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Review Article

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Optimizing Heart Failure Management: A Review of the Clinical Pharmacist Integration to the Multidisciplinary Health Care Team

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ABSTRACT

Heart failure (HF) stands as a prevalent chronic ailment, imposing a substantial burden on global healthcare systems due to recurrent hospitalizations, intricate management, persistent symptoms, and polypharmacy challenges. The augmentation of patient safety and treatment efficacy across various care stages, facilitated by a multidisciplinary HF team inclusive of a clinical pharmacist, emerges as paramount. Evidence underscores that the collaborative engagement of a physician and a clinical pharmacist engenders proficient and secure management, forestalling avoidable adversities stemming from drug reactions and prescription inaccuracies. This synergistic approach tailors treatments optimally to individual patients. Post-discharge, the vulnerability of HF patients to re-hospitalization looms large, historically holding sway as the foremost cause of 30-day readmissions. Diverse strategies have been instituted to fortify patient well-being, leading to the formulation of specialized transitional care programs that shepherd patients effectively from hospital to outpatient settings. These initiatives have demonstrably curtailed readmission rates. This review outlines a spectrum of roles assumed by clinical pharmacists within the healthcare cohort, spanning inpatient care, transitional phases, and outpatient services. Moreover, it traverses a compendium of studies spotlighting the affirmative impact instigated by integrating clinical pharmacists into these fields.

Keywords: Clinical pharmacist; Heart failure; Pharmaceutical services; Medication adherence

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INTRODUCTION

Heart failure (HF) is a significant and escalating chronic ailment with a global incidence, impacting more than 60 million individuals worldwide. This condition is marked by an insufficient capacity to pump blood effectively, resulting in compromised perfusion. It is known for recurrent episodes of decompensation, leading to frequent hospitalizations with readmission rates ranging from 30% to 40%.[1-5] In the United States of America and Europe, the prevalence of HF ranges from 1% to 2%, while in Asian countries like South Korea, it reached a maximum value of 2.24% in 2018.[6-8] The substantial prevalence of HF imposes a significant economic burden on healthcare systems worldwide. In 2012, the estimated annual cost of HF management was 30.7 billion USD in the United States, 33.14 billion USD in the European Union, and 1.1 billion USD in South Korea.[9-11]

Inadequate communication between healthcare providers in the inpatient and outpatient settings significantly contributes to an elevated risk of readmission and mortality. Collaborative care among healthcare professionals, including cardiologists, nurses trained in cardiology, and pharmacists, is crucial for improving patient outcomes.[12]

Transitions of care (TOC) often involve medication errors that can result in medication-related adverse reactions. A significant proportion of patients, up to 70%, experience unintended changes in their medication regimen during these transitions. Disturbingly, around 30% of these medication changes lead to worsened outcomes, and approximately 5–8% of patients require readmission to the hospital due to medication-related issues.[12,13]

The proactive engagement of pharmacists in prescription reviews, coupled with their seamless integration into multidisciplinary teams, holds immense significance. Their pivotal role in overseeing and detecting prescription errors to avert medication-related issues cannot be overstated. This synergistic methodology guarantees the execution of refined, secure, and effective therapeutic regimens, culminating in enhanced patient outcomes.[14] A recent study has highlighted the significant impact of a multidisciplinary TOC team, including clinical pharmacists, residents, students, and HF-trained nurses, in mitigating 30-day readmission rates for HF patients with cardiovascular symptoms. By integrating medication reconciliation at every juncture of the TOC process, a significant decrease of 2% in readmission rates was accomplished. These results underscore the efficacy of engaging a multidisciplinary team in mitigating hospital readmissions for individuals with HF, consequently enhancing patient outcomes and potentially diminishing healthcare expenditures.[15]

This review aims to elucidate the various activities that clinical pharmacists can undertake as part of the multidisciplinary management of HF across different stages of care and to evaluate the supporting literature for their effects.

