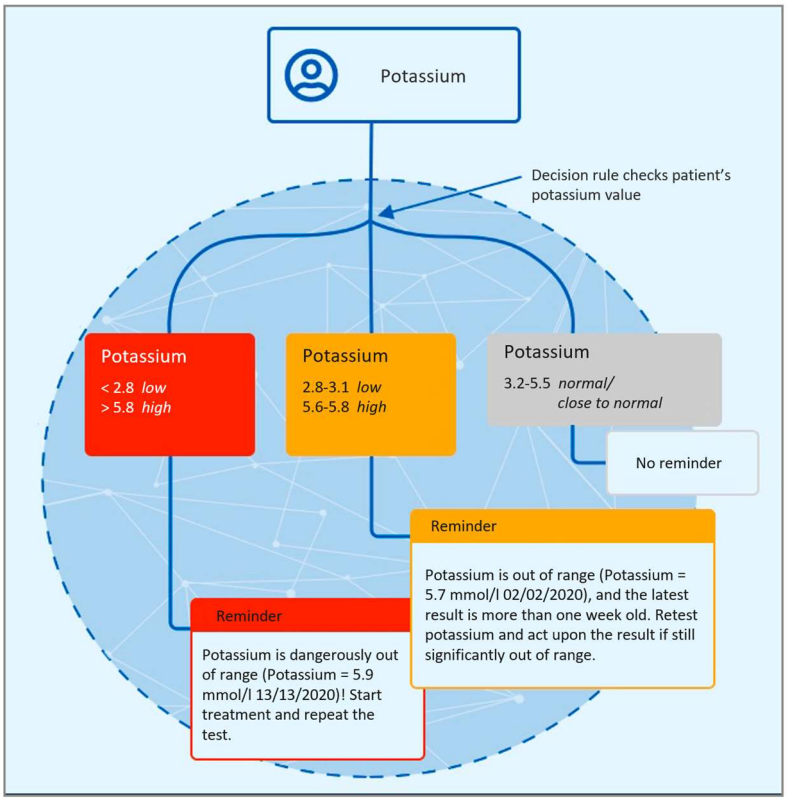
This uses a dosage database, which allows clinical decision support to produce reminders of possible overdoses. A reminder is generated when the daily dose of the drug exceeds the maximum daily dose based on the drug indication. If the indication is not known, the daily dose is checked according to the maximum allowed dose for any indication. Overdose feedback has no severity levels.

In many electronic health record systems, the dosing data is not available as structured data. In these cases, the clinical decision support features utilising the dosing data (including the overdose section) do not work.

3.3 Reasoning Assistant

3.3.1 Decision rules

The Reasoning Assistant provides a platform for healthcare professionals to develop clinical decision rules. The decision rules ("scripts") analyse the patient's diagnoses, risks, laboratory results, drugs/vaccines, and procedure data and draw conclusions that are displayed as **reminders** to the electronic health record system user. As an example, the figure below describes the operating principle of a single decision rule and reminders produced by the rule:



3.3.2 Classification of reminders

Reminders are classified according to severity/ urgency:

- Very important recommendation = alert ("If the recommendation is not followed, the patient may suffer serious harm")
- Important recommendation = request ("If the recommendation is not followed, the patient may suffer harm")
- Reasonably important recommendation = reminder ("If the recommendation is followed, it may be useful for the patient").

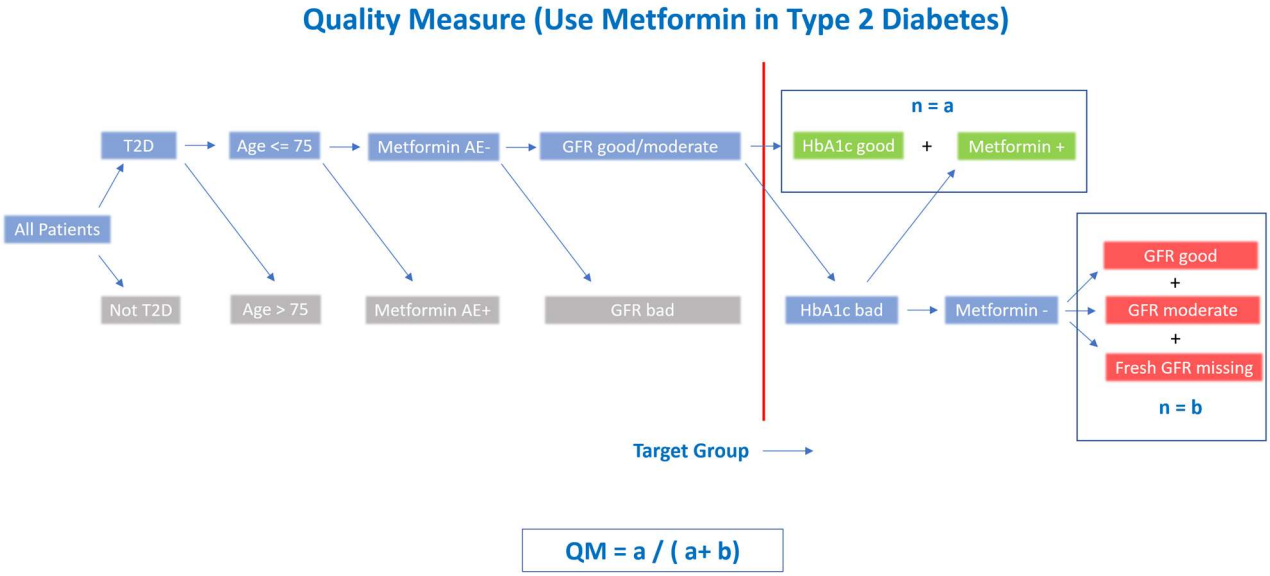
Severity levels are usually visualised with icons of different colours (see section 4.2.2).

3.3.3 Patient specific data displayed in reminders

The reminders may contain dynamic patient-specific data, such as laboratory test results and time stamps, as well as information about the patient's diagnoses or the drugs they use.

3.3.4 Triggering reminders as a quality indicator

As a rule, when a reminder is triggered, this means a quality deviation. Thus, the triggering of reminders can be used as quality indicators at the population level. The principle of quality measurement is shown in the following example:



This decision rule is based on the fact that metformin is recommended as the primary drug for type 2 diabetics. The rule first examines whether the patient has type 2 diabetes. If so, only those patients who are under 75 years old, who have not previously been recorded with adverse reactions to metformin and whose GFR is good enough will be included in the target group of the quality measurement. If the target group patient has metformin in use and/or HbA1c is at a good level, a quality deviation will not be triggered. However, if metformin is missing and HbA1c is not at a satisfactory level, a quality deviation is created. In the population review, the numeric value of the quality measurement is calculated using the formula a / (a + b), where a = the number of patients found without a quality deviation divided by the number of patients in the entire target group (a + b).

