ADHERENCE **PATIENT**

Guide for HEALTH PROFESSIONALS

The main objective of this manual is ordering, in a didactic manner, the actions that can be implemented by health professionals to improve patient adherence to treatment.

HEMORIO
BLOOD CENTER OF RIO DE JANEIRO

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PATIENT ADHERENCE

Guide for health professionals

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PREFACE

This booklet is intended to make a modest contribution about main concepts and actions of the patient's adherence to their treatment, targeting primarily the health care professionals.

With an interdisciplinary, represents in its essence, the experience of HEMORIO in search of quality health care to its patients, particularly those with hereditary chronic diseases or cancer, whose adherence is of particular significance in the outcome of treatment.

In part 1, are revised essential concepts to a proper orientation of the reader for that matter. Following is a list of compliance actions, supported by literature, mixed with the experiences of HEMORIO professionals.

The presentation of adhesion's actions, separated by profession, is purely didactic, because the biggest challenge being faced is to create strong links between all healthcare staff, patients and their families. The more harmonious is this tripod, the greater the chances of success.

Thus, if the patient and his family felt welcomed by all professionals working in the hospital, means that more than health professionals; they represent a team that works in several directions, to achieve the same target.

Finally, we present some observations, the fruit of our experience in clinical practice and we consider relevant to follow up with certain medications.

Vera Marra
Medical Director of HEMORIO

CONTENTS

CONCEPTS

Adherence is the reflection of the interactive behavior between patients and health professionals, focusing on the fulfillment of the requirements, not only correct but also of vaccines, the attendance to the clinic, changes in behavior with regard to hygiene personnel, adequate contraception, avoiding risky sexual behavior, poor diet, physical activity, among many other recommendations. [1, 2]

There are several synonyms for adherence, adherence, compliance, complacency loyalty and compliance. This latter terminology translated into Portuguese as "participatory obedience" would be possibly the best term to be employed. But remember not to passivity of the patient, the terms most used are adhesion and adhesion. [1, 2]

The term concordance reveals a new concept, broader than adherence or noncompliance with an idea where the focus is understanding and shared decision making in relation to drug treatment, drug user and the multidisciplinary team (doctors, nurses and pharmaceutical) on how, where and at what time the drugs will be used.[3]

There are few publications on this subject. Thus, there is no exact measure of the magnitude of the problem as to its consequences for health. According to some studies, about 40% of patients do not adhere to the proposed treatment.[4,5]

From the economic point of view, it is believed that the lack of adherence to treatment leads to a loss of $ 100 billion per year in the U.S.[6] In Brazil, there is no information on the subject.

DIMENTIONS OF ADHERENCE

For WHO adherence is a multidimensional phenomenon that is influenced by various factors that are didactically presented as the "five dimensions of adherence"[6]:

1 - Patient-related factors: The main factors are inherent to the patients, are sex, age, ethnicity, marital status and education level. For example, adolescents have a lower rate of adherence than children, not only because known rebellion own age, but also because they depend on responsible for the administration of medication, which increases the risk of noncompliance. In elderly patients, this risk is also relevant, due to impairment of cognitive functions.

2 - Therapy-related factors: chronic disease and its treatment and absence of symptoms, represent important factors affecting the degree of patient adherence to therapy. Study conducted in Brazil, with hypertensive patients reported that 36% of these were not adherent to treatment because they are asymptomatic, while 70% claimed to know the characteristic of chronic hypertension and its complications.

3 - Therapy-related factors: There are many factors that are related to therapy, such as complexity, duration, ineffectiveness of previous treatments, constant changes in treatment, immediate effects of medications, side effects and required the use of adjuvant drugs.

4 - Social and economic-related factors: The low socio-economic and education are mentioned as one of the more common modulators of adherence. Also related to socioeconomic conditions are: living away from the treatment center, high cost of transportation and / or medication, family problems and, above all, cultural issues that affect the perception and knowledge about the disease.

