comeo·check

Instructions for Use

comeo®

www.comeo.com

Identification	
Product:	ComeoCheck
Basic UDI-DI:	++B886COMEOCHECKV3
Versions:	v1.*
Title:	Instructions For Use
Sub-title:	ComeoCheck User Guide

Pending regulatory approval: *The regulatory information and labelling described in this document is not yet effective. It will be effective when the Notified Body will deliver the CE certificate for the EU MDR conformity.*

History of Changes

Version	Date	Change Description
1.0	31/03/2025	Initial version

Table of Contents

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1 Introduction

1.1 Purpose

This documentation aims at guiding the users for the safe use of the ComeoCheck software.

It delivers important notices, limitations, contraindications, precautions, and warnings, regarding the use of ComeoCheck, that must be considered carefully by all users before any use.

1.2 Scope

This document is the entry point to the ComeoCheck User Guides series.

It is meant to deliver general information, precautions, and warning and limitations for the Healthcare Professionals.

This document is part of the ComeoCheck User Guides series whose reading is mandatory in function of the person's roles:

- Healthcare Professionals who are using ComeoCheck through their Computerized Physician Order Entry system.
- Any stakeholder interested in medication appropriateness check and drugs information.

As a Healthcare Professional user, you remain the only decider and responsible of a medication decision.

1.3 Applicability

The information in this document applies to the versions of ComeoCheck mentioned on the first page of this document, for all markets where it is distributed, unless specifically mentioned otherwise in the text. When a certain chapter or subchapter is limited to a version, this is the case for all paragraphs within this section and its subsections.

1.4 Audience

Intended audience of this guide are:

- Healthcare Professionals that are users of ComeoCheck;
- Any other person in charge of- or making use of the application.

Technical staff and developers can refer to the [REL1] ComeoCheck - Integration Manual available from the manufacturer (see section 1.6).

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1.5 Paper copy

The present Instructions for Use deliverable is distributed electronically and is accessible through the link in the "About" page of the application. In conformity with the (EU) 2021/2226 Regulation on Electronic Instructions for Use of Medical Devices, it will be available from the manufacturer for 15 years after the last device has been placed on the market.

Users requiring a paper copy can submit a request to:

E-mail:	Online: https://support.comeo.com E-mail: support@comeo.com

Paper copies will be received to the latest within 7 calendar days.

1.6 Support, Complaints or Incidents

Any complaint about ComeoCheck or any incident that has occurred in relation to ComeoCheck should be reported with no delay to the manufacturer or its distributor.

The contact details are listed below:

Region	**Support**
[BE] Belgium	Online: https://support.comeo.com E-mail: support@comeo.com

Functional and Technical support is available from the same contact point. To help understanding and remediating the situation, please explain the circumstances and observed conditions.

Any **serious incident** that has occurred in relation to ComeoCheck should be reported with no delay to the manufacturer and the Competent Authority of the state in which the user and or patient is established:

Serious incident reporting	
Manufacturer	support@comeo.com
[BE] Belgium	FAGG Portal in Dutch: https://www.fagg.be/nl/MENSELIJK_gebruik/gezondheidsproducten/medische_hulpmiddelen_hulpstukken/materiovigilantie/wat_0 AFMPS Portal in French:

	https://www.afmps.be/fr/humain/produits_de_sante/dispositifs_medicaux/materiovigilance/que_notifier/professionnel_de_la

To help understanding and addressing the Serious Incident, please explain the circumstances and observed conditions.

1.7 Related documents

ID	Reference	Description
REL1	CCK-ITM	ComeoCheck - Integration Manual

1.8 Glossary of terms

Term	Definition
AFAP	As Far As Possible
Alert	Information Signal notifying the User of a condition of the Patient and the Prescription providing contextual awareness that is intended to improve the clinical workflow or understanding of the Patient condition, the awareness not being intended by the need to take immediate action but to prevent further implications.
APB	The Belgian Pharmacists Association. (French) Association Pharmaceutique Belge: https://www.apb.be/fr/corp/Pages/default.aspx (Dutch) Algemene Pharmaceutische Bond: https://www.apb.be/nl/corp/Pages/default.aspx This association gathers independent Belgian pharmacists and provides its members with a wide range of services and tools to support them in their daily work.