Utilising quality measurements requires the introduction of EBMEDS clinical decision support's Health Benefit Analysis application as a separate service. Use of the Health Benefit Analysis is described in a different user manual.

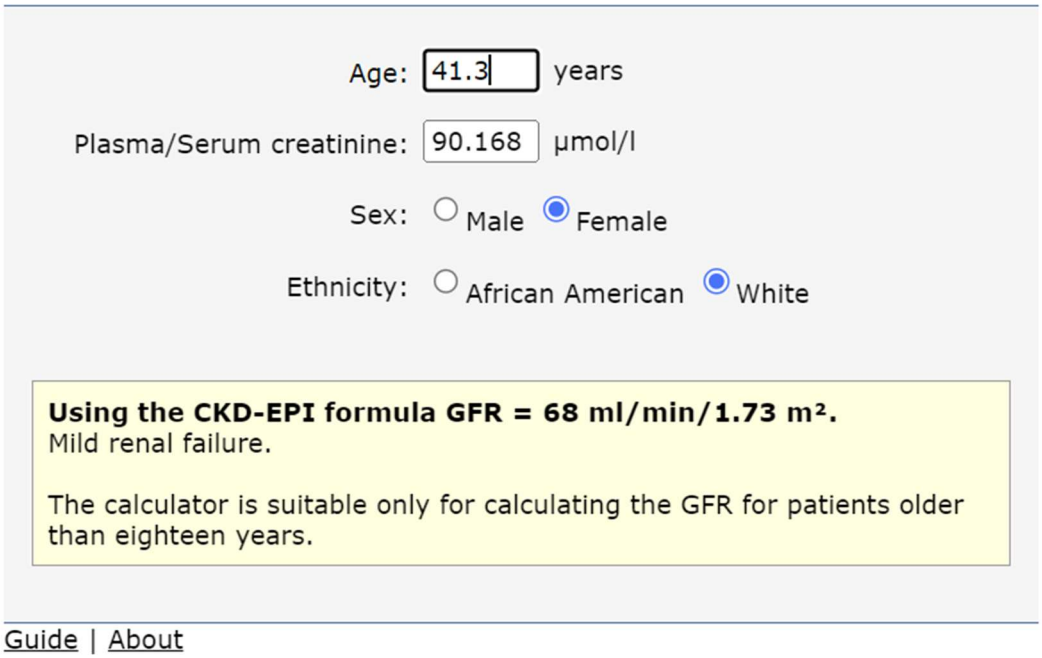
3.4 Form Assistant

3.4.1 Operating principle

The Form Assistant utilises information from the electronic health record system by transferring it to various electronic platforms ("forms"), such as calculators, referrals, flowcharts and quality registers.

3.4.2 Calculators

Many calculators are used in health care, and they take a lot of time to fill. The information needed for them is in fragments in several different locations. Clinical decision support pre-populates the calculators with the patient's data, saving significant working time.



It is always a good idea to check that the patient's diagnosis and medication are up to date and that the pre-filled information is correct[6]. Clinical decision support cannot fill in calculators with information that has not been recorded in a structured manner. You can always change the pre-filled information if necessary.

3.4.3 Registers

Clinical decision support can be used, for example, to transfer patient data to the input forms of the Conmedic company's quality registers. This eliminates the need to fill in the forms manually, which saves considerable time.

3.5 Treatment Recommendation Assistant

The Treatment Recommendation Assistant automatically creates patient-specific links to national and local clinical guidelines based on the patient's diagnosis information. The collection of links has been fine-tuned with age and gender restrictions. This way, for example, no child clinical guideline links are created for adults, and clinical guideline links intended for women are not displayed for men.

3.5.1 National clinical guidelines

Clinical decision support includes a standard collection of treatment recommendations, which includes clinical guidelines familiar from Terveysportti health portal and the Terveyskirjasto health library:

- Current care
- EBM Guidelines
- Sairaanhoitajan käsikirja (Nurse's handbook)
- Lääkärikirja Duodecim (a collection of treatment recommendations intended for the general public in the Terveyskirjasto service).

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3.5.2 Local treatment recommendations

Local organisations that use clinical decision support can also add their own local treatment recommendations and treatment paths to the Treatment Recommendation Assistant. In this case, the clinical decision support team must be provided with information on the location of the documents online, and a classification of the documents ("indexing") with ICD-10 diagnosis codes is also required.

4 Feedback from clinical decision support

4.1 Structured feedback

Many electronic health record systems utilise the structured feedback from clinical decision support. This means that the electronic health record system forms a user interface for the clinical decision support itself and displays the feedback produced by clinical decision support in a layout suitable for the electronic health record system. In principle, the electronic health record system can also utilise only part of the feedback from clinical decision support in the different work phases of the electronic health record system, for example in interaction checks in connection with prescriptions. However, this is not very common, as all feedback is usually in the same place and resembles the general feedback produced by Duodecim described in section 4.2. Electronic health record system suppliers provide additional information on the appearance and functionality of clinical decision support for individual electronic health record systems.

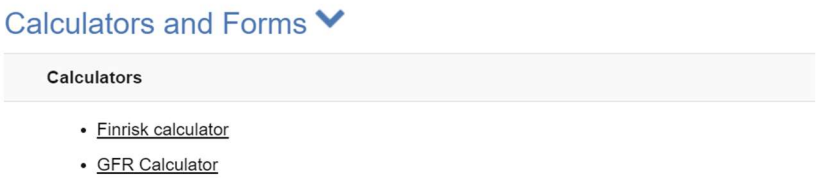
4.2 General browser feedback

EBMEDS provides a version of the general feedback on clinical decision support that can be read in a web browser. Some electronic health record systems display this feedback version as is in a browser embedded inside the electronic health record system, and some produce a corresponding version of the structured feedback on clinical decision support.

4.2.1 Form Assistant tools and links

There are links to additional information describing the EBMEDS service, the clinical decision support website and training materials (online courses and this manual) at the beginning of the general feedback. Under the *Tools* heading, you will find links to the Comprehensive Medication Review and the Diagnosis-specific Overview. These aggregate views are described in more detail in sections 4.3 and 4.4.

