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## Evaluation of antihypertension using ATC/DDD and DU 90% in outpatient care at Pekanbaru Medical Center (PMC) Hospital

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#### Abstract

**Background**: High blood pressure or hypertension is one of the non-communicable diseases that is still a health problem in Indonesia. A person is diagnosed with hypertension when systolic blood pressure  $\geq$ 140 mmHg or diastolic blood pressure  $\geq$ 90 mmHg on repeated examinations. If this is not treated and lasts for a long time it can cause damage to the kidneys, heart and brain. This study aims to evaluate the use antihypertensives with the ATC/DDD method and DU 90% in outpatients at Pekanbaru Medical Center (PMC) Hospital in 2023.

**Method**: This study is an observational study with a descriptive design and retrospective data collection using secondary data by searching medical records, purposive sampling technique. The sample in this study were all outpatients with the main diagnosis of hypertension. The sample used was 320 patient medical record. Quantitative data analysis using the ATC/DDD method and measuring the use of antihypertensives to obtain DDD values using Daily Dose based on guidelines issued by WHO and combined with DU 90%. Data is processed using Microsoft excel, then arranged in table format based on ATC/DDD codes.

**Results**: The results showed that based on the ATC/DDD methods and DU 90%, it can be concluded that there are 4 hypertension drugs with the highest quantity of use which are included in the DU 90% segment.

**Conclusion**: There are 4 drugs included in the 90% DU segment, namely Amlodipine of 519,66 DDD/1000 KPRJ (33,16%), Ramipril of 432,51 DDD/1000 KPRJ (27,60%), Candesartan of 374,64 DDD/1000 KPRJ (23,90%) and Furosemide of 64,06 DDD/1000 KPRJ (4,09%).Based on the results obtained it is recommended that hospitals continue to monitor availability and pay attention to the planning and procurement of antihypertensives which are included in the 90% DU Segment

Keywords: Antihypertension; ATC/DDD; DU 90%

### INTRODUCTION

Hypertension is a condition where a person experiences an increase in systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg in two measurements with an interval of five minutes in a state of sufficient rest or calm (Indonesian Ministry of Health, 2013a). Hypertension is often referred to as The Silent Killer because in general hypertensive patients do not show any signs or symptoms (1).

Data from the World Health Organization (WHO) in 2015 shows that the number of hypertension sufferers doubled between 1990 and 2019 from 650 million to 1.3 billion. Hypertension affects 1 in 3 adults

worldwide. Nearly half of hypertension sufferers throughout the world are currently unaware of their condition. More than threequarters of adults with hypertension live in low- and middle-income countries (2).

The prevalence of hypertension, based on the 2018 Basic Health Research data, shows that the most cases of hypertension in Indonesia occur in the age group  $\geq$  18 years, with a percentage of 25.8%. There was an increase in the incidence of hypertension in 2018, namely with a percentage of 34.11%. The prevalence of high blood pressure in women reached 36.85%. This figure is higher than the prevalence of high blood pressure in men, namely 31.34% (3). Based on data from the 2019 Riau Province Health Profile, the incidence of essential hypertension ranks second with 198,543 cases (17.8%) after upper respiratory tract infections with 378,307 cases (33.9%) (4).

Hypertension is a major risk factor for coronary and ischemic heart disease and hemorrhagic stroke. The risk of cardiovascular disease doubles for every 20/10 mmHg increase in blood pressure. Apart from coronary heart disease and stroke, other complications due to hypertension are heart failure, peripheral vascular disease, kidney problems, retinal hemorrhages and vision problems (1).

In order to avoid fatal complications of hypertension, good preventive measures must be taken (Stop High Blood Pressure), namely by using therapy which consists of two types, namely pharmacological therapy and non-pharmacological therapy. Pharmacological therapy by using is antihypertensive drugs which have been proven to reduce and control blood pressure. Compliance with taking medication regularly is required so that the patient's blood pressure controlled because can be regular examinations have an important meaning in treating hypertension so that the patient's blood pressure remains within normal limits. (5).

Evaluation of drug use can be done both quantitatively and qualitatively. Quantitative evaluation can be carried out using the ATC/DDD and DU 90% methods to evaluate the type and amount of antihypertensive used (6).

