



A Review on Vericiguat Intravenous Drug Delivery System

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ABSTRACT

Heart failure (HF) is a progressive cardiovascular disorder, where the heart can't pump enough blood to satisfy the body metabolic demands. Even with several treatment advances, people with chronic heart failure still have a high risk of being hospitalized, and also mortality. Vericiguat is a new oral soluble guanylate cyclase (sGC) stimulator, it was designed to improve cardiovascular outcomes in patients with symptomatic chronic heart failure after a recent decompensation event. The idea is that it directly stimulates soluble guanylate cyclase and boosts cyclic guanosine monophosphate (cGMP) production, so impaired nitric oxide signalling can be restored. That helps with vascular function and also overall cardiac performance. In this review we cover the entire drug profile, pharmacological properties, mechanism of action, pharmacokinetics, clinical efficacy, and the safety profile, plus the advantages and limitations, and future perspectives for Vericiguat in heart failure care.

Keywords: Vericiguat, Heart Failure, soluble guanylate cyclase stimulator, cGMP, chronic heart failure, HFREF, cardiovascular pharmacology, Verquvo, VICTORIA Trial, drug profile.

INTRODUCTION

Heart failure is a serious global health issue affecting millions of people across the world. It is tied to a lower quality of life, repeated hospital stays, and a higher risk of death. One of the main pathophysiological issues in heart failure involves the disruption of the nitric oxide (NO)-soluble guanylate cyclase-cyclic guanosine monophosphate (NO-sGC-cGMP) signalling axis. When nitric oxide availability drops, and oxidative stress goes up, cGMP generation falls. This seems to fuel endothelial dysfunction, vascular stiffness, as well as myocardial remodeling, which then contributes to the progression of heart failure symptoms. Vericiguat was created as a first in class oral soluble guanylate cyclase stimulator, to help re-activate this weakened NO-sGC-cGMP route. In practice, it has become a relevant treatment choice for patients with chronic, symptomatic heart failure, especially those who have had a recent worsening of their condition, like requiring hospitalization or intravenous diuretic management.^{12,13,14}

MECHANISM OF ACTION

Vericiguat works by kind of re-using, or restoring the impaired nitric oxide (NO) – soluble guanylate cyclase (sGC) – cyclic guanosine monophosphate (cGMP) signaling route, which gets disrupted in people living with chronic heart failure. Rather than just boosting cardiac contractility in a direct way, it supports overall cardiovascular function through things like vascular tone control, endothelial performance, myocardial rebuilding, and tissue perfusion. The main pharmacological target is soluble guanylate cyclase (sGC), an enzyme that's broadly present in vascular smooth muscle cells, endothelial cells, cardiac myocytes, platelets, and renal tissues.^{3,6,16,18}

In normal physiological conditions, endothelial cells release nitric oxide via endothelial nitric oxide synthase (eNOS). Then nitric oxide moves into the vascular smooth muscle cells and turns on soluble guanylate cyclase, this enzyme changes guanosine triphosphate (GTP) into cyclic guanosine monophosphate (cGMP). When cGMP levels rise, protein kinase G (PKG) gets activated, and that results in lower intracellular calcium, smoother muscle relaxation, vasodilation, less vascular resistance, better tissue blood flow, and overall reduced cardiac strain. This whole cascade, yes it matters a lot, because it helps keep cardiovascular homeostasis stable and in balance.^{3,16,18}

In heart failure, oxidative stress plus endothelial dysfunction kind of mess up nitric oxide production, and it also makes activation of soluble guanylate cyclase less effective. Because of that, intracellular cGMP drops down, and then you see persistent vasoconstriction, higher vascular resistance, myocardial fibrosis, cardiac hypertrophy, ventricular remodeling, fluid retention, and overall progressive worsening of cardiac performance. So, getting the NO-sGC-cGMP pathway back to speed has basically become a key therapeutic route for better cardiovascular outcomes. Vericiguat helps restore this pathway with a dual way of acting. It directly stimulates soluble guanylate cyclase even when nitric oxide levels are low, and at the same time it increases the enzyme's responsiveness to the remaining endogenous nitric oxide. In combination, this boosts intracellular cGMP production even in spite of endothelial dysfunction, which then supports sustained activation of that protective signaling cascade in people with chronic heart failure.^{3,6,14,18}

