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Commentary

COMMENTARY

An Ethical Framework for Allocating Scarce Life-Saving Chemotherapy and Supportive Care Drugs for Childhood Cancer

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Abstract

Shortages of life-saving chemotherapy and supportive care agents for children with cancer are frequent. These shortages directly affect patients' lives, compromise both standard of care therapies and clinical research, and create substantial ethical challenges. Efforts to prevent drug shortages have yet to gain traction, and existing prioritization frameworks lack concrete guidance clinicians need when faced with difficult prioritization decisions among equally deserving children with cancer. The ethical framework proposed in this Commentary is based upon multidisciplinary expert opinion, further strengthened by an independent panel of peer consultants. The two-step allocation process includes strategies to mitigate existing shortages by minimizing waste and addresses actual prioritization across and within diseases according to a modified utilitarian model that maximizes total benefit while respecting limited constraints on differential treatment of individuals. The framework provides reasoning for explicit decision-making in the face of an actual drug shortage. Moreover, it minimizes bias that might occur when individual clinicians or institutions are forced to make bedside rationing and prioritization decisions and addresses the challenge that individual clinicians face when confronted with bedside decisions regarding allocation. Whenever possible, allocation decisions should be supported by evidence-based recommendations. "Curability," prognosis, and the incremental importance of a particular drug to a given patient's outcome are the critical factors to consider when deciding how to allocate scarce life-saving cancer drugs.

Over the past decade, drug shortages, defined as a supply of a marketed drug inadequate to meet current or projected demand (1), have become increasingly common (2). Shortages of chemotherapy and supportive care agents (CASCA) related to cancer care have been particularly frequent (3,4). The typical CASCA in short supply is a generic sterile injectable drug (5,6). Drug shortages occur for a variety of reasons and are especially common in the United States (7–11). Although there have been fewer new drug shortages in the United States since 2012, the number of active drug shortages has steadily increased, reaching an all-time high of 320 as of September 30, 2014, with 265 drugs currently in shortage (12). Strategies to prevent shortages have been proposed (13–18) yet are unlikely to be fully effective. Proposed strategies to solve the drug shortages largely focus on the primary reasons for drug shortages, including economic, manufacturing, and quality and regulatory drivers. In this regard, proposed solutions include, but are not limited to, establishment of a national stockpile of critical drugs, creation of US Food and Drug Administration (FDA)–quality metrics to incentivize and reward high-quality manufacturing practice, amending federal

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policy to allow for greater price increases for generic oncology products, and promote sharing of drugs between hospitals. Adopting these changes will require multilevel stakeholder engagement, including involvement by pharmacists, clinicians, hospital administrators, drug manufacturers and distributors, patients and patient advocates, regulators, and members of institutional drug shortage committees. Moreover, a number of barriers constrain these recommendations. Challenges include disagreement about specific drugs deemed "critical," unproven effectiveness of new incentives, concern over increased cost and possible reduced access to generic cancer drugs, legal and institutional barriers, and resistance to sharing drugs. Although the number of drug shortages has increased over the past decade, physicians—and oncologists in particular—report little formal guidance in making decisions about allocating scarce drugs. Ongoing shortages of CASCA raise serious ethical challenges, necessitating a framework that allows for a reasoned and consistent response.

Beyond the associated economic costs (19–21), drug shortages directly affect patients' lives. Drug shortages have resulted in increased medication errors, delayed administration of life-saving therapy, inferior outcomes, and patient deaths (4,22–26). Drug shortages prevent clinicians from providing standard-of-care therapies and hinder critical clinical research efforts.

In the context of an emerging national debate on drug shortages, a multidisciplinary North American working group (WG) on chemotherapy drug shortages in pediatric oncology recently published its findings examining the ethical and policy implications of chemotherapy shortages in childhood cancer (27). The Consensus Statement focused on recommendations to prevent and mitigate shortages of essential drugs for children with cancer. The statement also provided a blueprint for effective and ethical management of drug shortages in pediatric oncology and other disease disciplines. Adopting the WG's recommendations will require an integrated framework with multilevel stakeholder engagement grounded in coordination and cooperation, including representation by government, industry, and relevant professional organizations. Until such a framework has been developed, and because the Consensus Statement did not provide specific recommendations for prioritization of scarce chemotherapy, we offer the following ethical framework for allocating CASCA among patients during a shortage.