The Anatomical Therapeutic Chemical (ATC) and Defined Daily Dose (DDD) classification systems are units of measurement for drug use in drug use research and development recommended by the World Health Organization (WHO) as international standards for research evaluating drug use. DDD is the average daily maintenance dose used for its main indication in adults. DDD is only available for drugs that have an ATC code (7).

The advantage of the ATC/DDD method is that it is a fixed unit that cannot be influenced by changes in currency and prices

and dosage forms, so that research results can be more easily compared between institutions, nationally, regionally and internationally. The weakness of the ATC/DDD method is that it is not a complete unit for all drugs (topicals, vaccines, local or general anesthetics, etc.) and is not yet used in children (8).

The ATC/DDD and DU 90% methods have been carried out by several researchers, Ulfa and Kautsar (2019) on 24,173 patient cases at Dr. Hospital. H. A Rotinsulu, antihypertensive drugs which include a DU of 90% are Amlodipine 270.54 DDD/1000 KPRJ, then Furosemide 45.29 DDD/1000 KPRJ and Irbesartan 43.74 DDD/1000 KPRJ (9). Research conducted by Destiani et al., (2016) on 4,179 cases of patients who received antihypertensive drugs in outpatient health facilities with the use of antihypertensive drugs including a DU of 90%, namely Amlodipine, was 171.8 DDD/1000 KPRJ, followed by Irbesartan 47.38 DDD/1000 KPRJ and Captopril 40.74 DDD/1000 KPRJ (10). Research conducted by Asih at the Sidomulyo Pekanbaru Inpatient Health Center in 2021 used antihypertensive drugs which included 90% namelv Amlodipine DU. 2678.78 DDD/1000 KPRJ. then there was Candesartan 222.64 DDD/1000 KPRJ and Furosemide 45.42 DDD/1000 KPRJ (11).

At PMC Hospital, research has never been conducted on evaluating the use of antihypertensives using the ATC/DDD and DU 90% methods and hypertension is the disease with the highest cases. As cases of hypertension and complications continue to increase, the use of antihypertensives is increasing and there is little research in several hospitals, especially in Pekanbaru City.

The research objectives are to determine the classification of drug use using ATC codes, look at the profile of antihypertensive use and determine the antihypertensive number of uses in outpatients using DDD calculations and evaluate drugs that fall into the 90% DU segment. It is hoped that the benefits of this research can be used as a source of additional information in terms of management such as planning and procurement of antihypertensives at PMC Hospital.

## METHOD

This research was carried out from March to July 2024 at Pekanbaru Medical Center (PMC) Hospital. This research is a descriptive observational studv with retrospective data collection techniques on outpatients at PMC Hospital in 2023. The population in this study were all patients with a primary diagnosis of hypertension in outpatients at PMC Hospital during January to December 2023, totaling 1448 patients. The inclusion criteria in this study were patient medical records that were complete and could be read clearly with a patient age limit of  $\geq 18$ years. The exclusion criteria were patient death and hypertension during pregnancy. Sampling was carried out using a non-random method. namely purposive sampling technique. The sample size calculation for this study used a formula from Taro Yamane and sample of 320 patients was obtained.

Data collection in this study was retrospective data. The data taken is secondary data in the form of medical records of outpatients at PMC Hospital. The data taken includes drug data in the form of the name of the antihypertensive, dose and number of uses which are then recorded on the data collection sheet.

Data is processed using Microsoft Excel, then arranged in table format based on ATC/DDD codes. Data processing and analysis is carried out in the following stages: 1. Patient Characteristics

Calculate the number and percentage of patients who received antihypertensive therapy during January to December 2023 based on gender and age.

### 2. ATC classification

Each drug is given an ATC code in accordance with the guidelines set by WHO, which can be seen at the following link: (<u>https://www.whocc.no/atc\_ddd\_index\_and\_uidelines/guidelines/</u>).

### 3. Defined Daily Dose

Each drug is given DDD in accordance with the guidelines set by WHO, which can be

seen	at	the	follov	ving	link:
(https://v	www.wl	hocc.no/atc	ddd	index	and
guideline	es/guid	elines/).			

