Digi-HTA Recommendation

The Orla INR Remote Monitoring

PRODUCT INFORMATION

The Orla INR Remote Monitoring supports warfarin treatment with the help of self-measurement or self-care. The product consists of a mobile application intended for patients and a web-based service intended for professionals. The patient measures the INR value by using the Roche Diagnostics CoaguChek® INRange measurement device, which is connected to the Orla INR Remote Monitoring mobile application with a Bluetooth connection. The patient mobile application includes an electronic warfarin card and it seeks to remind the patient of the measurements to be made as well as to notify of any adjustments in the warfarin dosage made by the health care professionals. The patient's measurement data are available for the health care professionals with an access through the cloud service.

According to the company's declaration, this product is not a medical device, so it should not be used in any intended uses of the medical devices.

Platform: ⊠ Android ⊠ IOS ⊠ MS Windows ⊠ Browser ☐ Other

Language: ⊠ Finnish ⊠ Swedish ⊠ English ⊠ User interface of a health care professional, Finnish

Certificates: ⊠ CE marking (the INR measurement device) ☐ Medical device, level ☐ US FDA

Information security management system: ☐ ISO 27001 ☐ ISO 27701 ☐ Other

Quality management system: ☐ ISO 13485 ☐ Other

Manufacturer: Orla DTx https://orladtx.com/healthcare-professionals/orla-inr-remote-monitoring/

RECOMMENDATION   19.1.2022
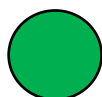
USE OF THE PRODUCT IS RECOMMENDED

The Orla INR Remote Monitoring is suitable for self-measurement or self-care of patients provided with warfarin treatment. Special attention must be paid to patient selection and patient counselling.

The recommendation is based on the information provided by the manufacturer.

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SUBAREAS OF ASSESSMENT		
Subarea	**Assessment**	Ponts
Effectiveness	**Sufficient** The service can be used in two ways: 1. Self-measurement: The patients measure the INR value by themselves, based on which the personnel within health care adjust the future doses of medicine. The patient sees the dose instructions through the mobile application. 2. Self-care: The patients both measure the INR value and adjust the doses of medicine by themselves. The personnel within health care see the measurement values and the doses of medicine (= remote monitoring). The service provider has completed a follow-up in five localities, on the basis of the actual use in respect of 58 patients. Based on this, the TTR (time in therapeutic range) was 70.71 % before the remote monitoring and 75.72 % at the end of the remote monitoring period (the difference is not statistically significant). Before the remote monitoring, 13 of the patients had reached the target level/value TTR > 80 %, at the end of the remote monitoring period 29 patients had reached the target level/value (the difference is statistically significant). The results show that for some patients the remote monitoring suits well and the care balance is improving, but, on the other hand, there are patients for which the remote monitoring is not suitable and the care balance is worsening.[1] There are ongoing studies carried out by the service provider on the actual use situations.[1] According to the satisfaction survey by the service provider, both the patients and the organisations have been satisfied with the service.[1] **Systematic reviews** Some systematic reviews[2,3,4] have been published on the subject, based on which self-measurement and self-care are at least as good as standard treatment. In the Cochrane review, both self-measurement and self-care were considered together. The relative risk, RR, with regard to thromboembolic events, decreased compared to standard treatment (RR = 0.58; the 95 % confidence interval, CI [0.45, 0.74]), but, when	

considering the risk of major bleeds (RR = 0.95; the 95 % confidence interval, CI [0.80, 1.12]) or mortality (RR = 0.85; the 95 % confidence interval, CI [0.71, 1.01]), there were no differences. When reviewing only self-care, the risk decreased with regard to thromboembolic events (RR = 0.47; the 95 % confidence interval, CI [0.31, 0.70]) and mortality (RR = 0.55; the 95 % confidence interval, CI [0.36, 0.84]), but there were not any difference with regard to major bleeds. When reviewing only self-measurement, the risk with regard to thromboembolic events (RR = 0.69; the 95% confidence interval, CI [0.49, 0.97]) decreased, but the risk did not decrease with regard to major bleeds or mortality. In 16 studies, the INR values were reported on with target level/value (tests in range). Of these in 15 cases, the results improved in groups of self-measurement or self-care. It should be noted that the quality of the evidence was moderate or low in the studies included.[2]

When it comes to all studies, it should be noted that the self-measurement and self-care patients have measured the INR values more often than those under standard treatment. In studies, the measurement interval has typically been one (1) week and in the follow-ups of the actual use two (2) weeks. In standard treatment, the INR values are measured once a month. This denser measurement of the INR values may be a component of better care balance.

All studies highlight that self-measurement or self-care is not suitable for all patients. Therefore, special attention must be paid to patient selection and, at the initial stage, success of treatment needs to be monitored closely. Services within remote monitoring used in studies have been different; all are based, however, on implementing communication between the personnel and the patients through digital methods.

