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# Optimising Event Detection in Body Weight Time Series from Heart Failure Telemonitoring Patients

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# AFFIDAVIT

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# Acknowledgement

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# Zusammenfassung

**Hintergrund:** Die Verhinderung von Hospitalisierungen als ein zu vermeidendes Ereignis in der Herzinsuffizienzbetreuung kann durch die Anwendung von automatischen Event-Erkennungsalgorithmen auf physiologische Daten, die durch Telemonitoring erfasst werden, unterstützt werden.
**Ziele:** Vergleich von automatischen Event-Erkennungsalgorithmen und Bestimmung von optimalen Arbeitsparametern.
**Methoden:** Ein Datensatz des Herzinsuffizienzversorgungsnetzwerks HerzMobil Tirol wurde mit Moving Average Convergence Divergence- (MACD) und Rule of Thumb- (RoT) Algorithmen analysiert. Für die Evaluierung wurden Receiver Operating Characteristic- (ROC) Kurven und Youden-Index berechnet und stratifizierte Kreuzvalidierungen wurden durchgeführt.
**Ergebnisse:** Bei Limitierung des maximal erlaubten Prozentsatzes an falschen Vorhersagen von Ereignissen auf 5% ergab sich für MACD und RoT eine maximale Sensitivität von 0,44. Eine Optimierung ohne Limitierung ergab eine maximale Sensitivität von 0,90, aber gleichzeitig eine Spezifität von nur 0,37.
**Schlussfolgerung:** Es gibt bei Klassifikationsalgorithmen immer einen Kompromiss zwischen Sensitivität und Spezifität. In der Praxis sind zu viele Fehlhinweise störend. Allerdings führte eine Limitierung der Spezifität auch zu relativ geringen Sensitivitätswerten. Aufgrund von ähnlichen Evaluierungsergebnissen konnte kein Unterschied zwischen MACD und RoT hinsichtlich der gewichtsbasierten Vorhersage von handlungsrelevanten Ereignissen in der Herzinsuffizienzbetreuung festgestellt werden.

**Schlagwörter:** Herzinsuffizienz, Zeitreihenanalyse, Gewichtsanstieg, Telemedizin, klinische Entscheidungsunterstützung

# Abstract

**Background:** The prevention of hospitalisations in heart failure disease management can be supported by applying automated event detection algorithms to physiological data, which are obtained by telemonitoring.
**Objectives:** Comparison of automated event detection algorithms and determination of optimal working parameters.
**Methods:** A dataset from the heart failure disease management network HerzMobil Tirol was analysed with Moving Average Convergence Divergence (MACD) and Rule of Thumb (RoT) algorithms. For evaluation, Receiver Operating Characteristic (ROC) curves and Youden Index were calculated and stratified cross validations were conducted.
**Results:** Limiting the maximum percentage of false positive predictions of events to 5%, the maximum sensitivity for MACD and ROC was 0.44. Optimising without limitation, led to a maximum sensitivity value of 0.90 with a specificity of just 0.37.
**Conclusion:** Event classification always needs a trade-off between sensitivity and specificity. In practice too many false notifications are disturbing. However, limiting the specificity led to relatively low sensitivity values. Due to similar evaluation results, no difference between MACD and RoT regarding the weight-based prediction of critical events in heart failure disease management could be determined.

**Keywords:** Heart Failure, Time Series Analysis, Weight Gain, Telemedicine, Clinical Decision Support

# Contents

# List of Abbreviations

**ACE-I** Angiotensin-Converting Enzyme Inhibitors

**AIT** Austrian Institute of Technology

**ARB** Angiotensin Receptor Blockers

**ARNI** Angiotensin Receptor Neprilysin Inhibitors

**AUC** Area Under the Curve

**BEAT-HF** Better Effectiveness After Transition - Heart Failure

**BB** Beta-Blockers

**BNP** B-type Natriuretic Peptide

**CSV** Comma Separated Values

**CUSUM** Cumulated Sums

**ESC** European Society of Cardiology

**FN** False Negative

**FP** False Positive

**FPR** False Positive Rate

**HFmrEF** Heart Failure with mid-range Ejection Fraction

**HFpEF** Heart Failure with preserved Ejection Fraction

**HFrEF** Heart Failure with reduced Ejection Fraction

**INTENSE-HF** INtegrated TElemonitoring and Nurse Support Evaluation in Heart Failure

**KNIME** Konstanz Information Miner

**LVEF** Left Ventricular Ejection Fraction

**MACD** Moving Average Convergence Divergence

**MOBITEL** MOBIle TELemonitoring in Heart Failure Patients

**MRA** Mineralocorticoid/Aldosterone Receptor Antagonists

**NFC** Near Field Communication

**NP** Natriuretic Peptides

**NT-proBNP** N-terminal pro-BNP

**OI** Output Index

**RAAS** Renin Angiotensin Aldosterone System

**ROC** Receiver Operating Characteristic

**RoT** Rule of Thumb

**SD** Standard Deviation

**TEMA-HF1** TElemonitoring in the MAnagement of Heart Failure

**TEN-HMS** Trans-European Network-Home-Care Management System

**TN** True Negative

**TP** True Positive

**TPR** True Positive Rate

**WISH** Weight monitoring In patients with Severe Heart failure

# Chapter 1

# Introduction

After hospitalisation, heart failure patients are at risk of recurring deterioration with regard to their health status, which might even entail their re-admission to hospital. Telemonitoring solutions show a positive effect on the prevention of hospitalisations by providing health professionals with continuous updates regarding the patients' health status. This particular procedure enables them to intervene in case of a deterioration of the patients' health status [1]. Therefore, in the course of the Tyrolean project "Herz-Mobil Tirol", heart failure patients were equipped with mobile observation devices after their discharge in order to avoid re-hospitalisation. The patients were instructed to transmit their vital signs to a server, which enabled physicians and heart failure nurses to monitor their health status. In case of irregularities, the respective health professionals could intervene and take the necessary measures in order to treat the patient. Furthermore, the health professionals could more easily track the patients' treatment trajectory by using the information transmitted. In addition to this manual supervision of the patients' vital signs, automated daily checks, which were performed by applying trend algorithms to the measured values to provide automated decision support to the health professionals, were carried out. Weight gains can be a sign for fluid retention and, therefore, be an indicator for an imminent hospitalisation. If fluid retention is recognised early enough, the hospitalisation can possibly be prevented by an adaptation of the medication and other interventions [1]. In order to find ways to further improve the reliability of the automated decision support, a comparison of trend algorithms was conducted. The results showed low sensitivity values as well as high variation, when applying cross validation. Hence, it was not possible to decide, which of the algorithms was better suited for the detection of critical events. To achieve a higher reliability of the detection of critical events, more physiological data than just weight data alone should be considered.

## 1.1 Background

### 1.1.1 Telemonitoring and Closed Loop Healthcare

In telemonitoring, a health professional can observe the health status of several patients with the help of mobile devices, which are used by the patients to transmit their vital signs to a health data center. In the health data center, the transmitted data is preprocessed and analysed to support the health professional. If the applied algorithms detect an incoming threat for the health of a patient, the respective health professional will be notified and can react to the signs. In the system, the vital data collected from the patients is visualised in order to give an overview of the patients' health status. In a closed-loop healthcare network, additionally, health professionals can communicate with their patients by the means of telemonitoring devices, such as the possibility to alter medication prescriptions, which will immediately be transmitted to the patients, or send notifications to the patients. The health data center also sends feedback reports and reminders to the patients and motivates them to follow the treatment plan and to transmit their data, by reminding them through automatically generated messages. Furthermore, a closed-loop healthcare network includes all stakeholders, who are involved in the care process. Heart specialists, physicians, heart failure nurses, network co-ordinators, technical support and the patients as well as their families are part of the network and communicate with each other to avoid losing important information. (see 1.1). [2]

### 1.1.2 Heart Failure

Heart failure is a severe disease. Many people are affected and, therefore, the European Society of Cardiology (ESC) published their "Guidelines for the diagnosis and treatment of acute and chronic heart failure", to provide information on the disease and on current treatments. Currently, the most recent version is from 2016. The following information about heart failure is based on these guidelines [3].

The risk to be affected by Heart failure rises with higher age: Whereas the prevalence of heart failure in adults is at about 1-2%, it climbs to 10% for people with an age of over 70 years. Heart failure leads to a deteriorated cardiac ability to efficiently pump blood through the body. Hence, a lack in oxygen supply causes affected patients to feel exhausted and easily stressed by physical exercise. Furthermore, restricted blood circulation leads to fluid retention and thus oedema might build up, which leads to weight gain. In the diagnostic of heart failure the plasma concentration of natriuretic peptides

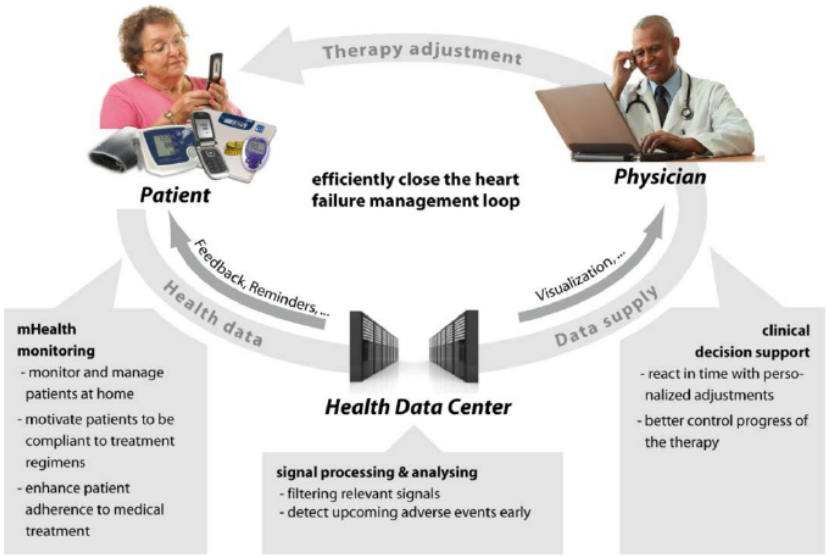



Figure 1.1: Closed-Loop Healthcare Monitoring. The patient transmits physiological data. The physician regularly checks the data and gives feedback to the patient (taken from [2]).

(NP) is of great interest. NP are produced, if there is an increased wall tension in the heart due to volume or pressure overload ([4]). Therefore, high levels of B-type NP (BNP) and of N-terminal pro-BNP (NT-proBNP) can be an indicator for heart failure.

### Organisation of Care

Heart failure patients are advised to record their weight on a daily basis and to react to a weight gain of 2kg or more in 3 days by increasing their diuretic dosage and by consulting their assigned physician.

As mentioned by Gheorghiade et al. in a paper from 2010 [4], congestion often leads to a gain in weight. Thus, fluid retention may be detected by raises in body weight. However, the interpretation has to be done carefully, as several factors can come into play. A weight gain over a long time period might be provoked by unhealthy nutrition or too little physical activity. Furthermore, the observed differences in weight are not too big. Thus, it is important for patients to always do the weight measurements in a similar way. The measurements should be done on the same time of day, before eating, after visiting the toilet and with no or the same clothing as usual. This procedure requires a precise weight scale, which should be placed on solid, even ground without any carpets or other objects, which could influence the

measurement [4].

Further recommendations for heart failure patients include knowledge about their disease and about its causes and symptoms. The patients should be able to recognise changes in their health status on their own. Furthermore, in various situations, they should be able to decide, whether they should contact a professional or not. For example, they should be able to decide, whether to change the amount of their diuretic intake themselves or to seek professional advice. Concerning their drugs, they should know, which drug has which effect (including side effects) and why it is necessary to take it. Also, heart failure patients should change their diet. Patients are advised to limit their intake of fluids, salt and alcohol, which can lead to a worsening in their health status. Heart failure patients should also stop smoking and should be encouraged to do regular exercise.

### Acute Heart Failure

The health status of a patient can deteriorate rapidly due to various reasons (e.g. infection, hypertension or incorrect/omitted drug intake). If no preventive steps are taken by the physician or by the patient, the situation can lead to a decompensation, which means that the heart cannot sufficiently supply the body any more and that - to avoid further deterioration - the patient has to be taken to the hospital immediately in most cases.

### Subdivision by Severity

Heart failure can be subdivided by the remaining percentage of the normal left ventricular ejection fraction (LVEF), which can be determined by echocardiography. The three groups of heart failure comprise "Heart failure with preserved ejection fraction" (HFpEF), "Heart failure with mid-range ejection fraction" (HFmrEF) and "Heart failure with reduced ejection fraction" (HFrEF).

### Pharmacological Treatment for Patients with HFrEF

Most studies focused on heart failure patients with HFrEF. Therefore, a high amount of knowledge is available for the treatment of HFrEF patients, whereas few known treatments are available for the other categories. For the treatment of patients with HFrEF, the following groups of drugs are recommended:

- **Angiotensin-converting enzyme inhibitors (ACE-I):** ACE-I regulate blood pressure by inhibiting the Renin Angiotensin Aldosterone

System (RAAS).

- **Angiotensin receptor blockers (ARB):** ARB also influence the RAAS and can be prescribed, if there is an intolerance to ACE-I.
- **Angiotensin receptor neprilysin inhibitors (ARNI):** ARNI can also be used to replace ACE-I.
- **Beta-blockers (BB):** Beta-blockers are used to reduce blood pressure. Due to undesirable adverse affects patients tend to reject the intake. Possible adverse effects are e.g. lethargy, sleep disturbance, visual hallucinations or depressions [5].
- **Mineralocorticoid/aldosterone receptor antagonists (MRA):** Aldosterone has an influence on the fluid and electrolyte balance. For heart failure patients an adverse effect caused by MRA is renal dysfunction and the possibility of a renal failure [6].

For the patients' prescribed medications, recommended target dosages can be defined and monitored by the professionals. If needed, the health professionals can adjust the medication by transmitting a dosage adjustment to the patient via the telemonitoring system of HerzMobil Tirol. Furthermore, diuretics are used to cope with congestion and fluid retention. For the HerzMobil Tirol dataset, Dr. Gerhard Pölzl, the clinical director of the HerzMobil heart failure network, defined the most important diuretic active components as:

- **Amilorid**
- **Furosemid**
- **Hydrochlorothiazid**
- **Torasemid**
- **Xipamid**

For diuretics, no standard dosages can be defined, as they should be dosed as low as possible. Nevertheless, one diuretic active component can be taken as a reference and the corresponding amount can be defined for another active component. (For reference dosages, see Appendix A.) Drug prescription adaptations are a common intervention in a telemonitoring setting and are continually required to obtain the optimal treatment of the patients.

### 1.1.3 HerzMobil Tirol

The HerzMobil Tirol project was established in late 2012. It was initiated as a collaboration of the tirol kliniken (health care company of Tyrol) and the Austrian Institute of Technology (AIT).

Heart failure patients, who had been hospitalised due to an acute heart failure, were offered the possibility to participate in HerzMobil Tirol and at their discharge they obtained a training to learn how to avoid a deterioration of their medical condition, how the medication works and why it is important to stick strictly to the medication plan. Furthermore, they were taught, how to handle the technical devices. Back at home, the patients were daily measuring their vital signs and stayed connected to their physicians, the heart specialists of the tirol kliniken and the heart failure nurses via a dedicated smartphone app. The smartphone app enabled communication between all involved persons and the gathering as well as secure transmission of data (see figure 1.2).


Figure 1.2: Heart failure disease management network. Via a smartphone and a dedicated application, the patients were connected to their physicians, the heart specialists of the tirol kliniken and their heart failure nurses (taken from [7]).

The transmitted data were systolic and diastolic blood pressure, heart rate, weight, well-being and drug compliance. These data were collected with a blood pressure measuring device, a body weight scale and a smartphone, which were able to communicate with each other via Near Field Communication (NFC). After touching the measuring devices with the smartphone, the vital signs were automatically transmitted to a server and were stored in a database at the IT centre of the tirol kliniken. The physicians performed weekly checks on the patients' health status in order to avoid re-hospitalisations by reacting to impending decompensations (e.g. they

adapted the medication, if needed). Furthermore, there were algorithms running on the server, which generated automated notifications in case of immanent threats for the patient. In addition, if a patient did not transmit all expected information, physicians and heart failure nurses were notified by the system. However, the system was no emergency system, and thus in the case of an emergency, the patients had to call an ambulance. The main goal of the HerzMobil Tirol project was to avoid hospitalisations. Moreover, the patients should be trained to understand the disease and to be able to adequately react to certain symptoms by self-care or by consulting health-care professionals. Thus, a long-term stability of the patients' health status should be achieved while requiring as little professional help as possible at the same time. The required knowledge and self-esteem was given to the patients through the design of the project as a closed-loop healthcare network. [8][9]

## 1.2 State of the Art of Clinical Decision Support in Telemonitoring Programs for Heart Failure Patients

### 1.2.1 Benefits of Telemonitoring

According to a paper of Inglis et al. from 2011, telemonitoring had positive effects on the patients' quality of life, there was a reduction in costs, the adherence to prescribed drugs was higher and the patients had better knowledge about their disease and about self-care procedures. They assumed, that patients, who participate in telemonitoring, are more likely to exactly follow the treatment guidelines and therefore an improvement of the therapy outcomes could be observed. The feeling of being supervised by a physician could give the patients an additional feeling of safety [10].

### 1.2.2 Relevant Physiological Data for Hospitalisation Prediction

In a paper from 2015 [1], Henriques et al. give an overview about previous attempts to detect decompensations. They list the following methods:

- **Body Weight:** Increases in body weight could be an indicator for fluid retention.

- **Blood Pressure:** High blood pressure can lead to a deterioration of the patient's health status.
- **Heart Rate:** Differences in heart rate can also be an indicator for a deterioration of the patient's health status.
- **Intrathoracic Impedance:** Impedance changes are related to the amount of fluid in the patient's body.
- **Arrhythmias:** Arrhythmias can be used for the prediction of impending hospitalisations.

### 1.2.3 Previous Studies Considering Weight Data

In several studies, researchers tried to find a reliable algorithm for the prediction of heart failure related hospitalisations. For this thesis, especially weight-related approaches are of interest, because only weight data was considered for the analyses. In the following, a selection of studies focusing on weight gains, are presented and information about the used algorithms is provided.

#### Detection Based on Thresholds and Simple Rules

The easiest approach of detecting a deterioration in the health status of a patient is to predict an event on the basis of measurement values that lie below or above a defined threshold. A number of telemonitoring studies, which were applying such rule sets, took place. In the following, some of them are described regarding the used algorithms.

In California 1500 patients participated in the Better Effectiveness After Transition - Heart Failure (BEAT-HF) trial. Half of them were treated with telemonitoring and therefore they daily transmitted their blood pressure, heart rate and weight values. The notification for a weight increase was triggered for more than 3lbs (1,36 kg) in 1 day or for 6lbs (2,72 kg) in 1 week [11].

Lynga et al. analysed data from the Weight monitoring In patients with Severe Heart failure (WISH) trial, which was conducted in Sweden. Half of the 344 patients were equipped with an electronic scale and transmitted data to a server. Notifications were generated, if there was a divergence of more than 2 kg from the target weight (= body weight at discharge) or if a weight gain of more than 2 kg in 3 days occurred. [12]

In the TElemonitoring in the MAnagement of Heart Failure (TEMA-HF1) study, 160 patients from Belgium took part from 2008 to 2010. The

patients' weight was measured at discharge and taken as a reference. The threshold was set as a divergence of 2 kg from the reference weight. An e-mail notification was automatically sent to the corresponding general practitioner, if the weight change of a patient exceeded the defined limit for two consecutive days [13].

28 patients were observed by telemonitoring in the TELBIL study in Spain, starting in 2010. The weight notification was triggered by a weight gain of more than 2 kg in 3 days [14].

In a paper from 2014 [15], Kropf et al. evaluated algorithms for automated decision support with datasets from the MOBIle TELemonitoring in Heart Failure Patients (MOBITEL) clinical trial and from the ELICARD telemonitoring system. At the time of their analysis, the same algorithms were applied in the INtegrated TElemonitoring and Nurse Support Evaluation in Heart Failure (INTENSE-HF) randomised controlled trial. During the INTENSE-HF study, physicians had the possibility to view the patients' vital signs and to adapt medication dosages to prevent readmissions. Along with other threshold-based rules, a rule for a maximum weight gain of 2 kg in 2 days was implemented in the decision support system to trigger notifications, which recommended drug dosage adaptations to the physicians. Kropf et al. concluded, that the results of a prospective study would be more reliable than a retrospective analysis of existing data. Furthermore, they mentioned the difficulty of defining a ground truth, which would be the reference for evaluations. The implemented rules were derived from existing heart failure treatment guidelines and seemed to be too static for a telemonitoring approach. In a paper from 2015 [16], Kropf et al. presented the results of the INTENSE-HF trial and concluded, that 13% of the system's recommendations resulted in medication adjustments by physicians and, thus, were correct.