Term	Definition
ATC	Anatomical Therapeutic Chemical. The Anatomical Therapeutic Chemical (ATC) Classification System is a drug classification system that classifies the active ingredients of drugs according to the organ or system on which they act and their therapeutic, pharmacological, and chemical properties. It is controlled by the World Health Organization Collaborating Centre for Drug Statistics Methodology (WHOCC). See structure and principles here: https://www.whocc.no/atc/structure_and_principles/
BMUC	Belgian Meaningful Use Criteria. The BMUC (Belgian Meaningful Use Criteria) is a Belgian public incentive system to promote the use of medical software systems within hospitals: https://www.health.belgium.be/en/node/28866
CAS Number	Chemical Abstracts Service. The Chemical Abstracts Service (CAS) Registry Number, also referred to as CASRN or CAS Number, is a unique numerical identifier assigned by the CAS to every chemical substance described in the open scientific literature (currently including all substances described from 1957 through the present, plus some substances from the early or mid 1900s), including organic and inorganic compounds, minerals, isotopes, alloys and non-structural materials (UVCBs, substances of unknown or variable composition, complex reaction products, or biological origin).
Check of Medication Appropriateness	The validation of the medication treatment of patients at risk for potentially inappropriate medication (PIM), including drug-related problems (DRPs) and ADEs by combining structured data available from the hospital information system (HIS) and by using standardized algorithms, also referred to as clinical rules.
Clinical relevance	The clinical relevance defines the meaning and severity of the drug-drug interaction. There are 7 levels defined by DelphiCare (contraindicated, severe, moderately severe, weak, warning from the producer, no expected inaction, no advice possible).
CNK	(French) Code National / (Dutch) Nationale Kode. This national code number is used for identifying unequivocally all the different packages of products available in pharmacies open to the public.

Term	Definition
Computerized Physician Order Entry system	The physician's use of computer assistance to directly enter medication orders from a computer or mobile device. The order is also documented or captured in a digital, structured, and computable format for use in improving safety and organization.
DelphiCare	DelphiCare is a scientific database over Belgian and foreign drugs, as well as parapharmaceutical products labeled by the APB. The "Centre d'Information Pharmaceutique (CIP) - Centrum voor Farmaceutische Informatie (CFI)" of the APB publishes DelphiCare.
Drug-Condition Interaction	An event in which a drug that is intended for therapeutic use causes some harmful effects in a patient because of a disease or condition that the patient has. This can be true for both prescription and over-the-counter drugs.
Drug-Drug Interaction	A change in a drug's effect on the body when the drug is taken together with a second drug. A drug-drug interaction can decrease or increase the action of either or both drugs or cause adverse effects.
eIFU	Electronic Instructions for Use
Healthcare Professional	Any member of the medical, pharmacy or nursing professions who, in the course of their professional activities, may prescribe, administer or dispense to a patient a medicinal product.
FAMHP	Federal Agency for Medicines and Health Products. https://www.famhp.be/en The Belgian competent authority for the quality, safety and efficacy of medicines and health products.
IFU	Instructions for Use
Intervention class	The intervention class defines the type of action to take in case of drug-drug interaction. There are 8 intervention classes defined by the legacy DelphiCare (from the most critical (1) to the weakest (8)). The intervention class is now obsolete and supported in the backward compatible mode only of API v1, it has been replaced by the clinical relevance concept. Refer to section 3.5 for more information.

Term	Definition
Monograph	The monograph is an exhaustive documentation on an interaction between two drugs. It contains the essential information about the interaction but also data on the type of interactions (pharmacokinetic or pharmacodynamics) and the substances affected by these interactions. On the other hand, it also describes the pharmacological effects, mechanisms, comments and contains the corresponding bibliography.
SMD or SaMD	Software as a Medical Device.
SPC	Summary of Product Characteristics.
Therapeutic Duplication	The practice of prescribing multiple medications for the same indication without a clear distinction of when one agent should be administered over another – for example, pain, nausea and vomiting, and constipation.
Web service	A Web service is a method of communications between two electronic devices over the Internet. It is a software function provided at a network address over the web with the service always on as in the concept of utility computing.
WHOCC	World Health Organization Collaborating Centre.

2 Intended Application

2.1 Intended use

ComeoCheck is a software as a service application designed to integrate with computerized physician order entry systems and intended to aid healthcare professionals in checking the appropriateness of patient medication prescriptions.

2.2 Intended indications

ComeoCheck is indicated for the check of medication prescriptions appropriateness involving all or part of the following aspects: drug-drug interactions, drug-conditions contraindications, and drug-drug therapeutic duplications.