When cGMP goes up it brings a bunch of good cardiovascular results, like vascular smooth muscle



loosening up, lower systemic vascular resistance, better coronary blood flow, less ventricular afterload, stronger ventricular filling, and even less myocardial oxygen demand. It also tends to block cardiac hypertrophy and fibrosis, which is kind of a big deal. On top of that, improved renal perfusion helps the body dump sodium and water, so fluid overload and edema go down. Put together these effects generally improve symptoms, support cardiac function, and lower the chance of being hospitalized for people living with heart failure. An intravenous form of vericiguat might add extra clinical benefits since the medicine can be delivered straight

into systemic circulation. That could mean a quicker onset of action and plasma drug concentrations that are more predictable. With IV, the drug skips gastrointestinal absorption, so you avoid the kind of day to day variability you get from food intake, or from impaired GI function. This makes IV especially helpful for critically ill patients or people already in the hospital. Continuous IV infusion could also keep drug levels more steady, allow a careful dose adjustment with real time clinical observation, and help maximize the NO-sGC-cGMP pathway activation while reducing swings in blood pressure.^{1,3,6,14}

Flow Chart:

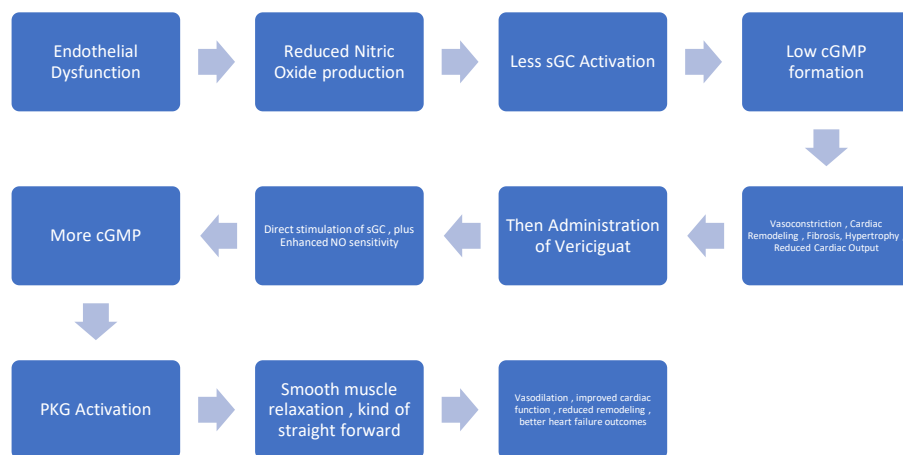


Figure 1: Mechanism of action.

ADVANTAGES

An intravenous (IV) formulation of vericiguat comes with a few clinical benefits that are kinda obvious once you think about it, because the drug goes straight into the systemic circulation, so bioavailability becomes immediate and the pharmacological effects start faster. Compared with oral administration, IV delivery skips gastrointestinal absorption, so you avoid the variability that can happen from food intake, gastric emptying, intestinal motility, or when gastrointestinal function is compromised. Because of that, the NO-sGC-cGMP signaling pathway gets restored more quickly, which in turn supports earlier improvement in vascular relaxation, less cardiac workload, and overall more consistent therapeutic drug concentrations.^{21,25}

Also, IV administration makes dose titration more controllable since infusion can be adjusted based on the patient's blood pressure, cardiac output, renal function, and the actual clinical response being seen. During the infusion, continuous hemodynamic monitoring helps spot adverse events early, like hypotension and then you can manage it promptly instead of waiting. On top of all that, IV vericiguat is especially useful for hospitalized patients who cannot take oral medications, for example due to reduced consciousness, mechanical ventilation, severe nausea or vomiting, dysphagia, recent gastrointestinal surgery, or intestinal edema. This basically helps keep the treatment

uninterrupted even during critical illness, when things are most unstable.^{4,21,25}