Methods

The current report represents an extension of the WG's initial efforts with recommendations from an allocation task force (TF). The primary audience includes pediatric oncologists and hospital administrators at institutions that care for children with cancer although the framework also has implications for pharmacists, regulators, pharmaceutical manufacturers, and patients and families.

Responding to a charge from the Chairman of the Children's Oncology Group (COG), three members of the WG steering committee convened the Allocation Task Force. The seven-member interdisciplinary and multi-institutional TF possesses expertise in pediatric oncology, nursing, psychiatry, research ethics, palliative care, pharmacy, pharmacology, and bioethics and includes a parent advocate. To inform the analysis and development of an ethical framework, TF members were provided with an annotated bibliography previously utilized by the WG (27). TF members were then presented with two vignettes describing national shortages of vincristine and methotrexate, which are essential chemotherapy agents in many pediatric oncology therapeutic protocols (Supplementary Materials, available online). Meeting initially in person and then via teleconferences and functioning as a hypothetical drug shortage committee, the TF discussed the vignettes and reached consensus on an ethical framework for rationing of life-saving CASCA. An independent panel of peer consultants with expertise in pediatric oncology, law, regulatory affairs, pharmacology, bioethics, and advocacy reviewed a preliminary version of the report. The consultants' feedback was incorporated into a revised report. Recommendations were reached after iterative discussion and input as noted above. Where consensus could not be reached, we note the range of opinion. The final report, endorsed by the leadership of COG and the American Society of Pediatric Hematology/Oncology, provides concrete recommendations and reasoning for explicit decision-making in the face of an actual drug shortage and specifically aims to assist COG member institutions in navigating this difficult decision-making process.

Ethical Principles

Fair allocation of scarce resources should be based upon sound ethical reasoning. Prioritization frameworks upon which to base such decisions have been previously proposed (28–32). Ideally, evidence-based recommendations should support decisions about allocating a particular drug in a given circumstance. However, the context of allocation is always complex. Clinicians must fulfill their fiduciary responsibilities to current patients while remaining mindful of obligations to other current and potential future patients. Moreover, they must consider how to utilize a scarce drug across patients who differ by disease, age, prognosis, and other salient factors. Approaches to such decisions might include utilitarian models that emphasize saving the most lives, life-years, or quality-adjusted life-years; impartial systems that allocate scarce resources according to chance (eg, by lottery); prioritarian models that allocate drug to the worst-off patients (eg, according to the urgency of their medical situations); or social value criteria based upon patients' perceived or potential value to society. The complete lives system (28), advocated by Persad and colleagues, incorporates five principles combining various features of the above systems. Daniels and Sabin's accountability for reasonableness (A4R) model (32) and Rosoff's (33) modification thereof combine various approaches and are most helpful as procedural approaches. None of these frameworks, however, readily provides the concrete guidance clinicians need when faced with difficult prioritization decisions among equally deserving children with cancer.

The TF's consensus framework for prioritizing life-saving CASCA starts from a utilitarian model that maximizes total benefit from the available supply of drug, modified by limited constraints to exclude unjustified differences in the treatment of individual patients. Such an approach emphasizes lives or life-years saved and has previously been used to allocate scarce resources such as influenza vaccines, penicillin, ventilators, and hospital beds in response to pandemics. Moreover, it is widely viewed as part of an acceptable framework to allocate scarce medications (28–33). In this guidance document, we emphasize maximizing lives rather than life-years saved because all patients within its scope are children and therefore fall within a narrow age range. Considering life-years saved might be appropriate when allocating a scarce resource within a population that involves greater diversity of age, but to a first approximation we assume that all pediatric oncology patients, if cured of their disease, have similar life expectancies. Our guidance aims at minimizing bias that might occur when individual clinicians

or institutions are forced to make bedside rationing and prioritization decisions and addresses the challenge that individual clinicians face when confronted with bedside decisions regarding allocation of CASCA. As the TF only included childhood cancer providers, the framework is limited to decisions within pediatric oncology and does not address how the claims of children with cancer might be weighed against those of adults with cancer or of patients with rheumatologic or other relevant diseases treated with CASCA.