CLINICAL PHARMACIST'S ACTIVITIES DURING OUTPATIENT HF MANAGEMENT

When managing HF, adopting a guideline-directed medical therapy (GDMT) approach has shown superior efficacy compared to limited treatment plans. GDMT has demonstrated a reduction in both mortality and morbidity within 30 days of commencing treatment.[16] Despite concerns surrounding the use of multiple medications (polypharmacy), GDMT has proven to be a beneficial strategy in managing HF, improving quality of life, increasing survival rates, and reducing mortality. However, the complexity of medication regimens can sometimes result in undesirable reactions and intolerance. It is crucial to regularly evaluate and adjust medications to ensure their safety and effectiveness. **Table 1** provides a summary of common adverse reactions that can occur with these medications.[17-26] Given the vast array of available drugs and the possibility of adverse reactions, it is essential to closely monitor the patient's response to therapy at every stage of care to achieve positive outcomes.[27]

Table 1. Common drug adverse of medication used for the management of chronic heart failure and acute decompensated heart failure[17-26]

Medication group	Potential adverse reactions
Angiotensin receptor-neprilysin inhibitor	· Dry cough · Angioedema
Angiotensin converting enzyme inhibitors	· Increased serum creatinine and potassium
Angiotensin receptor blockers	· Dizziness and hypotension
Beta-blockers	· Hypoglycemia · Insomnia · Fatigue · Dizziness · Hypotension
Diuretics	· Frequent urination may cause non-adherence · May precipitate gout
Mineralocorticoid receptor antagonists	· Hyperkalemia, this risk is increased on renal failure patients and in concomitant use with angiotensin converting enzyme inhibitor · Gynecomastia in men
Sodium-glucose cotransporter 2 inhibitors	· Genital mycosis · Urinary tract infections · Hypotension
Soluble guanylate-cyclase stimulants (Vericiguat)	· Hypotension · Syncope · Anemia

Medication compliance

One of the primary challenges faced by patients with HF lies in achieving medication compliance by providing appropriate treatment adherence guidance.[28] Educating patients, their families, and caregivers is one of the main points of interest in pharmacy care. Medication adherence is one of the most studied topics when referring to pharmaceutical care, which is achieved through education to patients and their close circle.[29] There have been numerous investigations into the impact of engaging a pharmacist in post-treatment consultations on patient adherence to prescribed medication. By complying with the recommended treatment plan, healthcare providers can more effectively monitor patient progress and evaluate their overall health outcomes.[30,31]

Certain authors expand the notion of treatment adherence when it comes to patients with HF, given the significance of dietary considerations and daily actions. Consequently, an inclusive approach that encompasses monitoring medication compliance, adherence to dietary recommendations, and fostering patient awareness of their condition has emerged as a relatively recent objective in the ambulatory management of HF. This holistic approach has been integrated into pharmacy consultations to address treatment adherence. The active practice of this new concept of treatment adherence is directly related to a better prognosis, being that non-adherent patients have an increased risk of 22% being hospitalized, in comparison to adherent patients.[28] For this reason, various strategies have been developed to measure HF medication adherence, including checking the prescription refill history of HF medication, insurance history, pill counts, serum drug levels, questionnaires, and patient self-reports.[32] **Table 2** [32,33] illustrates some common strategies used to improve medication adherence. When consulting a polymedicated patient, it's worth noting that some tendencies indicate if the patient may or may not be adherent to their treatment; these tendencies are shown in **Table 3**.[32]

Optimization of GDMT

Pharmacist-directed HF programs have demonstrated success in enhancing GDMT prescription rates. GDMT has proven to be significantly more effective than restricted treatment plans in promoting positive outcomes for HF patients. The presence of a clinical pharmacist within the HF program enables personalized dosing for each patient, facilitating timely adjustments and attainment of target doses. This not only benefits the patient's

Table 2. Strategies for improving patient's adherence to treatment[32,33]

Strategy to enhance medication adherence	Description
Educational strategies	· Identify barriers to medication use: medication disbelief, expectations about possible improvement, attitude about the disease, complex regimen and costs · Empower the patient to understand their disease, how the treatment works and how they can see a positive effect on their evolution · Empower the patient to understand how medication adherence translates to positive outcomes and fewer symptoms, fewer medical appointments, less risk of hospitalization and better quality of life
Non-educational strategies	· For economic limitations it's possible to look for social action programs inside and outside the institution or look for sponsors that are willing to give financial support · For complex medication regimens where organization is the issue it is possible to give the patients pill organizers and educate them about their correct use