Further, an IV formulation can keep the plasma drug levels fairly stable, cut down on how much the whole thing depends on patient compliance, and also work as a bridging therapy from acute inpatient care to longer-term oral management. With a more predictable pharmacokinetic profile, clinicians can fine tune dosing, look closely at infusion protocols, and even check pharmacodynamic responses in real time. Also, restoring cGMP signaling quickly may lessen myocardial stress and limit ventricular remodeling during acute heart failure, but these extra upsides still need solid confirmation through future clinical studies.^{21,22,25}

DISADVANTAGES AND CHALLENGES

Making an intravenous (IV) formulation of vericiguat comes with multiple pharma hurdles. Compared with oral tablets, an IV version has to be sterile, pyrogen-free, and particulate-free too, plus it needs to stay chemically stable. So the manufacturing process becomes more involved, almost like a whole extra layer of control. On top of that, there are other tough spots: getting enough aqueous solubility, picking the right co solvents, holding the optimal pH steady, blocking any drug precipitation, and also checking long term chemical stability. Finally, you still need to verify how it behaves with the container and infusion materials, because compatibility can be a quiet problem. All



of this, honestly, pushes up both the complexity and the overall cost of formulation development.^{21,22,,25,26}

Intravenous administration also has clinical and practical, kind of limitations. If you infuse too fast the drug can cause excessive vasodilation, and that may show up as symptomatic hypotension dizziness or even reduced organ perfusion, especially when infusion rates are not closely controlled. On top of that, IV therapy needs venous access. That access is not always straightforward, and complications can happen like phlebitis, catheter related infections thrombosis extravasation, and hematoma. Also, it leans on hospital infrastructure, trained healthcare professionals, proper infusion equipment, plus continuous patient monitoring, so overall it tends to be less convenient, and more costly compared with oral therapy.^{21,22,25}

Another big challenge is that there is limited clinical experience with intravenous vericiguat, since the medicine is presently approved only as an oral formulation. So things like IV dosing regimens and infusion rates, pharmacokinetics, long term safety, and clinical efficacy are still not established. Also, you would need a lot of preclinical work, including stability testing and sterility validation. You'd also need toxicity assessments, pharmacokinetic evaluations, and Phase I–III clinical trials before regulators could allow an IV formulation to be used in routine clinical practice.^{10,14,25}

PHARMACODYNAMICS

Pharmacodynamics is basically about how a drug does what it does inside the body, biologically and therapeutically. It covers receptor interactions, intracellular signaling paths that kinda “move messages” through cells, dose-response patterns, how fast the effect starts, how long it lasts, plus how effective it is overall in real life. In the case of vericiguat, its pharmacodynamics is more focused on fixing an impaired nitric oxide (NO)–soluble guanylate cyclase (sGC)–cyclic guanosine monophosphate (cGMP) signaling route, so vascular function gets better, myocardial stress goes down, and pathological cardiac remodeling is kept in check, instead of the drug just directly pushing the heart to contract harder.^{11,16,18}

So, in people who have chronic heart failure, nitric oxide availability is often lower and soluble guanylate cyclase activity becomes impaired. With that situation, intracellular cGMP levels drop. This shortfall doesn't stay quiet, it tends to drive endothelial dysfunction, ongoing vasoconstriction, higher vascular resistance, more myocardial fibrosis, ventricular reworking, poorer tissue blood supply, and then ultimately a worsening cycle of heart failure over time. Vericiguat helps by restoring cGMP generation— it directly stimulates soluble guanylate cyclase and makes it more responsive to the body's own nitric oxide. Then you get activation of protein kinase G (PKG) and you see improved vascular relaxation and better cardiac performance, at least in functional terms.^{3,6,16,18}

Also, the pharmacodynamic response to vericiguat depends on dose. As plasma drug concentrations rise, stimulation of

soluble guanylate cyclase and cGMP formation rises too, so the therapeutic effects become stronger. That's why clinical dose titration matters a lot, to chase the best possible benefit while also reducing risks like hypotension. And for an intravenous formulation, controlled infusion rates could make it easier to manage plasma concentrations more precisely, based on the patient's clinical status, without going too high too fast.^{3,6,11}