Decision-Making During a Shortage of Chemotherapy and Supportive Care Agents

Faced with a drug shortage, the TF recommends a two-step process. Step I includes strategies to mitigate an existing shortage by minimizing waste. Step II addresses actual prioritization across and within diseases grounded in a modified utilitarian model that maximizes total benefit while respecting limited constraints on differential treatment of individuals.

Shortages of CASCA preclude the use of standard of care therapies for some children. Accordingly, shortages compromise a child's best possible outcome. Thus, we recommend that institutions adopt a reasoned, explicit, transparent, and public prioritization framework in which decisions are not made at the bedside of individual patients. Given the challenging nature of bedside allocation decision-making, a multidisciplinary institutional drug shortage committee (DSC) or similarly appointed body should make prioritization decisions. In constituting such a committee, institutions must ensure appropriate stakeholder representation, including, but not limited to, physicians, nurses, psychosocial clinicians, pharmacists, administrators, ethicists, and patient advocates. Additionally, patient and family representatives should be proactively engaged in the allocation decision-making process. Because children, parents, or physicians, may question the allocation decision as it applies to their individual situation, we also recommend that the institutional framework include a process for appeal to a group with sufficient expertise and authority to make a final determination. Such a group should assure that allocation strategies are clearly stated, widely disseminated, and uniformly and fairly applied.

Legal considerations are beyond the scope and purview of this task force. It is important to note that in a true drug shortage some patients will not receive optimal therapy, either through planned allocation of drug or through random chance. Similarly, if required drugs are not available for patients on clinical trials, protocol deviations are inevitable. If a drug shortage compromises a trial's integrity and scientific validity, trial sponsors and oversight bodies may have little recourse other than to halt trial accrual. Moreover, if regimens within a trial are altered during the course of a drug shortage, it may be impossible to make substantive observations and reach conclusions related to a trial's objectives.

The two clinical scenarios presented in the Supplementary Materials (available online) illustrate the dilemmas that may arise during a scarcity of CASCA. The TF utilized the scenarios during its deliberations to facilitate consensus regarding principles and generate concrete recommendations. Although individual institutions will necessarily allocate scarce resources like CASCA in different ways based on the specific needs and unique features of the patients they serve, the following guidance is applicable to a shortage of any life-saving medication, including both scenarios described in the Supplementary Materials (available online), and should be considered when providers face a shortage of CASCA.

Step I – Mitigation

The first response to a shortage of CASCA should be to maximize efficiency and minimize waste. In order to meet this obligation, confronted with a CASCA shortage, members of the DSC require up-to-date information regarding the severity, extent, and anticipated duration of the shortage. When applicable, institutions should adopt additional practices as outlined in Table 1. Effective management of a drug shortage requires a coordinated effort by multiple stakeholders, including pharmacists, clinicians, hospital administrators, drug manufacturers and distributors, patients and patient advocates, regulators, and members of the institutional DSC. These efforts, as described in Table 2, should be pursued alongside the practices outlined in Table 1.