4. Number of antihypertensive doses Number of doses = Quantity of Drug Use (tablets) × Dosage Strength (grams)

5. Total antihypertensive DDD  
Total DDD = 
$$\frac{\text{Number of doses}}{\text{Value DDD}}$$

6. Number of KPRJ (Outpatient Visits) per year. The number of outpatient visits in 2023 will be 46,861 KPRJ.

7. Calculation of Quantity Use of Antihypertensives based on DDD (Defined Daily Dose)

8. Percentage of Antihypertensive Use

The results of the DDD/1000 KPRJ calculation are then converted into the percentage of antihypertensive

9. Calculation of Antihypertensive

Percentage and 90% DU segment Calculate the percentage of antihypertensives included in the 90% DU segment by sorting the percentage from largest to smallest followed by calculating the cumulative percentage of antihypertensives included in the 90% DU segment.

## RESULTS

After analyzing data on the use of antihypertensives in outpatients at Pekanbaru Medical Center (PMC) Hospital in 2023, data recapitulation was carried out and the following results were obtained:

a. Characteristics Based on GenderTable 1. Patient Characteristics Based on

Gender

Gender	Amount	Percentage
Woman	202	63,13%
Man	118	36,87%
Total	320	100%

Based on (table 1) data on patient characteristics based on gender, it is known

# that women receive the most antihypertensive therapy

b. Characteristics Based on Age

#### Table 2. Patient Characteristics Based on Age Range

Age Range	Amount	Percentage (%)	Female	Male
Late Adolescence (18-25 Years)	0	0	0	0
Early Adulthood (26-35 Years)	4	1,25%	1	3
Late Adulthood (36- 45 Years)	25	7,81%	16	9
Early Elderly Age (46-55 Years)	98	30,63%	66	32
Late Elderly Age (56-65 Years)	110	34,37%	70	40
Old Age (> 65 Tahun)	83	25,94%	49	34
Total	320	100%	202	118

Based on (table 2) data on patient characteristics based on age, those who received the most antihypertensive therapy were the late elderly (56-65 years).

 Table 3. Use of Antihypertensives in Outpatients Included in the 90% DU Segment at PMC Hospitals in 2023

No.	Drug Name	DDD/1000 KPRJ	Percentage (%)	Cumulative Percentage	DU 90%	
1.	Amlodipine	519,66	33,16	33,16		
2.	Ramipril	432,51	27,60	60,76	90%	
3.	Candesartan	374,64	23,90	84,66		
4.	Furosemide	64,06	4,09	88,75		
5.	Spironolactone	47,97	3,06	91,81		
6.	Bisoprolol	41,21	2,63	94,44		
7.	Valsartan	28,64	1,83	96,27		
8.	Hydrochlorothiazide	22,68	1,45	97,72		
9.	Nifedipine	11,18	0,71	98,43	1.09/	
10.	Clonidine	9,01	0,58	99,01	10%	
11.	Carvedilol	7,12	0,45	99,46		
12.	Captopril	6,42	0,41	99,87		
13.	Propranolol	1,17	0,07	99,94		
14.	Diltiazem	0,97	0,06	100		
Total		1.567,24	100		100%	

The data in (table 3) shows that the candesartan and drugs that fall into the 90% DU segment after spironolactone, b being cumulated are amlodipine, ramipril, hydrochlorothiazide,

candesartan and furosemide while spironolactone, bisoprolol, valsartan, hydrochlorothiazide, nifedipine, clonidine, carvedilol, captopril, propranolol and diltiazem fall into the DU segment 10%. Drugs that fall into the 90% DU segment are the drugs that are most widely used.

### DISCUSSION

Based on research that has been conducted, it is known that the largest number of patients who received antihypertensive therapy were women at 63.13%. This is caused by psychological factors. Women are more easily stressed than men due to several factors, including hormones, where women have hormone levels whose changes fluctuate more than men. In men, one hormone cycle is 24 hours, while women's hormones are 28 days and consist of several different phases. Then there are genetic factors and also personal relationship factors such as work and family (12).

Stress can be considered a causative factor for hypertension because stress can cause hyperactivity of the sympathetic nervous system and cause increased blood pressure due to increased catecholamine secretion. Catecholamines consistina of adrenaline, noradrenaline, thyroxine and cortisol will increase and have a significant effect on the homeostasis system. Then adrenaline, which works synergistically with the sympathetic nervous system, will cause vasoconstriction so that more blood is pumped. This will affect the increase in heart rate and blood pressure (3).