5 - Health System/Health Care Team-Related Factors: The role of health services and especially professionals who are extremely patient. The culture of consensus and negotiation with patients and families should come from those who are the actors who have the knowledge and that are ultimately responsible for the balance of this asymmetrical relationship.

INTERACTING DIMENSIONS

In many cases, there is not one single factor involved in the absence of adhesion. However, the factors related to the health system and especially the team of professionals who provide patient care corresponds to the central object of this manual.

As discussed above, adherence implies obedience participatory and this term refers to the pact, which must be clear to both the health professional for the patient and / or family, that the best outcome is the goal of both. In this way is not enough to provide them a paper with the requirements and recommendations because they can simply not be met. Similarly, consult a doctor and receiving him a prescription does not necessarily follow in a cure.

The majority of the studies in the area of adhesion suggests that the physician-patient relationship plays an important role in this process, however, there is no doubt that the multidisciplinary approach is the decisive factor and irreplaceable.

In order to answer the question "What are effective interventions to improve adherence to drug treatment?" Dalla[7] made an extensive research literature on this subject, focusing on articles that addressed chronic outpatient treatment and / or home care as well as articles addressing pharmacological treatments. Some of them are discussed.

Bellow we list the main interventions for improvement of adherence, trying to correlate them to different members of a health team. We must highlight that this is not intended to reflect an inflexibility of the actions by category, and that many or all should be followed by any health professional.

THE ROLE OF THE PHYSICIAN

"The patient compliance rests on the good relationship with the doctors who assist him."

Minchie [8] and collaborators showed strong evidence that the higher perception by patient's involvement in medical consultation, the greater will be its adherence to medication. According to Atreja[9], strategies to improve adherence are identified by what he called a mnemonic acronym, SIMPLE, in which each letter stands for an action, as described below:

Simplifying Therapeutic plan	Avoid, whenever possible, the use of multiple drugs in varying doses, daily.
Imparting knowledge:	Inform about the condition, the necessity of the therapy and what it seeks to achieve, as guide to all treatment options, assess risks and benefits with the patient and decide how best to treat it. It is recommended the distribution of textbooks with explanations in simple language and accessible to all. We recommend reading this leaflet, during consultations, in an attempt to stimulate the patient to get better acquainted with the recommendations. It is desirable to periodically make available to the patient and family time, for information about treatment, the results and future prospects, following the degree of adhesion.
Modifying patient beliefs:	It is worth addressing patients' beliefs and perceived ability to perform the recommended action. The doctor may tailor interventions to suit the unique needs of each patient.
Patient communication:	Making an excellent history and physical examination is not enough. It is necessary to engage with the feelings and concerns of the patient, strengthening the vital doctor-patient relationship, which is the foundation of trust and therefore adherence to treatment.
Leaving the bias:	Haynes[1] found no relationship between adherence, race, sex, educational background, intelligence, status, occupational status, income and ethnic or cultural backgrounds.
Evaluating adherence:	Evaluation of degree of compliance can be done by interviewing the patient, pills count and possibly measurement of serum levels of drugs in urine. Moreover, regular assessment of patient adherence alone can lead to increased patient compliance.