One of the major pharmacodynamic effects of vericiguat, is a mild kind of systemic vasodilation, it tends to bring systolic blood pressure down by about 1–2 mmHg on average when people take therapeutic doses. It seems to happen because vericiguat increases cGMP production, then activates protein kinase G, it also lowers intracellular calcium levels, relaxes vascular smooth muscle, and in turn reduces systemic vascular resistance. What's also important here is that vericiguat decreases vascular resistance but it does not directly mess with myocardial contractility, so it may be useful for patients who basically have limited hemodynamic reserve.^{1,3,16}

The pharmacodynamic profile of vericiguat really fits, the idea of developing an intravenous, (IV) drug delivery approach. With IV dosing you can get faster systemic drug exposure, and vasodilation can start right away, plus plasma levels are more predictable. There's also the benefit of titration, because you can adjust the dose precisely via controlled infusion. Having continuous monitoring of blood pressure, and cardiac function too, would likely help avoid overly low blood pressure, while still aiming for good therapeutic effect. So, intravenous vericiguat could be a promising option for critically ill patients who are dealing with acute or decompensated heart failure.^{1,13,21,25}

Overall, vericiguat pharmacodynamics support an IV formulation because the NO–sGC–cGMP pathway can be activated quickly, and therapeutic plasma concentrations can show up immediately, without the usual gastrointestinal absorption delays. IV delivery also gives precise dose control via infusion, and it becomes easier to keep watching blood pressure and cardiac function. In some settings, it may even lead to a faster reduction in ventricular stress. All these points make IV vericiguat a potentially strong candidate for critically ill patients with acute decompensated heart failure, especially when it is being used as a bridge, toward longer term oral therapy.^{1,3,4,7}

DRUG INTERACTION

Drug interaction studies are really important for judging both the safety and the overall effectiveness when medications are used together, especially in patients with heart failure, who often get several therapies at the same time. In clinical studies it has been shown that vericiguat comes with a low chance of clinically meaningful pharmacokinetic and pharmacodynamic drug interactions, so it tends to fit well with common heart failure regimens like ARNIs, beta-blockers, mineralocorticoid receptor antagonists, SGLT2 inhibitors, diuretics, anticoagulants and antiplatelet agents. This fairly calm interaction profile also



helps the move toward an intravenous, (IV) formulation, because people in hospital settings commonly end up needing a mix of intravenous as well as oral medications at the same time, and sometimes changes happen quickly.^{1,3,4,30}

Vericiguat in general has a pretty low risk for clinically meaningful drug–drug interactions, and most of those are more pharmacodynamic than pharmacokinetic, so not so much about metabolism changes. The main worry is this additive vasodilation effect, especially when its taken along with other vasodilators or antihypertensive agents. That can nudge blood pressure downward more than expected, so the chances of hypotension go up. For that reason, they really recommend careful monitoring of blood pressure during the start of therapy and again when the dose is increased. Also, vericiguat doesn't seem to change platelet function, coagulation pathways, or the metabolism of the usual cardiovascular medications you'd expect, so it should work fairly well for combination therapy in heart failure patients.^{1,3,4}

When it comes to creating an intravenous (IV) formulation, drug interaction studies become even more important, because IV dosing gives immediate whole-body drug exposure and fast pharmacological effects. Going forward, future work should look at compatibility with IV infusion fluids, stability when it's co infused with cardiovascular drugs, plus how it behaves alongside IV diuretics, vasopressors, and inotropes. It would also be useful to optimize the infusion rate, not just for efficacy but to reduce hypotension risk. Taken together, these studies can support safer, more effective clinical use of IV vericiguat in critically ill patients who often have multiple therapies running at the same time.^{21,25,30}

PHARMACOKINETICS

Pharmacokinetics kind of explains how a drug gets absorbed, spread out, biotransformed, and then eliminated (ADME) inside the body. So, getting the pharmacokinetics of vericiguat right is crucial for tuning its dose, choosing the route of administration, and also for improving therapeutic efficacy as well as overall safety. At the moment the available version is mainly an oral tablet, but if an intravenous (IV) formulation were developed, it might bypass gastrointestinal absorption, remove some of the variability linked to meals and stomach conditions, and allow near immediate systemic availability, with a fast start of action.^{19,20,28,29}