2.3 Intended use environment

ComeoCheck is intended to be used integrated by a Computerized Physician Order Entry system deployed for the exclusive use by Healthcare Professionals.

Restrictions on locations or environments in which the software can be used: the integration must have been successfully validated by Computerized Physician Order Entry system user representatives in an environment that is fully similar to the production environment.

2.4 Intended user profiles

ComeoCheck is intended to be used exclusively by Healthcare Professionals that have been trained for using the Computerized Physician Order Entry system integrated with ComeoCheck.

2.5 Target population

ComeoCheck targeted population encompasses any human patient being treated in a Healthcare Institution under the control of a Healthcare Professional.

3 Important Notices

3.1 Contra-Indications

The following are known contraindications preventing Healthcare Professionals to rely on ComeoCheck for performing a check of medication appropriateness.

The use of ComeoCheck is contraindicated for any of the following conditions:

a. For patients taking drugs that have been prescribed outside Belgium and/or are imported from another market and not reimbursed in Belgium and therefore not supported by the APB DelphiCare database.
b. For patients taking drugs that are unknown to the Computerized Physician Order Entry system. Reasons for this situation typically include but are not limited to:
    - One or several previous prescriptions have been performed using a different Computerized Physician Order Entry system in the same Healthcare Institution whose data are not shared or accessible to the Computerized Physician Order Entry system integrated with ComeoCheck.
    - One or several previous prescriptions have been performed in a different Healthcare Institution whose data are not shared or accessible or copied into the Computerized Physician Order Entry system integrated with ComeoCheck.
    - One or several previous prescriptions have been performed by one or several open care prescribers whose data are not shared or accessible or copied into the Computerized Physician Order Entry system integrated with ComeoCheck.
c. The Computerized Physician Order Entry system is permanently or temporarily not connected to the Internet preventing to establish a reliable access to the cloud ComeoCheck services.

The use of ComeoCheck drug-condition interactions detection service is contraindicated for any of the following conditions:

d. For patient for which conditions are not encoded or available in the Computerized Physician Order Entry system using a structured coding scheme compatible with ComeoCheck.

3.2 Side effects

There are no known side effects from the use of ComeoCheck.

3.3 Warnings

The following is a non-limitative list of important attention points to be reviewed and understood by Healthcare Professionals before considering using ComeoCheck within their Healthcare *Institution.*

3.3.1 Dependent on the Internet connectivity

ComeoCheck is an Internet hosted system, i.e., relying, and dependent on the Healthcare Institution network and Internet connectivity.

The ComeoCheck service is delivered online from the Internet, relying and dependent on the Healthcare Institution network and Internet connectivity. As such, it might not be available in case of network connectivity interruption occurring between the Healthcare Institution and the ComeoCheck server. In such case, you will be warned by the display of a non-verification error message.

It is advised that the Healthcare Institution take relevant mitigation measures (such as redundant Internet connectivity) to guarantee the availability of the network.

3.3.2 Exposed to software malfunction

ComeoCheck, the Computerized Physician Order Entry system and the connector in-between are Software, i.e., are subject to present defects (i.e., bugs) or vulnerabilities that could affect their performance.

The manufacturer has performed extensive set of verifications and tests and has deployed the highest level of security infrastructure to prevent cyber-attacks and contamination by malwares. However, as all technologies, it's always possible that despite all the precautions and verifications there could be a residual risk that can be reduced AFAP (As Far As Possible) by:

- Additional check procedures in Computerized Physician Order Entry system systems;
- Make sure you are using the latest version of your Computerized Physician Order Entry system. Contact your support department in case of doubt;
- Always ensure that your digital equipment is protected for malware and anti-virus contaminations;
- Always pay attention to alerts and their level.

ComeoCheck is a machine service intended to complement the Healthcare Professional expertise with an extra level of verification, but not to replace him/her. As a Healthcare Professional user, you remain the only decider and responsible of a medication decision.

The eIFU (Electronic Instructions for Use) are packaged in ComeoCheck itself, so there is only one latest version accessible. However, it's always possible that the eIFU will not be visible to the Healthcare Professionals despite all the precautions and verifications. This risk can be reduced AFAP (As Far As Possible) by:

- Providing required documentation such as the Instructions for Use, Terms of Use, and Labelling (About Page);
- Verifying the availability of the latest version of the eIFU (paper version can be received within 7 days if necessary);
- Using a device compatible with the display of the eIFU;
- Locating and differentiating the information coming from the Instructions for Use or the Integration Manual.