The prevalence of hypertension in men is the same as in women. However, women are protected from cardiovascular disease before menopause. Women who have not experienced menopause are protected by the hormone estrogen which plays a role in increasing High Density Lipoprotein (HDL) levels. High HDL cholesterol levels are a protective factor in preventing the process of atherosclerosis. The protective effect of estrogen is thought to explain the existence of premenopausal female immunity. In premenopause, women begin to lose bit by bit the hormone estrogen which protects blood vessels from damage (13). This is in line with the research results that there were 110

patients in the late elderly (56-65 years), with a greater number of women, namely 70 patients, affected by hypertension compared to 40 men.

34.37% more elderly people (56-65 years) received antihypertensive therapy compared to other age ranges. Age is one of the factors that influences blood pressure. Research by Liao et al (2017) found that the increased risk of hypertension in the elderly is related to a decrease in the longitudinal systolic strain of the atrium which loses its flexibility and becomes stiff because blood with each heart beat is forced to pass through narrower blood vessels than usual and causes blood pressure to rise (14).

As a person ages, they are more likely to suffer from hypertension too, this could be caused by structural changes in large blood vessels. This is in line with the results of research conducted by Maulidina (2019) which shows that there is a significant relationship between age and the incidence of hypertension because age >60 years increases the incidence of hypertension due to natural changes in the body which affect the elasticity of blood vessels (15).

The results of this study are in agreement with Zhu et al (2016) who stated that physiological changes associated with aging cause an increase in systolic blood pressure, an increase in mean arterial pressure, an increase in pulse pressure and a decrease in the ability to respond to sudden hemodynamic changes. The aging process is associated with changes in the vascular system, heart, and autonomic system (16).

in blood pressure The increase associated with the aging process is most likely related to changes in the arteries. Aging causes narrowing of the blood vessel lumen and hardening of the blood vessel walls through a process known as atherosclerosis. Atherosclerosis causes structural changes including increased vascular calcification that causes pressure waves that were previously reflected during blood pressure wave propagation. Pressure waves come back from the aortic root during systole and contribute to

Regarding vascular structure and function, in young individuals, the peripheral arterial system is stiffer than the central arterial system. Over time, this condition reverses, with older individuals having greater central arterial stiffness compared with peripheral arteries. This reversal and increase in stiffness of the greater central arteries is multifactorial in etiology. Changes in structural components, increased reactive oxygen species, inflammatory changes, and endothelial dysfunction are some of the causes that lead to changes in arterial structure and function seen in aging (17).

The most widely used antihypertensive is the Calcium Channel Blocker (CCB) group with the largest order of use, namely amlodipine at 33.16%, nifedipine at 0.71% and diltiazem at 0.06%. Amlodipine is a firststage CCB group, this drug can be used as a single or combination therapy. The this antihypertensive mechanism of in lowering blood pressure is by inhibiting the entry of calcium into arterial blood vessel cells, thereby causing dilatation of peripheral arteries. CCB is indicated for patients who have high risk factors for coronary disease and diabetes patients (18).

The highest DDD/1000 KPRJ value is amlodipine, namely 519.66 DDD/1000 KPRJ, this value means that in one year there are 519 patient visits who receive 1 DDD amlodipine 5 mg/day. It can be seen that amlodipine is an antihypertensive with the highest DDD value compared to other types of antihypertensives used, this is comparable to research conducted by Asih (2021) that the most antihypertensive drugs used are the CCB group, especially amlodipine.

Nifedipine with a DDD value of 11.18 DDD/1000 KPRJ, this value means that in one year there are 11 patient visits who receive 1 DDD of nifedipine of 30 mg/day. Nifedipine is rarely used, possibly because nifedipine is a short-acting drug. The use of nifedipine must be taken 3 times a day with a regimen that is

too frequent and patient compliance does not go according to the provisions, resulting in increased attack recurrence rates (19).

Diltiazem with a DDD value of 0.97 DDD/1000 KPRJ, this value means that in one year there is 1 patient visit who receives 1 DDD of diltiazem of 0.24 g/day. Diltiazem is a non-dihydropyridine CCB antihypertensive which reduces heart rate, slows atrioventricular node conduction and produces ionotropic effects (20).