Considerations for Mitigation

1. Drug shortages range in scope with some shortages limited to individual hospitals while other may affect a region or even the entire nation. The degree to which a given drug is scarce influences available choices and responses by clinicians and health systems. Shortages of CASCA should trigger a mechanism to assess the level of response required. Such responses may range from local measures to a national strategy akin to a national emergency. Viewing a drug shortage as a natural disaster or a natural emergency achieves more than raising public awareness; it also provides a mechanism for potential policy change (44) and

Table 1. Mitigation strategies to maximize efficiency and minimize waste during a shortage of chemotherapy and supportive care agents*

Verify if the scarce drug is listed either on the American Society of Health System Pharmacists (ASHP) (34) or the FDA (35) drug shortage websites
Determine supply and anticipated duration of the shortage to assist in the decision-making process regarding allocation
Anticipate drug needs for current and expected patients
If the preferred drug brand or strength is not available, contact manufacturers directly as alternate product sizes (ie, larger or smaller vial size) may be available
When possible, select alternative therapies with equivalent safety and efficacy profiles
Cohort patients receiving similar therapies on the same day in order to share vials that otherwise are meant for single use
Borrow drug(s) from, or share drug(s) with, neighboring institutions
If scarcity is expected to be short lived, administer the scarce drug out of sequence
If feasible, compound drug on own or acquire from a commercial compounding pharmacy
Acquire the scarce drug via FDA lending
If stability and sterility profile supports doing so, consider extending drug usage beyond labeled expiration date

* FDA = US Food and Drug Administration.

Table 2. Stakeholder responsibilities during a shortage of chemotherapy and supportive care agents*

Responsible party	Action
Pharmacist or designee	If the scarce drug is not listed either on the ASHP or the FDA drug shortage websites, notify ASHP and/or FDA to update their list
	Contact the drug company for an update on supply and anticipated duration of the shortage
	Insight into the expected duration can assist the institutional DSC in its decision-making process
	Contact other institutions to determine the extent of a shortage and verify if they are willing to share drug(s)
	As a result of varied distribution of a given product nationally (36), drug supplies may be unevenly distributed during a shortage, with some institutions having a relative surplus while others experience scarcity
	Order drug(s) strictly based on the hospital's typical needs (ie, no hoarding)
Drug manufacturers and distributors	To prevent hoarding, internally allocate drugs in a fair and transparent manner based on a hospital's ordering history
Clinician	If an alternative regimen exists that either avoids using the scarce drug or uses less of it, it should be employed
	To help drive allocation decisions, determine what the next best alternative is and how much worse (if at all) it is than the accepted standard
	As much as possible, consideration should be given to the (negative) impact of the alternative on survival as well as on quality of life both in the near term and the long term
	Alert the DSC when an alternative exists and be prepared to provide evidence-based facts to assist the committee in their deliberations
	Discuss with patients/families the process by which allocation decisions were reached
Institutional drug shortage or similarly appointed committee	Allocation and prioritization
	Arbitrate challenges to allocation decisions
Hospital administrator	Assure timely treatment without unnecessary interruptions or delays
Patients/patient advocates (parents/guardians)	Proactively engage in the allocation decision-making process
FDA	When manufacturers authorized by the FDA to sell drugs in the United States are unable to address a shortage in an expedient and timely manner, FDA should investigate the feasibility of securing an adequate supply of the drug from a non-US supplier until the shortage has been alleviated
	Previous examples of such FDA actions include importation of methotrexate injection, leucovorin injection, thiotepa, doxorubicin liposomal, sodium glycerophosphate, zinc injection, and IV saline solution (37–43)

* ASHP = American Society of Health System Pharmacists; DSC = Drug Shortage Committee; FDA = US Food and Drug Administration.

remediation (45). A recent example of such remediation includes the November 2013 joint Centers for Disease Control and Prevention and FDA initiative allowing importation of a Swiss vaccine to curtail an outbreak of (strain B) bacterial meningitis at two US universities (46).