You can find links to calculators, interactive algorithms, quality register input forms and referrals produced by the Form Assistant under the *Calculators and forms* heading Note! Opens with the "^" sign!). The selection of links of the Form Assistant is described in more detail in section 3.4.

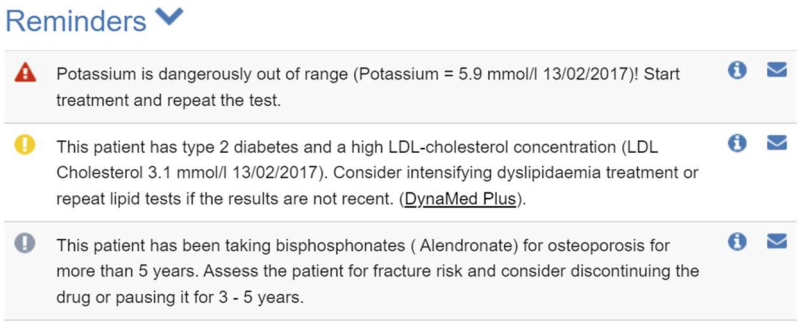


When items in the Form Assistant links are opened, clinical patient data extracted from the clinical decision support query message is automatically transferred to them.

The choice of calculators is not exactly the same for all patients - e.g. links to children's calculators are not displayed to adults.

4.2.2 Reasoning Assistant reminders

You can find Reasoning Assistant reminders generated based on the patient's data (see 3.3) under the heading *Reminders*. The severity level of the reminders (see 3.3.2) is indicated by red, yellow and grey icons:



There are two icons that act as a link on the right side of the reminders:

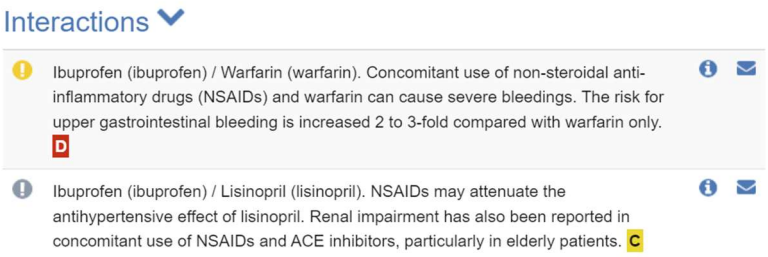
- The “i” icon
  - A link to the background information page of clinical decision support where the background of the reminder in question is specified. The following information can be found on the page:
    - Summary of purpose, context and function of the reminder
    - Other reminders generated by the decision rule behind the reminder (many rules can produce several reminders)
    - A report of the scientific evidence underlying the decision rule.
- Envelope icon
  - Provides a link to the clinical decision support feedback page.

4.2.3 Drug Assistant reminders

4.2.3.1 Interactions

Of the identified potential interactions (see 3.2.4), drug pairs (trade name + generic name of the active component) and the short text describing the interaction in the Inxbase database are shown in the section *Interactions*. The generic name of the active component is important, especially if the drug in question is a

combination drug containing several active components. In such case, the generic name confirms which of the components of the combination drug causes potential interaction. The text ends with a color-coded letter describing the severity of the interaction (yellow C or red D).

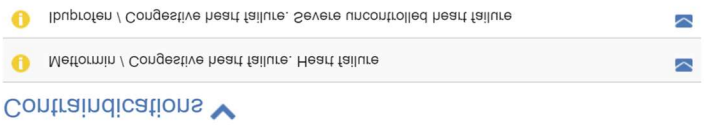


There are two icons that act as a link on the right side of the interaction reminders:

- The “i” icon
  - A link to the section of the Terveysportti portal’s Inxbase database, which contains a recommendation on the measures required by the interaction and information on the scientific evidence of the interaction.
- Envelope icon
  - Provides a link to the clinical decision support feedback page.

4.2.3.2 Contraindications

Of the identified potential contraindications (see 3.2.3), the drug diagnosis pairs (trade name of the drug + the entry associated with the ICD-10 code of the diagnosis) and, in certain cases, a short text specifying the contraindication are shown in the section *Contraindications*.

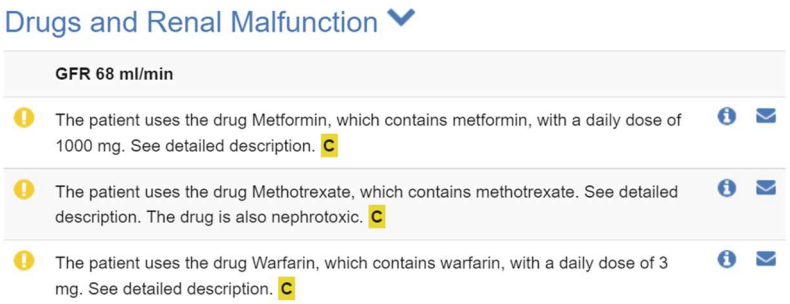


There is an envelope icon to the right of the interaction reminders, which provides a link to the clinical decision support feedback page.

4.2.3.3 Drugs and Renal Malfunction

If the patient's glomerular filtration rate (GFR) has decreased and this affects the patient's medication, feedback from the Renbase database (see 3.2.6) is presented in the section *Drugs and Renal Malfunction*. The section starts with a GFR value and possibly information about problems with its interpretation. After the GFR value, there are reminders related to the use of drugs (especially dosing). The reminder describes the trade name of the drug and the generic name of the active component. Combined preparations contain several active components, so the generic name indicates which component the reminder was generated from.

If the current daily dose is available in structured form, the daily dose is also shown in the reminder. The recommendation in the reminders is often to reduce the dose, and you can see from the daily dose if this has already been realised. Note! Unfortunately, clinical decision support is unable to reliably calculate patient-specific normal doses, so the **reminders are displayed even though appropriate dose changes have already been made**.



There is an icon on the left side of the reminders and a letter on coloured background at the end of the text indicating the severity of the potential problem and the scientific evidence (for more details, see 3.2.6):

- Yellow icon and a letter on yellow background: Severity level D (important reminder).
- Grey icon and a letter on grey background: Severity level B or C (relatively important reminder).