Table 3. Predictors associated with therapy adherence on heart failure patients

Influence-factors on adherence	Associated with decreased adherence	Associated with increased adherence
Patient-related factors	Race: Minorities	Advanced age (>65 years)
	Gender: Male, Female	Gender: Female
	Lapses in attention	Education level and years of education
	Excessive daytime sleepiness independent of mild cognitive limitations presence	
Condition related factors	Greater HF severity	Previous HF hospitalizations
	Greater number of concomitant diseases	
	Depression	
	Higher heart rate	
	Poor renal function or end-stage renal failure	
	Recent initial HF hospitalization	
Therapy related factors	Increased dosing (twice a day, three times a day)	Experience with the same class of HF medication
	Daily life changes in function of HF medication schedule	Concurrent use of cardiac medication
	Antiarrhythmic medication use	Patient knowledge of correct dosing times
Socio-economic related factors	Living alone	Health literacy
	Patient income	Reading ability
	No health insurance	Marital status-Married

Source: Adapted from Davis et al.[32]
HF = heart failure.

recovery but also optimizes the HF clinics' operations. The importance of timely and optimized dosing cannot be overstated, as studies have found that every month of delay in reaching the target dose is associated with a 1% decrease in survival rates.[16,34]

Due to the intricate dosing requirements of HF medications, patients face a clear disadvantage. In a multinational study involving 29,546 patients, the attainment of goal doses following HF guidelines was assessed. The findings revealed that only 30% of the population was able to achieve these goal doses. In a different cohort study in Germany with a sample of 26,191 patients similar results were found, where only 21% of patients reached goal doses. The causes attributed to these findings were a lack of medication compliance and the lack of knowledge from the clinicians about the clinical guidelines.[35] This tendency can represent a clear limitation if new promising drugs such as vericiguat, which proved to decrease mortality and hospitalization rates, are initiated, as the four-week titration period involves every follow-up to measure tolerability and clinical response.[19,36,37] The follow-ups from the clinical pharmacist during the different titration periods can play a crucial role in achieving goal doses early or treating the patients according to their tolerability.

According to a recent study conducted by University of California, Los Angeles, the inclusion of pharmacists in a HF clinic had a significant impact on patient outcomes. The study involved 153 patients and revealed that having a pharmacist present resulted in patients reaching their target doses more efficiently and promptly, resulting in a 94% fulfillment rate for GDMT. Furthermore, follow-up visits were reduced from an average of 23 days to just 13 days. Most notably, the study demonstrated a notable decrease in all-cause mortality rates.[16] Another study involving 1,568 patients also yielded positive results after incorporating clinical pharmacists into a HF clinic. The intervention group experienced a decrease in non-fatal cardiovascular events, which led to fewer hospital admissions and emergency room visits compared to the control group. Although not statistically significant, the study also observed a decrease in overall mortality rates in the intervention group.[38]

These positive outcomes are significant because, despite the well-known positive effects of angiotensin converting enzyme inhibitors, angiotensin receptor blockers, angiotensin receptor-neprilysin inhibitor, beta-blockers, and mineralocorticoid receptor antagonists, it is well-documented that these therapies are not prescribed with optimal doses.[29] For this reason, prescribing errors and dosing titration timing are monitored in clinical pharmacy care daily, evaluating patient needs, evolution with a determined drug regimen, and accomplished treatment compliance.[14,29] Pharmacists are well-trained to play a key role in this regard, given their expertise in promoting safe medication use, reducing prescribing errors, and providing dosing guidance for high-complexity patients or special populations such as those with renal or hepatic impairment patients, but these are just mere examples of how pharmacists can significantly contribute to the multidisciplinary management of HF.[27,39]

New strategies for outpatient pharmacy follow-up

Due to the COVID-19 pandemic, there has been an increased prevalence of telehealth or telephonic consultations with healthcare providers. In the tele-management of outpatients with HF, clinical pharmacists have been conducting follow-ups with high-risk, non-adherent patients. This intervention has yielded positive outcomes, leading to a significant 41% reduction in mortality over two years. It is important to note that this was a relatively small-scale study involving only 16 patients. Nonetheless, the study observed that efficient timing in therapy optimization remained evident despite the telehealth management, and there was also a notable reduction in the need for in-person hospital services.[40]

One of the key advantages of pharmacy consults in this context is the ability to thoroughly assess the patient's condition, monitor the progression of HF, and identify its correlations with comorbidities and treatment. This comprehensive evaluation allows for the timely prevention of decompensation or early initiation of medical referrals.[41]