Vericiguat shows relatively predictable pharmacokinetic behavior, including a gradual move toward steady state, moderate plasma accumulation, strong plasma protein binding of about 98%, a volume of distribution close to 44 L, plus a slow clearance roughly 1.6 L/h, and an elimination half-life around 30 hours. Taken together, these features back the idea of once-daily oral dosing. They also suggest that an IV formulation could help keep fairly steady therapeutic plasma concentrations, either via a controlled infusion or via well planned intermittent dosing, while

reducing the risk of too high peak exposure, and keeping drug exposure more consistent overall.^{1,3,19,20}

The pharmacokinetic properties of vericiguat kinda make it a promising candidate for building an intravenous formulation, like the IV route. With IV administration you skip gastrointestinal absorption, so you get an immediate systemic availability, fast onset of effects, and in general more reliable plasma drug levels. By removing the back and forth variability linked to food intake gastric emptying, and intestinal uptake, an IV formulation could help deliver steady drug exposure. Then clinicians can do more exact dose adjustments, based on the patient's blood pressure, cardiac output, renal function, and this overall clinical picture that matters so much.^{1,19,20,28}

An intravenous formulation might be especially useful for hospitalized, or critically ill, patients who can't take oral medications— swallowing difficulties are a big one, also severe nausea, vomiting, gastrointestinal edema, or diminished intestinal absorption. It may also support quick stabilization in people experiencing acute decompensated heart failure. After the patient improves, therapy could potentially be shifted from intravenous vericiguat to oral vericiguat for long term maintenance, though, this approach still needs additional clinical evaluation.^{12,13,27}

Absorption

Absorption is kind of the process where a drug gets into the systemic circulation from where it is given. Vericiguat, which is currently offered as an oral tablet, is absorbed well, with an absolute oral bioavailability around 93%, especially when it is taken with food. In other words food doesn't just "help", it really boosts overall drug exposure, pushes back the time needed to reach the peak plasma concentration, meaning the T_{max}, it also raises the peak concentration C_{max} and the area under the curve AUC, and it even lowers the patient to patient differences. So basically vericiguat should be taken with food so the therapeutic effects stay more consistent.^{19,20}

Clinical studies also suggest that crushed vericiguat tablets when dispersed in water can give pharmacokinetic exposure that is comparable to intact tablets, so they may work for patients who struggle with swallowing. Still, even with intact or crushed tablets, the drug is still largely relying on gastrointestinal absorption, and that process might be influenced by things like gastric emptying, intestinal motility, food intake, or gastrointestinal disorders. As a result, the start of action can come a bit later than expected.^{1,19}

An intravenous, or IV, formulation of vericiguat, would bypass that whole absorption phase by putting the drug straight into the bloodstream. In theory it could offer 100% bioavailability, a faster onset of action and more predictable plasma concentrations, meaning the effect would be less tied to food or gut function. That could be especially helpful in critically ill patients who have acute decompensated heart failure. But turning it into a real IV medicine means you still have to tackle a set of hurdles, like improving



aqueous solubility, making sure physicochemical stability holds up, ensuring sterility, checking compatibility with IV fluids, and fine tuning the infusion rates so the treatment stays both safe and effective.^{19,20,21,25}

Distribution

Distribution is the pharmacokinetic process where a drug moves out of the bloodstream and into tissues and organs after administration, more or less. Vericiguat shows a moderate volume of distribution, around 44 L, meaning it spreads beyond plasma into extracellular and cardiovascular areas, rather than getting heavily stored in fat, or in intracellular compartments. That kind of spread is kind of “ideal” because the therapeutic target, soluble guanylate cyclase (sGC), is mostly found in vascular smooth muscle, endothelial cells and cardiac tissues, so it helps ensure strong activation of the NO–sGC–cGMP pathway.^{15,17}

About 98% of vericiguat shows up bound to plasma proteins, mostly serum albumin, while roughly 2% is left free and pharmacologically active. This strong protein binding basically works like a kind of reservoir where the drug is gradually released, so plasma levels stay fairly steady. In turn, the therapeutic effect lasts longer, drug level swings are reduced, and the odds of acute toxicity drop. Also, while notable protein-binding drug interactions haven’t really been reported, certain situations, like severe liver disease or hypoalbuminemia, can shift things by increasing the fraction that’s free, then the drug can feel more potent pharmacologically.^{13,14,19}

