Appendix 15–1 Format for Drug Monograph

Institution Name Heading

Generic Name: Can include other common, nonofficial names, e.g., TPA for alteplase.
Trade or Brand Name: If more than one, indicate company that each is from.
Manufacturer (or source of supply): Include website address.
Therapeutic Category: For example, thrombolytic agent for alteplase.
Classification: Note—other classifications, such as the VA class, can also be used.

AHFS Number and Classification: If not in the book yet, see the list in the front of American Hospital Formulary Service—Drug Information book and figure out the most appropriate classification.

FDA Classification see Tables , , , and : Include specific FDA website URL concerning approval.

Status: Prescription, nonprescription, and/or controlled substance schedule (if applicable).
Similar Agents: A list of common treatments used for the same indication(s).
Summary: Includes a short summary of advantages and disadvantages of the drug, particularly in relation to other drugs or treatments used for each major indication, and any other significant information.
Recommendations: Indicate whether or not the drug should be added to the Drug Formulary of an institution, assuming they would have patients that would be treated for illnesses where this drug might be used. Also indicate specific formulary status for the drug (i.e., uncontrolled, monitored, restricted, and conditional—see ASHP guidelines) and whether the drug will replace any other product that might already be on the formulary. In addition, present any information on how the drug is to be placed in any clinical guidelines. For third-party payer monographs, information will need to be included regarding the payment tier.
Page one consists of the above information
Pharmacologic Data

Mechanism of action (usually brief)

Bacterial spectrum (if applicable)
Therapeutic Indications

Food and Drug Administration (FDA)-approved indications (see package insert)—clearly indicate which indications are FDA approved.

Potential unlabeled uses (list only if they are considered to be acceptable medical practice, although it is allowable to mention others that are early in investigation with a statement that the drug should not be used for them or that they require more study)—clearly indicate they are not FDA approved.

How the drug, and similar drugs, fit into clinical guidelines.

Clinical comparison (abstract at least two studies; see for more abstract guidelines. Include human efficacy studies and, where available, studies comparing the product to standard therapy. *Note*: if there are other supportive studies for an indication, they can be covered briefly, if desired, along with the major study covered in detail. Be sure to note any deficiencies in the studies). Also, pharmacogenomic information may need to be included here and elsewhere.

Bioavailability/Pharmacokinetics: A table summarizing the following, in comparison to the comparator agent(s) can be very useful.

Absorption

Distribution

Metabolism

Excretion

Dosage Forms

Forms and strengths: Compare to other agents (consider a table), since new products often have a limited number of dosage forms/routes as compared to established products. Purity and composition information should be included for herbal and alternative medications.

Explain any special information needed for preparation and storage, in comparison to other products. Sometimes a product will be so difficult to prepare or have such a limited shelf-life after preparation that it is not worth stocking.

Dosage Range

Adults

Children

Elderly

Renal or hepatic failure

Special administration requirements

Any anticipated problems in supplies (i.e., shortages) or restrictions in distribution (e.g., physician needs to be certified to prescribe)

Known Adverse Effects/Toxicities

Frequency and type (a table comparing the drug to others can be a clear and concise way of expressing this information)

Prevention of toxicity

Risk and benefit data

Special Precautions: Usually includes pregnancy and lactation
Contraindications
Drug Interactions: A simple one- or two-sentence statement for each—usually separate various interactions into separate short paragraphs and compare to other drugs.

Drug-drug

Drug-food

Drug-laboratory
Patient Safety Information

Includes medication error information
Patient Monitoring Guidelines

Includes effectiveness, adverse effects, compliance, and other appropriate items
Patient Information

Name and description of the medication

Dosage form

Route of administration

Duration of therapy

Special directions and precautions

Side effects

Techniques for self-monitoring

Proper storage

Refill information

What to do if a dose is missed
Cost Comparison: Use Average Wholesale Price (AWP) and institutional prices, and make sure there is a comparison with any similar products at equivalent doses—a pharmacoeconomic analysis (see) is the best method of comparing drugs in this section; remember to include any required concomitant therapy. Providing a spreadsheet file with information to consider different circumstances may be helpful.
Date Presented to Pharmacy and Therapeutics Committee, and Name and Title of the Person Preparing the Document
References

Follow guidelines as described in .