3.4 Precautions

ComeoCheck may partially or completely malfunction if it is not installed, configurated, maintained, operated, and used in accordance with the complete Instruction set, consisting in this documentation and the [REL1] ComeoCheck - Integration Manual. To ensure that the product always

operates properly and safely, it must be installed, maintained, operated, and used in accordance with the instructions provided in these documentations.

Besides the guidelines in the instruction set, this section contains a mandatory but non-limitative list of precautions to be taken by Healthcare Professionals in the integration and deployment of ComeoCheck within their Healthcare Institution.

3.4.1 Healthcare Professional awareness is required

The ComeoCheck features can be implemented separately and independently by the manufacturer of the Computerized Physician Order Entry system.

ComeoCheck does not require the Computerized Physician Order Entry system to request all the possible appropriateness verification on the medication prescription. The Healthcare Professional shall be aware of which verifications are performed, and which aren't, and make no assumption that a verification has been made.

For example, a Computerized Physician Order Entry system manufacturer may have decided to request verification of drug-drug interaction but not drug-condition interaction nor drug-drug therapeutic duplication due to technical reasons, e.g., structured data availability or format. The Healthcare Professional should then not assume that drug-condition interaction and drug-drug therapeutic duplication would be identified by the system.

The Computerized Physician Order Entry system provides, when calling ComeoCheck, a clinical relevance filter which will be used by ComeoCheck to filter the returned alerts (see section 4.1.2). The Healthcare Professional should be aware of the filter(s) which have been configured in the Computerized Physician Order Entry system.

3.5 Limitations

The following is a non-limitative list of relevant factors that may affect the device's performance or safety.

3.5.1 Limitations of Prescription Verification

The ComeoCheck service provides an aid medication appropriateness check but shall not be considered as comprehensive or deterministic in the prescription process.

The following limitations are applicable to the ComeoCheck Service:

a. It is limited to medicines commercialized on the Belgian market and officially identified by the APB using the Belgian CNK code.
b. It does not include all drug-drug interactions but only a subset that has been published and made available (localized to Belgian codes and translated in French and Dutch) by the APB.

c. It does not take into account situations where a magistral or radiopharmaceutical preparation is involved in the prescription with no tracing to the original product and/or substance CNK or ATC code.
d. It does not include all drug-condition interactions, but only a subset that has been structured and codified by the APB based on a limited defined list of illnesses, hyper-sensibilities, and physiological states (see section 0).
e. It does not include all drug-drug therapeutic duplications but only those that can be detected by a common substance (see section 0). More specifically drugs that have in common a substance and it's derivative, and/or drugs that have different substances but share a common indication are not detected by the Service for potential duplication.
f. The data are updated typically monthly, at the end of a publication process by the APB. Information that could already have been identified and published by/within the scientific community might not yet be available in the Service due to localization, translation, review and/or periodic server update delays.

As a Healthcare Professional user, you remain the only decider and responsible of a medication decision.

3.5.2 Limitations regarding Patient Data

ComeoCheck checks the medication appropriateness only based on the current medications and has no historical or external data awareness about the patient context and history.

The following limitations are applicable to the ComeoCheck Service regarding patient data:

a. It has no access to any patient administrative or medical data and is not connected to any third medical data vault or hub or network. It has no way of identifying the patient. It does not collect any personal data, including cookies.
b. It keeps no track of previous verifications for the same patient and is unable of correlating subsequent verifications between them.
c. It makes no difference between medication already being taken and medication about to be prescribed. By consequence it has no possibility to know if an alert is related to medications prescribed in the past, medications about to be prescribed, or a mix of the two.
d. It is not informed of any past decision, or if a bypass has previously been set by any prescriber, therefore subsequent verifications including bypassed alerts will again trigger the same alerts.

As a Healthcare Professional user, you remain the only decider and responsible of a medication decision.

3.6 System, error and fault messages

Medication alerts messages are meant to be self-explanatory to Healthcare Professionals and displayed according to their clinical relevance as described in section 4.1.2.

Technical error messages are meant to be catch by the Computerized Physician Order Entry system and are described for developers in the [REL1] ComeoCheck - Integration Manual.

3.7 Lifetime, decommissioning and disposal of ComeoCheck

3.7.1 Device lifetime

The device lifetime is defined to 3 years after the release date of the version to the market. The release date is mentioned on the About page.