CLINICAL PHARMACIST'S ACTIVITIES DURING INPATIENT HF MANAGEMENT

In the intensive care unit (ICU), pharmacists play a critical role in supporting patients who are in critical condition and face unique pharmacokinetic challenges. By working as part of a multidisciplinary critical care team, pharmacists can gain a comprehensive understanding of individual cases, which leads to well-informed decision-making. While there have been limited studies on the role of pharmacists in managing hospitalized patients with HF, many of the activities that are relevant to ICU patients can be applied to less complex cases for optimal quality of care. This section aims to explore the various activities that pharmacists undertake when caring for hospitalized patients.[42]

Preventable adverse drug reactions

Preventable adverse drug reactions (ADEs) are a focus of clinical pharmacists' activities, both for hospitalized and ambulatory patients. ADEs can be categorized into intrinsic and extrinsic harm. Intrinsic harm arises from the medication's pharmacologic properties, leading to proper adverse drug reactions. On the other hand, extrinsic harm results from medication errors, such

as administering medication intravenously instead of intramuscularly. While many drug-related adverse reactions are well-documented, some of them are preventable. Clinical physicians conduct follow-ups to assess the safety of therapies for patients and identify strategies to prevent or control high-risk ADEs before they manifest.[43]

Monitoring for preventable ADEs, their occurrence, and potential drug interactions are of paramount importance for patients with polypharmacy, a concern that is equally pertinent for HF patients, as previously discussed. In the management of complex patients characterized by a myriad of comorbidities and a multitude of prescribed medications, it becomes imperative to scrutinize the safety of the prescribed regimen. This entails a comprehensive analysis of parameters about drug efficacy and safety. Notably, it is not uncommon for HF patients to either already have or develop renal impairment, making it essential to monitor renal function closely and adjust medication doses accordingly. As an illustrative example, renal function can significantly impact the pharmacokinetics of certain medications, necessitating precise dose titrations. Additionally, populations such as older adults or individuals with significant weight fluctuations, who may present challenges in terms of anticoagulant therapy management, require careful attention and expertise to ensure safe and effective treatment. In these intricate scenarios, the active involvement of a clinical pharmacist can be invaluable, contributing substantively to the multidisciplinary healthcare team's efforts to optimize patient care and therapeutic outcomes.[42]

In the treatment of HF patients with multiple comorbidities, the multitude of medications involved can be overwhelming. Clinical pharmacists play a vital role in identifying potential drug-drug and food-drug interactions using various tools. These interactions are assessed based on probability, risk-benefit, and severity, allowing the clinical pharmacist to provide valuable guidance and support to the prescribing doctor in determining the most appropriate pathway when facing medication-related issues.[44]

Medication management

Patients with complex conditions, such as those with HF, require close monitoring of clinical parameters and overall clinical progress to determine the efficacy of treatment outcomes. Clinical pharmacists play a crucial role in assessing various aspects of the prescribed medication regimen, including its safety, appropriateness, indication, and effectiveness. They have the expertise to initiate, discontinue, modify, or adjust medication doses to achieve the most favorable patient outcomes. This comprehensive evaluation and the activities collectively constitute comprehensive medication management (CMM), which aims to personalize therapy based on the unique needs of each patient. CMM encompasses addressing current symptoms, managing existing conditions, and preventing future complications and can be applied in both inpatient and outpatient settings.[42,45]

The process of CMM comprises four essential steps. Firstly, the patient's needs are assessed, allowing for the identification of any medication-related issues. In the second step, the prescribed medication regimen is evaluated in terms of necessity, safety, and effectiveness. Based on this evaluation, a plan is developed in the third step to optimize medication therapy. Finally, the plan is implemented, and the patient's progress is continuously monitored and evaluated in the fourth step to ensure that desired outcomes are achieved.[42,45]

The studies on the effect of these activities show a decrease in the incidence of preventable ADEs caused by prescription errors, which translated to a more likely discharge, avoiding extension of hospital stays and the consequent economic savings. In complicated patients such as ICU patients, a substantial decrease in mortality due to bleeding was also found, this sort of study then led to the question of how high the rate of prescribing errors is associated with mortality. Because of this, some institutions recruited ICU-trained clinical pharmacists to reduce the incidence of ADEs, prescribing errors, and implementation of a CMM, but this sort of complication is not exclusive to critically ill patients and can be extended to less complicated patients to ensure the best quality of care, but the study of the effect of clinical pharmacists on different wards is yet to be conducted.[46]