Appendix 15–2 Example Drug Monograph

Note: This example is based on fictional products and is condensed. It shows examples of most sections in a real drug monograph, but often does not go into all of the details (e.g., a table of adverse effects is seen, but only a couple items are listed, whereas, a full drug monograph would list at least all common and/or serious reactions).

St. Anywhere Medical Center

Pharmacy & Therapeutics Committee

Drug Evaluation Monograph

Generic Name:	artiblood
Brand Name:	MegaBlood
Manufacturer:	MegaPharmics
Classification:	AHFS 16:00 Blood Derivatives
	FDA Classification:1A
	Status: Prescription Only

Summary

Artiblood is a new perfluorocarbon that has many similarities to the only other product in its class, fakered. Both products have the ability to temporarily replace the oxygen-carrying function of red blood cells in patients in whom use of whole blood or packed red blood cells is impossible due to medical or religious reasons. In general, artiblood was found to be more efficacious than fakered; however, it also has been shown to produce a greater number of adverse effects. The adverse effects are mostly gastrointestinal in nature; however, the increased INR can be a problem in some patients. Artiblood is not metabolized in the body, whereas fakered is approximately 50% metabolized to inactive components. These differences are generally not clinically significant, since the dose of either product is unlikely to need adjustment. Fakered is available in several different volume bags, allowing the dose to be matched more closely to the anticipated patient need. While the cost of fakered appears to be lower, a pharmacoeconomic analysis shows that artiblood would produce the greatest cost savings for the institution.

Recommendations

It is recommended that artiblood be added to the Drug Formulary for use restricted to those who cannot use natural blood replacement products because of religious reasons or because suitable blood types are not available.

Pharmacologic Data

Artiblood is a type of perfluorocarbon similar to fakered. These products have the

unique ability to freely bind with or give up oxygen, depending on the partial pressures of the gas where the product is located (i.e., in the lungs there is an abundance of oxygen, so the product adsorbs oxygen; in the tissues there is a relative deficiency of oxygen, so the product gives up the gas).[1,2] The products do not have direct immunologic properties, nor do they have the ability to aid in blood clotting, although there may be some affect on blood clotting (either interference by coating platelets or precipitation of the clotting pathway mechanism).[3]

In addition to oxygen-carrying capabilities, the products have some plasma volume expansion properties. Artiblood has a similar effect to Dextran 40,[1] whereas fakered's properties are relatively insignificant.[4] Maximum plasma volume expansion occurs within several minutes of administration and lasts for approximately one day in normal patients. This results in increased central venous pressure, cardiac output, stroke volume, blood pressure, urinary output, capillary perfusion, and pulse pressure. Microcirculation is improved.

Therapeutic Indications

Indications

Artiblood is FDA approved for the short-term replacement of the oxygen-carrying capabilities of blood in patients who cannot use normal whole blood.[1] In addition, the product has been used successfully in cardiac catheter procedures, although this use is not FDA approved.[5] There is some early research into the use of the product as a plasma expansion product, but there is not enough information to support this use.[6]

Fakered is approved only for use in cardiac catheterization,[2] although it is commonly used as a blood replacement product in patients who cannot or will not use whole blood products.[7]

Evidence-Based Clinical Guidelines

A search of the literature was performed to identify evidence-based clinical guidelines. This included MEDLINE®, EMBASE Drugs and Pharmacology, the National Guideline Clearinghouse website, the American College of Cardiology website, and approximately a dozen Internet search engines; however, no applicable guidelines were identified.