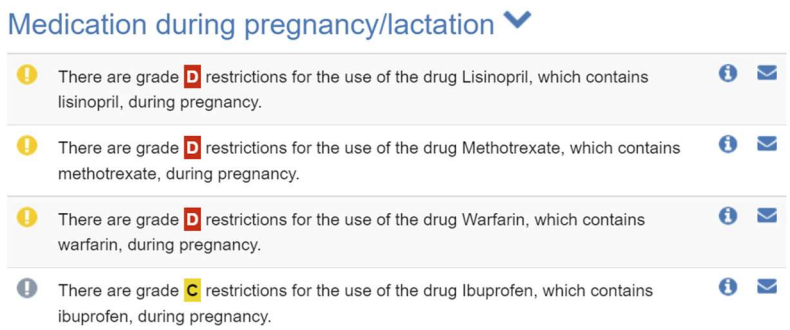
There are two icons that act as a link on the right side of the reminders:

- The “i” icon
    - The link takes you to the Renbase database page, which contains additional information on the dosing of the drug in case of renal failure. The page also includes the “Find a substitute product” function, which allows you to view the dosing restrictions of other drugs belonging to the same drug group in renal failure.
- Envelope icon
    - Provides a link to the clinical decision support feedback page.

4.2.3.4 Use of Drugs During Pregnancy and Breastfeeding

This section based on the Gravbase and Lactbase databases (see 3.2.7) contains reminders regarding restrictions on drug use during pregnancy and breastfeeding. The severity level of the reminders is described by the following icons on the left side of the reminder (for more information, see 3.2.7):

- Yellow icon: Severity level D.
- Grey icon: Severity level C.



There are two icons that act as a link on the right side of the reminders:

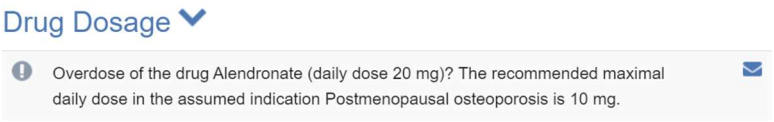
- The “i” icon

  - Using the info link at the end of the reminder, you can access the pages of the Gravbase and Lactbase databases, which contain additional information on restrictions on the use of the drug during pregnancy and breastfeeding. The page also includes the "Find a substitute product" function, which allows you to view the dosing restrictions of other drugs belonging to the same drug group during pregnancy and breastfeeding.
- Envelope icon
  - Provides a link to the clinical decision support feedback page.

4.2.3.5 Drug Dosage

An overdose reminder (see 3.2.8) is generated when the daily dose of the drug exceeds the drug's maximum daily dose based on the drug indication. If a suitable indication is found on the diagnosis list, the maximum daily dose for the drug is the dose specified for that indication, and this is informed in the text of the reminder. If no suitable indication is found, the maximum dose specified in the database for the drug is used as the maximum daily dose.

There are no severity levels associated with overdose reminders.

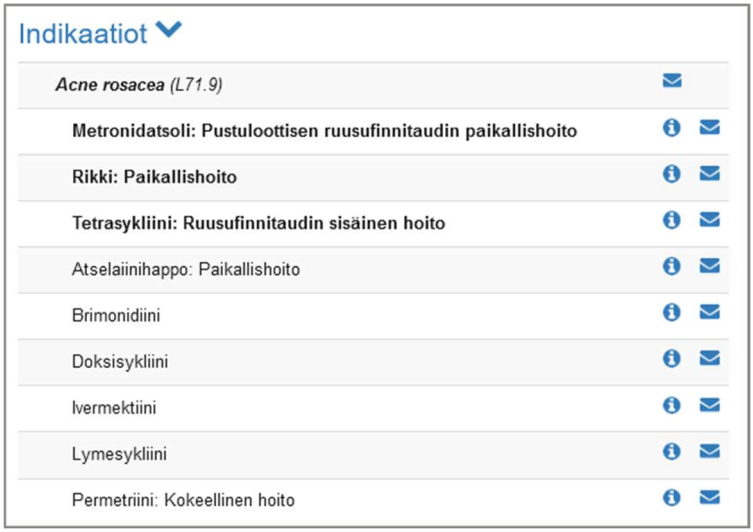


There is an envelope icon to the right of the reminders, which provides a link to the clinical decision support feedback page.

4.2.3.6 Indications

After a new diagnosis has been added (and only then), the primary and secondary drugs (see 3.2.2) used for the treatment of the diagnosis according to the clinical guidelines retrieved from the indication database will be shown in this section (which comes after the links of the Treatment Recommendation Assistant).

This section is not available in all languages and regions.



The primary drugs are in bold type.

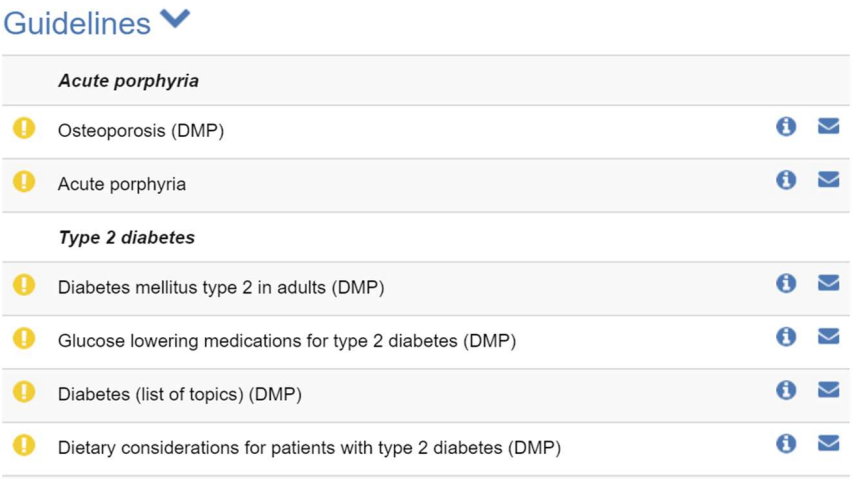
There are two icons that act as a link on the right side of the reminders:

- The "i" icon

  - You can access the drug database in Terveysportti portal to read more about the drug in question from the info link on the right side of the drug.
- Envelope icon
  - Provides a link to the clinical decision support feedback page.

4.2.4 Guideline Assistant links

The links to clinical guidelines (see 3.5) provided by the Treatment Recommendation Assistant are displayed grouped by diagnosis. If there are links to local treatment recommendations, this is explained (in parentheses) at the end of the relevant link texts.