CLINICAL PHARMACIST'S ACTIVITIES AS PART OF THE TOC TEAM

To ensure optimal treatment for HF patients, it is crucial to have a specialized team dedicated to TOC. This team should handle all aspects of the patient's treatment, from admission and hospitalization prescriptions to discharge medication. Due to the complex medical histories and comorbidities of HF patients, they are at a higher risk of adverse medication reactions and prescription errors. Therefore, a multidisciplinary TOC team is necessary to prevent undertreatment, overtreatment, duplication of therapy, omissions, and drug interactions. The TOC team works to ensure that the patient receives safe and efficient treatment tailored to their specific needs, and they also monitor the patient's medication history to prevent errors. To achieve this, the team coordinates patient care during transitions between healthcare settings, using interventions that optimize patient outcomes.[47]

Following discharge from the hospital, adherence to the prescribed ambulatory care medication regimen is of paramount

importance for the effective management of HF. This debilitating condition has been identified as the primary cause of 30-day readmissions for several years, underscoring the critical role of the TOC team in ensuring patient safety. Within the healthcare industry, 30-day readmission is widely regarded as an indication of suboptimal health management during the transition between stages of care. Contributing factors may include inconsistencies in medication administration, limited access to healthcare, inadequate knowledge of self-care practices, insufficient follow-up care, and financial constraints.[48] As a strategy to decrease the 30-day readmission rates transitional care pharmacists have implemented a system of medication reconciliation before discharge, patient education, discharge counseling, phone follow-ups, and multidisciplinary home visits, which have effectively decreased readmission rates of HF patients, eventually as part of the HF clinics that have implemented a HF-TOC patients then will be followed up in regular outpatient appointments.[49-53]

Numerous meta-analyses have explored the impact of TOC interventions. A noteworthy analysis delved into 53 clinical trials, encompassing more than 12,000 patients from 2000 to 2015. The findings indicate that individuals who received guidance from the TOC team during the post-discharge phase had a substantial drop in readmission rates, ranging from 20–35%.[51] A different meta-analysis intended to identify which actions contribute to an effective decrease in readmission rates, these different activities are presented in **Table 4**.[52]

The clinical pharmacist's role during discharge planning includes an integral overview of the condition of the patient and involves most of the different activities already mentioned in **Table 4**. Additionally, before discharge, a revision of contraindicated drugs in HF patients is conducted; these contraindicated drugs are illustrated in **Table 5**.[33,54] These actions are particularly important because the collaboration between physicians and pharmacists when establishing a management plan has proven positive on patient outcomes, achieving better prognosis and early results.[52,55] A general summary of the role of the clinical pharmacist in the multidisciplinary approach to HF treatment is presented in **Figure 1**.

CONCLUSIONS

Based on the reviewed literature, it is notable that pharmacists can play a crucial role in the multidisciplinary healthcare team, contributing to the optimal management of patients with HF in the different stages of care. As medication management is a critical aspect of HF treatment, the involvement of an expert in pharmacology, pharmacokinetics, therapeutics, and medication compliance can greatly favor treatment optimization, making treatment-based monitorization regular and achieving medication compliance possible, these different activities can improve patient's condition and help to accomplish positive outcomes. In conclusion, the pharmacists' inclusion in the multidisciplinary team can contribute to accomplishing an optimized and individualized therapy, active use of GDMT, accurate timing for medication titration, and an exhaustive review of how safe the prescribed regimen is, including not only HF treatment. The sum of these activities can influence importantly in achieving positive outcomes,

Table 4. Identified activities of the clinical pharmacist that cause a decrease in 30-day readmission through a HF-TCP[52]