Clinical Studies

Max and Sugar[6] conducted a comparison trial of artiblood (500 mL/day administered once over 1 hour—80 patients) and fakered (750 mL administered once over 90 minutes—82 patients) in patients (18–80 years of age) suffering from massive blood loss (>1 L), who could not use whole blood due to religious beliefs (e.g., Jehovah's Witnesses). In the artiblood group, all patients were undergoing open-heart surgery, as were 78 of the patients in fakered group. The remainder of the fakered group consisted of gunshot patients. Patients with renal insufficiency (creatinine clearance <50 mL/min) or diagnosed with liver dysfunction were eliminated from consideration. Both groups were similar, except that the artiblood group had more smokers, which may have had an affect on oxygen requirements. Withdrawals from

the artiblood group were for the following reasons: death due to failure of heart-lung machine (1 patient), noncompliance with protocol (10 patients), worsening symptoms (3 patients), and side effects (1 patient: vomiting). The authors noted that protocol compliance problems were due to inappropriate staff education and were not related to the drug itself. In the fakered group, withdrawals were due to side effects (1 patient: diarrhea, 1 patient: nausea, 1 patient: abdominal cramps) and noncompliance with protocol (2 patients). The patients were assessed on the following items: oxygen and carbon dioxide content of the blood (samples drawn immediately before and after administration, and every 4 hours for 24 hours), coagulation profile of patient (drawn within 2 hours before and after administration), affect on normal blood chemistry profiles (SMA-20) (drawn within 2 hours before and after administration), and time to discontinuation of supplemental oxygen to the patient. Adverse effects were also noted. Results were analyzed using appropriate statistical methods. Artiblood was found to increase the oxygen-carrying capabilities of the blood in comparison to fakered ($p < .01$), although fakered did significantly improve oxygen-carrying capabilities over baseline ($p < .05$). While fakered had minimal affect on blood chemistry and coagulation profile, it was noted that INRs were increased in patients receiving artiblood ($p < .001$). Other adverse effects, mostly gastrointestinal in nature, were more common with fakered, although the symptoms typically disappeared within 2 hours of administration. Other measured characteristics seemed similar between the two groups. The authors concluded that artiblood was the superior agent, due to increased oxygen-carrying capabilities. The authors downplayed adverse effects, although the effects on INRs do appear worrisome. (Other studies would be covered here for all likely uses within an institution.)

Bioavailability/Pharmacokinetics[16–18]

Absorption

Absorption is not applicable, since these agents are administered by IV infusion.

Distribution

Artiblood is found in the blood stream, with little being distributed to the tissues. Approximately 5% of fakered is found in the liver, with the rest being in the bloodstream.

Metabolism

Artiblood is not metabolized in the body, whereas approximately 50% of fakered is broken down to inactive components and is excreted in the bile.

Elimination

Artiblood has a half-life of 5 to 15 hours. It is excreted unchanged in the urine. The longer half-life is seen in patients with renal insufficiency. Since the drug is usually given as a single dose, renal insufficiency does not pose a significant problem. Fakered has a half-life of 4 to 7 hours in normal patients. Significant renal or hepatic impairment may double the half-life.

Dosage Forms

Large Volume Parenteral

Artiblood: 500 mL IV bags

Fakered: 500, 750, and 1000 mL IV bags

No other forms or strengths available. Artiblood will have limited availability for the next 6 months due to the ability of the manufacturer to produce an adequate amount to satisfy demands. No problems in availability are expected after that point.

Dosage Range

The normal dose of artiblood for blood replacement is 500 mL, which may be repeated once after 4 hours. Doses may be cut in half for patients weighing less than 50 kg. No dosage adjustments are necessary in renal or hepatic impairment. The product has not been tested in patients younger than 12 years of age and is not recommended in that population. No dosage adjustment is necessary in the elderly.[1]

Fakered is given in doses of 500 mL to 1 L, with a maximum daily dose of 1.5 L. The dose is adjusted based on clinical response of the patient. The product can be used in patients as young as 6 years of age; however, the initial dose is 250 mL.[2]

Known Adverse Effects/Toxicities

The two agents are compared in the following table

Adverse Effect	Artiblood (% of Patients)	Fakered (% of Patients)
Gastrointestinal		
Nausea	20	7
. . .	. . .	. . .

Special Precautions

Neither drug has been studied long-term, therefore, the effects are not known in that situation.

Both products are considered Pregnancy Category C. Tests in pregnant animals have shown adverse effects and no adequate, well-controlled studies have been conducted in humans. There is no information available on the excretion of the drug in human milk. Overall, when considering use in pregnant or lactating women, the physician must consider the benefits versus the risks.

Safety and effectiveness of artiblood in children have not been established, although

fakered may be used in children at least 6 years old.