For an intravenous, (IV) formulation, vericiguat would reach the bloodstream right away, then rapidly attach to plasma proteins, and spread toward cardiovascular tissues with no real absorption lag. Its moderate volume of distribution along with the extensive protein binding helps support plasma concentrations that are more predictable and pharmacological effects that stay more controlled during the infusion. Because of that, clinicians can better choose an appropriate loading dose, fine tune infusion rates, and move toward a faster therapeutic start. Taking together, these features make vericiguat look like a good candidate for IV use, but only with careful clinical monitoring, of course.^{22,23,27}

Metabolism

Drug metabolism is this biochemical process where medicines are broken down or reshaped into more water-soluble compounds, so they can be removed from the body easier. In the case of Vericiguat it is metabolized mainly by Phase II glucuronidation, not by the cytochrome P450 (CYP450) system. The core route uses UDP-glucuronosyltransferase (UGT) 1A9, but UGT1A1 also adds a smaller amount. Overall, this leads to formation of an inactive N-glucuronide metabolite. Because of that, people tend to have a pretty predictable metabolism pattern, with less variability, compared to some other drugs.^{7,9,19}

This “glucuronidation-leaning” setup brings multiple clinical perks. There is generally low potential for CYP450-mediated

drug interactions, and less of an influence from genetic polymorphisms. On top of that, the chances of metabolic inhibition or induction from other co-administered medications are reduced. Since CYP450 enzymes account for under 5% of vericiguat metabolism, even if CYP enzyme activity changes, the pharmacokinetics are affected only slightly. Also, the inactive metabolite doesn’t really drive therapeutic activity, so the clinical effects rely mostly on the parent drug.^{8,14,19}

For an intravenous (IV) formulation, the actual metabolic pathway of vericiguat doesn’t really switch, because the drug still undergoes hepatic glucuronidation after it enters systemic circulation. That said, IV dosing gives immediate therapeutic plasma concentrations, it skips the variability tied to gastrointestinal absorption, and it lets clinicians fine tune plasma drug levels by adjusting the infusion rate. So, the overall pharmacokinetic behavior becomes steadier and more predictable, especially in critically ill patients.^{23,25,27}

Elimination And Excretion

Elimination is this overall process where the body gets rid of a drug, kind of via metabolism AND excretion. Vericiguat has a long elimination half-life around 30 hours, and also a low systemic clearance, about 1.6 L per hour, which lets it keep relatively steady therapeutic plasma concentrations for a while. Because of these pharmacokinetic traits it is usually compatible with once daily dosing, it also helps dampen the swings in drug levels, and it may help patient adherence during longer term use, not just short cycles.^{1,2,27,29}

After metabolism happens, vericiguat is cleared through both the kidney related, and the fecal exit route. Roughly 53% of the given dose shows up in urine mostly as the inactive N glucuronide metabolite, while about 45% can be recovered in feces, mainly as the parent vericiguat without changes. This “two way” elimination setup means the body isn’t forced to depend on only one excretory pathway which in turn tends to support steady drug clearance in most people.^{7,9,20,28}

Those elimination features look helpful when thinking about making an intravenous formulation. The long half-life together with moderate clearance could make continuous infusion or some form of control dosing more realistic, with more predictable steady state plasma concentrations. Also, this elimination profile that stays kind of stable may make it easier to go from IV therapy to an oral maintenance phase, without overdoing frequent dose changes, especially in patients whose renal and hepatic function is stable.^{20,21,25}

CLINICAL PHARMACOLOGY

Clinical pharmacology shows how a drug interacts with the human body so we get the right therapeutic effects, but at the same time we try to reduce adverse reactions. Basically, it covers the study of how a drug works, then pharmacokinetics, pharmacodynamics, plus safety and clinical efficacy, all that stuff. When you understand the clinical pharmacology for vericiguat, it matters a lot for creating an intravenous (IV) formulation, because the route



of administration really changes drug absorption and distribution, the time to onset of action, dose optimization, and the final therapeutic outcomes too.^{16,17,18,30}