**Detection Based on Moving Average Convergence Divergence (MACD)**

In a paper from 2009, Zhang et al. compared Rule of Thumb (RoT) and Moving Average Convergence Divergence (MACD) algorithms regarding the detection of heart failure related events. They used data from the Trans-European Network-Home-Care Management System (TEN-HMS) study, which included data from 168 patients. 45 hospitalisation events due to worsening heart failure occurred. They concluded, that MACD is more specific, but also less sensitive than simple RoT algorithms. Furthermore, they mentioned, that in many cases, there was no weight gain before a hospitalisation [17].

Gyllensten et al. evaluated the predictive potential of weight measure-

ments and noninvasive transthoracic bio-impedance measurements by applying various algorithms (RoT, MACD, Cumulated Sums (CUSUM)). The underlying dataset was taken from the myHeart project, which started in January 2004 and had participants from 10 european countries. The dataset contained measurements of 148 patients from Spain and Germany and there were 24 heart failure related hospitalisation events. No data about prescribed drugs was considered. They concluded, that in comparison to weight measurements, impedance measurements enabled a more accurate prediction of decompensation events [18][19].

### Detection Based on Wavelet Transformation

In a paper from 2015, Henriques et al. also worked with the dataset from the myHeart project and used measurements of blood pressure, heart rate, body weight and respiration rate, as they wanted to focus on parameters that can easily be measured. The algorithm was based on the wavelet transformation and was applied to the mentioned biosignals to find underlying trends, which could be used for the prediction of heart failure related hospitalisations. They concluded, that their approach is very appropriate [1].

### Nuisance Notifications

In a paper from 2012, Vukovic et al. mention that clinical decision support systems have to cope with the generation of incorrect notifications. Clinical decison support systems are applying algorithms to decide, whether a notification should be generated or not. For real life situations, it is difficult to find a gold standard to distinguish between a normal condition and a threat for the patient's health. There has to be a balance between detecting every potential threat and avoiding too many false notifications. The main problem resulting from a high number of false notifications is the decrease in reliability of the system and, therefore, a decrease in the attention, that is given to the notifications. On the one hand, for physicians and heart failure nurses it is exhausting and annoying to be notified without real need, and on the other hand, it consumes time as well as other resources, which could be more effectively used for other tasks in patient care [20].

## 1.3 Aims

The goal of this thesis, was to create a framework for the assessment of existing algorithms to detect health-related events in data from an existing telemonitoring program and to find optimal parameter setting for these algorithms.

Thus, the received data should be prepared for the analyses by removing data, which is not valuable (e.g. outliers), and by transforming the data to be ready for the application of RoT and MACD algorithms. Further, RoT and MACD algorithms should be applied to data from the HerzMobil Tirol project and the results should be evaluated by applying suitable quality criteria. The results should be interpreted with regard to possible improvements of event detection algorithms, which are currently used in the closed-loop health care monitoring of HerzMobil Tirol.

# Chapter 2

# Methods

For the analyses, data from HerzMobil Tirol were used. The data consisted of the daily measurements of the participating heart failure patients, including systolic and diastolic blood pressure, heart rate, body weight and information about their well-being. Furthermore, data were collected in the course of a daily prompt, asking for every prescribed drug, and collecting information on whether it was taken as prescribed or not. Theoretically, for the trend analysis of the weight, only the weight curve is necessary. However, more detailed information about the health status of a patient contributes to a better understanding of the reasons of a weight change.

The data were given as a database dump and were pseudonymised via a Konstanz Information Miner (KNIME) [21] pipeline that removed all names, telephone numbers, etc. For the ability of viewing the data, a visualisation tool was developed, which was based on JavaScript and the Highcharts library [22]. For this visualisation tool, the respective tables of the database were combined to one comprehensive Comma Separated Value (CSV) file (see [23]). This process was done with KNIME. Further analyses concerning the algorithms were done in Eclipse Neon [24] with Python 3.5 [25].

## 2.1 Patient Cohort

HerzMobil Tirol started in late 2012 and there have been 4 phases so far, which had different monitoring time spans. The monitoring for patients of the first phase lasted 1 year, for patients of the second phase, the monitoring lasted 6 months and for patients of the third and fourth phase, the monitoring lasted 3 months each. Out of 136 patients, 106 patients were selected for the analyses (see section 3.1 for details). In total the patients had 105 hospitalisations.

## 2.2 Preprocessing

The transformation from the PostgreSQL database to the CSV-file was done with KNIME. KNIME allows to read data from a local PostgreSQL-server and to combine tables to a CSV-file. For the first two phases, the common database was structured in a different way than in phase III and IV. Therefore, the collection of the data had to be adapted for the various database structures. Some measurement values dated back long before the start of the respective phase due to incorrect settings of the patient terminal. Therefore, for phase I and II, measurements with a date prior to 2011 were removed, for phase III measurements prior to 2014 were removed and for phase IV measurements prior to 2015 were removed. Test users were removed from the database, as they were no valid participants of the program. Furthermore, patients were removed from the dataset, if they had less than two weeks of monitoring. Also, body weight measurement values were removed, if they were strong outliers in comparison to their neighbourhood (e.g. a measurement value, that has more than 10 kg offset to the measurement value of the day before or to the measurement value of the day after).

### 2.2.1 Active Component Curves

Every drug contains an active component, which has certain effects on the patient's body. There are several drug companies, that have different products for the various active components. For an easier observation of the currently prescribed drug dosages, similar active components were grouped and a curve was calculate, which showed the achieved percentage of the recommended reference dosage for every day. Especially, for diuretics, prescription raises were of high interest, as they could have been the reaction to a weight gain of the patient.

Thus, all drugs occurring in the database were added to a list. To this list, for every drug, all contained active components and their dosages were added. Reference dosages were defined for all active components by Dr. Gerhard Pölzl, the clinical director of the HerzMobil Tirol heart failure network. He also assigned them to groups (see Appendix A). Given this information, it was possible to calculate an active component curve for every patient for every group of medications (e.g. beta blockers). Diuretics were further divided into the most common diuretic active components (e.g. Furosemid).

### 2.2.2 Weight Measurement Values

For missing weight measurement values, the measurement value of the day before was substituted. To obtain exactly one weight measurement value per day, only the first measured value of each day was taken and further ones were ignored.

## 2.3 Event Detection Algorithms

For the automated generation of notifications, two different algorithms were used. The algorithms generated an output index, which triggered a notification, when reaching a defined threshold. The first one was the RoT algorithm, that compares the actual value to a value in the past. The second one was the MACD algorithm, which calculates two exponentially weighted sums and subtracts the one from the other.

The selection of the algorithms was based on a paper from 2016 by Gyllensten et al. [19], who applied RoT and MACD algorithms to weight data of a similar patient cohort.

### 2.3.1 RoT

The RoT algorithm can be found in equation 2.1 (taken from [19]). The output index is calculated by subtracting a measured value from a past day from the measured value of the current day. The parameter in this formula is time shift d, which defines the time difference between the two considered measurements.

$$OI\left(t\right) = w\left(t\right) - w\left(t - d\right) \tag{2.1}$$

### 2.3.2 MACD

The MACD algorithm can be found in equation 2.2 (taken from [19]). The output index is calculated by subtracting a sum, weighted with a long time window ($N_l$), from a sum ,weighted with a short time window ($N_s$). After choosing the time windows, the weight factors $\alpha_s$ and $\alpha_l$ can be calculated. The weighting is an exponential function that attenuates values more, if they lie farther in the past. The attenuation is controlled by the time windows. For the calculation of the sums, values from the past have to be available. As an infinite sum could not be computed, the sums were limited to 100 terms. For the beginning of the telemonitoring period, the first valid measurement

was used for all terms of the sum, for which no corresponding weight value was available.

$$OI(t) = \alpha_s \sum_{x=0}^{\infty} (1-\alpha_s)^x \, w(t-x) - \alpha_l \sum_{x=0}^{\infty} (1-\alpha_l)^x \, w(t-x)$$
$$with \quad \alpha_s = \frac{2}{N_s+1} \quad and \quad \alpha_l = \frac{2}{N_l+1} \tag{2.2}$$

## 2.4 Hospitalisation and Drug Adjustment Events

There were two types of events, that were considered in the evaluation of the algorithms:

- **Heart failure related hospitalisations:** 25 heart failure related hospitalisations were gathered from the patient data at the tirol kliniken.
- **Raises in the diuretic prescription:** 62 diuretic prescription raises were derived from the active component curves.

### 2.4.1 Hospitalisations

The reasons of the hospitalisations were assigned to three categories by health professionals of the tirol kliniken:

- **Heart Failure Related:** ascites, cardiac decompensation, cardiac decompensation with multiorgan failure, hypostatic pneumonia, pulmonary oedema
- **Cardiovascular:** atrial fibrillation, bradycardia, bypass (+ follow-up treatment), cardioangiography, cardiopulmonary resuscitation because of ventricular fibrillation (+ follow-up treatment), carotid endarterectomy + patch plastic, chronotropic incompetence, collapse with dehydration, congestive heart failure, drug intolerance, electively MitraClip, electrical cardioversion, heart valve surgery (+ follow-up treatment), hypertensive urgency, implantation of a pacemaker, ischemic cardiomyopathy, orthostatic syncope, pericardial effusion, severe aortic stenosis, transcatheter aortic valve implantation, transient ischemic attack, transthoracic echocardiogram, ventricular tachycardia

– **Other:** acute gouty arthritis, acute pancreatitis, arthritis urica, breathing-related sleep disorders, carpal tunnel syndrome, chronic periodontitis, chronic renal insufficiency, clarification sleep apnoea, delirium, diabetic neuropathy, enteritis, exsiccosis, femoral neck fracture, herpes zoster, infected joint endoprosthesis, influenzal infection, kidney failure, macular degeneration, nausea, other malaise and fatigue, pleural effusion, pneumocystis pneumonia, pneumonia, polyserositis, senile cataract, ventricular fibrillation

Thus it was possible to tag every hospitalisation with its category. For the analyses, only the heart failure related hospitalisations were considered.

### 2.4.2 Diuretic Prescription Raises

Raises in the diuretic prescription can be due to weight gains. Thus, they were considered as events, as they could have prevented a hospitalisation. Every raise in the total prescribed diuretic active component dosage was taken as an event. For changes from a drug, containing one diuretic active component, to another drug with another diuretic active component, no notification was generated, if there was no raise in the percentage of the reference dosage. If no drug compliance data was available, an event was detected only, if the next drug compliance entry was assigned to a higher prescription dosage than the previous. Events that occurred during the first seven days after hospitalisations were not considered.

## 2.5 Evaluation

The perfect decision support system would detect every threat and would never generate a notification, when it is not necessary. Therefore, the evaluation can be done by looking at the notifications, if they were justified or not, and further looking at the events, if they were detected or if notifications were missing.

For the evaluation of the algorithms, a similar method was used as described by Gyllensten et al. [19] in their paper from 2016. They also compared the capability of different body weight-based algorithms for the prediction of hospitalisations. Furthermore, they applied the algorithms to non-invasive transthoracic impedance measurements. A main difference to the study of Gyllensten et al. is the consideration of diuretic prescription

raises as events, that need to be detected through weight gains in the present analysis.

### 2.5.1 Evaluation Grid

The observation time span had to be divided into equal partitions (see figure 2.1). Therefore, beginning at the end of the observation time span, 7 consecutive days were grouped again and again until a preceding event was reached. If there were less than 7 days left, these days were not considered for the evaluation. Thus, the first stop would be either the last day of a heart failure related hospitalisation, or a diuretic prescription raise or the beginning of the whole observation time span (in case there was no event for this patient). After the first stop, this procedure of grouping 7 consecutive days, was continued until the beginning of the whole observation time span was reached. The obtained partitions were then classified as true positives, false positives, false negatives or true negatives (see section 2.5.3). The size of the partitions was varied, to compare the results for different evaluation time frames. The evaluation was done for 7 and 14 days considering all events (heart failure related hospitalisations and diuretic prescription raises), considering only heart failure related hospitalisations and considering only diuretic prescription raises. The dataset contained a total of 1980 monitoring weeks. Considering missing values, grouping of events as well as hospitalisation and absence durations, 1460 valid partitions remained.

### 2.5.2 Missing Values

Even the best algorithm can't predict an event, if it has no measurement values, that it can be related to. Therefore a minimum of 70% of the expected values for the given partition was taken as the limit for considering a partition as a valid one. This rule resulted in a maximum of 2 missing values being allowed for the 7-day-partitions and a maximum of 4 missing values being allowed for the 14-day-partitions. During hospitalisations, the evaluation of notifications does not entail any benefits, as there are other forms of supervision in a clinical setting. Furthermore, in many cases a drastic weight change occurs due to various treatments and also, there are frequent changes in the medication dosage. Thus, all measurement values of days during a hospitalisation were treated equal to missing values. Furthermore, the 7 days following any hospitalisation (this means also the first seven days of the whole measuring time span) were treated equally as missing values, as the first days after discharge are very likely to be accompanied by jumps in weight and changes in medication, as changing from the hospital stay to

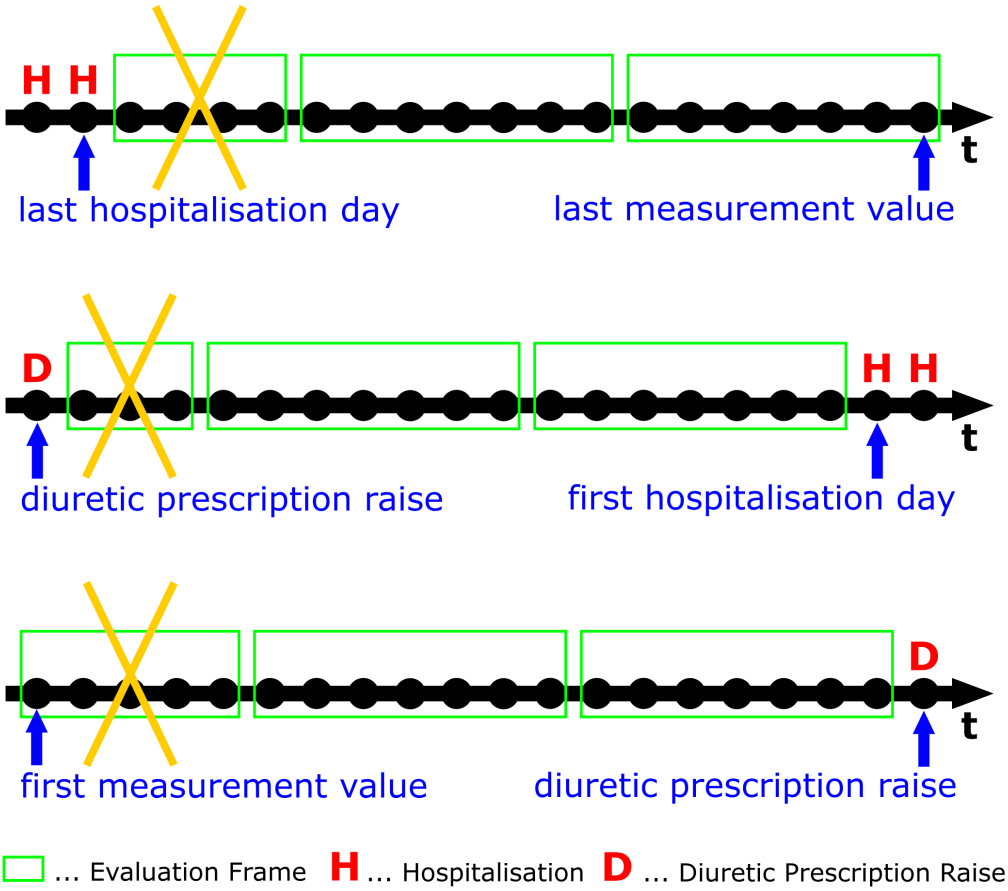



Figure 2.1: Visualisation of the evaluation grid. Beginning with the last day of the measurements, partitions are created, until a hospitalisation or diuretic prescription event is reached. If there are too few days for a further partition, these days are not considered for the analysis. This process is continued, starting from the day before the hospitalisation or diuretic prescription raise event, until the beginning of the measurement time span is reached.

being back at home again is a quick change in the environment and it takes a few days for the patient to acclimatise. Rehabilitation stays and holidays were also considered. For these time spans and the 7 days following the end of the absence, measurement values were treated like missing values.

### 2.5.3 Evaluation Tags

The following definitions were made to appraise the partitions (see figure 2.2):

- **True Positive (TP):** in a valid evaluation time frame preceding an event, at least one output index value exceeded the defined threshold.
- **False Positive (FP):** in a valid evaluation time frame **not** followed by an event, at least one output index value exceeded the defined threshold.
- **False Negative (FN):** in a valid evaluation time frame preceding an event, no output index value exceeded the defined threshold.
- **True Negative (TN):** in a valid evaluation time frame **not** followed by an event, no output index value exceeded the defined threshold.

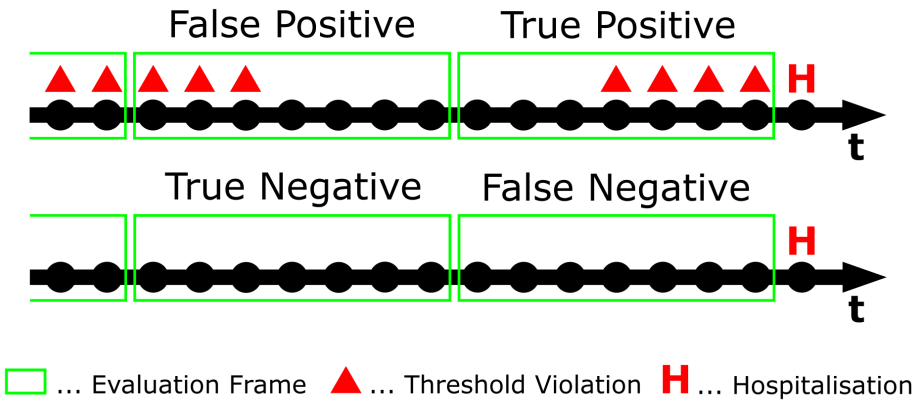



Figure 2.2: Visualisation of the evaluation tags.

### 2.5.4 Quality Criteria

For the evaluation, sensitivity (see formula 2.3), specificity (see formula 2.4) and the Youden Index (see formula 2.5) had to be calculated. For the parameter optimisation, Receiver Operating Characteristic (ROC) curves were

calculated and thus the calculation of the True Positive Rate (TPR, see formula 2.6) and the calculation of the False Positive Rate (FPR, see formula 2.7) were required.

$$sensitivity = \frac{TP}{TP + FN} \tag{2.3}$$

$$specificity = \frac{TN}{TN + FP} \tag{2.4}$$

$$Youden\,Index = sensitivity + specificity - 1 \tag{2.5}$$

$$TPR = sensitivity \tag{2.6}$$

$$FPR = 1 - specificity \tag{2.7}$$

### 2.5.5 Optimal Parameters

The algorithms were controlled by different parameters. These could be varied to make the algorithms behave differently. To find the optimal parameters, there had to be an evaluation criterion, which allowed to choose the best set of parameters.

### 2.5.6 ROC Measurements for the Assessment of Classifier Algorithms

The assessment of classifier algorithms is done by applying the algorithm to a dataset and to look at the concordance with reality. For example a classifier could be used to distinguish between persons, who suffer from a certain disease, and healthy persons. The classification would result in an appraisal for every person. Affected people would be classified as "positive", whereas healthy people would be classified as "negative". Now, if the truth is known, the appraisals can be compared to the truth. Thereupon, the decision for each person, which was made by the classifier, can be assessed as true positive, false positive, false negative or true negative. With the results of this assessment, specificity and sensitivity can be calculated. In the given scenario, sensitivity is the percentage of truly sick persons (positives), who are correctly classified as sick (true positives). The specificity is the percentage of truly healthy persons (negatives), who are correctly classified as healthy (true negatives). When evaluating an algorithm, the parameters are varied

and for a given parameter set, various thresholds are applied. Now for every threshold, sensitivity and specificity can be calculated.

These pairs of sensitivity and specificity can be converted to TPR (see formula 2.6) and FPR (see formula 2.7) and plotted as a graph, which is called a ROC. An example of a ROC is given in figure 2.3: The diagonal line would result from a random classifier. While the green curve (long dashes) could be the result of a perfect classifier, the red curve (few points) is beyond the random line and, thus, for this classification the evaluation tags (TP, FP, FN, TN) could have been defined in an inverse manner. Comparing the remaining curves, which run through point A and point B, the yellow curve (short dashes) would result from a better classifier than the orange curve (many points), as it has got a higher Area Under the Curve (AUC). For a random classification, the obtained graph will be a straight, diagonal line from (0,0) to (1,1). The more accurate the classification is, the more distance will be between this diagonal and the obtained points, which are defined by the pairs of sensitivity and specificity. A perfect classification would result in a sensitivity of 1 and a specificity of 1 and therefore the point would be at (0,1). For the ROC graph, the AUC can be calculated. For a random classification the area will be the area under the already mentioned diagonal straight line from (0,0) to (1,1). The AUC, therefore, would be 0.5. Thus a classifier, which will give a classification, that is assessed with an AUC of 0.5 is not better than a random decision. On the other hand, for a perfect classification the AUC will be 1, as the graph is connecting (0,0) with (0,1) and further (1,1). If the AUC results in a value between 0 and 0.5, theoretically, the false and positive classes were interpreted in an inverse manner. To sum this up: Whereas an AUC of 0.5 denotes a random classification, an AUC lying close to 0 or close to 1 denotes a very good classification.