4.3 Comprehensive Medication Review (CMR)

4.3.1 Introduction

The Comprehensive Medication Review is one of the most used and most important tools in Clinical Decision Support. It makes it possible to assess the patient's medication with a single click. Based on the patient's information, the tool provides a summary of the medication. Information that would otherwise have to be retrieved from several different locations has been quickly and easily made available. The Comprehensive Medication Review helps to identify problems related to medication and make better decisions in pharmacotherapy. In other words, it increases the safety of drug therapy while saving the professional's time.

The operation of the Comprehensive Medication Review is based on the diagnosis and medication data obtained from the electronic health record system, which is why this data must be up to date. The up-to-dateness of the list of drugs should always be reviewed, and missing diagnoses added if necessary. If this information is incomplete, the Comprehensive Medication Review does not work completely reliably.

4.3.2 Navigation in the application

CMR consists of the following sections:

- Medication list with indication checks
- Research results relevant to the drug therapy
- Drug reminders produced by the Reasoning Assistant
- Feedback provided by the Drug Assistant:

- Use of drugs in renal failure
- Cumulative adverse drug reactions of the drugs
- Interactions
- Contraindications
- Drug restrictions during pregnancy and breastfeeding
- Overdose warnings.

There is a navigation control on the right side of the tool to quickly navigate from one section to another. The control also shows how many issues the application has detected in those sections:

4.3.3 Medication and indications

The medication used is listed together with diagnostic indications (see 3.2.2). Drugs for which no indication is found will be marked with “No indication”. These drugs could potentially be discontinued or replaced with another drug. **However, it is very important to check that the indication has not been omitted from the diagnosis list by chance or, for example, recorded as a temporary diagnosis.** If necessary, the missing indications should be added to the diagnosis list. The material used by the indicator check is not yet fully comprehensive, and, as a result, unjustified notifications of missing indications may also be received. For example, painkillers have so many possible indications that not all of them can be found in the database.

Medication and Indications

Drug	Active ingredient	ATC	Strength	Dosage	Daily dose	Start Date
Metronidazol	metronidazole	P01AB01	400 mg	1 x 3	1200 mg	2017-02-13
• Please check the indication						
Alendronate	alendronate	M05BA04	10 mg	1 x 2	20 mg	2011-08-24
• Postmenopausal osteoporosis (2017-02-13)						
Ibuprofen	ibuprofen	M01AE01	400 mg	1 x 3	1200 mg	2015-06-24
• Rheumatoid arhthritis (2017-02-13)						
Methotrexate	methotrexate	L04AX03	10 mg			2017-02-13
• Rheumatoid arhthritis (2017-02-13)						
Warfarin	warfarin	B01AA03	3 mg	1 x 1	3 mg	2016-04-19
• Atrial fibrillation (2017-02-13)						
Metformin	metformin	A10BA02	500 mg	1 x 2	1000 mg	2015-06-24
• Please check the indication						
Ranitidine	ranitidine	A02BA02	150 mg	1 x 1	150 mg	2017-02-13
• Please check the indication						

The diagnosis code for the indication appears when you place the pointer over the diagnosis name.

4.3.4 Examination results

This section shows the laboratory results that are relevant to the safe drug therapy of the patient in question. The section reports missing and outdated laboratory tests and alerts you to abnormal results. The recommendations on the limits of the measurement results are based on clinical guidelines and the clinical expertise of the clinical decision support physician editors. The limits are often wider than the reference intervals given by laboratories.

If the result is in red, it is not within the desired range. Based on this, monitoring should be increased or changes to the patient's medication should be considered.

Measurement Results

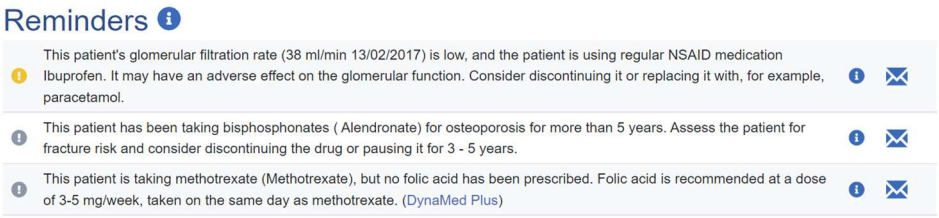
Name	Result	Date
Creatinine	115 umol/l	2017-02-13
BMI	24.5 kg/m^2	2017-02-13
GFR	38 ml/min	2017-02-13
HbA1c	5.993 %	2017-02-13
ALT	59 U/l	2016-02-09
Haemoglobin		
INR	3	2017-02-13
Platelet Count		

If the date is in red, the result is out of date and the examination will probably need to be renewed soon.

If the result is missing (the field is blank), the result is not available and the examination should probably be ordered.

4.3.5 Drug reminders of the Reasoning Assistant

This section displays the non-database based medication reminders produced by the Reasoning Assistant (see 3.3).



The reminders may include, for example:

- A request to order follow-up laboratory tests to improve patient safety
- A request to reduce the dose of certain pharmaceuticals
- A request to end medication with no positive risk/benefit balance or evidence that risks may outweigh the benefits (especially in older people)
- A request to end medication that is on the list of drugs to be avoided for older patients (e.g. 'European PIM' or 'STOPP' lists)
- A request to end medication that has been used for longer than specified in the clinical guideline
- A request to end medication that is not justified because of its minor or questionable effect.

The severity level of the reminders (see 3.3.2) is indicated by red, yellow and grey icons on the left side of the reminder.

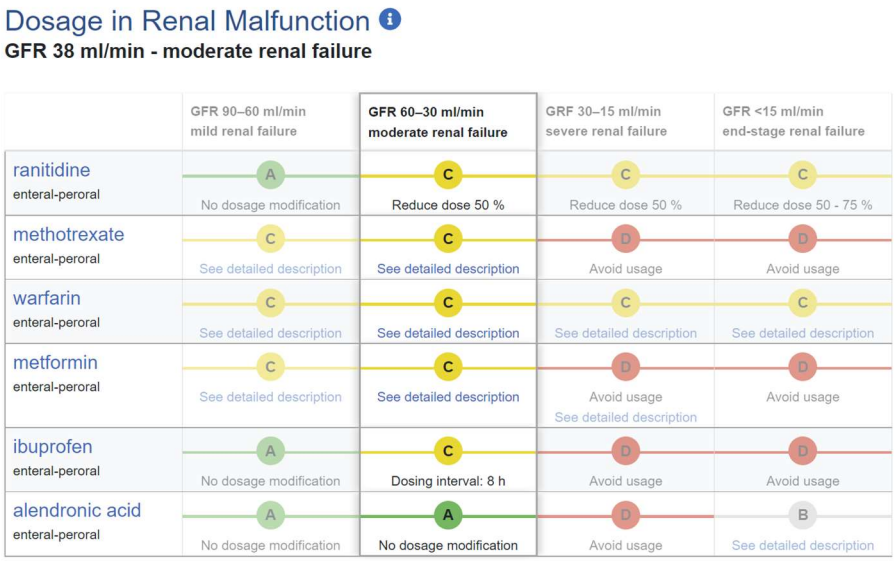
For more information about the background of the reminder, click the "info" icon to the right of the reminder. This opens a link to the EBMEDS website with a more detailed description of the reminder. The description presents, for example, the scientific evidence behind the reminder (see 4.2.2).

