

Guidance on Availability of Antidotes, Reversal Agents, and Rescue Agents

Created by the Section Advisory Group on Medication Safety

ASHP Section of Inpatient Care Practitioners (SICP)



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ASHP's Medication Safety Section Advisory Group (SAG), Section of Inpatient Care Practitioners (SICP)

Purpose

The Institute for Safe Medication Practices (ISMP) biannually publishes the *ISMP Targeted Medication Safety Best Practices for Hospitals* to prioritize and focus efforts on consensus-based approaches to mitigate medication safety risks. ISMP Best Practice 9 was first introduced in 2016 with a goal to ensure an antidote, reversal agent, or rescue agent is readily available to mitigate adverse drug reactions or the effects of toxic doses.

ISMP BEST PRACTICE 9: Ensure all appropriate antidotes, reversal agents, and rescue agents are readily available. Have standardized protocols and/or coupled order sets in place that permit the emergency administration of all appropriate antidotes, reversal agents, and rescue agents used in the facility. Have directions for use/administration readily available in all clinical areas where the antidotes, reversal agents, and rescue agents are used.

- Identify which antidotes, reversal agents, and rescue agents can be administered immediately in emergency situations to prevent patient harm.
- Use this list to develop appropriate protocols or coupled order sets to ensure that the above Best Practice is met.

Current guidelines broadly identify antidotes, reversal agents, and rescue agents, indications, and recommended dosing. An opportunity remains for practical application of access priority, health-system approaches to inventory management, and clinical decision support opportunities.

The purpose of this document is to provide guidance for organizations implementing or seeking to improve compliance with ISMP Best Practice 9. The following topics are covered: methods of this consensus document, definitions, *at minimum* recommended list of agents, additional considerations, and the role of the pharmacy department and the poison control center. The recommendations in these guidelines represent a consensus of documented evidence, expert opinion, and professional judgment. They are written to establish reasonable goals that are progressive and challenging yet attainable as best practices in applicable settings. Pharmacy professionals and health-care organizations are encouraged to exercise their professional judgment in assessing and adapting these recommendations to meet the specific needs of their organizations.

Methods

Antidote, reversal agent, and rescue agent lists from local/regional poison control centers (2) and large academic medical systems (4), which included two children's hospitals, were compared by an expert panel of pharmacists with expertise in Toxicology, Emergency Medicine, Critical Care, Medication Safety, and Pharmacy Operations. Recommendations from available clinical literature and guidelines were also reviewed and included, when applicable. Criteria for agent inclusion on the final list included presence on at least three to four facility-specific lists. Several specific agents were also added based on clinical expertise or guideline recommendations (see *Additional Considerations* for further details).

The Role of the Pharmacy Department and Poison Control Centers

The role of the Pharmacy Department and pharmacists is to exert leadership in the development, maintenance, and ongoing evaluation of the usage of antidotes, reversal agents, and rescue agents across the health-system. Pharmacists should facilitate an annual review of the antidote, reversal agent, and rescue agent list, including regular review of available literature and guidelines. Pharmacists with additional post-graduate training in critical

care, emergency medicine, and/or toxicology are ideally suited for this work. Order sets and/or clinical protocols are also essential to facilitate appropriate, safe, and timely application of these recommendations. Clinical decision support tools and protocols should be approved through appropriate organizational committees (e.g., Pharmacy & Therapeutics Committee). Departments of Pharmacy involved in this work should consult local experts for additional support, such as Poison Control Centers. For further guidance for stocking recommendations based on local trends and for assistance with finding certain antidotes, contact your Poison Control Center at 1-800-222-1222.

Definitions

Agent: for the purposes of this document, a drug or compound used as an antidote, reversal agent, or rescue agent.

Antidote: a drug or compound that counteracts or neutralizes a toxin.

Antivenin: a compound that functions like an antidote and counteracts or neutralizes toxins (venom) produced by animals, insects, or reptiles.

Reversal Agent: a drug or compound that reverses the effects of a drug or toxin by targeting its mechanism of action or function at the receptor.

Rescue Agent: a drug or compound that targets the symptomatic effects of a drug or toxin.

Vaccine: a compound used to stimulate the production of antibodies and provide immunity against bacterial or viral diseases.

Antidote, Reversal Agent, and Rescue Agent List

Organizations should create and maintain a list of antidotes, reversal agents and rescue agents.

An Antidotes, Reversal Agents, and Rescue Agents Critical Inventory List (Appendix 1) proposes an *at-minimum* recommendation of what agents should be considered. Pharmacy professionals and health-care organizations are encouraged to exercise their professional judgment in assessing and adapting these recommendations to meet the specific needs of their organizations. See the list below for an explanation of the various categories of information included in the list.

Classification: refers to the function of the agent listed for the indication. Classifications include antidote, reversal agent, rescue agent, antivenin, or vaccine. (See *Definitions*)

Indication: refers to the indication for the agent listed when used as an antidote, reversal agent, or rescue agent.

Access Priority Tiers: categorize urgency of access of agents for the listed indication. The purpose of the tiers is to provide actionable information to health-systems to help guide approach to inventory management. Tier 1 is immediate access, lifesaving situation, and/or can involve multiple victims. Tier 2 is immediate access, lifesaving situation of a single victim. Tier 3 is emergent access within 4 hours from presentation. Tier 4 is urgent access greater than 4 hours. Tier 5 is for emergent or urgent cases, but the agent is suspected to be a part of the general medication inventory for other indications (e.g., epinephrine).

Route: appropriate route of administration for each agent.

Minimum Quantity to Treat: based on the treatment of one 100 kg patient for the course of 24 hours.

Additional Consideration for Quantity-on-Hand: additional information for each agent including if the agent is high-cost, has a historic limited availability, or if it is appropriate for an alternate inventory strategy (e.g., city-level collaborative supply or hub and spoke model for health-systems).

Order Set or Clinical Protocol Recommendation: agents that were deemed to require clinical decision support and/or protocols due to rarity or complexity of use.

Additional Considerations

Anticoagulation Reversal Agents

Anticoagulation reversal agents were deemed outside the scope of this review due to the large number of agents that meet this classification. Organizations should consider patient population and anticoagulants listed on formulary to drive which anticoagulation reversal agents are available.

General Usage Agents

Agents in this section should be widely available and already stocked within the health-system setting (i.e., for other indications). These agents can also serve as antidotes, reversal agents, or rescue agents, and have been included to ensure a complete list of treatment options.

Targeted Agents: Animal Venom, Toxin, or Disease-specific

Animal-specific agents were reviewed for the purpose of this guidance document. Inclusion of these agents may vary regionally, depending on the presence of the offending animal or animal disease. Commercial access to these agents may be complicated, limited, or required direct contact with the manufacturer.

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References

1. Institute for Safe Medication Practices (ISMP). *ISMP Targeted Medication Safety Best Practices for Hospitals*. ISMP; 2022. <https://www.ismp.org/guidelines/best-practices-hospitals>.
2. Dart RC, Goldfrank LR, Erstad BL, et al. Expert consensus guidelines for stocking of antidotes in hospitals that provide emergency care. *Ann Emerg Med* 2018 Mar;71(3):314-25.

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