For the Youden Index a similar rule applies: If the Youden Index is 0, the point resulting from the pair of sensitivity and specificity lies on the diagonal and therefore denotes a random classification for a given threshold of a parameter set. If the Youden Index is 1, the point resulting from the pair of sensitivity and specificity lies at (0,1) and the classification for a given threshold of a parameter set is perfect. Thus a Youden Index of 0 denotes a random classification and a Youden Index lying close to -1 or 1 denotes a very good classification. [26]

### Range of Parameter Variation

For the RoT algorithm, the parameter, that was optimised, was the day shift d. In this analysis it was varied from 1 to 20 days with steps of 1 day. The

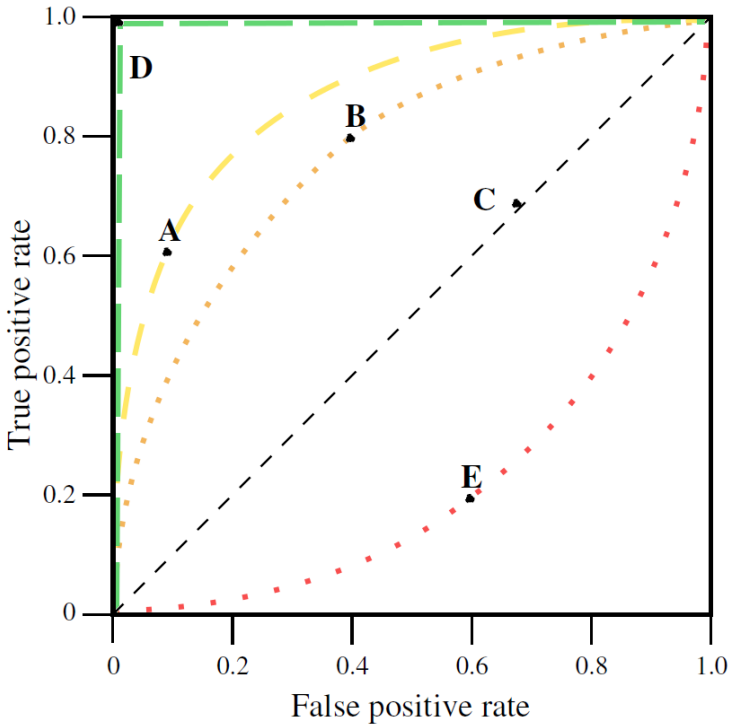



Figure 2.3: Example for a ROC Curve. Point A shows a classification with good sensitivity (ca. 0.6) and very high specificity (ca. 0.9). Furthermore, Point A has a bigger distance to the diagonal line than point B and, therefore, it is a better classifier. Point B shows a classification with high sensitivity (ca. 0.8) and good specificity (ca. 0.6). Point C shows a classification with good sensitivity (ca. 0.7) and low specificity (ca. 0.3). Moreover, it is very close to the diagonal line and thus could result from a random classification. Point D shows a classification with very high sensitivity (ca. 1.0) and very high specificity (ca. 1.0) and lies close to (0,1). Thus, it could result from a perfect classifier. Point E shows a classification with a quite low sensitivity (ca. 0.2) and low specificity (ca. 0.4) and lies beyond the random line, which tells, that the evaluation tags (TP, FP, FN, TN) might have been defined in an inverse manner. (taken from [26]).

threshold was varied from 0.1 to 5 kg with steps of 0.1 kg.

The MACD algorithm had two parameters, which were optimised. There were two windows $N_s$ and $N_l$ that changed the weighting of the weight measurement values. The short window $N_s$ was varied from 1 to 10 with steps of 1 and the long window $N_l$ was varied from 4 to 50 with steps of 2, whereas there was the condition that $N_s$ had to be smaller than $N_l$. The threshold was varied from 0.1 to 3 kg with steps of 0.1 kg.

#### Best Parameter Set with a Limited Number of False Notifications

To obtain better comparability to the results of Gyllensten et al. [19] the parameter optimisation was carried out in a similar way to the method mentioned in their paper. For all possible parameter sets in the defined ranges, a ROC curve was generated. This can be done by varying the threshold for one parameter set and calculating the TPR and the FPR for every threshold. Then the obtained points are plotted as a diagram to show the TPR (y-axis) versus the FPR (x-axis). From the resulting ROC curves, the best one was chosen by calculating the AUC for all threshold values with a FPR $< 5\%$. This is equal to a specificity $> 95\%$. Limiting the FPR to under 5% means that only 5% of all notifications, generated by the decision support system, are allowed to be false positive. The threshold for the resulting parameter set was chosen by looking for the threshold with the biggest Youden Index and at the same time with a specificity of more than 90%.

#### Best Parameter Set without Limitations

The limitation to a specificity higher than 95%, leads to quite low sensitivity values. In a further analysis, the best parameter set was searched without limitations. This means, the AUC was calculated for all thresholds and the threshold for the resulting ROC curve was chosen by the maximum Youden Index.

### 2.5.7 Cross Validation

The optimisation of an algorithm, using the whole dataset, leads to total over-fitting. This means that the algorithm is tailored specifically to the given data and will perform well on this particular dataset. However, it will not perform well on new data. A possible solution for this problem is to optimise only with a part of the data, which is called the "training set". The resulting parameter set can then be applied to the remaining part of the data, which is called the "test set", to evaluate the accuracy, when

confronted with "new" data. Our dataset was quite small and therefore, it was not practical to separate a part of the data and use it for testing only. To solve this problem, a cross validation can be used: For a cross validation the data has to be separated to groups. Then one group is left out and the others are combined. The combined groups are used as the training set and the left out group is used as the test set. This procedure is done, until every group was left out once and, subsequently, the mean and Standard Deviation (SD) of the obtained results can be calculated. To obtain groups that are quite homogeneous in comparison to each other, the selection of the patients, when assigning them to groups, can be done with respect to obtain a good distribution of events. This is called "stratified leave one out cross validation". Thus, a stratified 8-fold cross validation was applied.

### 2.5.8 Implementation in Python 3.5

After preprocessing, the weight data of the considered patients was available in a CSV-file. The further analyses were done in Eclipse Neon [24] with Python 3.5 [25]. For MACD, the structure of the Python script can be found in figure 2.4. At the beginning of the script, the evaluation frame could be chosen and the maximum number of missing values as well as the number of MACD terms could be defined. Furthermore, the ranges of the parameter variations and of the considered thresholds could be set. The "csv"-library was imported to make reading and writing of the CSV-files easier. Using the "datetime"- and "time"-libraries, functions were defined to transform timestamps to dates and vice versa. In the CSV-files, the date was given in the format "yyyy-mm-ddThh:mm:ss.s", because this format made it easier for humans to take a look at the data. For easier calculations, this format was transformed to a timestamp, which gives the milliseconds since 01.01.1970 - 00:00 Greenwich Mean Time. Thus, timepoints can be compared easily and an easy navigation is possible, without the need to consider the calendar. One of the pitfalls, which has to be considered, when working with timestamps, is the time change for summer and winter.

After these initial definitions, the event detection algorithm was implemented as a function, which takes a weight list, the current day of the measurement time span and the parameters of the algorithm as an input and gives back the output index for the current day. In this function, other event detection algorithms than MACD and RoT could be implemented too.

The next step was to import the weight data file and the file, which contained the hospitalisation events and the diuretic prescription events. The weight data of every patient was stored to a list and preprocessed to consist of exactly one weight measurement value per day (see section 2.2.2 for details).

These lists were stored to a further list. Subsequently, loops were defined for the algorithm parameters, which should be varied. Inside these loops, a loop iterated through all patients. For each patient, the output index curve was calculated for the given parameter set and a further loop for the range of the threshold was set up. Inside the threshold loop, all threshold violations for the given threshold were determined, all valid partitions were assessed and the respective counters for the evaluation tags were accordingly increased. After all patients' output index curves had been assessed in regard to all thresholds in the defined range, sensitivity and specificity could be determined for every threshold of the respective parameter set. After this procedure was finished for all parameter sets, the optimal parameter set could be determined by calculating the AUC of the ROC curves and selecting the highest one. Finally, for every threshold of every parameter set sensitivity and specificity values as well as the count of each evaluation tag and further the AUC of every parameter set were exported to a logging file.

For cross validation (see figure 2.5), this script was modified to initially separate the weight data to 8 groups. In a loop, each of the groups was left out once and used as the test set, while the other groups were combined to form the training set. After determining the optimal parameters for the training set, they were applied to the test set. Again, all measures were exported to a logging file in the end.

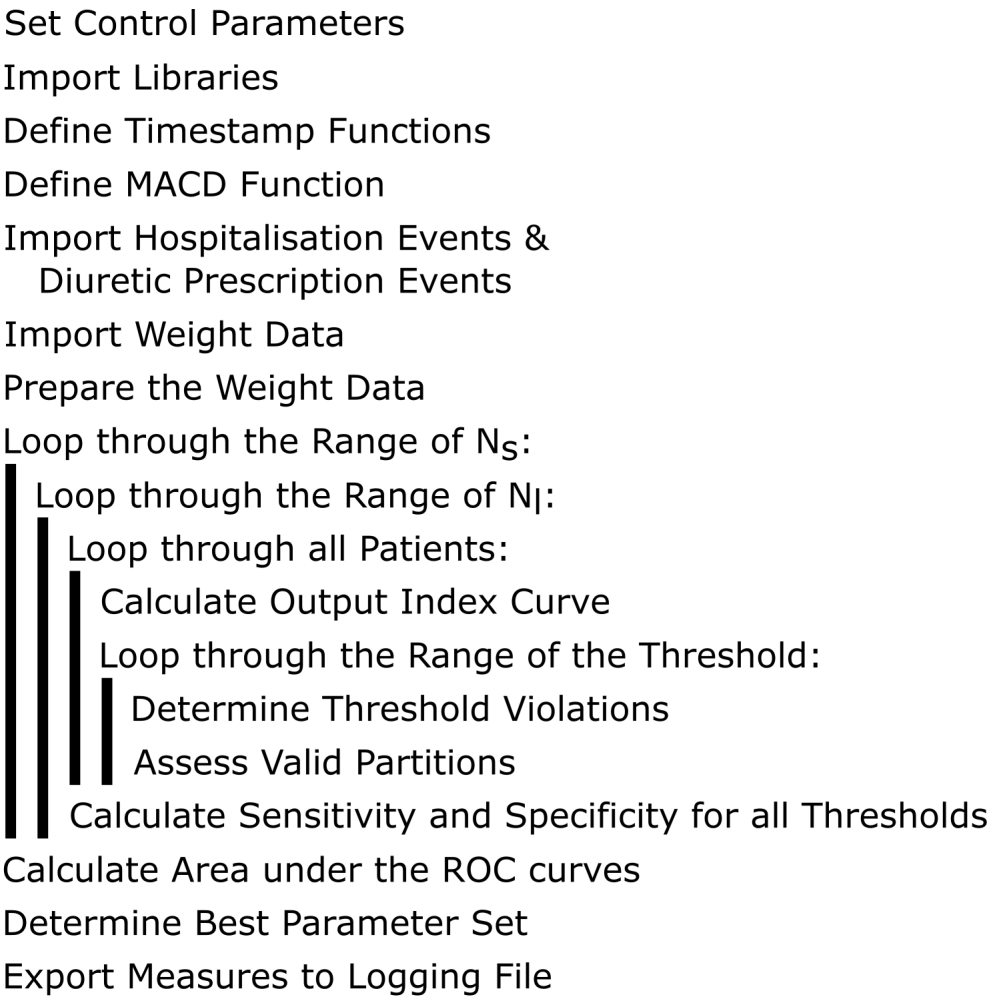



Figure 2.4: Structure of the Python script for the evaluation of the MACD algorithm.

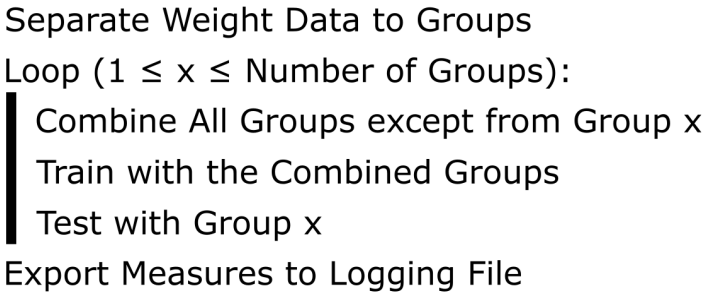



Figure 2.5: Scheme of the cross validation.

# Chapter 3

# Results

The search for the optimal parameter set was done, considering all events (heart failure related hospitalisations and diuretic prescription raises), considering only heart failure related hospitalisations and considering only diuretic prescription raises. The evaluation time frame was 7 days and 14 days. This results in six analyses each for MACD and for RoT. These 12 analyses were conducted with limiting the maximum number of false notifications to 5% and also without limitations.

## 3.1 Patient Statistic

So far, there have been 136 patients participating in the HerzMobil Tirol project. Based on the database and on information from the tirol kliniken, a patient statistic was developed, which can be found in table 3.1. Only patients, who started their measurements as expected, were selected for the further analysis. Never beginners and patients with less than 2 weeks of measuring data were not considered.

Table 3.1: Patient statistic for the four phases of the HerzMobil Tirol project. *One of the patients participated in phases II and IV.

| Phase | monitoring time span | Patients total | Patients selected | Mean age ± SD | men / women |
|---|---|---|---|---|---|
| - | months | - | - | years | - |
| I | 12 | 14 | 10 | 72.8 ± 8.7 | 8/2 |
| II | 6 | 51 | 40 | 75.4 ± 13.0 | 25/15 |
| III | 3 | 22 | 15 | 70.7 ± 10.0 | 8/7 |
| IV | 3 | 50 | 42 | 66.9 ± 11.3 | 34/8 |
| Total | - | 136* | 106* | 71.1 ± 12.1 | 74*/32 |

The mean (SD) age was 71 (12) years and there were 32 women and 74 men. In total the patients had 105 hospitalisations.

## 3.2 Best Parameter Set with Limited Number of False Notifications

Table 3.2 shows the resulting optimal parameters with the limitation to over 95% specificity for all MACD analyses. The optimal parameters resulted from the whole dataset. Considering all events with an evaluation frame of 7 days, the best parameters were a short window of $N_s$=4 and a long window of $N_l$=12 with a threshold of 0.8 kg. This parameter set resulted in an output index, which was slowly following the weight curve and showed no quick steps. Thus, its behaviour could be described as a low-pass characteristic. While outliers were filtered from the signal, the underlying long time trend was visible, as the course of the weight signal was smoothed (see plots in section 3.4). Varying the evaluation frame to 14 days, there were only small changes in the optimal parameters: the long window changed to $N_l$=10 and the threshold changed to 0.7 kg. Thus, the resulting output index curve also stayed very similar. Whereas leaving out the medication events did not make a big difference, looking at the medication events only led to a long window of $N_l$=8. This led to an output index curve, that reacted even slower than the curve obtained from a short window of $N_s$=4 and a long window of $N_l$=12. Table 3.3 shows the resulting optimal parameters with the limitation to over 95% specificity for all RoT analyses. The optimal parameters resulted from the whole dataset. For RoT with an evaluation time frame of 7 days, the optimal parameter was a time shift of 8 days with a threshold of 2.9 kg. When varying the evaluation time frame to 14 days, the optimal parameters

nearly stayed the same. For the consideration of prescription changes only and hospitalisations only, there also was not a big change in the optimal parameters.

Table 3.2: Optimal parameters estimated for the MACD algorithm with the limitation to over 95% specificity for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription raises (the optimal parameters resulted from the whole dataset).

| Considered Events | Frame | $N_s$ | $N_l$ | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|---|
| - | days | days | days | kg | 1 | 1 |
| all events | 7 days | 4 | 12 | 0.8 | 0.24 | 0.95 |
| all events | 14 days | 4 | 10 | 0.7 | 0.31 | 0.94 |
| hospitalisations | 7 days | 4 | 12 | 0.7 | 0.25 | 0.91 |
| hospitalisations | 14 days | 3 | 12 | 1.1 | 0.44 | 0.93 |
| prescription changes | 7 days | 5 | 8 | 0.3 | 0.25 | 0.92 |
| prescription changes | 14 days | 5 | 12 | 0.6 | 0.35 | 0.91 |

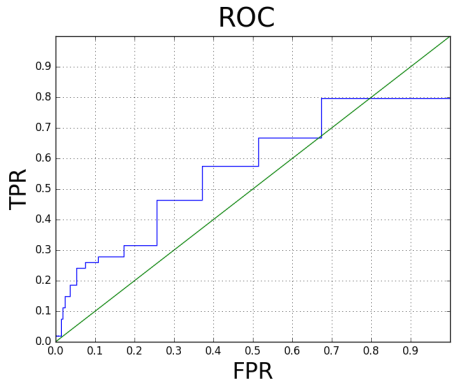
Table 3.3: Optimal parameters estimated for the RoT algorithms with the limitation to over 95% specificity for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription (the optimal parameters resulted from the whole dataset).

| Considered Events | Frame | Day Shift | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|
| - | days | days | kg | 1 | 1 |
| all events | 7 days | 8 | 2.9 | 0.24 | 0.93 |
| all events | 14 days | 8 | 2.8 | 0.36 | 0.91 |
| hospitalisation | 7 days | 6 | 2.6 | 0.33 | 0.91 |
| hospitalisation | 14 days | 6 | 4.0 | 0.44 | 0.97 |
| prescription changes | 7 days | 8 | 3.4 | 0.23 | 0.97 |
| prescription changes | 14 days | 7 | 2.9 | 0.26 | 0.91 |

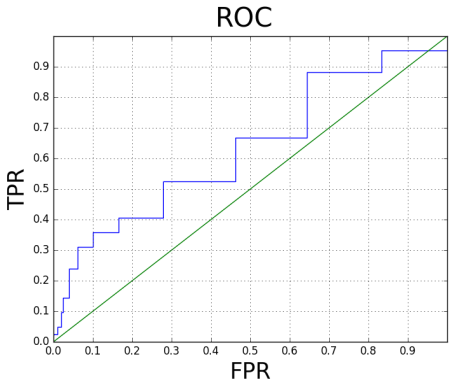
Figure 3.1 shows the ROC curves for the optimal MACD parameters with the limitation to over 95% specificity. Looking at figure (a), which shows the ROC curve for all events and an evaluation frame of 7 days, the optimisation for the AUC between an FPR of 0 and 0.05 can be observed. In this section the ROC curve bulges away from the diagonal line (which denotes a random classification). The remaining ROC curve stays quite close to the random line. The ROC of an evaluation frame of 14 days, which can be found in

figure (b), looks very similar to the one with a 7 day evaluation frame. Also for the other variations, the optimisation for the section with a FPR below 0.05 can be observed. Figure 3.2 shows the ROC curves for the optimal RoT parameters with the limitation to over 95% specificity. In figure (a), the ROC curve for all events and for an evaluation frame of 7 days is shown. In comparison to the MACD ROC curves, there are more steps, which is caused by a bigger range of the threshold estimation (50 values from 0.1 to 5.0 kg). Again, the optimisation for the FPR range between 0 and 0.05 is obvious, whereas the remaining ROC curve is very close to the diagonal random line. For 14 days the curve bulges away from the random line a little bit more than for 7 days. For the RoT, looking at hospitalisations only, the area under the ROC curve is bigger than for all events. Furthermore, the evaluation frame of 14 days results in a bigger AUC than the evaluation frame of 7 days.

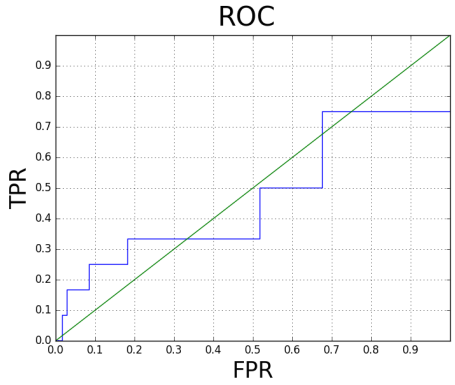
For all variations a stratified 8-fold cross validation was performed. The results for MACD can be found in table 3.4. The MACD parameters and the thresholds stayed quite constant for the consideration of all events and for the consideration of hospitalisations only. Considering the medication changes only, there were higher variations. Whereas the specificity values were limited to over 0.90 and thus did not vary much, the sensitivity values had a SD of up to 46%. The mean sensitivity values were relatively low at all. The results for RoT can be found in table 3.5. For RoT, again, there was a higher variation for the day shift parameter, when considering diuretic prescription changes only. The highest variation of the threshold could be observed for hospitalisations only with an evaluation frame of 7 days. Sensitivity and specificity showed a similar behaviour as the values of the MACD evaluation.