THE ROLE OF THE PHARMACIST

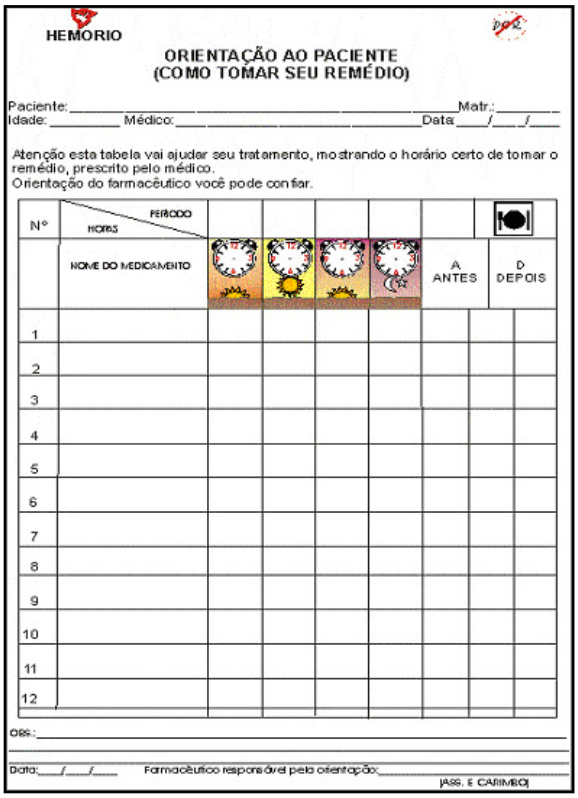
"The pharmacist has a fundamental commitment to play in regard to patient compliance with drug treatment. Pharmacotherapy allows obtaining adequate health care safe and economical, with important consequences for patients, health management, and society in general. "

In general, the pharmacist is the professional core of the process of adhesion, since pharmaceutical care is primarily to explain the doctor's prescription to the patient, family and caregiver.

The pharmacist can assist in finding appropriate treatment results and prevent to a large extent, the emergence of drug-related problems (DRP) and negative outcomes associated with drugs[12] through the practice of pharmaceutical care, according to the proposal Brazilian Consensus on Pharmaceutical Care, the practice of pharmaceutical care has six components[13]:

HEALTH EDUCATION	Includes the promotion of rational use of medicines, along with the patient and family.
PHARMACEUTICAL ORIENTATION	It involves helping the patient in the correct decisions for self care of their health. It is important to make clear to patients what effects
CONSULTATION OR PHARMACEUTICAL ASSISTANCE	The pharmacist will trace the patient profile about his degree of adherence, in order to plan with other team members, the most appropriate strategy for the patient.
PHARMACEUTICAL MONITORING AND FOLLOW-UP	It is based on monitoring and systematic recording of the therapy and contributes decisively to the adherence.
RESULTS EVALUATION	The use of instruments such as ROMI scale (Rating Of Medication Influences) may be useful to evaluate the individual or collective adherence. Morisky test [14] is another evaluation tool. ROMI scale was developed by Weiden and collaborators[10] for evaluation of the factors that influence the behavior of schizophrenic patients with neuroleptic treatment, believing that non-adherence is the major barrier to these patients. Although, it can be used in other types of patients.

During the dispensation is important to check the patient's understanding about the correct way to use and instructing him to his rational, and if necessary, use auxiliary tools. Figures 1 and 2 show the forms used by HEMORIO for this purpose.



HEMORIO

ORIENTAÇÃO AO PACIENTE
(COMO TOMAR SEU REMÉDIO)

Paciente: _____ Matr.: _____
Idade: _____ Médico: _____ Data: ___/___/___

Atenção esta tabela vai ajudar seu tratamento, mostrando o horário certo de tomar o remédio, prescrito pelo médico.
Orientação do farmacêutico você pode confiar.