Other observations made in the studies

There have been published several follow-up studies of actual use with a larger group of patients and with a longer follow-up period. Related to these studies, the Spanish study concluded that self-measurement and self-care are at least as effective as standard treatment[5]. In the Danish registry study, self-care was compared to

	direct anticoagulants (DOAC, direct oral anticoagulant). The study showed that self-care is safe and effective in respect of properly trained patients. The self-care patients have a lower risk of a stroke than those under the DOAC treatment, there were no differences in risks concerning bleeds or mortality.[6] **Health Technology Assessment (HTA) Reports** In England, the National Institute for Health and Care Excellence (NICE) has assessed self-measurement and self-care in 2014.[7] The Canadian Agency for Drugs and Technologies in Health (CADTH) examined the patients' and the closest relatives' experiences.[8] In Sweden, cost-effectiveness of self-measurement and self-care was examined in 2015.[9]
Safety	**Sufficient** According to the company, the product has been in use from 2017 onwards and during that period of time no patient safety incident or adverse event related to the use of the product has been reported[1]. The company complies with the risk management system to the appropriate extent in accordance with the ISO 14971:2019, but compliance with the standard has not been formally assessed[1]. The risk analysis of the product is comprehensive and it is constantly updated by the company[1]. The company has necessary processes and notification procedures available along with a designated responsible person for the purpose of ensuring product safety[1]. The instructions for use of the product introduce how to prevent any potential error conditions and situations[1].
Costs	**Reasonable** Monthly costs consist of two parts, customer-specific maintenance costs and patient-specific costs. Monthly costs include the Roche Diagnostics CoaguChek® INRange measurement device for the patient's self-measurement, test strips (24 pieces a year) as well as use of the service. It is possible to buy more test strips.[1] Introduction of the product may cause some costs, whose more detailed description will be discovered during the introduction planning of the device. Introduction training for the personnel within the organisation is included in the price of the service.[1]

	The organisation decides whether to charge the patient for the use. As for the patients, transferring to self-measurement or self-care eliminates the need for visiting the laboratory for the purpose of sampling and thus save both the time and travel expenses. Based on the information given by the service provider, it appears that the cost of using the service is reasonable when compared with the provision of an equivalent service in another way.[1]	
Data security and data protection	The assessment was carried out using the list of data security and data protection requirements for social welfare and health care procurement and the response material provided by Orla DTx[10]. **Sufficient** Based on the response material, the service clearly meets the data security and data protection requirements. **Risk management and information security testing** The company has processes for the purpose of • managing information security incidents and threat scenario based information security risks • developing secure software and testing of security features/capabilities is included as part of the testing process • managing security vulnerabilities in the third party software. **Log management** The company has processes for centralised log management. An audit log related to use of patient data by health care professionals is available. **User management** The service utilises role-based access rights management. The service clearly follows modern good practices in respect of passwords and the requirements for password strength are definable. The service does not support two-factor authentication, but access to service may be restricted on the basis of the IP addresses. The single sign-on (SSO) support can be added at extra cost. Support for card login is available through the single sign-on integration.	

	Equipment The measurement device (Roche Diagnostics CoaguChek® INRange) transfers the measurement results into the service through the Orla INR phone application and the Bluetooth Low Energy (BLE) connection. The measurement device is not included in this assessment. The data link from the phone into the service is encrypted. **Data protection** Orla DTx acts as a data processor and the client organisation as a data controller. Orla DTx has drawn up an assessment of data protection effects, which includes an assessment of data protection risks. Personal data of patients to be entered into the service are kept in Finland and the data in question are encrypted at rest. Data related to a client relationship are retained within the European Economic Area. **Other considerations** The service is available only as Software as a Service, SaaS software distribution model. This assessment does not include any connections to external services. If a client organisation introduces integrations, these connections must be assessed separately. **General guidelines on procurements** At the procurement stage, you should always communicate with the organisation's information management, information security expert and data protection expert. Discuss with them whether the product in question meets your requirements. In addition, we recommend that health care districts use the Procurement Guidelines for Cybersecurity in Hospitals by the European Union Agency for Cybersecurity (ENISA) as support[11].
Usability and accessibility	**Sufficient** The Roche Diagnostics CoaguChek® INRange measurement device is not included in this assessment of usability and accessibility. The patient application has been implemented in accordance with the design guidelines for iOS and Android platforms[1]. Both health care

professionals and patients have been involved in product testing[1]. The language and layout of the textual content in the application is, according to the company, designed in cooperation with the health care professionals[1]. According to the company, the functionality and comprehensibility of the textual content has been tested on test subjects and real patients[1].

The patient mobile application meets three key requirements set by the Act on the Provision of Digital Services[13,14,15]. The application meets the Web Content Accessibility Guidelines, WCAG 2.1 criteria levels A and AA and there is an Accessibility Statement available for it[15]. It is possible to give feedback on the product accessibility through electronic feedback channel and the company will respond to it within 14 days[15]. According to the notice by the company, the minimum version of the operating system in respect of the accessibility functionalities is iOS 15.0 and Android 11[15]. The minimum version of the mobile software is 2.0[15].