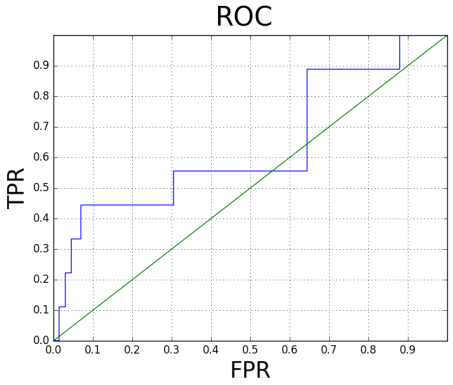

(a) $N_s$=4, $N_l$=12, hospitalisations and diuretic prescription events, evaluation frame = 7 days



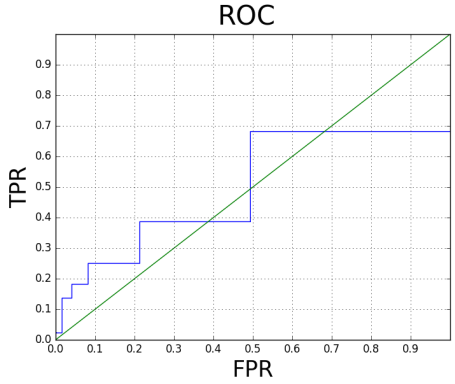

(b) $N_s$=4, $N_l$=10, hospitalisations and diuretic prescription events, evaluation frame = 14 days



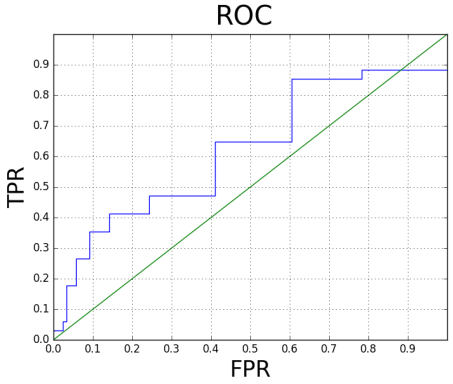

(c) $N_s$=4, $N_l$=12, hospitalisations only, evaluation frame = 7 days




(d) $N_s$=3, $N_l$=12, hospitalisations only, evaluation frame = 14 days

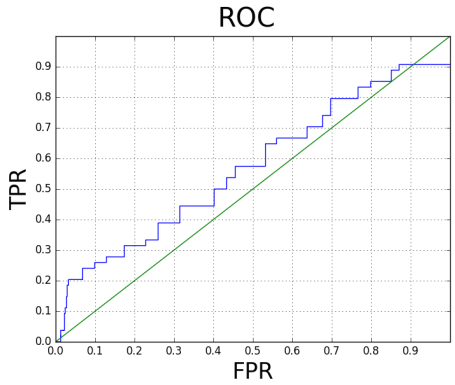



(e) $N_s$=5, $N_l$=8, diuretic prescription events only, evaluation frame = 7 days

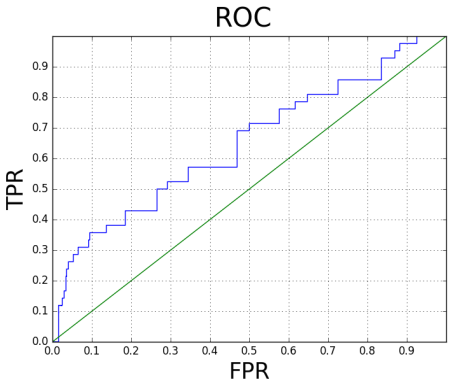



(f) $N_s$=5, $N_l$=12, diuretic prescription events only, evaluation frame = 14 days

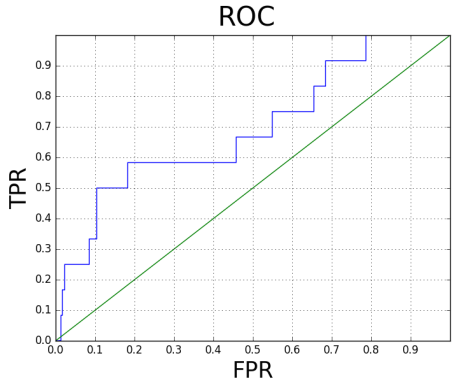
Figure 3.1: ROC curves for the optimal parameters of the MACD algorithm obtained by maximising the AUC for all thresholds with a specificity over 95%.



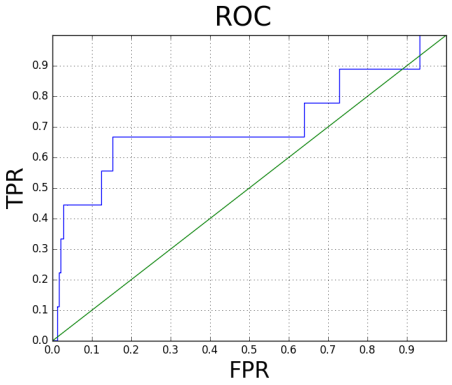

(a) d=8, hospitalisations and diuretic prescription events, evaluation frame = 7 days



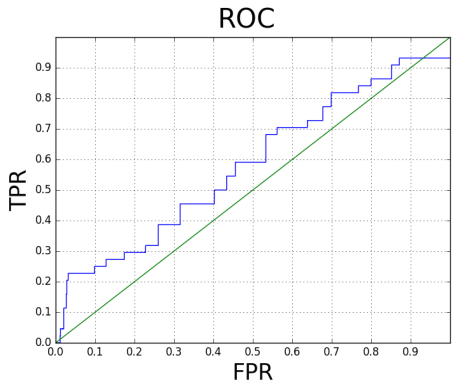

(b) d=8, hospitalisations and diuretic prescription events, evaluation frame = 14 days



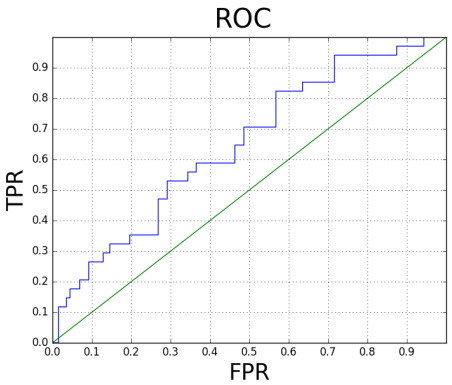

(c) d=6, hospitalisations only, evaluation frame = 7 days




(d) d=6, hospitalisations only, evaluation frame = 14 days




(e) d=8, diuretic prescription events only, evaluation frame = 7 days




(f) d=7, diuretic prescription events only, evaluation frame = 14 days

Figure 3.2: ROC curves for the optimal parameters of the RoT algorithm obtained by maximising the AUC for all thresholds with a specificity over 95%.

Table 3.4: Results of the cross validation for the MACD algorithm for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription raises. (With limited number of false notifications.) The mean value (± SD) is given.

| Considered Events | Frame | $N_s$ | $N_l$ | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|---|
| - | days | days | days | kg | 1 | 1 |
| all events | 7 days | 3.88 ± 0.83 | 12.50 ± 2.33 | 0.76 ± 0.16 | 0.26 ± 0.20 | 0.93 ± 0.03 |
| all events | 14 days | 4.12 ± 0.35 | 12.25 ± 3.28 | 0.76 ± 0.16 | 0.34 ± 0.17 | 0.92 ± 0.05 |
| hospitalisations | 7 days | 4.62 ± 1.41 | 11.75 ± 0.71 | 0.66 ± 0.20 | 0.19 ± 0.37 | 0.92 ± 0.03 |
| hospitalisations | 14 days | 3.50 ± 0.53 | 10.25 ± 1.67 | 0.88 ± 0.17 | 0.31 ± 0.46 | 0.93 ± 0.04 |
| prescription changes | 7 days | 3.88 ± 0.99 | 15.25 ± 8.35 | 0.85 ± 0.47 | 0.23 ± 0.21 | 0.93 ± 0.04 |
| prescription changes | 14 days | 5.88 ± 2.59 | 19.00 ± 15.53 | 0.95 ± 0.65 | 0.31 ± 0.30 | 0.92 ± 0.04 |



Table 3.5: Results of the cross validation for the RoT algorithm for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription raises. (With limited number of false notifications.) The mean value (± SD) is given.

| Considered Events | Frame | Day Shift | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|
| - | days | days | kg | 1 | 1 |
| all events | 7 days | 9.12 ± 2.70 | 2.92 ± 0.15 | 0.18 ± 0.15 | 0.94 ± 0.04 |
| all events | 14 days | 8.00 ± 0.93 | 2.99 ± 0.19 | 0.28 ± 0.14 | 0.93 ± 0.06 |
| hospitalisation | 7 days | 6.38 ± 1.51 | 2.83 ± 0.51 | 0.17 ± 0.36 | 0.92 ± 0.07 |
| hospitalisation | 14 days | 7.50 ± 2.07 | 4.01 ± 0.16 | 0.17 ± 0.36 | 0.96 ± 0.03 |
| prescription changes | 7 days | 8.12 ± 0.35 | 3.41 ± 0.04 | 0.18 ± 0.16 | 0.97 ± 0.02 |
| prescription changes | 14 days | 8.75 ± 4.56 | 2.98 ± 0.18 | 0.17 ± 0.15 | 0.90 ± 0.07 |

## 3.3 Best Parameter Set without Limitations

Table 3.6 shows the resulting optimal parameters without limitations of specificity for all MACD analyses. The optimal parameters resulted from the whole dataset. Considering all events with an evaluation frame of 7 days, the best parameters were a short window of $N_s$=1 and a long window of $N_l$=6 with a threshold of 0.4 kg. This parameter set results in an output index, which is quickly following the weight curve and shows quick steps. Thus, its behaviour can be described as a high-pass characteristic. While outliers are followed by the signal, the underlying long time trend cannot be observed (see plots in section 3.4). Varying the evaluation frame to 14 days, caused only small changes in the optimal parameters: the long window changed to $N_l$=10 and the threshold changed to 0.6 kg. Thus, the resulting output index curve stayed very similar. With respect to hospitalisations only, the parameters remained a short window of $N_s$=1 and a long window of $N_l$=6. Considering diuretic prescription changes only and choosing an evaluation frame of 14 days, there was a change in the optimal parameters to $N_s$=2 and a long window of $N_l$=12. This curve was a bit smoother than the curve of the other variations. While the highest sensitivity values resulted from the estimation considering all events, the specificity values were higher for the estimation considering only hospitalisations. Table 3.7 shows the resulting optimal parameters without limitations for all RoT analyses. The optimal parameters resulted from the whole dataset. In the evaluation of RoT, a longer day shift could be observed for an evaluation frame of 14 days. Whereas for an evaluation frame of 7 days the day shift was d=5 days, the day shift for an evaluation frame of 14 days was up to d=12 days. The highest sensitivity was obtained for considering all events and applying an evaluation frame of 7 days. The highest specificity was achieved considering all events and applying a 14 day evaluation frame.

Table 3.6: Optimal parameters estimated for the MACD algorithm without limitations regarding the number of false notifications for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription raises (the optimal parameters resulted from the whole dataset).

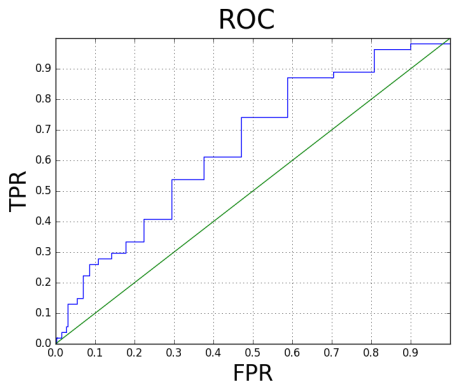
| Considered Events | Frame | $N_s$ | $N_l$ | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|---|
| - | days | days | days | kg | 1 | 1 |
| all events | 7 days | 1 | 6 | 0.4 | 0.87 | 0.41 |
| all events | 14 days | 1 | 10 | 0.6 | 0.90 | 0.37 |
| hospitalisations | 7 days | 1 | 6 | 0.6 | 0.75 | 0.62 |
| hospitalisations | 14 days | 1 | 6 | 0.8 | 0.78 | 0.63 |
| prescription changes | 7 days | 1 | 6 | 0.4 | 0.86 | 0.41 |
| prescription changes | 14 days | 2 | 12 | 0.5 | 0.85 | 0.45 |

Table 3.7: Optimal parameters estimated for the RoT algorithm without limitations regarding the number of false notifications for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription raises (the optimal parameters resulted from the whole dataset).

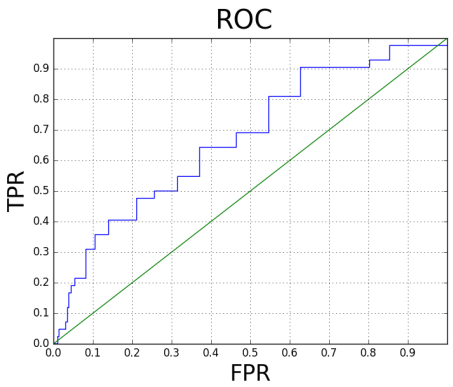
| Considered Events | Frame | Day Shift | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|
| - | days | days | kg | 1 | 1 |
| all events | 7 days | 5 | 1.0 | 0.76 | 0.57 |
| all events | 14 days | 11 | 3.1 | 0.38 | 0.92 |
| hospitalisation | 7 days | 5 | 1.9 | 0.58 | 0.84 |
| hospitalisation | 14 days | 7 | 2.2 | 0.67 | 0.79 |
| prescription changes | 7 days | 5 | 1.4 | 0.61 | 0.71 |
| prescription changes | 14 days | 12 | 1.8 | 0.65 | 0.31 |

Figure 3.3 shows the ROC curves for the optimal MACD parameters without limitations of the maximum number of false notifications. Especially, the ROCs for hospitalisations only show a bigger AUC, than observed for the optimisation of the limited AUC (see figures (c) and (d)). The distance to the diagonal random line is equally distributed over all thresholds. Figure 3.2 shows the ROC curves for the optimal RoT parameters without limitations of the maximum number of false notifications. For RoT, again, the variations with considering hospitalisations only have the biggest AUC and the algorithm seems stable over all thresholds.

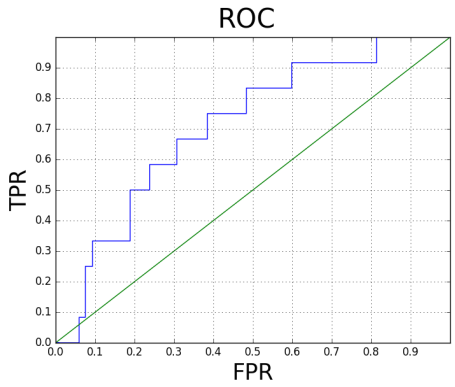
For all variations, a stratified 8-fold cross validation was performed. The results for MACD can be found in table 3.8. The variations for the MACD parameters and corresponding thresholds were quite low. While for all variations with a 7 day evaluation frame the sensitivity was higher, the specificity was higher for all variations with a 14 day evaluation frame. The results for RoT can be found in table 3.9. While the variations with an evaluation frame of 7 days showed very small differences in the day shift, there was a higher variance for the variations with a 14 day evaluation frame. The higher sensitivity was achieved for the variations with a 7 day evaluation frame.



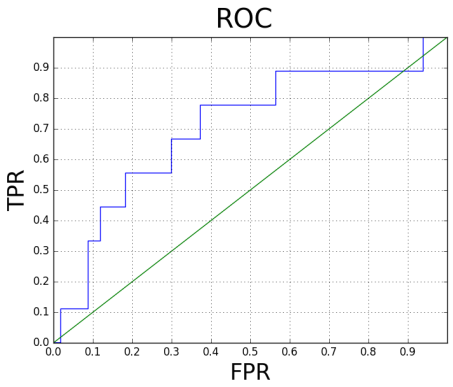

(a) $N_s$=1, $N_l$=6, hospitalisations and diuretic prescription events, evaluation frame = 7 days



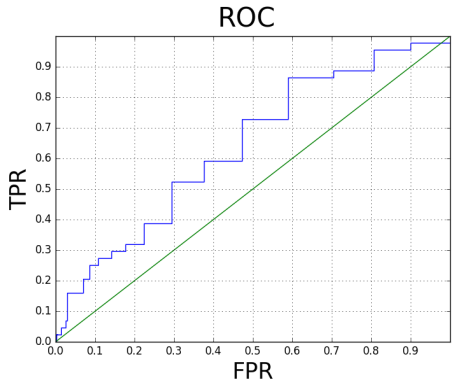

(b) $N_s$=1, $N_l$=10, hospitalisations and diuretic prescription events, evaluation frame = 14 days



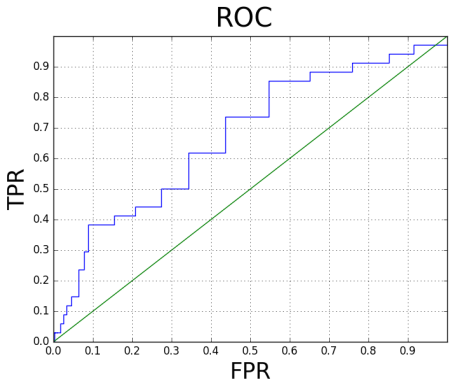

(c) $N_s$=1, $N_l$=6, hospitalisations only, evaluation frame = 7 days




(d) $N_s$=1, $N_l$=6, hospitalisations only, evaluation frame = 14 days

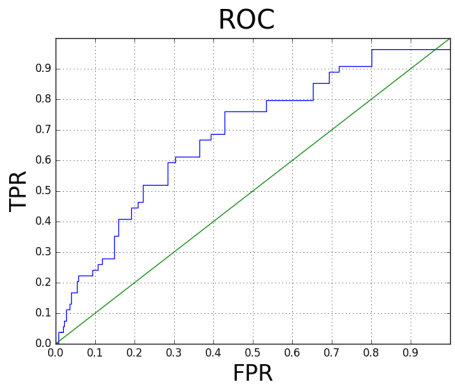



(e) $N_s$=1, $N_l$=6, diuretic prescription events only, evaluation frame = 7 days

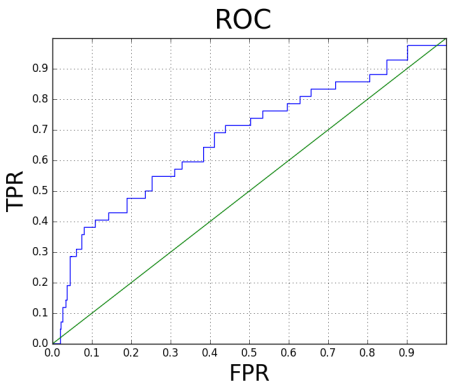



(f) $N_s$=2, $N_l$=12, diuretic prescription events only, evaluation frame = 14 days

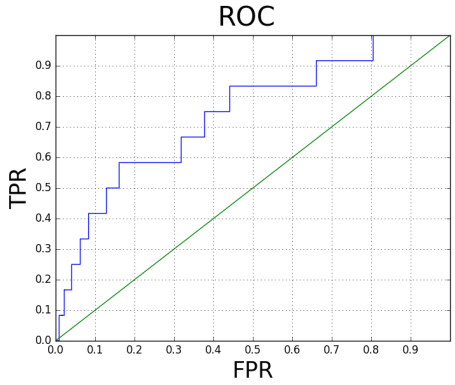
Figure 3.3: ROC curves for the optimal parameters of the MACD algorithm obtained by maximising the AUC for all thresholds (no limitations).



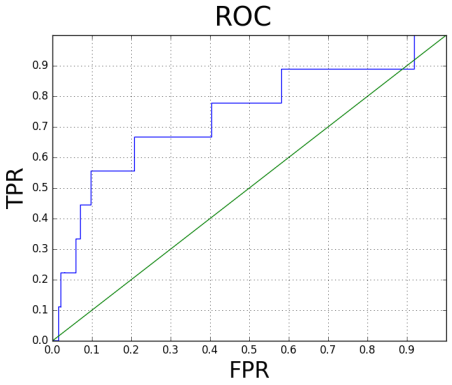

(a) d=5, hospitalisations and diuretic prescription events, evaluation frame = 7 days



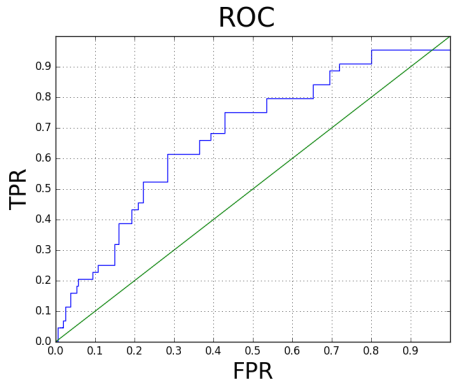

(b) d=11, hospitalisations and diuretic prescription events, evaluation frame = 14 days



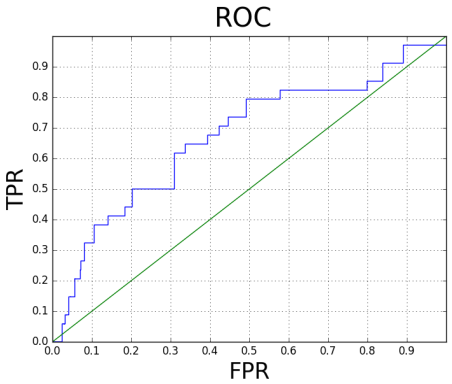

(c) d=5, hospitalisations only, evaluation frame = 7 days




(d) d=7, hospitalisations only, evaluation frame = 14 days




(e) d=5, diuretic prescription events only, evaluation frame = 7 days




(f) d=12, diuretic prescription events only, evaluation frame = 14 days

Figure 3.4: ROC curves for the optimal parameters of the RoT algorithm obtained by maximising the AUC for all thresholds (no limitations).