Nº	PERÍODO / HORAS						
	NOME DO MEDICAMENTO					A ANTES	D DEPOIS
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							

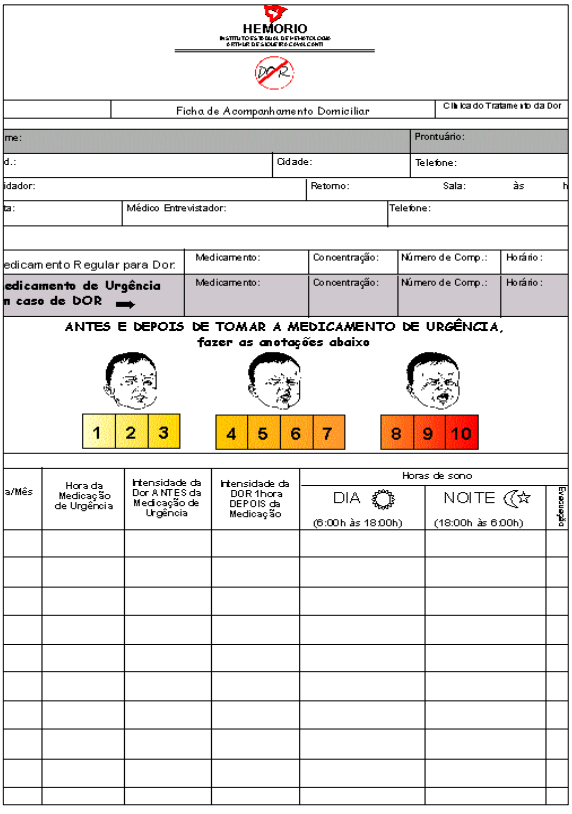
OBS: _____

Data: ___/___/___ Farmacêutico responsável pela orientação: _____
ASS. E CARIMBO

Figure 1: Orientation form of prescription drugs, used by Hemorio.

When properly used, the drug is the therapeutic option with greater cost-effectiveness. Your misuse, however, is a major public health problem worldwide, with major economic consequences. The purpose of this tool is to promote rational and safe use of these products[13].

It is known that socioeconomic factors have a decisive influence in the delivery of health care and rational use of medicines. Taking as a basis for the WHO publication, 2007 (Use of Concordance to Improve Patient Adherence)[11], poor adherence to drug treatment in patients with chronic illnesses undermines the effectiveness of treatment, becoming a critical public health both in terms of increasing quality of life, and in relation to the economic impact generated.



HEMORIO

Ficha de Acompanhamento Domiciliar — Clínica do Tratamento da Dor

me: Prontuário:
d.: Cidade: Telefone:
idador: Retorno: Sala: às
ta: Médico Entrevistador: Telefone:

edicamento Regular para Dor:	Medicamento:	Concentração:	Número de Comp.:	Horário:
edicamento de Urgência n caso de DOR ➡	Medicamento:	Concentração:	Número de Comp.:	Horário:

ANTES E DEPOIS DE TOMAR A MEDICAMENTO DE URGÊNCIA, fazer as anotações abaixo

1 2 3 | 4 5 6 7 | 8 9 10

a/Mês	Hora da Medicação de Urgência	Intensidade da Dor ANTES da Medicação de Urgência	Intensidade da DOR 1hora DEPOIS da Medicação	Horas de sono: DIA (6:00h às 18:00h)	NOITE (18:00h às 6:00h)	Observações

Figure 2: Type of monitoring side effects in patients with chronic use of opioids used by Hemorio:

The WHO recommends reducing drug associations and introduces the use of single medication, in the face of the observation that the toxicity of drugs increases in direct proportion to the number of competing drugs. Therefore the consequences of interactions should be evaluated carefully before the application of therapy with multiple medications[15].

The effects of many drugs are altered by the excipient or solvent used to prepare medicamentos[16] as well as for food, through its nutrients, which interfere with medications, thus altering the effects of these [17].

THE ROLE OF THE SOCIAL WORKERS

"Identifying and overcoming the barriers of social nature that interfere with patient compliance to treatment is one of the activities of social workers in hospitals, justifying the presence of this professional in health teams."

ACTIVE SEARCH FOR THE ACCESSION TREATMENT CLINICAL	The professional seeks to identify whether patient is not attending the scheduled appointments, calls for interviews and advice on the importance of treatment, acting directly and in a personalized way in each case.
MEETING WITH PATIENTS AND FAMILY	These are spaces for presentation of the institution, exchange experiences and information about rights and benefits and the importance of treatment compliance.
ASSISTANCE DIRECTED TO THE PATIENTS' RIGHTS	Calls are directed to patients and their families toward the rights of patients, identification of demands and routing to relevant resources.

THE ROLE OF THE PSYCHOLOGIST

"People do not" adhere "just to" treatment", but make connections with professionals who care for the various aspects of their health by treating them with attention, care and respect. It is through these ties that they will be able to trust, listen and better meet the recommendations."