There is an envelope icon to the right of the reminders, which provides a link to the clinical decision support feedback page.

4.3.6 Drugs and Renal Malfunction

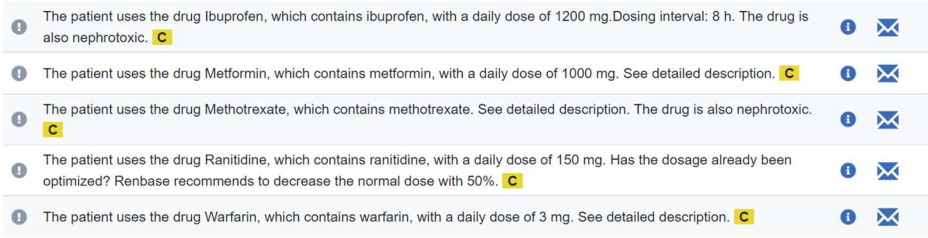
This section contains reminders related to drug dose changes or restrictions on use in renal failure, using the Renbase database (see 3.2.6). The degree of renal failure of the patient is classified on the basis of the GFR value at the beginning of the section.

To understand the overall picture, the recommendations for action are displayed in all GFR groups in tabular form:



The GFR area to which the patient currently belongs is highlighted in the table.

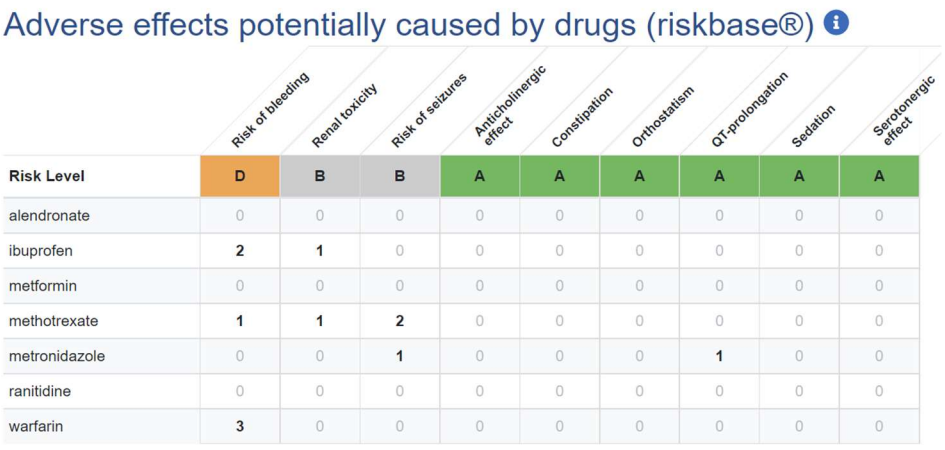
After the table, deviations in the table are displayed in the reminder format. The structure of these reminders is described in section 4.2.3.3.



Please note that the reminders are received even though the dosage has already been changed because the system is unable to evaluate the "normal doses" of an individual patient and the changes made to them.

4.3.7 Cumulative adverse drug reactions

This section is based on the Riskbase cumulative adverse drug reactions database (see 3.2.5). The table contains nine key adverse drug reactions (columns) and the active agents (rows) of the patient's drugs. The cells in the table show the typical adverse drug effect risks on a scale of zero (no risk or very low risk) to three (high risk).



	Risk of bleeding	Renal toxicity	Risk of seizures	Anticholinergic effect	Constipation	Orthostatism	QT-prolongation	Sedation	Serotonergic effect
Risk Level	**D**	**B**	**B**	**A**	**A**	**A**	**A**	**A**	**A**
alendronate	0	0	0	0	0	0	0	0	0
ibuprofen	2	1	0	0	0	0	0	0	0
metformin	0	0	0	0	0	0	0	0	0
methotrexate	1	1	2	0	0	0	0	0	0
metronidazole	0	0	1	0	0	0	1	0	0
ranitidine	0	0	0	0	0	0	0	0	0
warfarin	3	0	0	0	0	0	0	0	0

The overall risk of each adverse effect for that drug combination is indicated by a letter code:

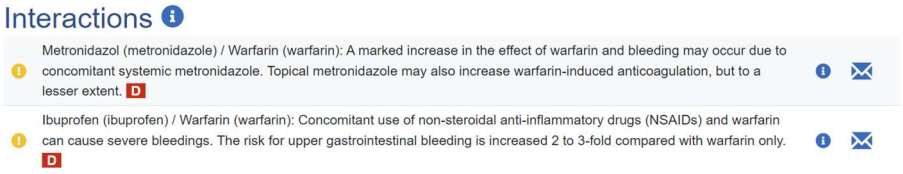
- A: No known increased risk.
- B: The risk is slightly increased.
- C: The risk is moderately increased.
- D: The risk is significantly increased.

You can display the overall risk classification in the tip window by hovering the mouse over the letter code.

By clicking the names or letter codes of the adverse drug reactions, you will receive instructions on how to avoid the adverse drug reactions. At the same time, you can search substitute preparations with a lower tendency to cause such adverse effects.

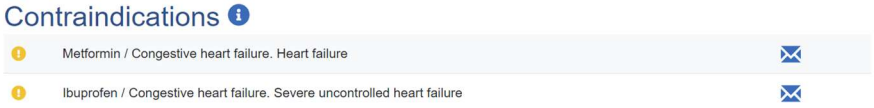
4.3.8 Interactions

This section contains reminders of possible drug interactions based on the information in the Inxbase database (3.2.4). Only clinically significant reminders (level C and level D reminders) are displayed. The syntax and severity levels of reminders are described in more detail in section 3.2.4.