Activities	Description
Medication management and optimization during hospital stay through CMM evaluation	The patient's medication regimen is evaluated, ensuring proper selection of medications, dosages, and routes of administration to optimize treatment efficacy and safety.
Early assessment of patients regarding post-discharge care	Prior to discharge, patient assessments are performed to plan their post-discharge care. This helps identify potential challenges or specific needs the patient may have during the transition from hospital to home, increasing the likelihood of therapy effectiveness.
Pre-discharge education and counseling	Providing predischarge education and counseling ensures that patients fully understand their medication regimens, including dosing instructions, potential side effects, and the importance of medication adherence.
Discharge instructions	Clinical pharmacists help to formulate clear discharge instructions. These instructions may include details about medication use, medication schedules, and lifestyle modifications.
Discharge planning with the prescribing doctor	Clinical pharmacists collaborate with the prescribing physician to establish an appropriate discharge plan for the patient. This plan may include medication adjustments or changes, considering the patient's response to treatment and any necessary follow-up care.
Evaluation of effectiveness, safety, and indication of discharge prescription	Assessing the efficacy and safety of prescription medications to verify their suitability for the patient's medical condition and compliance with evidence-based guidelines. This includes the evaluation of preventable ADEs, presented ADEs, and drug-drug and food-drug interactions, especially in polymedicated patients, to mitigate adverse effects and optimize therapeutic results.
Daily monitoring during post-discharge care through telehealth and home visits	As part of post-discharge care, clinical pharmacists can engage in daily monitoring of patients through telehealth consultations and home visits. This type of accompaniment significantly increases adherence to medication regimens, identifies issues, and provides timely intervention if necessary.
Regular follow ups in ambulatory care through a HF clinic, enhancing medication compliance	These follow-ups focus on monitoring medication compliance, evaluating treatment outcomes, and addressing any concerns or adjustments necessary for ongoing patient care.

HF = heart failure; TOC = transitions of care; CMM = comprehensive medication management; ADE = adverse drug reaction.

Table 5. Drugs with the capability of causing or exacerbating heart failure

Drug or therapeutic class	Magnitude	Level of evidence*	Possible mechanism
Analgesics	Major	B	Prostaglandin inhibition leads to sodium and therefore water retention, increasing vascular resistance and decreasing diuretics action
COX non-selective inhibitors			
COX-2 selective inhibitors			
Volatile anesthetics	Major	B	Myocardial depression, decreased sympathetic activity and peripheral vasodilation
Desflurane			
Enflurane			
Halothane			
Isoflurane			
Sevoflurane			
Intravenous anesthetics		B	
Dexmedetomidine	Moderate		α_2-Adrenergic agonist
Etomidate			Adrenal function depression
Ketamine	Major		Negative inotrope
Propofol	Moderate		Negative inotrope and vasodilation
Diabetes mellitus medication	Major		
Metformin		C	Increased anaerobic metabolism and lactic acidosis
Thiazolidinediones		A	Possible calcium channels blockade
Saxagliptin		B	Unknown
Sitagliptin		B	
Antiarrhythmic medication	Major		
Flecainide		B	Negative inotrope effect, proarrhythmic effect
Disopyramide			
Sotalol			Proarrhythmic effect and β blockade properties
Dronedarone		A	Negative inotrope
Antihypertensive, α adrenergic and peripheral vasodilators medication			
Doxazosin	Moderate	B	β_1 agonist and increases renin-aldosterone
Diltiazem	Major	B	Negative inotrope effect
Verapamil			
Nifedipine	Moderate	C	
Moxonidine	Major	B	Possible sympathetic withdrawal
Minoxidil	Moderate	C	Unknown
Antifungal medication		C	
Itraconazole	Major		Negative inotrope effect
Amphotericin B	Major/Moderate		Unknown
Anticancer medication			
Doxorubicin	Major	A	Prolonged oxidative stress caused by alcohol metabolite
Daunorubicin			
Epirubicin			
Idarubicin			
Mitoxantrone			
Cyclophosphamide	Major/Moderate	B	Oxidative stress
Ifosfamide			
Mitomycin	Moderate	C	Oxidative stress
5-FU	Major/Moderate	B	Unknown, possible coronary spams
Capecitabine		C	
Bevacizumab		A	VEGFA
Imatinib	Moderate	B	PDGFR
Interferon	Major/Moderate	C	Unknown
Interleukin-2	Major	C	Cytotoxic damage to myocardium
Lapatinib	Major/Moderate	A	ErbB2
Pertuzumab		C	
Sorafenib	Minor	B	VEGFR, PDGFR
Sunitinib	Major	B	VEGFR, PDGFR
Trastuzumab	Major/Moderate	A	Erb2
Paclitaxel	Moderate	B	Anthracyclines potentiation
Docetaxel			
Thalidomide	Minor	C	Unknown
Lenalidomide	Major		Hypersensitivity myocarditis
Anagrelide	Major	A	Possible inhibition of PD IV
Cilostazol			Inhibition of PD III, resulting in arrhythmias