Table 3.8: Results of the cross validation for the MACD algorithm for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription raises. (Without limitations regarding the number of false notifications.) The mean value (± SD) is given.

| Considered Events | Frame | $N_s$ | $N_l$ | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|---|
| - | days | days | days | kg | 1 | 1 |
| all events | 7 days | 1.00 ± 0.00 | 6.50 ± 1.41 | 0.45 ± 0.11 | 0.76 ± 0.20 | 0.45 ± 0.16 |
| all events | 14 days | 1.25 ± 0.46 | 9.50 ± 0.93 | 0.74 ± 0.33 | 0.62 ± 0.34 | 0.54 ± 0.22 |
| hospitalisations | 7 days | 1.12 ± 0.35 | 6.50 ± 0.93 | 0.60 ± 0.12 | 0.58 ± 0.50 | 0.63 ± 0.10 |
| hospitalisations | 14 days | 1.25 ± 0.71 | 5.75 ± 0.71 | 0.84 ± 0.25 | 0.31 ± 0.46 | 0.71 ± 0.16 |
| prescription changes | 7 days | 1.00 ± 0.00 | 6.50 ± 1.41 | 0.44 ± 0.07 | 0.73 ± 0.26 | 0.44 ± 0.15 |
| prescription changes | 14 days | 1.88 ± 0.35 | 9.75 ± 1.98 | 0.61 ± 0.29 | 0.57 ± 0.44 | 0.56 ± 0.20 |

Table 3.9: Results of the cross validation for the RoT algorithm for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription raises. (Without limitations regarding the number of false notifications.) The mean value (± SD) is given.

| Consid. Events | Frame | Day Shift | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|
| - | days | days | kg | 1 | 1 |
| all events | 7 days | 5.00 ± 0.00 | 1.05 ± 0.14 | 0.70 ± 0.26 | 0.59 ± 0.12 |
| all events | 14 days | 9.50 ± 5.15 | 2.00 ± 0.53 | 0.43 ± 0.23 | 0.70 ± 0.15 |
| hospitalisation | 7 days | 4.25 ± 1.16 | 1.67 ± 0.37 | 0.31 ± 0.46 | 0.78 ± 0.14 |
| hospitalisation | 14 days | 6.88 ± 2.42 | 2.35 ± 0.36 | 0.23 ± 0.37 | 0.81 ± 0.12 |
| prescription changes | 7 days | 5.00 ± 0.00 | 1.25 ± 0.21 | 0.62 ± 0.22 | 0.66 ± 0.15 |
| prescription changes | 14 days | 8.62 ± 5.42 | 1.52 ± 0.50 | 0.47 ± 0.34 | 0.55 ± 0.19 |

## 3.4 Comparison of the MACD Output Index Curves

Using the visualisation tool, the estimated optimal parameters could be used to plot the resulting output index curves. Figure 3.5 shows a fluctuating weight curve and the corresponding output index curves for the parameter sets obtained by the optimisations. The blue curve shows the output index curve plotted for the parameter set, which resulted from the optimisation for a limited AUC ($N_s$=4, $N_l$=12, Threshold=0.8). The black curve shows the output index curve plotted for the parameter set, which resulted from the optimisation with no limitations ($N_s$=1, $N_l$=6, Threshold=0.4). The blue curve shows low-pass characteristics and thus the underlying trend of the signal can be observed. The black curve shows high-pass characteristics and thus follows the weight signal very quickly. Steps in the weight signal result in steps in the output index. In the same setup, Figure 3.6 shows a rising weight curve and the corresponding output index curves. The blue curve with the low-pass character responds slowly to the weight gain and does not trigger a notification. The black curve with the high-pass character quickly follows the weight signal and generates a notification.

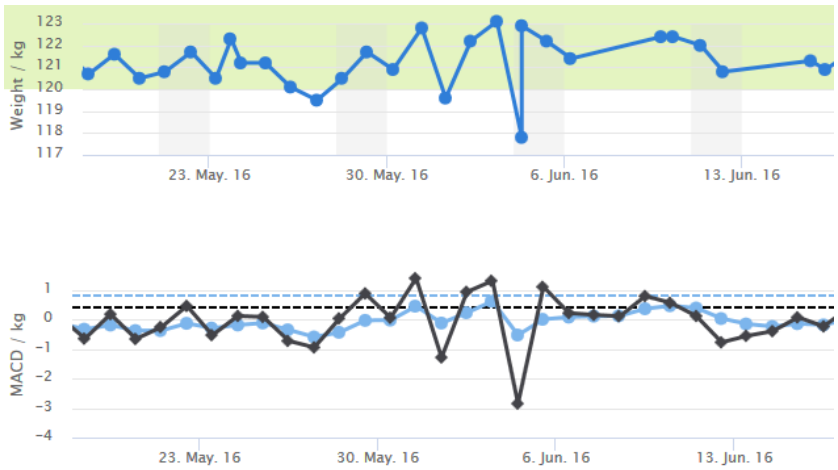



Figure 3.5: Fluctuating weight curve (top). MACD Output index resulting from optimised parameters (bottom): Blue curve: $N_s$=4, $N_l$=12, Threshold=0.8, optimised for limited AUC; Black curve: $N_s$=1, $N_l$=6, Threshold=0.4, optimised for total AUC

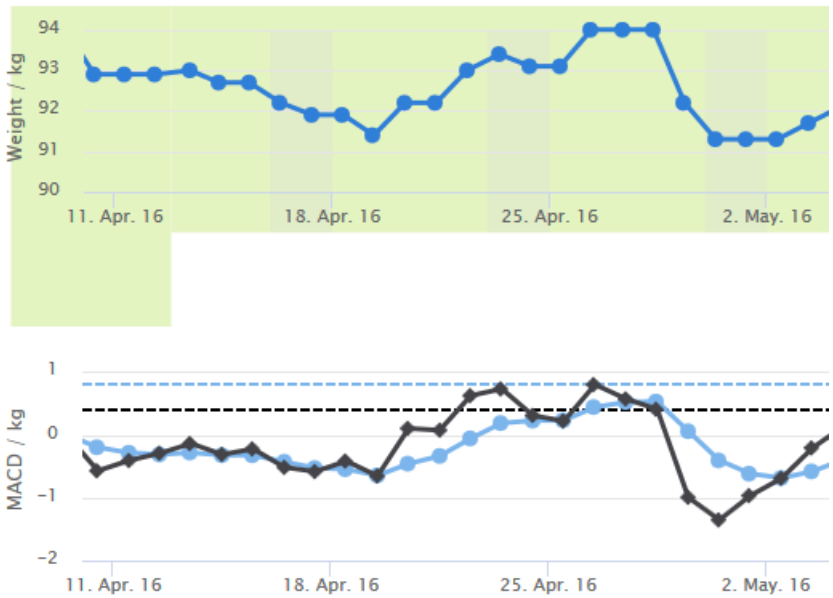



Figure 3.6: Rising weight curve (top). MACD Output index resulting from optimised parameters (bottom): Blue curve: $N_s$=4, $N_l$=12, Threshold=0.8, optimised for limited AUC; Black curve: $N_s$=1, $N_l$=6, Threshold=0.4, optimised for total AUC

## 3.5 Performance of ESC Guideline Rule and HerzMobil Tirol Rule

To the patients, the ESC guidelines recommend to consult the corresponding physician or adapt diuretics, when experiencing a weight gain of more than 2 kg in 3 days. The evaluation results for this rule can be found in table 3.10. The specificity was high for all variations. The sensitivity was higher for the variations with a two week evaluation frame. Further, the rule seemed to be better suited for hospitalisations than for diuretic prescription raises.

In the current system of HerzMobil Tirol, a RoT of 2 kg in 2 days was applied for the generation of weight notifications. The evaluation results for this rule can be found in table 3.11. Similar to the rule from the ESC guidelines, the specificity was high for all variations. The sensitivity, again, was higher for the variations with a two week evaluation frame. Also, there was a much higher sensitivity in hospitalisations than in diuretic prescription raises.

Table 3.10: Results of the evaluation of the ESC guidelines rule for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription raises (considering the whole dataset).

| Considered Events | Frame | Day Shift | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|
| - | days | days | kg | 1 | 1 |
| all events | 7 days | 3 | 2.0 | 0.22 | 0.89 |
| all events | 14 days | 3 | 2.0 | 0.31 | 0.84 |
| hospitalisation | 7 days | 3 | 2.0 | 0.33 | 0.89 |
| hospitalisation | 14 days | 3 | 2.0 | 0.44 | 0.83 |
| prescription changes | 7 days | 3 | 2.0 | 0.20 | 0.90 |
| prescription changes | 14 days | 3 | 2.0 | 0.29 | 0.83 |

Table 3.11: Results of the evaluation of the RoT implemented in the systems of HerzMobil Tirol for 7 and 14 days and for all events, only heart failure related hospitalisations and only diuretic prescription raises (considering the whole dataset).

| Considered Events | Frame | Day Shift | Thre. | Sens. | Spec. |
|---|---|---|---|---|---|
| - | days | days | kg | 1 | 1 |
| all events | 7 days | 2 | 2.0 | 0.19 | 0.91 |
| all events | 14 days | 2 | 2.0 | 0.24 | 0.86 |
| hospitalisation | 7 days | 2 | 2.0 | 0.33 | 0.91 |
| hospitalisation | 14 days | 2 | 2.0 | 0.56 | 0.85 |
| prescription changes | 7 days | 2 | 2.0 | 0.14 | 0.91 |
| prescription changes | 14 days | 2 | 2.0 | 0.18 | 0.85 |

# Chapter 4

# Discussion

## 4.1 Optimal Parameters

### 4.1.1 MACD

Optimising the MACD algorithm by maximising the limited AUC, led to a parameter set, which had low pass characteristics. The resulting output index curve showed the trend of the underlying weight signal. For a physician, the visualisation of this curve could give a good impression of the weight trend of a patient and thus be useful for the assessment of long term changes like the slow build-up of oedema or a weight gain caused by unhealthy eating habits. On the other hand, no quick changes in weight could be detected, as the curve follows the weight quite slowly. Optimising the MACD algorithm by maximising the total AUC led to a parameter set, which had high pass characteristics. With this variation no long term trend became visible, but the reaction to quick changes in weight was very fast. Considering the results of the cross validation, which showed high variations in the sensitivity values, no decision can be made, which parameters for MACD were better. Thus, for a real world scenario, a combination of both algorithms might be suitable to address both long time trends and quick weight gains.

### 4.1.2 RoT

For the RoT algorithm, the rule, which is actually recommended by the ESC guidelines (2 kg in 3 days), and the HerzMobil Tirol rule (2 kg in 2 days) showed high specificity and, therefore, seem to be a good choice in a real world scenario. The optimisation for RoT resulted in longer day shift intervals from 5 to 12 days with thresholds from 1 to 4 kg. For limited specificity values, the sensitivity values were only slightly higher than for the

guideline rule and for the HerzMobil Tirol rule. Considering the results of the cross validation, which showed high variations in the sensitivity values, no decision can be made, which parameters for RoT were better.

### 4.1.3 Comparison of MACD and RoT

Due to similar evaluation results, no difference between MACD and RoT regarding the weight-based prediction of critical events in heart failure disease management could be determined.

## 4.2 Limitations

For MACD, an infinite sum should be calculated. As no infinite sum could be computed, the sum was limited to 100 terms. This number of terms was chosen due to preceding tests, which showed, that for the applied ranges, the output index curves did not change in their appearance, if further terms were added. Only the magnitude of the signal became smaller, if more terms were added. Thus, it is important to calculate the MACD with the same number of terms as it was used, when the corresponding threshold was estimated.

## 4.3 Sources of Error

In the preprocessing step, outliers had to be handled. There were several possible reasons for outliers in the given setting. An interesting outlier in the weight measurements was a weight of 224,5 kg. This value seemed to be the maximum possible measurement value, that the scale could return. This value was found in the data of several patients and might be the result of a measurement, which was not correctly executed, or an error of the scale. A further possibility for divergences in the weight measurements could be the way the patients were dressed. Although the patients had been instructed to not wear clothing, when measuring their body weight, it could happen occasionally. Especially, if patients wanted to measure their weight during the day, they wouldn't completely undress. Thus, only the first weight measurement value of each day was used for the analyses.

## 4.4 Missing Values

Missing values were measurement values, which were expected, but the measurement was not executed or the data was not transmitted to the server

correctly. Due to the elderly patient population, most users were not used to the handling of a smartphone. Although the application was kept as easy to use as possible, there could be problems. Common problems were due to a missing connection to the mobile internet provider. This lost connection could e.g. be caused by the activation of the flight mode, which was integrated in the operating system of most smartphones. Moreover, some patients couldn't manage to restart the application, if they accidentally closed it. Another source of missing values was the absence of patients. Possible reasons for an absence were holidays or stays in a foreign country, rehabilitation stays or hospitalisations. A further important aspect, which is caused by the fact, that the analyses were retrospective, is data, which was transmitted with a delay. Measurement data sometimes was not transmitted for some days due to technical issues and thus, the physician was not able to react to the vital signs of the patient, as they were not present on the server. Due to the fact, that all values were assigned with timestamps, they were added to the measurement data as soon, as the technical problems were solved. Therefore, there might be situations in the final dataset, when the need for an intervention should have been obvious, but no physician reacted (as they were not able to).

## 4.5 Evaluation

The reason of limiting the calculation of the AUC to thresholds, that achieve a specificity higher than 95%, was the ambition, to keep the number of false notifications as low as possible. In this context, a false notification is a notification, given by the algorithm, that is not followed by an event. Maximising the AUC for all thresholds, led to higher sensitivity values, but there also was a decrease in specificity. For a decision support system it is important to be reliable. A trade-off appears between missing no event and giving no false notifications. In this context, when applied in the monitoring of heart failure patients, it is important that there are as few false notifications as possible, as on the one hand, it is stressful for everyone involved to react to a notification and the time and other resources could be used better, and on the other hand, the notifications will not be taken for serious and, thus, a notification, preceding an event, could be ignored. In HerzMobil Tirol, patients' data were routinely viewed once a week. It was better to implement an algorithm, which did not give many false notifications in cases, where they would not have been accurate, because they would have been wasted effort of the health professionals. It was less of a problem, if the worsening of a patient's health status was not reported by the decision support algorithm,

as it was most likely discovered by the next routine check.

### 4.5.1 Stratified Cross Validation

To perform an 8-fold stratified cross validation, all patients were assigned to 8 groups. For a stratified cross validation, the groups should be quite homogeneous and, therefore, the events should be distributed equally. In the evaluation, finally, 54 events were considered, of which 10 were heart failure related hospitalisations and 44 were diuretic prescription raises (these numbers slightly varied, if the evaluation frame was changed to 14 days due to the possible grouping of events, which occurred close to another event). Thus, every group consisted of about 13 patients with 1 or 2 heart failure related hospitalisations, about 5 diuretic prescription events and about 90 weeks with no event. Despite this distribution, every group consisted of datasets from real patients and therefore there was no guarantee, that in every group all events could be detected by weight data alone. Therefore, for example, if only the hospitalisations were considered and the testing group contained only 1 hospitalisation, and if this 1 hospitalisation was not detected, the sensitivity was 0. This could have been a reason for the high variation of the parameters.

## 4.6 Events

In the first seven days after hospitalisations, events were not considered, as during a hospital stay changes in medication are common and it may take some time until the prescription adaptations are stored in the database of the health data center. Furthermore, it was very likely, that there would be prescription changes in the days after discharge due to the change in the patient's environment.

The dataset contained a total of 1980 monitoring weeks. Considering missing values and grouping of events, as well as hospitalisation and absence durations, 1460 valid weeks remained. In this 1460 weeks only 54 events occurred, which is a relatively low number of events. For a prediction algorithm it would be suitable to have a lot more events.

Heart failure related hospitalisations were considered as events. For the possibility of the prediction of such an hospitalisation by looking at weight changes only, a preceding weight gain was required. However, not all acute decompensations were triggered by fluid retention and, thus, not always a weight gain was observable. Furthermore, not all weight gains had to be caused by heart failure. Patients could also gain weight by an increased

intake of food or because of unhealthy eating habits. This might have been a further reason for the relatively low sensitivity values.

While in the most comparable studies only hospitalisations were considered as events, in this analysis also diuretic prescription raises were considered events. HerzMobil Tirol was a disease management program, that monitors the patients vital data and further collects data on well-being, drug prescriptions as well as drug compliance. Suspicious weight gains were observed by the physicians and, if they were a potential threat for the patient, an immanent hospitalisation was prevented by adapting the medication of the patient. Often, weight gains were caused by liquid retention, which were countered with the prescription of diuretics. Thus, there was a high probability that, without an intervention of the physician, the patient would have had a cardiac de-compensation. Therefore, it made sense to include diuretic prescription raises, because a notification at this point would have been justified.

Diuretic prescription raises were derived from the compliance data. There also were database entries for prescriptions, but they were not always correct, as e.g. they were prescribed in hospital before discharge, but they were entered into the telemonitoring system after discharge. Furthermore, the notation in the database was quite complicated, as there was a prescription time span and additionally a flag to set the medication active for the adherence monitoring. Thus, for better reliability the compliance data was used, as it can be assumed, that the patient had a certain prescription, if it was displayed for the medication adherence check of that day. For diuretics, it is not possible to define usually prescribed dosages, as the goal is to treat the patient with the lowest possible dosage of diuretics. Therefore, for the possibility to compare various diuretics according to their prescribed dosage, reference dosages were defined for all active components by Dr. Gerhard Pölzl, the clinical director of the HerzMobil Tirol heart failure network. This way, it could be avoided, that a change from one prescribed diuretic to another one, without a change in the percentage of the reference dosage, resulted in an event. However, not all diuretic prescription events were necessarily related to heart failure, which could have led to a worse assessment of the algorithms. For example, in some cases diuretics were adapted in the case of high NT-proBNP values.

The events considered in this analysis were hospitalisations and diuretic prescription raises. The goal of all stakeholders, who participated in the HerzMobil network was to prevent hospitalisations. Thus, not only the physicians changed the drug prescriptions, but also the patients adapted their nutrition and even their medication, if they did not feel well. This behaviour could not be tracked by the system and, therefore, some imminent hospitalisations could not be detected, if they were prevented by such actions.

Therefore, it would make sense to consult heart specialists and physicians in order to look at the development of vital signs and to annotate time points, when a notification would be appropriate. This way, based on their knowledge and experience, they could decide, which changes in the vital signs should be a trigger for the automated generation of notifications by the decision support algorithms. The visualisation tool, which was created in the course of this thesis, allows for such an annotation and thus the data is currently annotated by health professionals.

## 4.7 Implementation

For the evaluation of real datasets, a lot of preparation was required to obtain a comprehensive dataset, which was ready to be used for further analyses. Not only the structure of the databases of the different phases was slightly different, but also in some cases the data had various formats. For example, there were differences in the way the timestamps of the measurements were stored and medications had various descriptions, ids or names in the various databases. Thus, a lot of time and effort was put into transforming the data into a common format to be able to merge the different databases.

The algorithms were evaluated using a python script. A detailed description can be found in section 2.5.8. The script could also be used to test further algorithms. The event detection algorithm is located in a separate function, which takes a parameter set, the current day of the measurement time span as well as a list containing the weight data. The function gives back an output index for the current day. Thus, the only limitation for the implementation of further algorithms would be the capability to generate an output index for a specific day based on a list of weight values. Furthermore, the loops for the variation parameters would have to be adapted. For the current analyses, the program was set up for RoT (one parameter) and for MACD (two parameters). If an algorithm, which takes more than two parameters, should be evaluated, further loops would have to be added.

## 4.8 Conclusion

A method was established to evaluate the performance of event detection algorithms regarding their reliability. With the created tools, data from various databases can be combined and preprocessed to obtain a comprehensive dataset. In a Javascript-based tool, the dataset can be visualised to obtain an overview of the patients' health status and annotations can be added to

create reference data for further analyses. The evaluation script takes ranges for algorithm parameters and thresholds as an input, tests all possible combinations and returns detailed results for all parameter sets as well as the optimal parameter set with the optimal threshold.

In comparison to the rather simple RoT algorithm, the results of this analysis showed no significant improvement, when implementing the more complex MACD algorithm. Concerning weight data, RoT seems to be a good choice for the application in a telemonitoring environment, as it is robust, easy to understand as well as easy to implement.