Treatment reminds disease, something that most people looking to keep the thought away, or remember the minimum necessary to keep an eye on other aspects of life maintenance.

It is basically through interviews with the patient and family - used as an instrument technician and therapeutic psychologist observes, perceives and evaluates the various factors involved in the care of these people.

Firstly, we evaluate how the patient is dealing with the fact of having an acute or chronic illness and how the body changes, habits and routines are impacting your personal life and family.

The story of a person's life influences the way she deals with what happens in their daily lives. It is in pursuit of psychological and work to discover the degree of understanding about the severity of disease, as this depends not only on aspects of conscious and rational. These factors affect directly the adherence.

The acceptance and assimilation of the information you were given and the details about the treatment depend on a personal time of preparation of their inner fears,

fantasies, defenses and resistances. These resistances are often triggered by the situation that the treatment is: a worsening of their clinical condition, a further effort to keep well and stay alive. Many treatments also require a significant change in routine, and / or are very painful, others require postponement of dreams and plans of the present and future of the individual and the family.

We can also mention that in this type of specialty, the treatments are long, requiring a prolonged relationship between professionals and patients, which may cause noise in the communication, generating friction, misunderstanding and distress. Each case requires a different solution from the psychodynamic aspects involved in it.

Consultations with other healthy team members is one of the working tools used by the psychologist to give a view of the subjective aspects involved, both on the part of caregivers as those are cared for.

The complexity of life brings difficulties, but also wealth, beauty and uniqueness. Living with quality of life. This is the great challenge!

THE ROLE OF THE NURSES

"In promoting adherence to treatment, the Health Education and Self-Care is the foundation of nursing."

The low level of adherence to treatment can negatively affect clinical outcome and quality of life, thus becoming relevant problem, which has consequences of personal, social and economic.

For the success of treatment adherence are needed at three different levels of commitment. The first relates to the offered services: laboratory tests, specialties, facilitated scheduling, bonding and host. The second is related to the quality of care provided by professionals in their commitment to listen, interact, educate, and adjust your language. Finally, we have the role of the patient, who needs to know, understand and accept the proposed treatment, adhering to strategies for self-care and guidance on the treatment proposed[19].

The adherence happens from the moment the patient accepts his condition of health believes the mechanisms of disease and opts for self-care[20]. Thus, there is need for actions aimed at establishing stronger link between patient and institution, with the aim of offering information and assistance to support patients and their families following their treatment and care of their healthy.

Therefore, the performance of professional nurses in their role as an educator born is fundamental to the extent of patient compliance and consequently treatment success. Accordingly, we direct nursing care to educational measures, as described below.

Thermometer Club	Assessment and training of patients, families and caregivers to measure the correct temperature in mercury and digital thermometers.
PIDMI - Infusion Program Household Injectable Drugs	Assessment and training of patients, families and caregivers for administration intramuscular or subcutaneous drugs.
Nursing Queries	It is a tool for implementing the nursing process that contributes to the detection and resolution of healthy problems of patients, Their interventions can be individual or collective, stands out in these consultations the responsibility of nurses in promoting adherence to treatment.
NAS- Nursing Assistance Systematization	The implementation of the NAS is formally recorded in the patient being composed of nursing history, physical examination, prescription nursing care. Each of these stages includes actions aimed at compliance treatment.
Pain as 5th Vital Sign	The education of patients, managers and healthy professionals in the measurement of pain using a visual analogue scale of pain is fundamental for ensuring adherence to treatment, because such records will subsidize the medical decision-making and interventions.
Self-care Project	This project is aimed to ensure compliance through the guidance of patients with sickle cell disease on how to treat leg ulcers at home, encouraging the practice of self-care.

LESSONS LEARNED

PAIN:

1 - Never use analgesics SOS. The treatment of acute pain has to be performed at regular intervals.

2 - It is very important to remember that morphine cannot be used "SOS". Morphine should only be used every four hours.