2. In a shortage, hospitals should not order more drug than they typically require in a given period, ie, hospitals should not hoard drugs. Drug hoarding is common, with 85% of hospitals having purchased excess inventory in response to drug shortages (47). Rather, as much as possible, hospitals should honestly anticipate their drug needs, allocating drug(s) for current and expected patients.
3. If a hospital lacks one or more drugs required by the patient, rather than delay treatment or select an inferior regimen, the hospital should attempt to secure a supply for that patient from another institution or refer the patient to another institution able to provide the necessary care. The good of the patient supersedes financial consequences to the hospital or physician.
4. If a drug's stability and sterility profile supports doing so, institutions should consider extending usage beyond typical and accepted practice. For example, in some centers intrathecal methotrexate vials are disposed of four hours after the vial has been punctured (opened) to minimize the risk of microbial contamination, while in reality vials may be used for up to 24 hours, especially when the drug is prepared in an appropriate hood-utilizing aseptic technique. In the United States, administering an expired drug violates pharmacy law and practice standards, but during a national emergency or national disaster such as a drug shortage, permission to administer an expired drug should be sought when evidence supports the safety of doing so (48). Pharmacies may also consider engaging their risk management or legal department to determine which steps should be taken to document noncompliance with these laws, when applicable. Other strategies to optimally utilize scarce CASCA include scheduling patients with similar diseases on the same day in order to share vials that otherwise are meant for single use.

Step II – Allocation

Allocation decisions must be transparent and public. Just allocation of scarce CASCA requires one to consider the perspectives of patients who are denied access, as well as the perspectives

of legitimate decision-makers such as the DSC. When decision-makers must articulate and justify the principles behind their choices, the result is likely to be more reasoned, thoughtful, and explicit decision-making. Such accountability is also more likely to gain patients', families', and the public's trust that institutions are acting in a legitimate and fair manner. Limit-setting should be reasoned and based upon values and principles.

In formulating its recommendations, in addition to maximizing lives, the TF considered several overarching principles, including, but not limited to, fairness, maximizing benefit, and minimizing harms. For example, fairness, related to the ethical principle of justice, requires that there be equitable access to drugs across and within institutions. That is, all similarly situated people deserve the same opportunity to receive the scarce drug. As a corollary, fairness requires justifying decisions to treat some people differently. Employing representative examples across and within diseases, Table 3 provides specific guidance for allocating scarce drugs during a shortage of CASCA.

Considerations for Allocation

1. Shortages of CASCA preclude the use of standard of care therapies for some children. As such, shortages compromise a child's best possible outcome. In such unjust circumstances, "curability" and prognosis should be emphasized in the allocation of scarce CASCA. Furthermore, in extreme cases, it may be acceptable to compromise relapse-free survival if second-line therapy using drugs that are not in shortage accomplishes the same overall survival in the event of recurrent disease (eg, early-stage Wilms tumor) (52).
2. In its deliberations, the TF discussed the various ways "curability" may be applied in practice. One approach is the so-called threshold of "curability" as occurs when a child with an 80% chance of survival receives priority over a child with a 40% chance of survival. This approach requires a degree of precision regarding prognosis that may only be possible to achieve in practice when the magnitude of difference is large. In contrast, we do not advocate prioritizing treatment between two children whose chances of survival are closer to one another, eg, 80% vs 70%. This approach becomes more complicated in scenarios involving patients whose overall chance of survival differs but who have an identical numerical difference in survival (eg, when one child has an 80% chance of survival and the other a 60% chance of survival, the difference between them is the same as that between a child with a 30% chance of survival and another with a 10% chance).
3. The incremental impact of the agent on survival represents another aspect of "curability" that merits consideration. While overall curability might favor prioritizing treatment of a child who has an 80% chance of survival with the drug and a 70% chance of survival with an alternative regimen that does not include it, priority should also be considered for patients with "less curable" diseases, especially when the particular scarce drug is necessary to offer the chance of cure (eg, a child who has a 40% chance of survival with the drug and a 5% chance of survival without it). In this case, the second child should receive priority because the drug gains her a larger increment in expected survival. It is rare, however, to have such precise estimates of a drug's contribution to outcome, especially with agents like vin-

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Table 3. Allocation considerations across and within diseases during a shortage of chemotherapy and supportive care agents*