An improvement of the detection of critical events in heart failure monitoring could be achieved by considering more data, than weight measurements alone. Thus, modern, data-driven methods like e.g. clustering or predictive modelling should be applied to all available data to develop reliable decision support systems with the ultimate goal to spare patients from unscheduled hospital re-admissions and help healthcare providers and health professionals to utilise their resources in a way to maximise the quality of life of patients with heart failure.

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# List of Figures

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# Appendices

# Appendix A

## Lists of Drugs, Active Components, Dosages, Groups & Indications

| uid | Medikamentenname | Name_1 | Dosis_1 | Zieldosis_1 | Gruppe_1 | Indikation_1 | Name_2 | Dosis_2 | Zieldosis_2 | Gruppe_2 | Indikation_2 | Name_3 | Dosis_3 | Zieldosis_3 | Gruppe_3 | Indikation_3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 35084 | ACECOMB - semi - Tabletten | Lisinopril | 10 | 20 | ACE-I | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. | | | | | |
| 32423 | ACECOMB - mite - Tabletten | Lisinopril | 20 | 20 | ACE-I | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. | | | | | |
| 31643 | ACEMIN 5 mg - Tabletten | Lisinopril | 5 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 31642 | ACEMIN 10 mg - Tabletten | Lisinopril | 10 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 31644 | ACEMIN 20 mg - Tabletten | Lisinopril | 20 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 39257 | ADAMON long retard 150 mg - Filmtabletten | Tramadolhydrochlorid | 150 | 1 | Schmerzmittel | Schmerzmed., | | | | | | | | | | |
| 46428 | ADENURIC 80 mg - Filmtabletten | Febuxostat | 80 | 1 | Uricostatikum | Herzinsuff. | | | | | | | | | | |
| 34281 | AEROMUC 600 mg - loesliche Tabletten | Acetylcystein | 600 | 1 | TAH | Herzinsuff. | | | | | | | | | | |
| 44070 | AGLANDIN retard 0,4 mg - Kapseln | Tamsulosinhydrochlorid | 0.4 | 1 | Alphablocker | Prostatahyperplasie | | | | | | | | | | |
| 20442 | AKTIFERRIN - Kapseln | Getrocknetes Eisen(II)-sulfat | 110 | 1 | Eisen | Anämie | D,L-Serin | 129 | 1 | x | NaN | | | | | |
| 20443 | AKTIFERRIN - compositum - Kapseln | Getrocknetes Eisen(II)-sulfat | 110 | 1 | Eisen | Anämie | D,L-Serin | 129 | 1 | x | NaN | Folsäure | 0.65 | 1 | Folsäure | Anämie |
| 20455 | ALDACTONE - Hartkapseln 100 mg | Spironolacton | 100 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 20454 | ALDACTONE - ueberzogene Tabletten 50 mg | Spironolacton | 50 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 35728 | ALLOPURINOL "G.L." 300 mg - Tabletten | Allopurinol | 300 | 1 | Harnsäuresenker | Herzinsuff. | | | | | | | | | | |
| 22067 | ALLOPURINOL "Hexal" 300 mg - Tabletten | Allopurinol | 300 | 1 | Harnsäuresenker | Herzinsuff. | | | | | | | | | | |
| 36522 | ALLOPURINOL "Sandoz" 100 mg - Tabletten | Allopurinol | 100 | 1 | Harnsäuresenker | Herzinsuff. | | | | | | | | | | |
| 49795 | ALLOPURINOL "Teva" 100 mg - Tabletten | Allopurinol | 100 | 1 | Harnsäuresenker | Herzinsuff. | | | | | | | | | | |
| 35775 | ALNA retard 0,4 mg - Kapseln | Tamsulosinhydrochlorid | 0.4 | 1 | Alphablocker | Prostatahyperplasie | | | | | | | | | | |
| 37008 | ALPRAZOLAM "Arcana" 0,5 mg - Tabletten | Alprazolam | 0.5 | 1 | Benzodiazepin | Schlafmedikation | | | | | | | | | | |
| 44969 | AMLODIPIN "1A Pharma" 5 mg - Tabletten | Amlodipin | 5 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 44971 | AMLODIPIN "1A Pharma" 10 mg - Tabletten | Amlodipin | 10 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 46965 | AMLODIPIN "Actavis" 5 mg - Tabletten | Amlodipin | 5 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 46966 | AMLODIPIN "Actavis" 10 mg - Tabletten | Amlodipin | 10 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 42222 | AMLODIPIN "Genericon" 5 mg - Tabletten | Amlodipin | 5 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 42223 | AMLODIPIN "Genericon" 10 mg - Tabletten | Amlodipin | 10 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 45000 | AMLODIPIN "Hexal" 5 mg - Tabletten | Amlodipin | 5 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 22737 | ANTIFLAT - Kautabletten | Simeticon | 42 | 1 | Carminativum | Völlegefühl, Verdauungsstörung | | | | | | | | | | |
| 20610 | APREDNISLON 5 mg - Tabletten | Prednisolon | 5 | 1 | Cortison | system. Enzündungserkrankung | | | | | | | | | | |
| 20626 | AQUAPHORIL - Tabletten | Xipamid | 40 | 40 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 39319 | AROMASIN 25 mg - Tabletten | Exemestan | 25 | 1 | Aromatasehemmer | Mamma-Carcinom | | | | | | | | | | |
| 42455 | ASS "Hexal" 100 mg - Tabletten | Acetylsalicylsäure | 100 | 1 | TAH | Herzinsuff. | | | | | | | | | | |
| 37036 | ATACAND 4 mg - Tabletten | Candesartancilexetil | 4 | 32 | ARB | Herzinsuff. | | | | | | | | | | |
| 37038 | ATACAND 8 mg - Tabletten | Candesartancilexetil | 8 | 32 | ARB | Herzinsuff. | | | | | | | | | | |
| 51195 | ATORVALAN 10 mg - Filmtabletten | Atorvastatin | 10 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 49132 | ATORVASTATIN 1A Pharma 10 mg - Filmtabletten | Atorvastatin | 10 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 49133 | ATORVASTATIN 1A Pharma 20 mg - Filmtabletten | Atorvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 49134 | ATORVASTATIN 1A Pharma 40 mg - Filmtabletten | Atorvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 49135 | ATORVASTATIN 1A Pharma 80 mg - Filmtabletten | Atorvastatin | 80 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 48140 | ATORVASTATIN Actavis 20 mg - Filmtabletten | Atorvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 50497 | ATORVASTATIN Bluefish 80 mg - Filmtabletten | Atorvastatin | 80 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 48796 | ATORVASTATIN Genericon 20 mg - Filmtabletten | Atorvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 48797 | ATORVASTATIN Genericon 40 mg - Filmtabletten | Atorvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 50739 | ATORVASTATIN Genericon GmbH 80 mg - Filmtabletten | Atorvastatin | 80 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 49854 | ATORVASTATIN ratiopharm 20 mg - Filmtabletten | Atorvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 49855 | ATORVASTATIN ratiopharm 40 mg - Filmtabletten | Atorvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 51049 | ATORVASTATIN Stada 10 mg - Filmtabletten | Atorvastatin | 10 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 51051 | ATORVASTATIN Stada 40 mg - Filmtabletten | Atorvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 52102 | ATORVASTATIN Teva 20 mg - Filmtabletten | Atorvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 54062 | ATOZET 10 mg/40 mg - Filmtabletten | Ezetemib | 10 | 1 | Statine | Herzinsuff. | Atorvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | |
| 20812 | BERODUAL - Dosieraerosol | Fenoterolhydrobromid | 0.05 | 1 | Inhalativa | COPD | Ipratropiumbromid | 0.02 | 1 | Inhalativa | COPD | | | | | |
| 20813 | BERODUALIN - Inhalationsloesung | Fenoterolhydrobromid | 0.5 | 1 | Inhalativa | COPD | Ipratropiumbromid | 0.261 | 1 | Inhalativa | COPD | | | | | |
| 46791 | BISOPROLOL "1A Pharma" 1,25 mg - Filmtabletten | Bisoprololfumarat | 1.25 | 10 | BB | NaN | | | | | | | | | | |
| 46794 | BISOPROLOL "1A Pharma" 5 mg - Filmtabletten | Bisoprololfumarat | 5 | 10 | BB | NaN | | | | | | | | | | |
| 46804 | BISOPROLOL "Sandoz" 2,5 mg - Filmtabletten | Bisoprololfumarat | 2.5 | 10 | BB | NaN | | | | | | | | | | |
| 36968 | BLOPRESS 8 mg - Tabletten | Candesartancilexetil | 8 | 32 | ARB | Herzinsuff. | | | | | | | | | | |
| 36969 | BLOPRESS 16 mg - Tabletten | Candesartancilexetil | 16 | 32 | ARB | Herzinsuff. | | | | | | | | | | |

| uid | Medikamentenname | Name_1 | Dosis_1 | Zieldosis_1 | Gruppe_1 | Indikation_1 | Name_2 | Dosis_2 | Zieldosis_2 | Gruppe_2 | Indikation_2 | Name_3 | Dosis_3 | Zieldosis_3 | Gruppe_3 | Indikation_3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 39530 | BLOPRESS Plus Tabletten - 16 mg/12,5 mg | Candesartancilexetil | 16 | 32 | ARB | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. | | | | | |
| 52053 | BONVIVA - Injektionsloesung 3 mg (Parallelimport Emra-Med) | Ibandronsäure | 3 | 1 | Bisphosphonat | Osteoporose | | | | | | | | | | |
| 52827 | BOSULIF 500 mg - Filmtabletten | Bosutinib | 500 | 1 | Tyrosinkinaseinhibitor | Carcinom | | | | | | | | | | |
| 49822 | BRILIQUE 90 mg - Filmtabletten | Ticagrelor | 90 | 1 | TAH | Herzinsuff. | | | | | | | | | | |
| 49042 | CALCIDURAN Vit. D3 500 mg/800 I.E. - Kautabletten | Calcium | 500 | 1 | Calciumsubst. | Osteoporose | Colecalciferol | 0.02 | 1 | Vitamin D | Osteoporose | | | | | |
| 42924 | CALCIMAGON-D3 - Kautabletten | Calcium | 500 | 1 | Calciumsubst. | Osteoporose | Colecalciferol | 0.01 | 1 | Vitamin D | Osteoporose | | | | | |
| 413 | CALDVITA - Kautabletten | Calcium | 600 | 1 | Calciumsubst. | Osteoporose | Colecalciferol | 0.01 | 1 | Vitamin D | Osteoporose | | | | | |
| 47588 | CANDESARTAN 1A Pharma 8 mg - Tabletten | Candesartancilexetil | 8 | 32 | ARB | Herzinsuff. | | | | | | | | | | |
| 49664 | CANDESARTAN Genericon 8 mg - Tabletten | Candesartancilexetil | 8 | 32 | ARB | Herzinsuff. | | | | | | | | | | |
| 47584 | CANDESARTAN Sandoz 8 mg - Tabletten | Candesartancilexetil | 8 | 32 | ARB | Herzinsuff. | | | | | | | | | | |
| 51053 | CANDESARTAN Stada 4 mg - Tabletten | Candesartancilexetil | 4 | 32 | ARB | Herzinsuff. | | | | | | | | | | |
| 51054 | CANDESARTAN Stada 8 mg - Tabletten | Candesartancilexetil | 8 | 32 | ARB | Herzinsuff. | | | | | | | | | | |
| 51055 | CANDESARTAN Stada 16 mg - Tabletten | Candesartancilexetil | 16 | 32 | ARB | Herzinsuff. | | | | | | | | | | |
| 49865 | CANDESARTAN/HCT ratiopharm 8 mg/12,5 mg - Tabletten | Candesartancilexetil | 8 | 32 | ARB | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. | | | | | |
| 52724 | CANDESARTAN/HCT Sandoz 32 mg/12,5 mg - Tabletten | Candesartancilexetil | 32 | 32 | ARB | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. | | | | | |
| 38782 | CAPTOPRIL "ratiopharm" 25 mg - Tabletten | Captopril | 25 | 150 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42012 | CARVEDILOL "1A Pharma" 25 mg - Tabletten | Carvedilol | 25 | 50 | BB | Herzinsuff. | | | | | | | | | | |
| 44614 | CARVEDILOL "Sandoz" 12,5 mg - Tabletten | Carvedilol | 12.5 | 50 | BB | Herzinsuff. | | | | | | | | | | |
| 44615 | CARVEDILOL "Sandoz" 25 mg - Tabletten | Carvedilol | 25 | 50 | BB | Herzinsuff. | | | | | | | | | | |
| 40110 | CASODEX 150 mg - Filmtabletten | Bicalutamid | 150 | 1 | Antiandrogen | Prostatacarcinom | | | | | | | | | | |
| 45817 | CIALIS 5 mg - Filmtabletten | Tadalafil | 5 | 1 | PDE5 Inhib. | Herzinsuff., Erektionsstörung | | | | | | | | | | |
| 44373 | CITALOPRAM "+pharma" 20 mg - Filmtabletten | Citalopram | 20 | 1 | Antidepressivum | Depression | | | | | | | | | | |
| 35517 | CLAVAMOX 1 g - Filmtabletten | Amoxicilin | 875 | 1 | Antibiotika | Infektion | Clavulansäure | 125 | 1 | Antibiotika | Infektion | | | | | |
| 48051 | CLOPIDOGREL 1A Pharma 75 mg - Filmtabletten | Clopidogrel | 75 | 1 | TAH | NaN | | | | | | | | | | |
| 48309 | CLOPIDOGREL Acino 75 mg - Filmtabletten | Clopidogrel | 75 | 1 | TAH | NaN | | | | | | | | | | |
| 47890 | CLOPIDOGREL Krka 75 mg - Filmtabletten | Clopidogrel | 75 | 1 | TAH | NaN | | | | | | | | | | |
| 47717 | CLOPIDOGREL Sandoz 75 mg - Filmtabletten | Clopidogrel | 75 | 1 | TAH | NaN | | | | | | | | | | |
| 31821 | CODIDOL retard 60 mg - Filmtabletten | Dihydrocodein-hydrogen-tartrat | 60 | 1 | Opiat | Schmerzmedikament | | | | | | | | | | |
| 21240 | COLCHICIN "Agepha" - Tabletten | Colchicin | 0.372 | 1 | Antiphlogistika | Entzündung | | | | | | | | | | |
| 31061 | CONCOR - Filmtabletten 5 mg | Bisoprololfumarat | 5 | 10 | BB | NaN | | | | | | | | | | |
| 39041 | CONCOR Cor 1,25 mg - Filmtabletten | Bisoprololfumarat | 1.25 | 10 | BB | NaN | | | | | | | | | | |
| 39042 | CONCOR Cor 2,5 mg - Filmtabletten | Bisoprololfumarat | 2.5 | 10 | BB | NaN | | | | | | | | | | |
| 39043 | CONCOR Cor 3,75 mg - Filmtabletten | Bisoprololfumarat | 3.75 | 10 | BB | NaN | | | | | | | | | | |
| 39044 | CONCOR Cor 5 mg - Filmtabletten | Bisoprololfumarat | 5 | 10 | BB | NaN | | | | | | | | | | |
| 39046 | CONCOR Cor 10 mg - Filmtabletten | Bisoprololfumarat | 10 | 10 | BB | NaN | | | | | | | | | | |
| 50908 | COVALSAX 160 mg/25 mg - Filmtabletten | Valsartan | 160 | 320 | ARB | Herzinsuff. | Hydrochlorothiazid | 25 | 50 | Diuretika | Herzinsuff. | | | | | |
| 41932 | CRESTOR 10 mg - Filmtabletten | Rosuvastatin | 10 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 41933 | CRESTOR 20 mg - Filmtabletten | Rosuvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 53527 | CRESTOR 20 mg - Filmtabletten (Parallelimport P01) | Rosuvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 53528 | CRESTOR 40 mg - Filmtabletten (Parallelimport P01) | Rosuvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 34618 | DANCOR 10 mg - Tabletten | Nicorandil | 10 | 1 | Vasodilator | KHK | | | | | | | | | | |
| 34619 | DANCOR 20 mg - Tabletten | Nicorandil | 20 | 1 | Vasodilator | KHK | | | | | | | | | | |
| 51650 | DESLORATADIN Genericon 5 mg - Filmtabletten | Desloratadin | 5 | 1 | Antihistaminikum | COPD | | | | | | | | | | |
| 40360 | DIAMICRON MR 30 mg - Tabletten mit veraend. Wirkstofffreisetzung | Gliclazid | 30 | 1 | Sulfonyharnstoff | Diabetes | | | | | | | | | | |
| 21505 | DIBONDRIN - Dragees | Diphenhydraminhydrochlorid | 50 | 1 | Antihistaminikum | Übelkeit, Einschlafstörung | | | | | | | | | | |
| 21523 | DIGIMERCK - Tabletten 0,07 mg | Digitoxin | 0.07 | 1 | Digitalis | Herzinsuff. | | | | | | | | | | |
| 31585 | DIGIMERCK - Tabletten 0,1 mg | Digitoxin | 0.1 | 1 | Digitalis | Herzinsuff. | | | | | | | | | | |
| 35981 | DILATREND 6,25 mg - Tabletten | Carvedilol | 6.25 | 50 | BB | Herzinsuff. | | | | | | | | | | |
| 35982 | DILATREND 12,5 mg - Tabletten | Carvedilol | 12.5 | 50 | BB | Herzinsuff. | | | | | | | | | | |
| 32494 | DILATREND 25 mg - Tabletten | Carvedilol | 25 | 50 | BB | Herzinsuff. | | | | | | | | | | |
| 40848 | DIOVAN - Filmtabletten 80 mg | Valsartan | 80 | 320 | ARB | Herzinsuff. | | | | | | | | | | |
| 40851 | DIOVAN - Filmtabletten 160 mg | Valsartan | 160 | 320 | ARB | Herzinsuff. | | | | | | | | | | |
| 21609 | DOMINAL forte - Filmtabletten 80 mg | Prothipendyl-Hydrochloridmonohydrat | 80 | 1 | Neuroleptikum | Schlafmedikation | | | | | | | | | | |
| 42543 | DOXAZOSIN "1A Pharma" 2 mg - Tabletten | Doxazosin | 2 | 1 | AntiHyp | NaN | | | | | | | | | | |
| 42544 | DOXAZOSIN "1A Pharma" 4 mg - Tabletten | Doxazosin | 4 | 1 | AntiHyp | NaN | | | | | | | | | | |
| 42546 | DOXAZOSIN "Hexal" - Tabletten 4 mg | Doxazosin | 4 | 1 | AntiHyp | NaN | | | | | | | | | | |
| 30848 | EBRANTIL retard 60 mg - Kapseln | Urapidil | 60 | 1 | AntiHyp | NaN | | | | | | | | | | |
| 47029 | EFIENT 10 mg - Filmtabletten | Prasugrel | 10 | 1 | TAH | Herzinsuff. | | | | | | | | | | |
| 50608 | ELIQUIS 2,5 mg - Filmtabletten | Apixaban | 2.5 | 1 | AK | Herzinsuff. | | | | | | | | | | |