3.7.2 Decommissioning and disposal

ComeoCheck is a cloud software system that has no local components installed within the Healthcare Institution infrastructure, network or user local machine. It can be safely decommissioned at any time by stopping to call the service, with no specific measure to be taken for disposal.

3.8 Compatibility Notices

Version notes

ComeoCheck is fully compatible with the software MedCheck v3.* (*) for both the API v1 and API v2 versions.

The below section describes the changes brought by the API v2 compared to the API v1. Healthcare Institutions using the API v2 can ignore this section. Refer to the manufacturer of the Computerized Physician Order Entry system to understand which API version is being used by your Computerized Physician Order Entry system.

(*) MedCheck is a product of Pfizer Inc., 400 Webro Rd, Parsippany, New Jersey 07054, United States

3.8.1 Change in the Principle of Operation

Interactions by pair of substances

The conceptual modification brought by API v2 is that it better reflect the new DelphiCare database (from the Belgian Pharmacists Association):

- Previous versions of DelphiCare database provided the description of interactions at the level of the class or group of substances. By consequence, the interaction text was often relating to several substances belonging to these classes. This may have made it more difficult to find information about the specific interaction reported by the Computerized Physician Order Entry system.
- In the new version of DelphiCare database leveraged by API v2, interactions between e.g., ritonavir and itraconazole, ketoconazole, miconazole or posaconazole are individually described with, if necessary, a specific interaction text and clinical relevance. They are therefore not, as is the case in the previous database, grouped into a single common interaction between HIV protease inhibitors and azole derivatives. The action information after reporting therefore only deals with that specific combination of interacting substances, which speeds up the processing of the information and makes consideration of the interaction more efficient.

3.8.2 How backward compatibility is ensured

Despite the above change, the API v1 remains supported, so that any Computerized Physician Order Entry system that was integrated successfully with API v1 will continue to operate.

Note that to fully benefit from the new DelphiCare database, the Computerized Physician Order Entry system must be adapted by its manufacturer to API v2. Inquire to the manufacturer of the Computerized Physician Order Entry system for upgrade information.

When the Computerized Physician Order Entry system has not been upgraded to be compatible with the new DelphiCare database through API v2, it is by default running in backward compatible mode.

In this mode, the following adjustments are automatically provided:

The intervention class can continue to be used

The intervention class is mapped to the following levels of clinical relevance as follow:

Intervention class [API v1]	**Clinical relevance** [API v2]
Contraindicated	Contraindicated
Contraindicated in case of risk factors	
Contraindicated for caution	Severe
Concomitant use not recommended	
Follow-up / adaptation(s)	Moderately severe

Intervention class [API v1]	**Clinical relevance** [API v2]
Follow-up / adaptation(s) required in certain cases	
Follow-up by caution	Weak
No measures to take	Warning from the producer
	No expected inaction
	No advice possible

Please note that the intervention class and the clinical relevance are different concepts, therefore this mapping is only an approximation.

Fields are adapted in the essential information

The essential information data set contains short information that, in most cases, will be sufficient to manage the interaction. It is adapted as follows:

Information fields [API v1]	**Backward compatible content** [API v2]
Left interaction group	This field content will be populated with the more specific left interaction substance.
Right interaction group	This field content will be populated with the more specific right interaction substance.
Intervention class	As the intervention class isn't existing anymore, this field content is populated by recreating the intervention class based on the clinical relevance as described in the mapping table above.
Effect	No change, the effect field content is preserved.
Management	This field content is populated with the measures to take field that contains the same information.
Pharmacologic effect	No change, the pharmacologic effect field is preserved.
Unlikely substance	This field is not existing anymore and will remain empty.

Fields are adapted in the monograph

The monograph data set contains detailed scientific information. It is adapted as follows:

Information fields [API v1]	**Backward compatible content** [API v2]
Left interaction group	This field content will be populated with the more specific left interaction substance.
Right interaction group	This field content will be populated with the more specific right interaction substance.
Intervention class	As the intervention class isn't existing anymore, this field content is populated by recreating the intervention class based on the clinical relevance as described in the mapping table above.
Effect	No change, the effect field is preserved.
Comments	This field content is populated with the important remarks field that contains the same information.
Management	This field content is populated with the measures to take field that contains the same information.
Bibliography	No change, the bibliography field is preserved.
Pharmacologic effect	No change, the pharmacologic effect field is preserved.
Pharmacokinetic effect	This field is not existing anymore and will remain empty.
Pharmacodynamic effect	This field is not existing anymore and will remain empty.
Other interaction type	This field is not existing anymore and will remain empty.
Interaction substance described	This field is not existing anymore and will remain empty.
Interaction substance expected	This field is not existing anymore and will remain empty.
Interaction substance any	This field is not existing anymore and will remain empty.
Interaction substance unlikely	This field is not existing anymore and will remain empty.