Vericiguat itself is a first-in-class soluble guanylate cyclase (sGC) stimulator, and it is used in patients who have chronic symptomatic heart failure with reduced ejection fraction (HFrEF). Its main way is pretty direct: it stimulates sGC and increases the sensitivity to nitric oxide, so the disturbed NO–sGC–cGMP signaling pathway that is often impaired in heart failure can get restored again. As a result, you see higher intracellular cGMP, then activation of protein kinase G (PKG), vasodilation, better endothelial function, less myocardial fibrosis and hypertrophy, and overall improved cardiac performance.^{1,3,4,12,13}

Although it is at the moment available only as an oral tablet, some intravenous formulation of vericiguat might give meaningful clinical benefits for critically ill patients, especially those with acute decompensated heart failure, plus gastrointestinal dysfunction, or simply when they can't take oral medications properly. With IV use, gastrointestinal absorption is essentially bypassed, systemic availability comes in right away, therapeutic drug levels can be reached faster, and dosing can be tuned very precisely during continuous observation. In the end, these perks make the clinical pharmacology of vericiguat kind of a key baseline, for building a safe and effective intravenous drug delivery system.^{1,4,12,13,30}

FUTURE PERSPECTIVES

Creating an intravenous (IV) formulation of vericiguat looks like a promising next step for pharmaceutical research, but a few key things still need work before it is actually put into clinical use. First, aqueous solubility has to be tuned, then you have to pick co-solvents that are both safe and effective. After that, the formulation must be made sterile and also pyrogen free, and you still have to check physicochemical stability during storage and also while it is being infused. On top of that, compatibility matters a lot with the intravenous fluids clinicians already use, and with the infusion devices in routine practice. Finally, the pharmacokinetic behavior needs to be clarified after IV administration.^{21,22,25,26}

Beyond that, dose escalation studies are necessary, infusion-rate optimization too, plus a broad set of preclinical and clinical trials to show safety, efficacy, and whether IV vericiguat really offers therapeutic advantages, especially in people with acute or advanced heart failure. It will also be important to run comparative work against the oral formulation that is currently available, just to understand where the real clinical value lies. If these scientific and regulatory hurdles are handled well, intravenous vericiguat could turn into a useful therapeutic option for hospitalized patients who need quick cardiovascular stabilization, and it may also meaningfully widen the heart failure treatment options clinicians can choose from.^{4,21,25,30}

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CONCLUSION

The pharmacokinetic profile of vericiguat, with that pretty good oral bioavailability, a moderate volume of distribution, strong plasma protein binding, and mainly UGT - driven glucuronidation, plus the long elimination half-life, and the fact it leaves the body via dual excretion routes, basically all together make a solid argument for its role in long-term control of chronic heart failure. And honestly it also gives a strong scientific foundation for looking into an intravenous (IV) formulation. If an IV dosage form were available, it could give immediate systemic drug levels, a faster start of action, more predictable pharmacokinetics, and even more precise dose titration. That would be especially useful for patients who can't take oral medication, like, for instance, hospitalized individuals with acute or advanced heart failure.

That said, getting a successful intravenous vericiguat product isn't simple, because there are big pharmaceutical, clinical, and regulatory hurdles to jump over. Things like sterile formulation development, physicochemical stability during storage and use, infusion safety, and how well it behaves with intravenous lines and related systems. Then there is also the need for broad preclinical and clinical testing to confirm safety, efficacy, and the most appropriate dosing. So, at this point, intravenous vericiguat should be seen as a promising research idea rather than something established in routine therapy, and future studies will be needed to turn its pharmacological potential into a truly practical option for quick cardiovascular stabilization.