| uid | Medikamentenname | Name_1 | Dosis_1 | Zieldosis_1 | Gruppe_1 | Indikation_1 | Name_2 | Dosis_2 | Zieldosis_2 | Gruppe_2 | Indikation_2 | Name_3 | Dosis_3 | Zieldosis_3 | Gruppe_3 | Indikation_3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 52485 | ELIQUIS 5 mg - Filmtabletten | Apixaban | 5 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 40056 | ENALAPRIL "1A Pharma" 5 mg - Tabletten | Enalaprilmaleat | 5 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 40053 | ENALAPRIL "1A Pharma" 10 mg - Tabletten | Enalaprilmaleat | 10 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 40055 | ENALAPRIL "1A Pharma" 20 mg - Tabletten | Enalaprilmaleat | 20 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 39596 | ENALAPRIL "Sandoz" 5 mg - Tabletten | Enalaprilmaleat | 5 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 45943 | ENALAPRIL/HCT "Teva" 20 mg/12,5 mg - Tabletten | Enalaprilmaleat | 20 | 20 | ACE-I | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. | | | | | |
| 55175 | ENTRESTO 24 mg/26 mg - Filmtabletten | Sacubitril | 24.3 | 200 | ARNI | Herzinsuff. | Valsartan | 25.7 | 320 | ARB | Herzinsuff. | | | | | |
| 55176 | ENTRESTO 49 mg/51 mg - Filmtabletten | Sacubitril | 48.6 | 200 | ARNI | Herzinsuff. | Valsartan | 51.4 | 320 | ARB | Herzinsuff. | | | | | |
| 51532 | EPLERENON Genericon 25 mg - Filmtabletten | Eplerenon | 25 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 51533 | EPLERENON Genericon 50 mg - Filmtabletten | Eplerenon | 50 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 52985 | EPLERENON Pharmathen 25 mg - Filmtabletten | Eplerenon | 25 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 52986 | EPLERENON Pharmathen 50 mg - Filmtabletten | Eplerenon | 50 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 51237 | EPLERENON ratiopharm 25 mg - Filmtabletten | Eplerenon | 25 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 21888 | EUSAPRIM forte - Tabletten | Trimethoprim | 160 | 1 | Antibiotika | Infektion | Sulfamethoxazol | 800 | 1 | Antibiotika | Infektion | | | | | |
| 40627 | EUTHYROX 25 Mikrogramm - Tabletten | Levothyroxin-Natrium | 0.025 | 1 | Thyroxin | Hypothyreose | | | | | | | | | | |
| 40628 | EUTHYROX 50 Mikrogramm - Tabletten | Levothyroxin-Natrium | 0.05 | 1 | Thyroxin | Hypothyreose | | | | | | | | | | |
| 40629 | EUTHYROX 75 Mikrogramm - Tabletten | Levothyroxin-Natrium | 0.075 | 1 | Thyroxin | Hypothyreose | | | | | | | | | | |
| 45532 | EUTHYROX 88 Mikrogramm - Tabletten | Levothyroxin-Natrium | 0.088 | 1 | Thyroxin | Hypothyreose | | | | | | | | | | |
| 40630 | EUTHYROX 100 Mikrogramm - Tabletten | Levothyroxin-Natrium | 0.1 | 1 | Thyroxin | Hypothyreose | | | | | | | | | | |
| 40633 | EUTHYROX 175 Mikrogramm - Tabletten | Levothyroxin-Natrium | 0.175 | 1 | Thyroxin | Hypothyreose | | | | | | | | | | |
| 45064 | EXFORGE 5 mg/ 80 mg - Filmtabletten | Amlodipin | 5 | 1 | CC-Blocker | Hypertonie | Valsartan | 80 | 320 | ARB | Herzinsuff. | | | | | |
| 45066 | EXFORGE 5 mg/160 mg - Filmtabletten | Amlodipin | 5 | 1 | CC-Blocker | Hypertonie | Valsartan | 160 | 320 | ARB | Herzinsuff. | | | | | |
| 45065 | EXFORGE 10 mg/160 mg - Filmtabletten | Amlodipin | 10 | 1 | CC-Blocker | Hypertonie | Valsartan | 160 | 320 | ARB | Herzinsuff. | | | | | |
| 48022 | EXFORGE HCT 5 mg/160 mg/12,5 mg - Filmtabletten | Amlodipin | 5 | 1 | CC-Blocker | Hypertonie | Valsartan | 160 | 320 | ARB | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. |
| 48032 | EXFORGE HCT 5 mg/160 mg/25 mg - Filmtabletten | Amlodipin | 5 | 1 | CC-Blocker | Hypertonie | Valsartan | 160 | 320 | ARB | Herzinsuff. | Hydrochlorothiazid | 25 | 50 | Diuretika | Herzinsuff. |
| 48033 | EXFORGE HCT 10 mg/160 mg/12,5 mg - Filmtabletten | Amlodipin | 10 | 1 | CC-Blocker | Hypertonie | Valsartan | 160 | 320 | ARB | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. |
| 48034 | EXFORGE HCT 10 mg/160 mg/25 mg - Filmtabletten | Amlodipin | 10 | 1 | CC-Blocker | Hypertonie | Valsartan | 160 | 320 | ARB | Herzinsuff. | Hydrochlorothiazid | 25 | 50 | Diuretika | Herzinsuff. |
| 41966 | EZETROL 10 mg - Tabletten | Ezetemib | 10 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 36186 | FEMARA 2,5 mg - Filmtabletten | Letrozol | 2.5 | 1 | Aromatasehemmer | Mamma-Carcinom | | | | | | | | | | |
| 43832 | FINASTERID "Sandoz" 5 mg - Filmtabletten | Finasterid | 5 | 1 | Alphablocker | Prostatahyperplasie | | | | | | | | | | |
| 40524 | FOSAMAX-70 mg - einmal woechentlich Tabletten | Alendronsäure | 70 | 1 | Bisphosphonat | Osteoporose | | | | | | | | | | |
| 43525 | FOSINOPRIL "Interpharm" 20 mg - Tabletten | Fosinopril-Natrium | 20 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 45239 | FOSTER 100/6 Mikrogramm/Spruehstoß, Druckgasinhalation, Loesung | Beclometasondipropionat | 0.1 | 1 | Inhalativa | COPD | Formoterolfumarat-Dihydrat | 0.006 | 1 | Cortsion | COPD | | | | | |
| 50854 | GABAPENTIN "Pfizer" - Filmtabletten 800 mg | Gabapentin | 800 | 1 | Antikonvulsivum | Epilepsie, neuropathische Schmerzen | | | | | | | | | | |
| 45726 | HCT G.L. 50 mg - Tabletten | Hydrochlorothiazid | 50 | 50 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 36491 | HYDAL retard 2 mg - Kapseln | Hydromorphon-Hydrochlorid | 2 | 1 | Opiat | Schmerzmedikament | | | | | | | | | | |
| 31452 | HYPREN - Kapseln 2,5 mg | Ramipril | 2.5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 22482 | IMUREK - Filmtabletten | Azathioprin | 50 | 1 | Immunsuppressiva | Entzündung | | | | | | | | | | |
| 22490 | INDERAL 40 mg - Filmtabletten | Propranolol-Hydrochlorid | 40 | 60 | BB | Herzinsuff. | | | | | | | | | | |
| 43249 | INEGY 10 mg/40 mg - Tabletten | Ezetemib | 10 | 1 | Statine | Herzinsuff. | Simvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | |
| 32463 | INHIBACE "Roche" 5 mg - Filmtabletten | Cilazapril wasserfrei | 5 | 5 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 40289 | INKONTAN 30 mg - Filmtabletten | Trospiumchlorid | 30 | 1 | Anticholinergicum | Inkontinenz | | | | | | | | | | |
| 43085 | INSPRA 25 mg - Filmtabletten | Eplerenon | 25 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 43086 | INSPRA 50 mg - Filmtabletten | Eplerenon | 50 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 38255 | INSUMAN Comb 25 - 100 I.E./ml - Inj-Susp. Patrone | Insulin human | 3.5 | 1 | Insulin | Diabtes | | | | | | | | | | |
| 22581 | IRENAT - Tropfen | Natriumperchlorat | 300 | 1 | Natriumsubstitution | Herzinsuff. | | | | | | | | | | |
| 22611 | ISOMONAT 20 mg - Tabletten | Isosorbidmononitrat | 20 | 1 | Nitrate | Herzinsuff. | | | | | | | | | | |
| 39999 | ITERIUM 1 mg - Tabletten | Rilmenidin | 1 | 1 | AntiHyp | NaN | | | | | | | | | | |
| 46319 | JANUMET 50 mg/ 850 mg - Filmtabletten | Sitagliptin | 50 | 1 | Gliptin | Diabetes | Metforminhydrochlorid | 850 | 1 | Metformin | Diabetes | | | | | |
| 45158 | JANUVIA 100 mg - Filmtabletten | Sitagliptin | 100 | 1 | Gliptin | Diabetes | | | | | | | | | | |
| 22376 | KALIORAL "Fresenius" - Pulver | Tri-Kalium-citrat wasserfrei | 1940 | 1 | Kaliumersatz | Herzinsuff. | Kaliumhydrogencarbonat | 2000 | 1 | Kaliumsubst. | Herzinsuff. | Citronensäure wasserfrei | 1874 | 1 | x | NaN |
| 22399 | KCL-retard Slow-K 600 mg - Dragees | Kaliumchlorid | 600 | 1 | Kaliumsubst. | Herzinsuff. | | | | | | | | | | |
| 22380 | KREON - Kapseln 10.000 Einheiten | Pankreatin | 150 | 1 | Verdauungsenzym | Völlegefühl, Verdauungsprobleme | | | | | | | | | | |

| uid | Medikamentenname | Name_1 | Dosis_1 | Zieldosis_1 | Gruppe_1 | Indikation_1 | Name_2 | Dosis_2 | Zieldosis_2 | Gruppe_2 | Indikation_2 | Name_3 | Dosis_3 | Zieldosis_3 | Gruppe_3 | Indikation_3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 42837 | KREON - Kapseln 40.000 Einheiten | Pankreatin | 400 | 1 | Verdauungsenzym | Völlegefühl, Verdauungsprobleme | | | | | | | | | | |
| 49087 | LAEVOLAC - Loesung zum Einnehmen 10 g/15 ml | Lactulose | 10000 | 1 | Disaccharid | Obstipation | | | | | | | | | | |
| 34743 | LAMICTAL - Kau-/Schmelztabletten 100 mg | Lamotrigin | 100 | 1 | Antikonvulsivum | Epilepsie | | | | | | | | | | |
| 22693 | LANITOP - Tabletten 0,1 mg | Metildigoxin | 0.1 | 1 | Digitalis | Herzinsuff. | | | | | | | | | | |
| 262 | LANITOP - Tabletten 0,15 mg | Metildigoxin | 0.15 | 1 | Digitalis | Herzinsuff. | | | | | | | | | | |
| 42996 | LANSOBENE 30 mg - Kapseln | Lansoprazol | 30 | 1 | Protonenpumpenhemmer | NaN | | | | | | | | | | |
| 22700 | LASILACTON 20 mg/ 50 mg - Kapseln | Furosemid | 20 | 80 | Diuretika | Herzinsuff. | Spironolacton | 50 | 50 | MRA | Herzinsuff. | | | | | |
| 22701 | LASILACTON 20 mg/100 mg - Kapseln | Furosemid | 20 | 80 | Diuretika | Herzinsuff. | Spironolacton | 100 | 50 | MRA | Herzinsuff. | | | | | |
| 22706 | LASIX - retard 30 mg - Kapseln | Furosemid | 30 | 80 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 36977 | LASIX - retard 60 mg - Kapseln | Furosemid | 60 | 80 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 22709 | LASIX - Tabletten 40 mg | Furosemid | 40 | 80 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 22710 | LASIX - Tabletten 80 mg | Furosemid | 80 | 80 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 22711 | LASIX - Tabletten 500 mg | Furosemid | 500 | 80 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 257 | LENDORM 0,25 mg - Tabletten | Brotizolam | 0.25 | 1 | Benzodiazepin | Schlafmedikation | | | | | | | | | | |
| 48048 | LERCANIDIPIN Sandoz 10 mg - Filmtabletten | Lercanidipinhydrochlorid | 10 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 34944 | LESCOL 40 mg - Kapseln | Fluvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 39837 | LESCOL MR 80 mg - Filmtabletten | Fluvastatin | 80 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 22777 | LEXOTANIL "Roche" 3 mg - Tabletten | Bromazepam | 3 | 1 | Benzodiazepin | Schlafmedikation | | | | | | | | | | |
| 42107 | LISINOPRIL "1A Pharma" 5 mg - Tabletten | Lisinopril | 5 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42108 | LISINOPRIL "1A Pharma" 10 mg - Tabletten | Lisinopril | 10 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42109 | LISINOPRIL "1A Pharma" 20 mg - Tabletten | Lisinopril | 20 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 40739 | LISINOPRIL "Arcana" 5 mg - Tabletten | Lisinopril wasserfrei | 5 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 40738 | LISINOPRIL "Arcana" 10 mg - Tabletten | Lisinopril wasserfrei | 10 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 40740 | LISINOPRIL "Arcana" 20 mg - Tabletten | Lisinopril wasserfrei | 20 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 43216 | LISINOPRIL "Arcana" comp. 20 mg/12,5 mg - Tabletten | Lisinopril | 20 | 20 | ACE-I | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. | | | | | |
| 40881 | LISINOPRIL "Genericon" 10 mg - Tabletten | Lisinopril wasserfrei | 10 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 40882 | LISINOPRIL "Genericon" 20 mg - Tabletten | Lisinopril wasserfrei | 20 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 40416 | LISINOPRIL "Sandoz" 20 mg - Tabletten | Lisinopril | 20 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42436 | LISINOPRIL-HCT "Sandoz" 20 mg/12,5 mg - Tabletten | Lisinopril wasserfrei | 20 | 20 | ACE-I | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. | | | | | |
| 42437 | LISINOPRIL-HCT "Sandoz" 20 mg/25 mg - Tabletten | Lisinopril wasserfrei | 20 | 20 | ACE-I | Herzinsuff. | Hydrochlorothiazid | 25 | 50 | Diuretika | Herzinsuff. | | | | | |
| 45335 | LOSARTAN "1A Pharma" 50 mg - Filmtabletten | Losartan-Kalium | 50 | 150 | ARB | Herzinsuff. | | | | | | | | | | |
| 45438 | LOSARTAN "Sandoz" 50 mg - Filmtabletten | Losartan-Kalium | 50 | 150 | ARB | Herzinsuff. | | | | | | | | | | |
| 47539 | LOSARTAN /HCT "Sandoz" 100 mg/25 mg - Filmtabletten | Losartan-Kalium | 100 | 150 | ARB | Herzinsuff. | Hydrochlorothiazid | 25 | 50 | Diuretika | Herzinsuff. | | | | | |
| 45629 | LOSARTEX 50 mg .... siehe LOSARTAN "Sandoz" | Losartan-Kalium | 50 | 150 | ARB | Herzinsuff. | | | | | | | | | | |
| 31155 | LOVENOX - Spritzampullen 40 mg | Enoxaparin-Natrium | 40 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 35710 | LOVENOX - Spritzampullen 60 mg | Enoxaparin-Natrium | 60 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 35712 | LOVENOX - Spritzampullen 100 mg | Enoxaparin-Natrium | 100 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 22864 | LUDIOMIL - Filmtabletten 75 mg | Maprotilinhydrochlorid | 75 | 1 | Antidepressivum | Depression | | | | | | | | | | |
| 43031 | LYRICA - Hartkapseln 25 mg | Pregabalin | 25 | 1 | Antikonvulsivum | Epilespie | | | | | | | | | | |
| 43035 | LYRICA - Hartkapseln 150 mg | Pregabalin | 150 | 1 | Antikonvulsivum | Epilespie | | | | | | | | | | |
| 37810 | MADOPAR "Roche" 100 mg/25 mg - Tabletten | Levodopa | 100 | 1 | DOPA Inhibitor | Parkinson | Benserazid | 25 | 1 | DOPA Agonist | Parkinson | | | | | |
| 31876 | MADOPAR CR "Roche" 100 mg/25 mg - Kapseln | Levodopa | 100 | 1 | DOPA Inhibitor | Parkinson | Benserazid | 25 | 1 | DOPA Agonist | Parkinson | | | | | |
| 22906 | MAGNESIUM Verla - Filmtabletten | Magnesiumcitrat | 436.8 | 1 | Magnesiumersatz | Krämpfe | Magnesium-L-Glutamat Tetrahydrat | 165.4 | 1 | Magnesiumersatz | Krämpfe | | | | | |
| 31621 | MAGNOSOLV - Granulat | Magnesiumcarbonat | 670 | 1 | Magnesiumersatz | Krämpfe | Magnesiumoxid | 342 | 1 | Magnesiumersatz | Krämpfe | | | | | |
| 22926 | MARCOUMAR - Tabletten | Phenprocoumon | 3 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 22935 | MAXI-KALZ 500 mg - Brausetabletten | Calciumcarbonat | 500 | 1 | Calciumsubst. | Osteoporose | | | | | | | | | | |
| 35675 | MAXI-KALZ Vit.D3 1000 mg/880 I.E. - Granulat | Calcium | 1000 | 1 | Calciumsubst. | Osteoporose | | | | | | | | | | |
| 49900 | METFORMIN "Actavis" 500 mg - Filmtabletten | Metforminhydrochlorid | 500 | 1 | Metformin | Diabetes | | | | | | | | | | |
| 43172 | METOHEXAL retard 47,5 mg - Filmtabletten | Metoprololsuccinat | 47.5 | 190 | BB | Herzinsuff. | | | | | | | | | | |
| 43174 | METOHEXAL retard 95 mg - Filmtabletten | Metoprololsuccinat | 95 | 190 | BB | Herzinsuff. | | | | | | | | | | |
| 47193 | METOPROLOLSUCCINAT "Actavis" 47,5 mg - Retardtabletten | Metoprololsuccinat | 47.5 | 190 | BB | Herzinsuff. | | | | | | | | | | |
| 47848 | METOPROLOLSUCCINAT "Stada" 47,5 mg - Retardtabletten | Metoprololsuccinat | 47.5 | 190 | BB | Herzinsuff. | | | | | | | | | | |
| 101 | MEXALEN500 mg - Tabletten | Paracetamol | 500 | 1 | Antiphlogistika | Schmerzmed., Fiebersenken | | | | | | | | | | |
| 42057 | MIRTABENE - Filmtabletten 30 mg | Mirtazapin | 30 | 1 | Antidepressivum | Depression | | | | | | | | | | |
| 43254 | MIRTAZAPIN "G.L." 30 mg - Filmtabletten | Mirtazapin | 30 | 1 | Antidepressivum | Depression | | | | | | | | | | |
| 47323 | MIRTAZAPIN "Teva" 30 mg - Filmtabletten | Mirtazapin | 30 | 1 | Antidepressivum | Depression | | | | | | | | | | |
| 23431 | MODURETIC 5 mg/50 mg - Tabletten | Amilorid | 5 | 10 | Diuretika | Herzinsuff. | Hydrochlorothiazid | 50 | 50 | Diuretika | Herzinsuff. | | | | | |
| 23432 | MOGADON - Tabletten | Nitrazepam | 5 | 1 | Benzodiazepin | Schlafmedikation | | | | | | | | | | |
| 48440 | MOLAXOLE - Pulver zur Herstellung einer Loesung zum Einnehmen | Macrogol 3350 | 13125 | 1 | Magnesiumersatz | Krämpfe | Natriumchlorid | 350.7 | 1 | Natriumsubstitution | Herzinsuff. | Kaliumchlorid | 46.6 | 1 | Kaliumsubst. | Herzinsuff. |