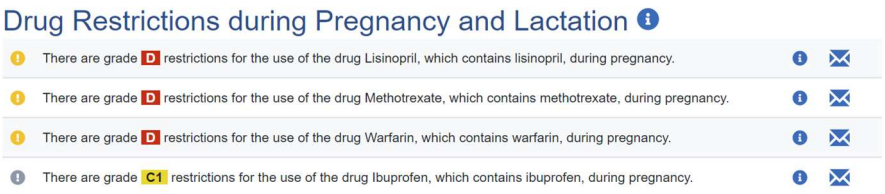
4.3.9 Contraindications

This section generates a contraindication reminder when a drug is found on the patient's list of medications that has a contraindication on the diagnosis list (see 3.2.3). The syntax and severity levels of reminders are described in more detail in section 4.2.3.2.



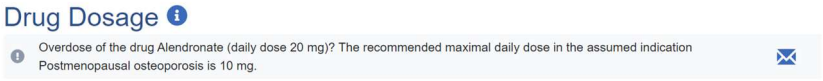
4.3.10 Drug restrictions during pregnancy and breastfeeding

This section contains reminders related to the use of drugs during pregnancy and breastfeeding (see 3.2.7). The syntax and severity levels of reminders are described in more detail in section 4.2.3.4.



4.3.11 Overdose check

This section generates an overdose reminder when the daily dose of the drug exceeds the maximum daily dose based on the drug indication (3.2.8). The syntax of reminders is described in more detail in section 4.2.3.5.



4.4 Diagnosis-specific Overview (DSO)

4.4.1 Introduction

Patients with multiple diseases challenge treatment chains around the world. Ageing causes many diseases, but many lifestyle diseases and their complications are beginning to be seen in younger and younger patients. These patients need comprehensive care, in which case it is essential that the clinicians have a cross-cutting view of the patient's care.

A Diagnosis-specific Overview collects the different diagnoses of the patient and the associated treatment in one place. The summary provides an overall picture of the patient's situation. This facilitates orientation to the patient’s situation and treatment planning, especially for patients with multiple diseases, and reduces the time required to open different forms.

The Diagnosis-specific Overview is comprised of boxes that represent different perspectives on the patient's overall situation. The summary presents diagnoses, reminders, drugs, clinical guidelines, laboratory results, calculators and procedures.

The Diagnosis-specific Overview serves as a checklist of issues that should be taken into account. It can be used to check, for example, the appropriateness of medication or the up-to-datedness of laboratory tests at a glance. For more information on the section, use the info links (i).

4.4.2 List of diagnoses

A diagnosis is selected from the Current diagnoses list, in which case a summary of the diagnosis is displayed: Only reminders, treatment recommendations, laboratory results, calculators and procedures relevant to the diagnosis are displayed.

4.4.3 List of medications

This section displays the patient's entire medication, but the drugs associated with the selected diagnosis are at the top of the list in bold. Drug strength and dosage information is displayed only if it is available as structured information.

Current Medication

Drug	Strength	Unit	Dosage
Warfarin	**3**	**mg**	**1x1**
Alendronate	10	mg	1x2
Esomeprazol	20	mg	1x1
Ibuprofen	400	mg	1x3
Lisinopril	10	mg	1x2
Metformin	500	mg	1x2
Methotrexate	10	mg	

4.4.4 Examination results

This section displays laboratory and physiological measurement results, which are classified to be associated with the selected diagnosis. If the examination result is outside the limits, it is displayed in yellow. If the result is too old to be interpreted, the examination date is marked with a yellow background colour.

Current Laboratory Results

Name	Result	Unit	Date
BMI	24.5	kg/m^2	2017-02-13
Creatinine	90.168	umol/l	2017-02-13
GFR	68	ml/min	2017-02-13
INR	3		2017-02-13

4.4.5 Procedures

This section lists procedures classified to be related to the diagnosis. If the date of the procedure is too old with regard to follow-up (e.g. too old fundus photography for a diabetic), the date is indicated in yellow.

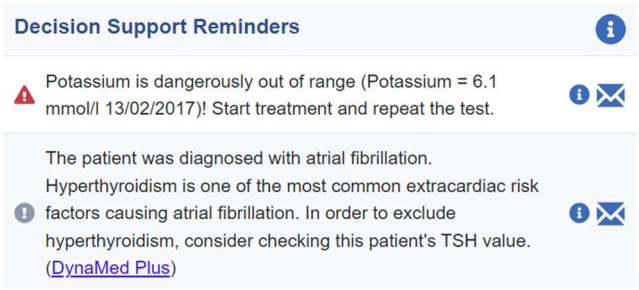
Relevant Procedures

Name	Date
Cardioversion	2016-12-05

4.4.6 Reasoning Assistant reminders

This section lists the recommendations and warnings provided by the Reasoning Assistant for the selected diagnosis (see 3.3.2). Critical reminders are marked with a red triangle. Reminders marked with a yellow icon are more important/urgent than reminders marked with a grey icon. By clicking the reminder, you can

move to the description page of the decision rule that produced the reminder, where the background of the reminder is explained (see 4.2.2).



4.4.7 Links to clinical guidelines

In this section, links to the main (yellow icons) and secondary (grey icons) treatment recommendations related to the selected diagnosis have been collected using the Treatment Recommendation Assistant (see 3.5).

4.4.8 Links to calculators

In this section, the Form Assistant (3.4) has been used to gather links to calculators associated with the selected diagnosis. When the calculators are opened, the patient's clinical data has been automatically transferred to them in part or in full (4.2.1see).

5 Sources of error

5.1 Important sources of error[7]

This chapter focuses on the sources of error of the clinical decision support system in the logical analysis of patient data and the production of reminders. These sources of error are similar regardless of the electronic health record system to which the clinical decision support system is connected. Those sources of error that depend on the specific implementation of the clinical decision support system to the electronic

health record system (presentation of reminders, indication of the urgency category, selection of information to be sent to the clinical decision support system, etc.) are not dealt with in detail here. In terms of taking these sources of error into account, the instructions and training provided by the supplier of the electronic health record system play a key role.

Errors in clinical decision support can mainly be caused by three reasons:

1) Errors or deficiencies in the patient's structured data,
2) Errors in the logic of the analysis carried out by EBMEDS, and
3) Delays in updating clinical decision support rules as medical information develops and treatment practices change.

It is also important to understand that clinical decision support can never cover all clinically significant situations. Therefore, even if clinical decision support does not respond to the situation in any way, the patient may have serious health problems.