4 Device Description

4.1 How ComeoCheck achieves its intended use

4.1.1 General Principle

ComeoCheck is a software service integrated with Computerized Physician Order Entry system and providing near real-time detection of:

- **Drug-Drug interactions**: by alerting a prescriber who is about to prescribe new medicinal products to a patient where potential adverse interaction(s) could arise from the simultaneous use of medicines. Upon detection of an interaction, a scientific contextual information can be provided by the mean of essential information (concise information) or a monography (detailed information).
- **Drug-Condition interactions**: by alerting a prescriber who is about to prescribe new medicinal products to a patient where potential adverse effect(s) could arise due to a particular patient condition or physiological state (i.e., disease, hyper-sensibility to a substance, pregnancy, breastfeeding, …). Upon detection of an interaction, a concise scientific contextual information can be provided.
- **Drug-Drug therapeutic duplication**: by alerting a prescriber who is about to prescribe new medicinal products to a patient where potential adverse effect(s) could arise due to duplication of the therapeutic effect of several drugs. Upon detection of a therapeutic duplication, a reference to the common chemical substance is provided.

4.1.2 Alerts

The alerts are delivered using the following scale based on the clinical relevance:

Clinical relevance	Description and meaning
Contraindicated	The interaction partners cannot be combined with each other, that is, they are contraindicated.
Severe	The interaction could be mortal or have serious, sometimes irreversible consequences for the patient.
Moderately severe	The interaction can have therapeutically significant consequences for the patient.
Weak	The interaction has no clear therapeutic consequences but should be monitored under certain circumstances.
Warning from the producer	For this interaction, only specific information from a pharmaceutical company is available, most often from the SPC.

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Clinical relevance	Description and meaning
No expected interaction	There are indications in the literature that no interactions occur or that no interactions are to be expected on the basis of structure, pharmacokinetics or pharmacodynamics.
No advice possible	An assessment based on the available literature is not possible.

This scale can be adapted by the Computerized Physician Order Entry system manufacturer.

Depending on the implementation choice within the Computerized Physician Order Entry system, clinical relevance can typically be used as an alert filter as needed and might be represented in a specific color to enhance the signal.

Frequency (probability) of occurrence

It is not always straightforward to assess a reported interaction solely based on clinical relevance. Therefore, the ComeoCheck also mentions the frequency of occurrence: very common (≥ 1/10), frequent (≥ 1/100 to < 1/10), uncommon (≥ 1/1.000 to < 1/100), rare (≥ 1/10.000 to < 1/1.000), very rare (< 1/10.000) or not known.

Assessment of the sources and nature of the sources

ComeoCheck indicates the quality of the data available (unknown, insufficient, poor, sufficient, good) and the nature of the sources consulted for the interaction (clinical studies, case observations, summary of product characteristics).

Interaction direction

The direction of the interaction describes whether one interaction partner influences the other (one-way interaction), whether the action of the two interaction partners is changed (two-way interaction) or whether the effect cannot be defined more precisely (without direction).

Side effects and symptoms

Adverse reactions and symptoms that may result from them are listed in a dedicated section. The use of layman's language supports the user in communicating with the patient.

Risk factors

The risk factors that may influence the occurrence of certain interactions are recorded in a structured manner.

Interaction monitoring

If patient follow-up is required when managing the interaction, this information is available in a structured way: parameters for follow-up, start of follow-up, duration of follow-up and any follow-up data after stopping one of the interacting substances.

Adjustment of the dose as part of the management of the interaction

This also applies to any adjustments to the dose or to the dosing schedule, which are necessary when considering certain interactions: taken or administered over time, adjustment of the dose and the dose interval, recommendations for short-term treatment and other recommendations.

4.1.3 Illustrative Example

A patient receiving chronic treatment with Marcoumar 3 mg tablets and Lanoxin 0,125 mg tablets should take Brufen 400 mg tablets.

CNK code	ATC code	Description
0119065	B01AA04	Marcoumar (c) 3mg
0127928	C01AA05	Lanoxin (c) 0,125mg
3607462	M01AE01	Brufen (c) 400mg

The way the Computerized Physician Order Entry system detects an interaction is system specific but basically consist in raising an alert notification.