Contraindications

Both agents are contraindicated in patients with hypersensitivities to the drug or any component of the dosage form.

Drug Interactions

Drug-Drug Interactions

Affects of heparin or low-molecular weight heparins may be significantly increased by either artificial blood replacement agent, although the affect by artiblood tends to be greater. There is no effect on either artiblood or fakered, although the heparin may improve circulation of the products to underperfused tissues. (Other interactions for both drugs would be listed and compared.)

Drug-Food Interactions

None are known or expected, since these agents are given intravenously and do not undergo enterohepatic recirculation.

Drug-Laboratory Test Interactions

INRs can be increased by both agents, although the effect is more noticeable with artiblood. (Other interactions for both drugs would be listed and compared.)

Patient Safety

This product has a good patient safety profile, with relatively minor adverse effects (e.g., nausea). Since the product has no coagulation or immunologic activity, health care providers must be aware that it is only used for temporary help in oxygen-carrying capabilities.

Patient Monitoring Guidelines

Monitor patient for objective evidence of effectiveness (e.g., oxygen content of blood and clinical effects). Obtain baseline INR and normal chemistry values, and monitor regularly. Monitor for adverse effects.

Patient Information

In a patient receiving the product due to trauma, it is likely that he or she will not be able to be given information. In that case, provide the information to the next of kin or guardian. Inform patients that the product is an intravenous product that does not contain any blood products. The patient or family should know that he or she may receive this product once or more during the first day after surgery. The patient or family should be informed that the drug has few noticeable adverse effects other than some gastrointestinal upset; however, the physician or pharmacist should be consulted if anything unusual occurs. The patient or family should know that some blood tests

will be regularly performed to exclude the possibility of adverse effects. The nurse will keep the drug refrigerated until approximately 30 minutes before infusion. Warnings about missed doses are irrelevant.

Cost Comparison

General Pricing Information

	AWP	Daily Dose*	St. AMC	Daily Dose*
Artiblood 500 mL	$2500/bag	$2500	$2310/bag	$2310
Fakered 500 mL	$1000/bag	$1000	$800/bag	$800
Fakered 750 mL	$1500/bag	$1500	$1200/bag	$1200
Fakered 1000 mL	$2000/bag	$2000	$1600/bag	$1600

*Assume used one bag of each strength.

Pharmacoeconomic Analysis

Problem definition: The objective of this analysis is to determine which artificial blood product should be included on our drug formulary.

Perspective: This will be from the perspective of the institution.

Specific treatment alternatives and outcomes: There are two drugs to be compared, artiblood and fakered. It will be assumed that natural blood products are not an alternative, since the ability to use natural products would preclude consideration of the artificial products. The outcomes to be measured are hospital costs.

Pharmacoeconomic model: A cost-benefit analysis will be performed. A cost-utility analysis would be desirable, but insufficient information is available. *Note:* no published pharmacoeconomic analysis is available. The following table is based on information obtained from the literature concerning efficacy, adverse effects, monitoring, and so forth and uses St. AMC costs, since outside prices would be irrelevant.

	Cost per Patient	Benefit-to-Cost Ratio	Net Benefit
Cost of artiblood (including administration, monitoring, adverse reactions, and so forth)	$5120	$7430/$5120 = 1.45:1	$7430–$5120 = $2310
Benefits of artiblood (money saved by early patient discharge from ICU)	$7430		
Cost of fakered (including administration, monitoring, adverse reactions, and so forth)	$4000	$4500/$4000 = 1.125:1	$4500–$4000 = $500

Benefits of fakered (money saved by early patient discharge from ICU)	$4500		

NOTE: The above information is a summary of information, including averages, decision analysis, and sensitivity analysis that would be used in a pharmacoeconomic evaluation. While the details could be presented here, that may be distracting and confusing to some readers—a decision must be made as to whether all of the details will be presented. See for details on how to prepare a pharmacoeconomic analysis of a drug being evaluated by the P&T Committee.

SOURCE: Presented by John Q. Doe, Pharm.D. to the Pharmacy and Therapeutics Committee on February 30, 20XX.

References

References would be listed in the order in which they are cited in the text—see for format and details.