5.2 Incomplete structured data

The quality of structured information cannot always be relied on.[8] Storing and maintaining information in a structured manner can be difficult. In our experience, this applies especially to patient diagnoses and medication and their validity information. The diagnosis classification is not always unambiguous and it may take time to find the exact code, which is why the codes may not be recorded with an accuracy that would provide the best possibility to offer clinical decision support. On the other hand, the medication list may be more similar to a list of prescriptions, which makes it difficult to determine what the patient's current medication really is. The reliability of recording procedures and radiological examinations may depend on whether the procedure is ordered from the electronic health record system or through a separate system: If the procedure code is only in a separate system, clinical decision support may not receive it at all. The transmission of structured information between, for example, a hospital and a health centre may be incomplete, as the information is often in free text form in referrals and epicrises, from which it cannot be directly used for clinical decision support. Laboratory results, on the other hand, are usually in a pre-structured format, but the codes may contain laboratory and organisation specific variations. It is important that the EBMEDS team is informed of any local laboratory codes[9]. These are particularly common in quick tests (e.g. INR and CRP). An effort will be made to map local codes in connection with the introduction of clinical decision support, but they may also be found during use.

The most common disadvantage of incorrect or missing structured data is unjustified reminders. For example, clinical decision support may suggest measuring blood pressure even though it has actually been done, but the result has not been recorded in structured form. On the other hand, justified reminders may not be given. For example, if a patient has previously been on a course of warfarin due to a venous occlusion, but the end of treatment has not been indicated on the drug list, a patient who needs warfarin again (e.g. as a chronic atrial fibrillation develops) may be left without a reminder.

5.2.1 Sources of error in diagnosis information

The ICD-10 classification is extensive and complex and is often experienced as difficult to use. In addition, recording diagnoses has served administrative needs to a large extent, and accurate recording has not been of significant benefit in the immediate planning or implementation of the patient's care. It is therefore not surprising that there are often shortcomings in structured diagnostic data. However, as clinical decision support systems become more widespread, the benefits of more accurate recording of diagnoses may move closer to clinicians and patients.

Possible errors related to diagnoses may be caused by at least:

- A completely missing diagnosis code
- Inaccurate diagnosis code (e.g. non-insulin-dependent diabetes with multiple complications should be coded E11.7, but E11 is often used to cover all non-insulin-dependent diabetes patients)
- Incorrect diagnosis code
- In particular, the end date of the diagnosis data may be incorrectly transferred to clinical decision support if the information about the permanent diagnosis is not recorded or if the end date of the diagnosis is not recorded.

Because the end dates of diagnoses are often inadequately recorded, clinical decision support has automatic filtering, which recognises long-term diagnoses and, as a rule, ignores diagnoses that are intended to be short-term and are more than six months old. This feature is used in most clinical decision support installations in Finland.

5.2.2 Sources of error in risk information

From the perspective of clinical decision support, the most important risk information is smoking status, information on the ongoing pregnancy and information on clinically significant adverse effects caused by drugs. If this information is entered non-structured in the patient record text, it is not available for clinical decision support. If possible, this information should always be recorded in the electronic health record system in a structured manner. The best way to record the pregnancy status is to enter the due date in the appropriate field, if available. There is usually a view for adverse drug effect data, in which the information can be recorded in a structured manner.[10]

5.2.3 Sources of error in drug information

- Changes in medication prescribed elsewhere or implemented by the patient himself or herself or changes in the medication’s dosing.
- Old drugs or medication courses that are no longer in use have remained on the medication list.
- Old vaccinations have not been recorded in a structured format in the electronic health record system.

5.2.4 Sources of error related to laboratory results

- EBMEDS does not recognise the existence of a laboratory tests performed on a patient if the code used by the electronic health record system for that test is missing from the EBMEDS code list. For example, an abnormal code used by an individual laboratory for a test may be the cause.

- The electronic health record system does not have direct access to the results, so they are not transmitted to EBMEDS (in this case, the laboratory results are often viewed from a separate system, e.g. via a browser)
- Laboratory errors (sample confusion, sample handling, etc.)
- Clinical decision support usually does not have access to all patient laboratory and other measurement results, as the number of results may be limited by test to maintain acceptable system performance. In this case, typically a few most recent readings of all the measurements are sent.
- The laboratory referral may remain hanging, unused, on the referral list, and EBMEDS may interpret the test as ordered even if the patient is not going to the test.

5.2.5 Sources of error related to procedure codes

- Procedures performed in another care facility (e.g. a hospital) may not be transferred to the patient's own (e.g. a health centre) electronic health record system as structured information.
- If the ordered procedure or imaging examination is not performed for some reason, the order information may hang on the list even if it no longer reliably describes the future events.
- The procedure classification may be used differently in different units (the same procedure is recorded with a different code).

5.3 Errors in the analysis logic

The decision rules for clinical decision support are carefully planned and reviewed by the editors of clinical decision support who have both medical and technical expertise. The editor-in-chief approves the decision rules before publication. Nevertheless, errors may sometimes remain in the logic of the decision rule, causing it to act inappropriately.

If the user suspects an error in the logic of the decision rule, the user should first read the description of the rule on the clinical decision support website. The description aims to describe the logic of the decision rule with sufficient accuracy to be useful when investigating an incorrect reminder.

5.4 Rapid development of medical knowledge

An attempt is made to maintain scripts on a regular basis, but if treatment practices suddenly change due to, for example, observed adverse effects of the drug or the emergence of better treatment, EBMEDS may provide advice based on old practices until the relevant decision rule has been updated and the electronic health record system supplier has installed the update in the electronic health record system.

If you suspect that the decision rule's advice is based on outdated information, you should first check the description on the clinical decision support website. The description of the decision rule is linked to the medical evidence on which the advice given by the decision rule is based. The description also shows the last update date of the decision rule, which, however, reflects the situation on the Duodecim server, where the latest versions of the decision rules can always be found. Depending on the patient system-specific update schedules, the introduction of new decision rule versions in electronic health record systems may take a long time.

6 Feedback and development suggestions

The EBMEDS decision team is happy to receive feedback on errors or shortcomings identified by users and ideas for developing current or new content. In some electronic health record systems, the feedback function is built directly in connection with the reminders provided by the system. In addition, you can always provide feedback through the feedback function on the clinical decision support website. If there is a technical problem in the clinical decision support system (for example, a connection problem), you should primarily contact your own system support.

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