3 - Replacement for codeine by morphine, to obtain a higher rate of analgesia, should be done by calculating the equivalent dose. For example, if patient had been using 60mg of codeine, or the equivalent of 7.5 mg of morphine, can substitute for oral morphine at dose of 10mg, which corresponds to a higher dose of codeine dose he was taking.

4 - After discharge, patients with sickle cell disease should maintain regular use of opioids for at least another 3 days, once the painful crisis lasts around 7 to 10 days.

5 - Haloperidol should be used to treat nausea caused by morphine in a single dose 1-2 mg (10 to 20gts) in the morning. At these doses are not observed extrapyramidal side effects.

6 - Nausea and vomiting with the use of methadone are early signs of overdose. Therefore, when using opioid, it should avoid the use of antiemetics for not mask the warning.

7 - You can treat painful crisis from moderate to strong with an extra dose of opioid, also called rescue dose, which can be calculated in two ways; 1st) 50% to 100% of regular dose is the dose that would be given every 4h or 2nd) 1 / 6 to 1 / 10 of total daily dose of opioid use, or the equivalent in a fast-acting morphine.

8 – We should always prescribe medication in addition to rescue medication for opioid maintenance. The frequent repetition of the rescue dose (twice or more) indicates the need to increase the total daily dose or adding adjunctive medication, if there is neuropathic pain.

9 - The recommended starting dose of morphine, 15 to 30 mg each four hours to find the desired level of analgesia.

10 - The opioid agonists have no ceiling dose; the optimal dose is that which relieves pain with the least side effects. In practice, the maximum dose of morphine is limited by the occurrence of adverse reactions (drowsiness, uncontrollable vomiting, myoclonus, respiratory depression). Respiratory depression is the great fear for the prescription of morphine, but the pain is the best analeptic. While there is pain, doses can climb even higher, without risk, because you do it gradually. The biggest problem is in association with general anesthetics on postoperative residual or when they partner with other neuro depressants.

11 - Morphine tablets are scored and if necessary, can be divided or crushed to better eating, but Dimorf's capsules has inside granules that cannot be violated. If they are, they will lose quality slow-release and immediate release morphine occurs, causing risk of overdose. However the microgranules can be administered via gastrostomy.

12 - The effect of metoclopramide is very short (around four hours) and repeated doses, especially in the elderly, can cause restlessness, drowsiness and extrapyramidal symptoms.

13 - Constipation is the most common side effect with the use of morphine. The optimal laxative should be able to soften the stool and cause peristalsis. These patients should be referred to the nutritionist.

14 - Drowsiness and sedation occur with some frequency at the beginning of opioid therapy (first 10 days), soon settles tolerance for this phenomenon. The patient using these drugs should not drive vehicles and do not perform any activity that requires skill to avoid accidents. In cases of excessive sleepiness, the dose should be reduced.

15 - The increase in dose at night may facilitate sleep. When there is a need to tackle a crisis of depression, we used tricyclic antidepressants, which are also analgesics with action on neuropathic pain.

16 - Orthostatic hypotension with the use of opioids may be result of dehydration or concurrent use of other drugs. Its usage indicates the patient should be directed to the postural changes are made slowly.

17 – For profuse perspiration with the use of morphine, that is more common in liver disease there is no preventive therapy, but the use of small doses of corticosteroids (5 to 20 mg of prednisone) may alleviate these symptoms.

18 - Before respiratory depression can be observed clinical signs such as nausea and vomiting, drowsiness or stupor, bradycardia, and cyanosis. In case of respiratory depression by morphine, naloxone it should initiate appropriate intravenous dose (duration of action is 45-90 minutes) and if necessary, measures of ventilatory support should be initiated.

FOR HYDROXYUREA SICKLE CELL DISEASE:

1 - INITIAL DOSE: 10mg/kg/day in taken once daily. Can be considered the real or ideal weight, whichever is less.

2 - For children unable to swallow capsules:

A- Family should be advised to dilute the drug in 5 ml of filtered water and boiled.

B- Powder dissolves completely.