Table 4 shows that the most widely used type of antihypertensive is the Angiotensin Receptor Blocker (ARB) group with the highest order of use, namely candesartan at 23.90% and valsartan at 1.83%. The DDD value for candesartan is 374.64 DDD/1000 KPRJ, this value means that in one year there are 374 patient visits who receive 1 DDD candesartan of 8 mg/day. The DDD value of valsartan is 28.64 DDD/1000 KPRJ, this value means that in one year there are 28 patient visits who receive 1 DDD of valsartan of 80 mg/day. The antihypertensive mechanism is by blocking the binding of angiotensin II to its receptor, both ACEI and ARB have a vasodilation effect which can lighten the burden on the heart. ARB drugs have no effect on bradykinin metabolism, and are more selective inhibitors of angiotensin effects compared to ACEIs (21).

The next antihypertensive used is the diuretic group consisting of furosemide at 4.09%. spironolactone 3.06% and at hydrochlorothiazide at 1.45%. Furosemide is a diuretic drug with a DDD value of 64.06 DDD/1000 KPRJ, this value means that in one year there are 64 patient visits who receive 1 DDD of furosemide of 40 mg/day. Spironolactone with a DDD value of 47.97 DDD/1000 KPRJ, this value means that in one year there are 47 patient visits who receive 1 DDD spironolactone of 75 mg/day. Hydrochlorothiazide with a DDD value of 22.68 DDD/1000 KPRJ, this value means that in one year there are 22 patient visits who receive 1 DDD of hydrochlorothiazide of 25 mg/day.

Furosemide works by increasing the body's sodium excretion thereby reducing blood volume and extracellular fluid which results in a decrease in cardiac output and blood pressure. Diuretics are effective in lowering blood pressure in most patients by 10-15 mmHg, this class of diuretic drugs is an adequate treatment for mild or moderate essential hypertension (21).

The next antihypertensive used is the Angiotensin Converting Enzyme Inhibitor (ACEI) group which consists of ramipril at 27.60% and captopril at 0.41%. Ramipril with a DDD value of 432.51 DDD/1000 KPRJ, this value means that in one year there are 432 patient visits who receive 1 DDD of ramipril of 2.5 mg/day. Captopril with a DDD value of 6.42 DDD/1000 KPRJ, this value means that in one year there are 6 patient visits who receive 1 DDD captopril of 50 mg/day.

The antihypertensive mechanism of the ACEI class is to inhibit the conversion of angiotensin I to angiotensin II, resulting in vasodilation and decreased aldosterone secretion. In addition, bradykinin degradation is also inhibited so that bradykinin levels in the blood increase and play a role in the vasodilation effect. Vasodilation will directly reduce blood pressure, while reduced aldosterone will cause water and sodium excretion and potassium retention. Both ACEI and ARB have a vasodilation effect which can lighten the burden on the heart. ACEI/ARBs are used for therapy in all patients, except those with certain contraindications. All hypertensive patients accompanied by diabetes mellitus must be treated with ACEI/ARB because this drug has no effect on the total blood volume in the cerebral blood vessels and reduces the risk of kidney dysfunction in diabetes patients (18).

The next antihypertensive used in the Beta Blocker group is bisoprolol at 2.63%, carvedilol at 0.45% and propranolol at 0.07%. Bisoprolol is a Beta Blocker drug with a DDD value of 41.21 DDD/1000 KPRJ, this value means that in one year there are 41 patient visits who receive 1 DDD of bisoprolol of 10 mg/day. Carvedilol with a DDD value of 7.12 DDD/1000 KPRJ, this value means that in one year there are 7 patient visits who receive 1 DDD carvedilol of 37.5 mg/day. Propranolol with a DDD value of 1.17 DDD/1000 KPRJ, this value means that in one year there is 1

patient visit who receives 1 DDD of propranolol of 0.16 g/day.

The beta blocker class works bv inhibiting beta 1 receptors by reducing heart rate and reducing myocardial contractions, thereby lowering blood pressure. Use of a combination of beta blockers such as bisoprolol to control blood pressure and reduce the risk of infarction, coronary heart disease, reduce oxygen demand from the heart, and to stabilize myocardial contractility. Beta blocker drugs are effective in 50 - 70%of patients with mild to moderate hypertension. The antihypertensive use of bisoprolol is more common than carvedilol and propranolol because bisoprolol is a selective beta blocker and has a higher affinity for beta 1 receptors than beta 2 (21).