(continued to the next page)

Table 5. (Continued) Drugs with the capability of causing or exacerbating heart failure

Drug or therapeutic class	Magnitude	Level of evidence*	Possible mechanism
Neurological and psychiatric medication			
Stimulants	Minor/Major (Dose dependent)	B	Peripheral αβ agonism
Carbamazepine	Major	C	Negative inotrope and chronotrope effect, AV and sinus node conduction suppression
Pregabalin	Minor to Moderate	C	L-type calcium channel blockade
Tricyclic antidepressants	Moderate	C	Negative inotrope effect and proarrhythmic properties
Citalopram	Major	A	Dose-dependent QT prolongation
Bromocriptine		B	Increased serotoninergic activity, leading to valvular damage
Pergolide		A	
Pramipexole		B	Unknown
Clozapine	Major	C	Calcium channel blockade
Ergotamine	Major	C	Increased serotoninergic activity, leading to valvular damage
Methysergide			
Appetite suppressants	Major	A	Valvular damage
Lithium	Major	C	Myofibrillar degeneration, adrenergic stimulation and calcium ion influx interference
Pulmonary medication			
Albuterol	Major/Moderate	B	Suppresses β receptors
Bosentan	Major	A	Unknown
Epoprostenol			
Urological medication	Moderate	C	β_1 Stimulator, increases renin and aldosterone
Doxasin			
Prazosin			
Tamsulosin			
Terazosin			

Table adapted from Page et al.[33] and Amabile and Spencer.[54]
COX = cyclooxygenase; FU = fluorouracil; VEGFA = vascular endothelial growth factor A; PDGFR = platelet-derived growth factor receptor; VEGFR = vascular endothelial growth factor receptor; HF = heart failure.
*This classification refers to the amount of evidence available to these contraindications. Level A signifies a strong recommendation against the use in HF, as it consistently demonstrates unfavorable outcomes across multiple studies. Level B constitutes a recommendation to avoid employing the treatment in HF due to generally consistent findings. Level C is presented as an alternative to consider; it is not a definitive recommendation since the evidence regarding these contraindications is inconclusive. Level D evidence denotes a scarcity or absence of systematic empirical evidence.[22]

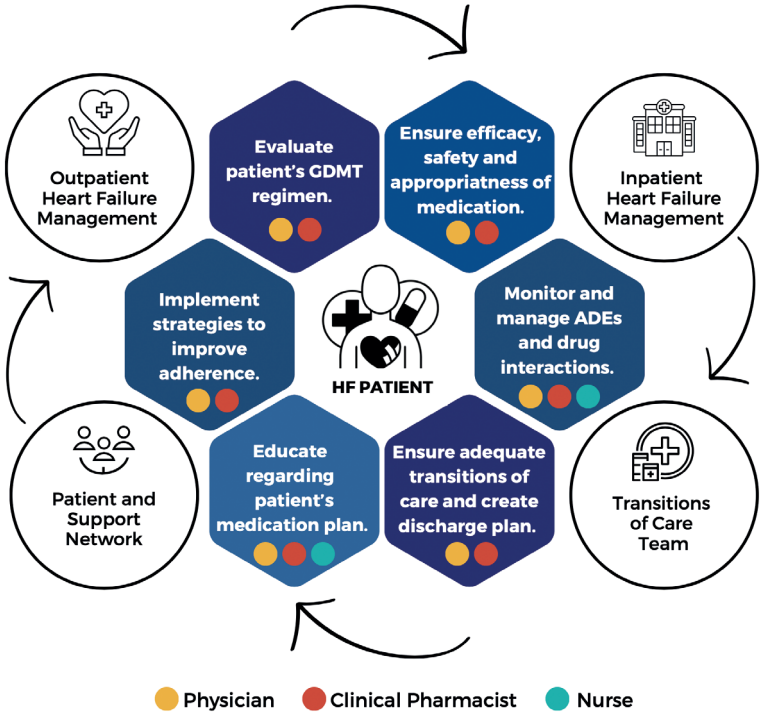

Figure 1. Role of the clinical pharmacist in the multidisciplinary approach to heart failure treatment.

maintaining a stable disease, preserving the quality of life, and consequently, decreasing mortality and hospitalization rates.

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