C- The product will then be at a concentration of 100mg/ml and the doctor can calculate the amount to be administered.

D- Use 5 ml syringe for better accuracy of the dose.

E- In case of over dose maintain aseptic conditions in the refrigerator, for up to 24 hours after dilution.

DEFERASIROX:

1 - It is a medicine available as a dispersible tablet, should be taken once a day, always at the same time, with empty stomach and 30 minutes before eating.

2 - The recommended dose is 10 30 mg / kg / day.

3 - The tablets should be dispersed in water, apple juice or orange.

4 - Must be monitored monthly with serum creatinine and ferritin.

5 - Not to be combined with other iron chelator therapies.

6 - Should not be used during pregnancy or breastfeeding.

7 - Can be used in individuals over the age of 2 years.

8 - The most common side effects are gastrointestinal and skin rash, transient.

9 - There may be decreased concentration of deferasirox with the drugs rifampicin, carbamazepine, phenytoin, phenobarbital, ritonavir, because they induce UGT (an enzyme that metabolizes the drug).

10 - There should be administered with antacids containing aluminum.

DEFERIPRONE:

1 - Must be taken three times daily.

2 - It has good penetration into the myocardium, providing cardioprotection.

3 - Its most important adverse effect is agranulocytosis. Therefore, in case of neutrophils below 1500/mm^3, treatment should be stopped temporarily, and in case of neutrophils below 500/mm^3, treatment should be discontinued permanently.

4 - Should not be used during pregnancy or breastfeeding.

IMATINIB MESYLATE:

1 – Imatinib is a frontline treatment of patients with chronic myeloid leukemia. Initial dose of 400 mg PO daily should be used for patients in chronic phase and 600 mg for patients in accelerated phase or blast crisis.

2 – The dose should be administered after a light meal with full glass of water to prevent nausea and vomiting. Use antiemetics if needed.

3 - In case of peripheral edema may be administered thiazide diuretics. The swelling usually regresses or even disappears with continued use of Imatinib.

4 - The presence of cramps responds well to regular ingestion of tonic water.

5 – Avoid antiacids. If absolutely necessary it can be given between periods of imatinib administration.

6 – Some drugs may have their action changed by Imatinib, as Cyclosporine, Warfarin and simvastatin.

7 - Avoid alcohol and paracetamol due to hepatotoxicity.

8 – Response monitoring tests should be performed periodically, such as blood counts, cytogenetic and PCR tests.

1. The dose of imatinib should only be changed for a second-line tyrosine kinase inhibitor.
2. Drugs Interactions:

INDUCTORS ENZYME ACTIVITY Decrease the action of imatinib	Amiodarone	Fenobarbital	Omeprazole
	Anastrazole	Fluconazol	Oxcarbamazepin
	Azitromicine	Fluoxetin	Oxiconazole
	Carbamazepine	Grape fruit	Paroxetine
	Cetoconazol	Griseofulvin	Primidone
	Ciclosporin	Indinavir	Propoxifene
	Cimetidine	Isoniazide	Ranitidine
INHIBITORS OF THE ENZYME ACTIVITY Increase the action of imatinib	Claritromicine	Itraconazole	Ritonavir
	Danazole	Metronidazole	Rofecoxibe
	Dexametasone	Miconazol	Saquinavir
	Diltiazem	Nelfinavir	Sertraline
	Dissulfiram	Nelfinavir	Sulfadimidine
	Eritromicin	Nevirapine	Troglitazone
	Etinilestradiol	Nevirapine	Valproic acid
	Fenilbutazon	Norfloxacin	Verapamil
	Fenitoin	Norfluoxetine	

3. What to do in the following situations :

You missed a single dose (400mg)	Take the medicine as soon as remembered. Do not double the dose on the next day
You forgot taken in a day (600mg or 800mg)	Take the medicine as soon as remembered. Avoid double dose
You took the medicine and threw up BEFORE 30 minutes.	Repeet the dose
You took the medicine and threw up AFTER 30 minutes.	Do not repeet the dose.
You took a higher dose of medicine than prescribed.	Inform your doctor or pharmacist, because there is a risk of adverse event
You did not take the medicine for more than two days.	Return to your doctor.