An Accessibility Assessment has been performed for the professional user interface by an external party in accordance with the WCAG2.1 standard, level AA[1]. The user interface does not fully meet the requirements for the WCAG 2.1 level AA and the development needs have been reported to the company in the Accessibility Assessment Report[1]. According to the notice by the company, color blindness and contrasts have been taken into account when designing the user interface[1,15].

During introducing the product, health care professionals should make an assessment of the suitability of the product for each patient and when the system is being introduced by a new patient, he/she should be intensively monitored at first[1]. The company will train the health care professionals for the purpose of supporting the patient when introducing the product[1]. Instructions for use of the application will be distributed through the website and the professionals will provide the patients with the printed quick start guide[1,12]. Those patients who take care of adjusting the warfarin dosage by themselves (self-care patients) will also obtain a so-called INR driving licence under the supervision of a professional.[1]

Other things to consider when using the product	The patient mobile application is available with the iOS (9.0 or a newer version) and the Android (7.0 or a newer version) operating systems. The professional application supports modern browsers and the Internet Explorer version 9 or a newer one.[1]
	Interoperatibility
	The Roche Diagnostics CoaguChek® INRange measurement device connects with the Orla Remote Monitoring application through the Bluetooth Low Energy (BLE) connection.[1]
	The system stores the data in structural form and the data can be exported to other systems, by using for example the HL7 V2 or FHIR interfaces.[1]
	The product supports the single sign-on integration (SSO).[1]
	Technical functionality
	The company has specified testing processes for different stages of product development. The company has continuous processes for the purpose of receiving error messages and correcting errors. According to the company, there have been no interruptions in the service nor has it been out of use due to some error condition in the last six months. The contact persons in the user organisations will be informed about system updates by email in advance. If necessary, the health care professionals will be responsible for informing the patients. The system updates are to be performed outside office hours and this, according to the company, causes only short interruptions in the functioning of the system.[1]
	Training and technical support
	The service provider will train the personnel of the organisation. The organisation must train the patients in order to be able to use the service. Technical/product support will be provided by email and over the phone in Finnish, Swedish and English. The company has a Project Plan in order to support device introductions.[1]
	Distribution
	The product is in use in four health and social services centres in Finland and through these in more than ten health centres[1].

	Other recommendations related to the product
	There are recommendations in several countries for using self-measurement or self-care aimed at those patients who are willing to use the service and meet the criteria.[7,16,17]
Assessment Team	Petra Falkenbach, Senior Planning Officer, FinCCHTA Jari Haverinen, Senior Planning Officer, FinCCHTA Jari Jääskelä, Information Security Expert, Oulu University

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Key Assessment Domains

Points	Effectiveness	Safety	Cost	Data security and protection	Usability and accessibility
2	Sufficient	Sufficient	Reasonable	Sufficient	Sufficient
1	Promising but more evidence is needed	Probably at a sufficient level but not known well enough	High	Minor shortcomings	Minor shortcomings
-4	Weak or unknown	Weak or unknown	Unreasonably high	Shortcomings	Shortcomings

Recommendation Scale

Total score	Definition
10	**USE OF THE PRODUCT IS RECOMMENDED** The use of this product is recommended because of strong evidence for its effectiveness. Safety, data security and protection, and usability and accessibility of the product are at an adequate level. The cost of using the product is reasonable.
9	**THERE IS ONE THING TO CONSIDER WHEN USING THE PRODUCT** An organization considering the deployment of the product should note that **in one key area there are things to consider**. Information about the effectiveness of the product could be promising, but the information is scarce. Product safety could be at a sufficient level but not known well enough. Product costs may be high. There could be minor shortcomings in the product's data security and protection or in usability and accessibility.
7-8	**THERE ARE A FEW THINGS TO CONSIDER WHEN USING THE PRODUCT** An organization considering the deployment of the product should note that **in two or three key areas there are things to consider**. Information about the effectiveness of the product could be promising, but the information is scarce. Product safety could be at a sufficient level but not known well enough. Product costs may be high. There could be minor shortcomings in the product's data security and protection or in usability and accessibility.
5-6	**THERE ARE MANY THINGS TO CONSIDER WHEN USING THE PRODUCT** An organization considering the deployment of the product should note that **in four or five key areas there are things to consider**. Information about the effectiveness of the product could be promising, but the information is scarce. Product safety could be at a sufficient level but not known well enough. Product costs may be high. There could be minor shortcomings in the product's data security and protection or in usability and accessibility.
≤4	**THERE ARE CRITICAL THINGS TO CONSIDER WHEN USING THE PRODUCT** An organization considering the deployment of the product should note that **there are shortcomings in one or more key areas.** Information about the effectiveness of the product is untrustworthy or of low quality. There may be shortcomings in the product's safety, or information related to it may be unreliable or of low quality. Product costs may be prohibitively high. There could be shortcomings in the product's data security and protection or in usability and accessibility.