The next antihypertensive used in the Central Alpha Agonist group is clonidine at 0.58%. Clonidine with a DDD value of 9.01 DDD/1000 KPRJ, this value means that in one year there are 9 patient visits who receive 1 clonidine of 0.45 mg/day. DDD The mechanism of action of this drug is via agonist alpha-2 adrenoceptors in the posterior hypothalamus and medulla. This effect causes sympathetic outflow to the central nervous system to decrease, which clinically lowers arterial blood pressure. This class of drugs is the main choice for hypertensive patients who have high sympathetic nerve activity such as tachycardia, anxiety, hyperhidrosis, etc. The types of Central Alpha Agonist that are widely circulated are reserpine, clonidine and methyldopa (21).

Based on this research, a very high difference was obtained, namely that the DDD value of amlodipine was much greater than the DDD value of other antihypertensives. This could be because the high amount of antihypertensive use can cause the number of grams of antihypertensive use to increase, causing the amount of antihypertensive use to be higher and this has an effect on the high DDD/1000 KPRJ value produced.

Amlodipine is a dihydropyridine CCB group. Systolic Hypertention-Europe conducted a placebo-controlled trial that showed that long-acting dihydropyridine CCBs reduced the risk of cardiovascular events. CCB causes relaxation of the heart and smooth muscles by inhibiting voltagesensitive calcium channels, thereby reducing the influx of extracellular calcium into cells. Vascular muscle relaxation causes vasodilation and is associated with a reduction in blood pressure. Amlodipine is vasculoselective, has relatively low oral bioavailability, has a long half-life, and slow absorption, thereby preventing sudden drops in blood pressure (22).

The dihydropyridine group is usually used in patients whose blood pressure is not well controlled with ACEI/ARB, because dihydropyridine CCBs have a good ability to lower blood pressure in a short time and from the results of this study, hypertensive patients with diabetes mellitus comorbidities mostly use amlodipine and it is appropriate with antihypertensive therapy guidelines according to JNC VIII. When someone has hypertension and is accompanied by diabetes mellitus, the treatment management is to use ACEI/ARB, but if the patient is intolerant to this group then they can be given the CCB class of drugs (23).

In this study, antihypertensives were used either alone or in combination. Hypertensive patients, if their blood pressure is far from the target, the target is difficult to achieve, or patients with various compelling indications such as elderly patients, combination therapy is often needed (24).

Based on the results of the evaluation of antihypertensives used in outpatients at Pekanbaru Medical Center (PMC) Hospital, it can be seen from (table 4) that there is an order of antihypertensive use from largest to smallest. The results show 4 antihypertensives which are included in the 90% DU segment, namely amlodipine, ramipril. candesartan and furosemide. Antihypertensives that fall into the 10% segment are spironolactone, bisoprolol, valsartan, hydrochlorothiazide, nifedipine, clonidine, carvedilol, captopril, propranolol and diltiazem.

Based on these data, it shows that there are similarities between the use of antihypertensive drugs in outpatients at PMC Hospital in 2023 with the treatment Evaluation of Antihypertension Using ATC/DDD and DU 90% In Outpatient Care At Pekanbaru Medical Center (PMC) Hospital

management in JNC VIII which recommends therapy starting with lifestyle modification and if the goal is not achieved then the CCB group is used first for hypertension without indication. comorbidities and also adjusted for comorbidities such as diabetes mellitus. The CCB class of drugs has a vasodilation effect, slows the heart rate and reduces myocardial contractility, causing a decrease in blood pressure (25).

Amlodipine is a calcium antagonist antihypertensive which is used as monotherapy or in combination with other classes of drugs such as ACEI, ARB, diuretics or beta blockers in the management of Amlodipine hypertension. is also recommended by JNC VIII as a first-line antihypertensive because it has a long halflife and slow absorption, thereby preventing sudden drops in blood pressure (23).

## CONCLUSIONS

Based on studies of the assessment of the use of antihypertension in outpatient patients at the Pekanbaru Medical Center (PMC) in 2023 with ATC/DDD and DU 90% methods. it concluded is that 4 antihypertension coupled with the highest number of uses included in segment DU 90% of amlodipin is 519,66 DDD/1000KPRJ (33,16%), ramipril of 432,51 DDD/1000 KPRJ (27,60%), The candesartan is 374,64 DDD/1000KPRJ (23,90%) and furosemide is 64,06 DDD/ 1000/KPRJ (4,09%).

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