REFERENCES

1. Armstrong PW, Pieske B, Anstrom KJ, Ezekowitz J, Hernandez AF, Butler J, et al. Vericiguat in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2020;382(20):1883-93.
2. Armstrong PW, Roessig L, Patel MJ, Anstrom KJ, Butler J, Voors AA, et al. A multicenter, randomized, double-blind, placebo-controlled trial of the efficacy and safety of the oral soluble guanylate cyclase stimulator: The VICTORIA Trial. *JACC Heart Fail*. 2018;6(2):96-104.
3. Trujillo ME, Ayalasomayajula S, Blaustein RO, Gheys F. Vericiguat, a novel sGC stimulator: Mechanism of action, clinical, and translational science. *Clin Transl Sci*. 2023;16(12):2458-66.
4. Markham A, Duggan S. Vericiguat: First approval. *Drugs*. 2021;81(6):721-6.
5. Vannuccini F, Campora A, Barilli M, Palazzuoli A. Vericiguat in heart failure: Characteristics, scientific evidence and potential clinical applications. *Biomedicine*. 2022;10(10):2471.
6. Follmann M, Ackerstaff J, Redlich G, Wunder F, Lang D, Kern A, et al. Discovery of the soluble guanylate cyclase stimulator vericiguat (BAY 1021189) for the treatment of chronic heart failure. *J Med Chem*. 2017;60(12):5146-61.



7. Gheorghiade M, Greene SJ, Butler J, Filippatos G, Lam CSP, Maggioni AP, et al. Effect of vericiguat on quality of life in patients with chronic heart failure. *Eur Heart J*. 2015;36(Suppl):Abstract.
8. Pieske B, Maggioni AP, Lam CSP, Pieske-Kraigher E, Filippatos G, Butler J, et al. Vericiguat in patients with worsening chronic heart failure and reduced ejection fraction: Results of the SOCRATES-REDUCED study. *Eur Heart J*. 2017;38(15):1119-27.
9. Butler J, Anstrom KJ, Felker GM, Givertz MM, Kalogeropoulos AP, Konstam MA, et al. Effect of vericiguat in patients with worsening chronic heart failure. *N Engl J Med*. 2020;382:1883-93.
10. McMurray JJV, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med*. 2014;371:993-1004.
11. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med*. 2020;383:1413-24.
12. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42:3599-726.
13. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure. *Circulation*. 2022;145:e895-e1032.
14. Braunwald E. Heart failure. *JACC Heart Fail*. 2013;1(1):1-20.
15. Mann DL, Zipes DP, Libby P, Bonow RO. Braunwald's Heart Disease. 12th ed. Philadelphia: Elsevier; 2022.
16. Brunton LL, Hilal-Dandan R, Knollmann BC. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 14th ed. New York: McGraw-Hill; 2023.
17. Katzung BG, Trevor AJ. Basic and Clinical Pharmacology. 16th ed. New York: McGraw-Hill; 2021.
18. Rang HP, Ritter JM, Flower RJ, Henderson G. Rang and Dale's Pharmacology. 10th ed. London: Elsevier; 2023.
19. Shargel L, Yu ABC. Applied Biopharmaceutics and Pharmacokinetics. 8th ed. New York: McGraw-Hill; 2022.
20. Rowland M, Tozer TN. Clinical Pharmacokinetics and Pharmacodynamics. 5th ed. Philadelphia: Wolters Kluwer; 2019.
21. Aulton ME, Taylor KMG. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 6th ed. London: Elsevier; 2022.
22. Allen LV. Remington: The Science and Practice of Pharmacy. 23rd ed. London: Pharmaceutical Press; 2020.
23. Sinko PJ. Martin's Physical Pharmacy and Pharmaceutical Sciences. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2017.
24. Allen LV, Popovich NG, Ansel HC. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. 11th ed. Philadelphia: Wolters Kluwer; 2020.
25. Allen LV Jr. Injectable Drug Delivery Systems. *Int J Pharm Compd*. 2019;23(4):280-9.
26. Banker GS, Rhodes CT. Modern Pharmaceutics. 5th ed. New York: CRC Press; 2009.
27. Florence AT, Siepmann J. Modern Pharmaceutics. Boca Raton: CRC Press; 2017.
28. Gibaldi M, Perrier D. Pharmacokinetics. 2nd ed. New York: Marcel Dekker; 1982.
29. Winter ME. Basic Clinical Pharmacokinetics. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2010.
30. DiPiro JT, Yee GC, Posey LM, Haines ST, Nolin TD, Ellingrod V. Pharmacotherapy: A Pathophysiologic Approach. 12th ed. New York: McGraw-Hill; 2023.

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