| uid | Medikamentenname | Name_1 | Dosis_1 | Zieldosis_1 | Gruppe_1 | Indikation_1 | Name_2 | Dosis_2 | Zieldosis_2 | Gruppe_2 | Indikation_2 | Name_3 | Dosis_3 | Zieldosis_3 | Gruppe_3 | Indikation_3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 210 | MOLSIDOLAT 2 mg - Tabletten | Molsidomin | 2 | 1 | Nitrate | KHK, Herzinsuff. | | | | | | | | | | |
| 272 | MOLSIDOLAT 4 mg - Tabletten | Molsidomin | 4 | 1 | Nitrate | KHK, Herzinsuff. | | | | | | | | | | |
| 329 | MONOKET retard 50 mg - Kapseln | Isosorbidmononitrat | 50 | 1 | Nitrate | Herzinsuff. | | | | | | | | | | |
| 39286 | MUCOBENE- loesbare Tabletten 200 mg | Acetylcystein | 200 | 1 | TAH | Herzinsuff. | | | | | | | | | | |
| 47291 | NEBILAN 5 mg - Tabletten | Nebivolol | 5 | 10 | BB | Herzinsuff. | | | | | | | | | | |
| 45735 | NEBIVOLOL 1A Pharma 5 mg - Tabletten | Nebivolol | 5 | 10 | BB | Herzinsuff. | | | | | | | | | | |
| 47462 | NEBIVOLOL Arcana 5 mg - Tabletten | Nebivolol | 5 | 10 | BB | Herzinsuff. | | | | | | | | | | |
| 46824 | NEBIVOLOL G.L. 5 mg - Tabletten | Nebivolol | 5 | 10 | BB | Herzinsuff. | | | | | | | | | | |
| 48143 | NEBIVOLOL Genericon 5 mg - Tabletten | Nebivolol | 5 | 10 | BB | Herzinsuff. | | | | | | | | | | |
| 23633 | NERISONA - Creme | Diflucortonvalerat | 1 | 1 | x | NaN | | | | | | | | | | |
| 34462 | NEURONTIN 300 mg - Hartkapseln | Gabapentin | 300 | 1 | Antikonvulsivum | Epilepsie, neuropathische Schmerzen | | | | | | | | | | |
| 37949 | NEURONTIN 600 mg - Filmtabletten | Gabapentin | 600 | 1 | Antikonvulsivum | Epilepsie, neuropathische Schmerzen | | | | | | | | | | |
| 48903 | NICOLAN 20 mg - Tabletten | Nicorandil | 20 | 1 | Vasodilator | KHK | | | | | | | | | | |
| 44720 | NICOTINELL TTS 10 ( 7 mg/24 h) - transdermale Pflaster | Nicotin | 17.5 | 1 | Nikotinersatz | Nikotinentzug | | | | | | | | | | |
| 44681 | NICOTINELL TTS 30 (21 mg/24 h) - transdermale Pflaster | Nicotin | 52.5 | 1 | Nikotinersatz | Nikotinentzug | | | | | | | | | | |
| 23670 | NITROLINGUAL 0,4 mg - Pumpspray | Glyceroltrinitrat | 0.4 | 1 | Nitrate | KHK, Herzinsuffizienz | | | | | | | | | | |
| 35695 | NOMEXOR - Tabletten 5 mg | Nebivolol | 5 | 10 | BB | Herzinsuff. | | | | | | | | | | |
| 42493 | NORMOHEX 0,4 mg - Filmtabletten | Moxonidin | 0.4 | 1 | AntiHyp | NaN | | | | | | | | | | |
| 32043 | NORVASC 5 mg - Tabletten | Amlodipin | 5 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 23716 | NOVALGIN - Tropfen | Metamizol-Natrium | 500 | 1 | Pyrazolon | Schmerzmed., Fiebersenken | | | | | | | | | | |
| 40912 | NOVOMIX 30 FlexPen 100 Einheiten/ml - Inj-Susp. in einem Fertigpen | Insulin aspart | 10.5 | 1 | Insulin | Diabetes | | | | | | | | | | |
| 40690 | NOVOMIX 30 Penfill 100 Einheiten/ml - Inj-Susp. in einer Patrone | Insulin aspart | 10.5 | 1 | Insulin | Diabetes | | | | | | | | | | |
| 44082 | NOVOMIX 70 FlexPen 100 Einheiten/ml - Inj-Susp. in einem Fertigpen | Insulin aspart | 10.5 | 1 | Insulin | Diabetes | | | | | | | | | | |
| 25285 | OLEOVIT D3 - Tropfen | Colecalciferol | 0.01 | 1 | Vitamin D | Osteoporose | | | | | | | | | | |
| 38272 | PANTOLOC 20 mg - Filmtabletten | Pantoprazol | 20 | 1 | Protonenpumpenhemmer | Gastritis, Ulcus | | | | | | | | | | |
| 34947 | PANTOLOC 40 mg - Filmtabletten | Pantoprazol | 40 | 1 | Protonenpumpenhemmer | Gastritis, Ulcus | | | | | | | | | | |
| 405 | PANTOLOC 40 mg - Trockenstechampulle | Pantoprazol | 40 | 1 | Protonenpumpenhemmer | Gastritis, Ulcus | | | | | | | | | | |
| 47197 | PANTOPRAZOL "Ranbaxy" 40 mg - magensaftresistente Tabletten | Pantoprazol | 40 | 1 | Protonenpumpenhemmer | Gastritis, Ulcus | | | | | | | | | | |
| 52388 | PANTOPRAZOL "ratiopharm GmbH" 40 mg - magensaftresistente Tabletten | Pantoprazol | 40 | 1 | Protonenpumpenhemmer | Gastritis, Ulcus | | | | | | | | | | |
| 23965 | PASPERTIN - Filmtabletten | Metoclopramidhydrochlorid | 10 | 1 | Antiemetikum | Übelkeit, Erbrechen | | | | | | | | | | |
| 51857 | PASSEDAN - Tropfen (HERB) | Flüssigextrakt aus Passionsblumenkraut | 50 | 1 | x | NaN | | | | | | | | | | |
| 24102 | PILOCARPIN PUROPTAL 1% - Augentropfen | Pilocarpinhydrochlorid | 10 | 1 | Parasympathomimetikum | Grüner Star | | | | | | | | | | |
| 37919 | PLAVIX 75 mg - Filmtabletten | Clopidogrel | 75 | 1 | TAH | NaN | | | | | | | | | | |
| 46138 | PRADAXA 110 mg - Hartkapseln | Dabigatranetexilat | 110 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 50828 | PRADAXA 150 mg - Hartkapseln | Dabigatranetexilat | 150 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 51379 | PRAMIPEXOL Accord 0,18 mg - Tabletten | Pramipexol | 0.18 | 1 | DOPA Agonist | Parkinson | | | | | | | | | | |
| 42915 | PRAVASTATIN "1A Pharma" 20 mg - Tabletten | Pravastatin-Natrium | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 42901 | PRAVASTATIN "Sandoz" 10 mg - Tabletten | Pravastatin-Natrium | 10 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 43353 | PRAVASTATIN "Stada" 40 mg - Filmtabletten | Pravastatin-Natrium | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 24165 | PRAXITEN 15 mg - Tabletten | Oxazepam | 15 | 1 | Benzodiazepin | Schlafmedikation | | | | | | | | | | |
| 24170 | PREDNISOLON "Nycomed" 25 mg - Tabletten | Prednisolon | 25 | 1 | Cortison | system. Enzündungserkrankung | | | | | | | | | | |
| 43990 | PROCORALAN 5 mg - Filmtabletten | Ivabradin | 5 | 15 | Procoralan | Herzinsuff. | | | | | | | | | | |
| 43989 | PROCORALAN 7,5 mg - Filmtabletten | Ivabradin | 7.5 | 15 | Procoralan | Herzinsuff. | | | | | | | | | | |
| 24275 | PSYCHOPAX - Tropfen | Diazepam | 12.5 | 1 | Benzodiazepam | Schlafmedikation | | | | | | | | | | |
| 46571 | QUETIAPIN Genericon 25 mg - Filmtabletten | Quetiapin | 25 | 1 | Neuroleptikum | Depression | | | | | | | | | | |
| 42791 | RAMICOMP "Genericon" - Tabletten | Ramipril | 5 | 10 | ACE-I | Herzinsuff. | Hydrochlorothiazid | 25 | 50 | Diuretika | Herzinsuff. | | | | | |
| 42288 | RAMIPRIL "1A Pharma" 1,25 mg - Tabletten | Ramipril | 1.25 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42287 | RAMIPRIL "1A Pharma" 2,5 mg - Tabletten | Ramipril | 2.5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42286 | RAMIPRIL "1A Pharma" 5 mg - Tabletten | Ramipril | 5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42284 | RAMIPRIL "1A Pharma" 10 mg - Tabletten | Ramipril | 10 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42798 | RAMIPRIL "Genericon" - Kapseln 2,5 mg | Ramipril | 2.5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42799 | RAMIPRIL "Genericon" - Kapseln 5 mg | Ramipril | 5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |

| uid | Medikamentenname | Name_1 | Dosis_1 | Zieldosis_1 | Gruppe_1 | Indikation_1 | Name_2 | Dosis_2 | Zieldosis_2 | Gruppe_2 | Indikation_2 | Name_3 | Dosis_3 | Zieldosis_3 | Gruppe_3 | Indikation_3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 42800 | RAMIPRIL "Genericon" - Kapseln 10 mg | Ramipril | 10 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42795 | RAMIPRIL "Genericon" - Tabletten 5 mg | Ramipril | 5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42298 | RAMIPRIL "Hexal" 1,25 mg - Tabletten | Ramipril | 1.25 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42297 | RAMIPRIL "Hexal" 2,5 mg - Tabletten | Ramipril | 2.5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42295 | RAMIPRIL "Hexal" 10 mg - Tabletten | Ramipril | 10 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 50103 | RAMIPRIL "Krka" 2,5 mg - Tabletten | Ramipril | 2.5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42945 | RAMIPRIL "ratiopharm" 2,5 mg - Tabletten | Ramipril | 2.5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42946 | RAMIPRIL "ratiopharm" 5 mg - Tabletten | Ramipril | 5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 42947 | RAMIPRIL "ratiopharm" 10 mg - Tabletten | Ramipril | 10 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 46542 | RANEXA 375 mg - Retardtabletten | Ranolazin | 375 | 1 | Protonenpumpenhemmer | NaN | | | | | | | | | | |
| 46543 | RANEXA 500 mg - Retardtabletten | Ranolazin | 500 | 1 | Protonenpumpenhemmer | NaN | | | | | | | | | | |
| 177 | RENITEC - Tabletten 20 mg | Enalaprilmaleat | 20 | 20 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 47476 | RENVELA - Filmtabletten 800 mg | Sevelamercarbonat | 800 | 1 | Phosphatbinder | Niereninsuffizienz | | | | | | | | | | |
| 42394 | RESTEX 100 mg/25 mg - Tabletten | Levodopa | 100 | 1 | DOPA Inhibitor | Parkinson | Benserazid | 25 | 1 | DOPA Agonist | Parkinson | | | | | |
| 43991 | REVATIO - Filmtabletten 20 mg | Sildenafil | 20 | 1 | PDE5 Inhib. | Herzinsuff., Erektionsstörung | | | | | | | | | | |
| 37680 | ROCALTROL-"Roche" 0,25 Mikrogramm - Kapseln (Parallelimport P3) | Calcitriol | 0.00025 | 1 | Vitamin D | Osteoporose | | | | | | | | | | |
| 46212 | SAFLUTAN 15 Mikrogramm/ml - Augentropfen im Einzeldosisbehaeltnis | Tafluprost | 0.00045 | 1 | Prostaglandin | Grüner Star | | | | | | | | | | |
| 293 | SANGENOR - Trinkampullen | Mono-L-Arginin-L-Aspartat | 1000 | 1 | Arginin | Aufbaustoff | | | | | | | | | | |
| 29 | SEDACORON 200 mg - Tabletten | Amiodaronhydrochlorid | 200 | 1 | Antiarrhythmika | Herzinsuff. | | | | | | | | | | |
| 31496 | SELOKEN retard 47,5 mg - Filmtabletten | Metoprololsuccinat | 47.5 | 190 | BB | Herzinsuff. | | | | | | | | | | |
| 31497 | SELOKEN retard 95 mg - Filmtabletten | Metoprololsuccinat | 95 | 190 | BB | Herzinsuff. | | | | | | | | | | |
| 38350 | SERETIDE Diskus forte 50 µg/500 µg einzeldos. Pulver zur Inhalation | Salmeterol | 0.047 | 1 | Inhalativa | COPD | Fluticasonpropionat | 0.46 | 1 | Cortison | COPD | | | | | |
| 39312 | SEROQUEL 100 mg - Filmtabletten | Quetiapin | 100 | 1 | Neuroleptikum | Depression | | | | | | | | | | |
| 45964 | SEROQUEL XR 200 mg - Retardtabletten | Quetiapin | 200 | 1 | Neuroleptikum | Depression | | | | | | | | | | |
| 43861 | SERTRALIN "Ranbaxy" 50 mg - Filmtabletten | Sertralin | 50 | 1 | SSRI | Depression | | | | | | | | | | |
| 48021 | SIFROL - Retardtabletten 0,52 mg | Pramipexol | 0.52 | 1 | DOPA Agonist | Parkinson | | | | | | | | | | |
| 41581 | SIMVASTATIN "1A Pharma" 20 mg - Filmtabletten | Simvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 41582 | SIMVASTATIN "1A Pharma" 40 mg - Filmtabletten | Simvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 47362 | SIMVASTATIN "Bluefish" 20 mg - Filmtabletten | Simvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 41125 | SIMVASTATIN "Genericon" 40 mg - Filmtabletten | Simvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 40871 | SIMVASTATIN "Hexal" 40 mg - Filmtabletten | Simvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 42201 | SIMVASTATIN "Interpharm" 20 mg - Filmtabletten | Simvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 24666 | SINTROM - Tabletten | Acenocoumarol | 4 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 36422 | SORTIS - Filmtabletten 10 mg | Atorvastatin | 10 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 36423 | SORTIS - Filmtabletten 20 mg | Atorvastatin | 20 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 36424 | SORTIS - Filmtabletten 40 mg | Atorvastatin | 40 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 41308 | SORTIS - Filmtabletten 80 mg | Atorvastatin | 80 | 1 | Statine | Herzinsuff. | | | | | | | | | | |
| 41278 | SPIRIVA 18 Mikrogramm - Kapseln mit Inhalationspulver | Tiotropiumbromid-Monohydrat | 0.0225 | 1 | Inhalativa | COPD | | | | | | | | | | |
| 45656 | SPIRIVA Respimat 2,5 Mikrogramm - Loesung zur Inhalation | Tiotropium | 0.0025 | 1 | Inhalativa | COPD | | | | | | | | | | |
| 35376 | SPIROBENE 50 mg - Tabletten | Spironolacton | 50 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 35377 | SPIROBENE 100 mg - Tabletten | Spironolacton | 100 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 21480 | SPIRONO "Genericon" 50 mg - Tabletten | Spironolacton | 50 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 51682 | SPIRONOLACTON "Agepha" - Tabletten | Spironolacton | 100 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 31618 | SPIRONOLACTON "Agepha"-Tabletten | Spironolacton | 100 | 50 | MRA | Herzinsuff. | | | | | | | | | | |
| 53424 | STRIVERDI Respimat 2,5 Mikrogramm - Loesung zur Inhalation | Olodaterol | 0.0025 | 1 | Inhalativa | COPD | | | | | | | | | | |
| 37471 | SULTANOL - Dosieraerosol | Salbutamol | 0.1 | 1 | Inhalativa | COPD | | | | | | | | | | |
| 31089 | SUPRESSIN 4 mg - Tabletten | Doxazosin | 4 | 1 | AntiHyp | NaN | | | | | | | | | | |
| 40344 | SYMBICORT Turbohaler 160 µg/4,5 µg pro Dosis - Pulver zur Inhalation | Budesonid | 0.16 | 1 | Inhalativa | COPD | Formoterolfumarat-Dihydrat | 0.0045 | 1 | Cortsion | COPD | | | | | |
| 41668 | SYMBICORT Turbohaler 320 µg/9 µg forte pro Dosis Pulver zur Inhalation | Budesonid | 0.32 | 1 | Inhalativa | COPD | Formoterolfumarat-Dihydrat | 0.009 | 1 | Cortsion | COPD | | | | | |
| 36451 | TAMOXIFEN "ratiopharm" 20 mg - Tabletten | Tamoxifen | 20 | 1 | Östrogenrezeptormodulator | Mamma-Carcinom | | | | | | | | | | |
| 44071 | TAMSULOSIN "ratiopharm" retard 0,4 mg - Kapseln | Tamsulosinhydrochlorid | 0.4 | 1 | Alphablocker | Prostatahyperplasie | | | | | | | | | | |
| 37199 | TAVANIC - Filmtabletten 250 mg | Levofloxacin | 250 | 1 | Antibiotika | Infektion | | | | | | | | | | |
| 37198 | TAVANIC - Filmtabletten 500 mg | Levofloxacin | 500 | 1 | Antibiotika | Infektion | | | | | | | | | | |
| 24952 | TEMESTA - Tabletten 1,0 mg | Lorazepam | 1 | 1 | Benzodiazepin | Schlafmedikation | | | | | | | | | | |

| uid | Medikamentenname | Name_1 | Dosis_1 | Zieldosis_1 | Gruppe_1 | Indikation_1 | Name_2 | Dosis_2 | Zieldosis_2 | Gruppe_2 | Indikation_2 | Name_3 | Dosis_3 | Zieldosis_3 | Gruppe_3 | Indikation_3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 24953 | TEMESTA - Tabletten 2,5 mg | Lorazepam | 2.5 | 1 | Benzodiazepin | Schlafmedikation | | | | | | | | | | |
| 24967 | TEPILTA - Suspension | Oxetacain | 10 | 1 | Lokalanästhetikum | Gastritis, Ulcus | Aluminiumhydroxid | 291 | 1 | x | NaN | Magnesiumhydroxid | 98 | 1 | Magnesiumersatz | Krämpfe |
| 21931 | THIAMAZOL Sandoz 20 mg - Tabletten | Thiamazol | 20 | 1 | Imidazolon | Hperthyreose | | | | | | | | | | |
| 33038 | THROMBO ASS 50 mg - Filmtabletten | Acetylsalicylsäure | 50 | 1 | TAH | Herzinsuff. | | | | | | | | | | |
| 33029 | THROMBO ASS 100 mg - Filmtabletten | Acetylsalicylsäure | 100 | 1 | TAH | Herzinsuff. | | | | | | | | | | |
| 25048 | THYREX 50 Mikrogramm - Tabletten | Levothyroxin-Natrium | 0.05 | 1 | Thyroxin | Hypothyreose | | | | | | | | | | |
| 25049 | THYREX 100 Mikrogramm - Tabletten | Levothyroxin-Natrium | 0.1 | 1 | Thyroxin | Hypothyreose | | | | | | | | | | |
| 44812 | THYREX 125 Mikrogramm - Tabletten | Levothyroxin-Natrium | 0.125 | 1 | Thyroxin | Hypothyreose | | | | | | | | | | |
| 42702 | TORASEMID "Hexal" 5 mg - Tabletten | Torasemid | 5 | 20 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 42703 | TORASEMID "Hexal" 10 mg - Tabletten | Torasemid | 10 | 20 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 42704 | TORASEMID "Hexal" 20 mg - Tabletten | Torasemid | 20 | 20 | Diuretika | Herzinsuff. | | | | | | | | | | |
| 50959 | TRAJENTA 5 mg - Filmtabletten | Linagliptin | 5 | 1 | Gliptin | Diabtes | | | | | | | | | | |
| 33378 | TRITACE - Tabletten 2,5 mg | Ramipril | 2.5 | 10 | ACE-I | Herzinsuff. | | | | | | | | | | |
| 39074 | TRITTICO retard 75 mg - Tabletten | Trazodonhydrochlorid | 75 | 1 | Antidepressivum | Depression | | | | | | | | | | |
| 39075 | TRITTICO retard 150 mg - Tabletten | Trazodonhydrochlorid | 150 | 1 | Antidepressivum | Depression | | | | | | | | | | |
| 53327 | ULTIBRO Breezhaler 85 µg/43 µg - Hartkapseln mit Pulver zur Inhalation | Indacaterol | 0.085 | 1 | Inhalativa | COPD | Glycopyrronium | 0.043 | 1 | Inhalativa | COPD | | | | | |
| 22990 | URBASON - Tabletten 4 mg | Methylprednisolon | 0.043 | 1 | Cortison | system. Enzündungserkrankung | | | | | | | | | | |
| 22991 | URBASON - Tabletten 40 mg | Methylprednisolon | 40 | 1 | Cortison | system. Enzündungserkrankung | | | | | | | | | | |
| 23023 | UROSIN 100 mg - Tabletten | Allopurinol | 100 | 1 | Harnsäuresenker | Herzinsuff. | | | | | | | | | | |
| 23024 | UROSIN 300 mg - Tabletten | Allopurinol | 300 | 1 | Harnsäuresenker | Herzinsuff. | | | | | | | | | | |
| 50970 | VALSARCOMP 80 mg/12,5 mg - Filmtabletten | Valsartan | 80 | 320 | ARB | Herzinsuff. | Hydrochlorothiazid | 12.5 | 50 | Diuretika | Herzinsuff. | | | | | |
| 47297 | VALSARTAN Actavis 40 mg - Filmtabletten | Valsartan | 40 | 320 | ARB | Herzinsuff. | | | | | | | | | | |
| 47298 | VALSARTAN Actavis 80 mg - Filmtabletten | Valsartan | 80 | 320 | ARB | Herzinsuff. | | | | | | | | | | |
| 49315 | VALSARTAN Sandoz 160 mg - Filmtabletten | Valsartan | 160 | 320 | ARB | Herzinsuff. | | | | | | | | | | |
| 50915 | VALSAX 80 mg - Filmtabletten | Valsartan | 80 | 320 | ARB | Herzinsuff. | | | | | | | | | | |
| 50916 | VALSAX 160 mg - Filmtabletten | Valsartan | 160 | 320 | ARB | Herzinsuff. | | | | | | | | | | |
| 23101 | VERTIROSAN - Dragees 50 mg | Dimenhydrinat | 50 | 1 | Antihistaminikum | Übelkeit, Erbrechen | | | | | | | | | | |
| 31124 | XANOR 0,5 mg - Tabletten | Alprazolam | 0.5 | 1 | Benzodiazepin | Schlafmedikation | | | | | | | | | | |
| 51305 | XARELTO 15 mg - Filmtabletten | Rivaroxaban | 15 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 51306 | XARELTO 20 mg - Filmtabletten | Rivaroxaban | 20 | 1 | AK | Herzinsuff. | | | | | | | | | | |
| 40401 | XATRAL uno 10 mg - Retardtabletten | Afluzosinhydrochlorid | 10 | 1 | Alphablocker | Prostatahyperplasie | | | | | | | | | | |
| 42371 | YOMOGI - Kapseln | Trockenhefe | 250 | 1 | x | NaN | | | | | | | | | | |
| 44184 | ZANIDIP 20 mg - Filmtabletten | Lercanidipinhydrochlorid | 20 | 1 | CC-Blocker | Hypertonie | | | | | | | | | | |
| 23283 | ZANTAC - Filmtabletten 150 mg | Ranitidin | 150 | 1 | Protonenpumpenhemmer | NaN | | | | | | | | | | |
| 31006 | ZANTAC - Filmtabletten 300 mg | Ranitidin | 300 | 1 | Protonenpumpenhemmer | NaN | | | | | | | | | | |
| 40906 | ZOLDEM 10 mg - Filmtabletten | Zolpidemtartrat | 10 | 1 | 0 | Schlafmedikation | | | | | | | | | | |
| 23296 | ZYLORIC 100 mg - Tabletten | Allopurinol | 100 | 1 | Harnsäuresenker | Herzinsuff. | | | | | | | | | | |
| 23297 | ZYLORIC 300 mg - Tabletten | Allopurinol | 300 | 1 | Harnsäuresenker | Herzinsuff. | | | | | | | | | | |
| 31661 | ZYRTEC - Filmtabletten 10 mg | Cetrizindihydrochlorid | 10 | 1 | Antihistaminikum | Allergie, Juckreiz, COPD | | | | | | | | | | |