In this example, two drug interactions are reported:

Interaction code	Clinical relevance	Interaction drug 1	Dir	Interaction drug 2
009904	Severe	Lanoxin (c) 0,125mg	←	Brufen (c) 400mg
000706	Severe	Marcoumar (c) 3mg	–	Brufen (c) 400mg

The first interaction is unidirectional. It is here represented by an arrow to the left (←) between the two interacting specialties. The right specialty influences the left.

The second interaction is directionless, which implies mutual reinforcement of adverse effects. This is indicated by a dash (–) between the names of the specialties.

The two reported clinical interactions are of "severe" clinical relevance.

4.1.4 Information

As side features, ComeoCheck is also able to:

- Provide **informative textual posology guidelines** including usual and max doses.
- Provide access to the official drug medical **Summary of Product Characteristics (SPC)**.

4.1.5 Integration in the Computerized Physician Order Entry system

ComeoCheck is available in the cloud as a machine-to-machine service to be used exclusively through software integration by the Computerized Physician Order Entry system manufacturer.

Consequently, ComeoCheck does not consist in an application for the Healthcare Professional. The Healthcare Professional is entirely using ComeoCheck from/through the user interface of the Computerized Physician Order Entry system, that must have been enhanced for this purpose by its manufacturer.

Another direct consequence is that in case the Computerized Physician Order Entry system becomes unavailable, then ComeoCheck will also become unavailable preventing the Healthcare Professionals to be aided for the check of medication appropriateness.

ComeoCheck relies on several data sources, mostly provided by the APB (Belgian Pharmaceutical Association) that provides updates of the data files typically monthly, and the AFMPS/FAGG (Belgian Agency of Drugs and Medical Devices).

4.2 Clinical benefits to be expected

No direct clinical benefit, understood as a positive impact of the device on the health of individual, is expected from the use of ComeoCheck. ComeoCheck is not intended to supplant the decision-making role of the physician, nor provide pivotal information to justify the adequacy of prescribed medication plans.

The indirect clinical benefit of the software lies in providing alerts and information on potential *drug-drug interactions, drug-condition interactions, therapeutic duplications, and drug contraindications* as documented within the DelphiCare APB pharmaceutical knowledge database, relative to medication orders made within a Healthcare Institution.

4.3 Performance characteristics of ComeoCheck

The following table lists the device performance characteristics:

Feature	Characteristics description
Medication Alerting Service	
Drug-drug Interactions Alerting	• Medication identification by APB CNK medication coding scheme. • Medication identification by WHO ATC medication coding scheme. • Filtering out by Clinical Relevance on 7 levels. • Provide Essential Information and Monograph for each reported interaction.
Drug-Condition Interactions, Advice and Precautions Alerting	• Medication identification by APB CNK medication coding scheme. • Condition identification by APB DelphiCare condition coding scheme. • Support alerting for the following conditions: ○ Asthma; ○ Hypersensitivity to rifamycins; ○ Hypersensitivity to polymyxins; ○ Hypersensitivity to nitrates; ○ Hypersensitivity to derivatives; ○ Hypersensitivity to barbiturates; ○ Hypersensitivity to an ACE inhibitor; ○ Photodermatosis (history of ...); ○ Hypersensitivity to NSAIDs; ○ Parkinson's disease; ○ Renal insufficiency; ○ Hepatic insufficiency; ○ Neuroleptic malignant syndrome (history); ○ Hypersensitivity to iodine; ○ Contact lenses; ○ Diabetes; ○ Hypersensitivity to cephalosporins; ○ Heart failure; ○ Open-angle glaucoma; ○ Hypertension; ○ Hypersensitivity to sulfonamides; ○ Prostatic hypertrophy; ○ Narrow-angle glaucoma; ○ Hypersensitivity to penicillins; ○ Hypersensitivity to tetracyclines; ○ Hypersensitivity to lincosamides; ○ Aminoglycoside hypersensitivity; ○ Phenylketonuria; ○ Quinolone hypersensitivity;