NILOTINIB:

1. Nilotinib interferes with the action of the following medications: midazolam and warfarin.
2. In vitro data suggest that nilotinib has the potential to prolong the QT interval. The ECG is recommended prior to initiation of therapy with nilotinib and should be repeated after 7 days and when clinically indicated. Certain antiarrhythmic drugs are known to slow cardiac repolarization (eg amiodarone, disopyramide, procainamide, quinidine, sotalol) and other drugs such as chloroquine, halofantrine, claritromocina, haloperidol, methadone, moxifloxacin, pimozide and bepridil.
3. Hypokalemia or hypomagnesemia, should be corrected prior to nilotinib administration and blood levels of potassium and magnesium should be monitored periodically during therapy in patients at risk for electrolyte abnormalities.
4. Drugs Interaction:

INDUCTORS ENZYME ACTIVITY Decrease the action of nilotinib	carbamazepine dexametasone fenobarbital fenitoin rifampicin
INHIBITORS OF THE ENZYME ACTIVITY Increase the action of nilotinib	cetoconazole claritromicine itraconazole moxifloxacin ritonavir telitromicine voriconazole

DASATINIB:

1- Dasatinib interferes with the action of the following medicines: cyclosporine, alfentanil, fentanyl, pimozide, sirolimus, tacrolimus and ergotamine.

2- Gastric pH helps the absorption of the drug, so no one should use it, along with antacids that neutralize the gastric. You should maintain a distance of two hours before and after meals.

3- You should avoid the use of cimetidine, ranitidine, famotidine, omeprazole, pantoprazole, esomeprazole, rabeprazole and lansoprazole. In all these associations have a reduction of approximately 60% in the concentration of dasatinib.
4- You should be aware of associated use with anticoagulants like warfarin or aspirin.
5- The tablets are coated and should not be broken or crushed;
6- Drug interactions:

INDUCTORS ENZYME ACTIVITY Decrease the action of dasatinib	carbamazepin dexametasone fenobarbital fenitoin rifampicin
INHIBITORS OF THE ENZYME ACTIVITY Increase the action of dasatinib	atazanavir cetoconazole claritromicin eritromicin indinavir itraconazole moxifloxacin ritonavir nelfinavir saquinavir telitromicine voriconazole

THALIDOMIDE:

1 - Thalidomide is indicated for patients with Multiple Myeloma.

2 - Initial dose is 100mg orally daily.

3 - Thalidomide is a potent sedative and association with other sedatives may increase the depressant effects on the central nervous system. It should be administered at night to sleep by inducing drowsiness.

4 - The main side effect is constipation. Laxative drugs should be administered if necessary.

5 – It is forbidden the use of thalidomide in pregnant women for high risk of fetal malformation.

6 - Men partners of women of childbearing age and women of childbearing potential should be advised to make use of at least two contraceptive methods.

7 – Aspirin 100mg daily should be given to prevent venous thrombosis. In cases of additional risks, such as use of erytrooietin or anthracyclines, we should preferwarfarin.

8 – You should avoid fatty foods because it may increase by 6 hours the time needed to achieve the best effect of Thalidomide.

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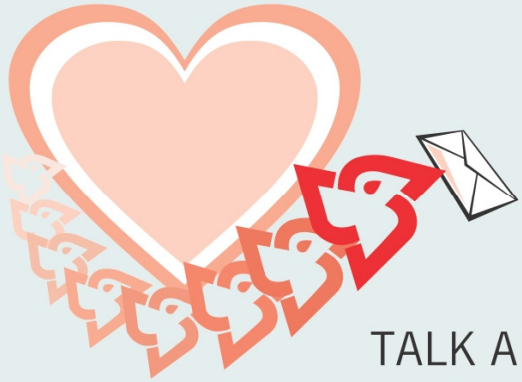

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