Feature	Characteristics description
	○ Macrolides hypersensitivity; ○ Sulfite hypersensitivity; ○ Epilepsy; ○ Carbapenem hypersensitivity; ○ Depression; ○ Pregnancy; ○ Breastfeeding; ○ Glucose-6-phosphate dehydrogenase deficiency; ○ Benzodiazepine hypersensitivity. • Filtering out by Risk Level.
Drug-Drug Therapeutic Duplications Alerting	• Medication identification by APB CNK medication coding scheme. • Support alerting for the following situations of duplications: ○ Two or more medications having the same active substance in common; ○ Two or more medications having the same ATC level 5 class.
Medication Information Service	
Drug Contraindications, Advice and Precautions Information	• Medication identification by APB CNK medication coding scheme. • Information delivered for the same conditions as for the alerting service.
Drug Composition Information	• Medication identification by APB CNK medication coding scheme. • Substances identification by CAS registry number.
Consult Drug Posology Guidelines	• Medication identification by APB CNK medication coding scheme. • Deliver unstructured text posology guidelines.
Summary of Product Characteristics Document	• Medication identification by APB CNK medication coding scheme. • Deliver summary of product characteristics documents in PDF.

4.4 Applications that can be used together with ComeoCheck

The table below lists the information flows that are supported by ComeoCheck and the applications that can be used together to provide extra functions.

Integration	Application	Details
Medication Appropriateness Service	Computerized Physician Order Entry system	**Intended purpose:** Provide alerts intended to aid the Healthcare Professionals in checking the appropriateness of a patient medication prescription. **Supported protocols:** Specific JSON REST protocol **Qualified software for safe combination:** The qualification for safe combination must be performed by the Computerized Physician Order Entry system manufacturer. **Known restrictions or constraints:** Requires a valid license token and Internet connectivity (see section 5).

For a more detailed technical view on how to integrate a Computerized Physician Order Entry system with ComeoCheck, please refer to the [REL1] ComeoCheck - Integration Manual.

4.5 Configuration

For ComeoCheck to function properly, the Computerized Physician Order Entry system must be configured with the license token allowing the use of ComeoCheck.

ComeoCheck can be configured by the means of a clinical relevance filter influencing the way alerts are filtered out.

5 User Device Technical requirements

5.1 Minimum Hardware Requirements

There are no specific hardware requirements for the user device other than the compliance with the Computerized Physician Order Entry system hardware requirements.

5.2 Minimum Software Requirements

On top of the Computerized Physician Order Entry system software requirements, using the ComeoCheck Public API web service might require a configuration of the network infrastructure.

The communication middleware is fully based on HTTPS requests/responses and does not differ from regular browser-based integrations with Internet web sites. The responses are formatted in simple JSON format that can be natively handled by most of the programming languages and/or frameworks.

In case of proxy and/or outbound routing rules are in place, we recommend that the Computerized Physician Order Entry system codebase gets access to:

URL	https://*.comeocheck.net/*
Port	443

Regarding the coding aspects, please refer to the [REL1] ComeoCheck - Integration Manual for technical details and coding guidelines about the integration of the ComeoCheck Public API in the Computerized Physician Order Entry system.

5.3 Security considerations

When using ComeoCheck, it is essential to follow security best practices to ensure the safety of patient data and the proper functioning of the system. The next table contains a non-exhaustive list of general security considerations:

Topic	Considerations
Secure Access to the System	• Always use unique login credentials and never share them with others. • Ensure multi-factor authentication (MFA) is enabled and complete the authentication process for every login. • Do not allow unauthorized individuals to view or access the application while it is in use. • Lock your device or application screen if you step away from your workstation • Log out of the system when not in use
Use of Approved Devices	• Access ComeoCheck only from devices that are approved and compliant with your organization's security policies. • Keep your devices updated with the latest operating system and security patches.
Data Handling and Export	• Avoid exporting sensitive patient data unless strictly necessary and authorized. • Ensure exported data is stored securely, encrypted, and deleted when no longer required. • Use data anonymization techniques to remove identifiable information before exporting or sharing data, in compliance with privacy regulations. • Do not transfer sensitive data using unsecured channels such as email

Responding to Alerts	• Take all system alerts and notifications seriously. • If you encounter a security alert, follow the recommended action steps provided by the system or notify your IT/security team immediately.
Reporting Suspicious Activity	• Report any suspicious activity, such as unexpected account logins or data anomalies, to your organization's IT/security team promptly. • Use the designated incident reporting system to log potential breaches or concerns.
Compliance with Organizational Policies	• Follow your organization's security policies and guidelines while using ComeoCheck. • Participate in regular security awareness training to stay informed about potential risks and best practices.
Keep Personal Information Secure	• Do not save passwords or sensitive information in unsecured locations (e.g., sticky notes, text files). • Use password managers if needed, ensuring they comply with organizational security requirements.

6 Regulatory information

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