Guiding principle	Representative chemotherapeutic	Representative disease(s)	Allocation rationale
Drug allocation should be evidence-based	Methotrexate	ALL NHL Osteosarcoma	Based on the strength of evidence, patients with ALL and NHL should receive priority over those with osteosarcoma (49,50) IT-MTX in ALL should be prioritized over systemic MTX in osteosarcoma
Maximize benefit according to total lives saved/life-years saved given the available supply of drug	Methotrexate	ALL NHL	Escalating dose Capizzi regimen should be prioritized over superior HD-MTX
Incremental importance of a particular drug to a given patient's prognosis, including diseases with poor prognosis	Doxorubicin Cisplatin Vincristine	Sarcomas GCT Many	Because of its crucial role in offering the chance for cure, doxorubicin should be prioritized to patients with sarcomas over patients with Hodgkin's lymphoma (51)
Total amount of the scarce drug required per regimen	Dactinomycin	WT (low risk)	Dactinomycin should be prioritized to patients with a curable disease requiring a relatively small amount of the scarce drug (eg, some lower-risk WT) over diseases that require more of the drug and have a lower overall survival (eg, high-risk RMS)
Phase of therapy	Vincristine	ALL NHL	Patients with a larger disease burden, early on in the course of treatment, should receive priority access to a scarce drug

* ALL = acute lymphoblastic leukemia; GCT = germ cell tumor; HD-MTX = high-dose methotrexate; IT-MTX = intrathecal methotrexate; MTX = methotrexate; NHL = non-Hodgkin's lymphoma; RMS = rhabdomyosarcoma; WT = Wilms tumor.

cristine and methotrexate that have been in use for more than 50 years.

4. During a shortage, whenever possible, drug allocation should be evidence-based, including evidence for a particular drug in treating a given disease. For example, when allocating injectable methotrexate in the face of a shortage, patients with acute lymphoblastic leukemia (ALL) should receive priority over those with osteosarcoma because of the lack of consensus as to the role for methotrexate in the treatment of osteosarcoma (53–55) and much stronger evidence for the benefit of methotrexate in the treatment of ALL. In addition, proven uses of a drug should be prioritized over promising but still unproven uses.
5. Phase of therapy is another consideration. Arguably, vincristine is more critical to a child with ALL who is in the initial induction phase of therapy and who therefore has a large disease burden than it is to a child with ALL with no detectable residual disease who is nearing the end of maintenance.
6. The total amount of the scarce drug required per regimen should also be a factor. Patients with a curable disease who require a relatively small amount of a scarce drug should receive priority over patients with a more difficult to treat disease that requires a larger amount of the scarce drug (eg, prioritizing dactinomycin for patients with low-risk Wilms tumor not eligible for treatment with single-agent vincristine or with surgery alone over patients with high-risk rhabdomyosarcoma). In the case of methotrexate for the treatment of ALL, compared with escalating-dose Capizzi-based regimens, high-dose methotrexate is associated with a superior five-year event-free survival. However, Capizzi methotrexate utilizes 20% of the total methotrexate dose per patient per cycle (1 g/m^2 vs 5 g/m^2). Therefore, based on the premise of total lives or life-years saved, patients should receive the lower-dose Capizzi methotrexate regimen rather than the marginally superior high-dose methotrexate.
7. In the context of a clinical trial, uses of a scarce drug within the standard-of-care backbone should receive priority over investigational uses of the same drug.
8. As many children with cancer ultimately participate in clinical trials, the question arises of whether or not children enrolled in a clinical trial should receive preferential access to a scarce drug over children who opt not to participate in a trial. Given the risks that research participants accept and the fact that patients who participate in trials contribute to generalizable knowledge that helps future patients, a moral argument might be made that investigators have a reciprocity-based obligation to prioritize research participants over nonparticipants (56,57). At the same time, valid reasons exist against offering research participants access to a scarce drug. These include concerns about coercion if patients and parents fear being denied access to a scarce drug unless they enroll in a trial, public perception, and the imperative to use drugs for indications for which evidence of benefit exists (27). Thus, trial participants should not receive priority access over non–trial participants.
9. Factors that should not play a role in allocating scarce CASCA include patient age, development, ability to pay, race, ethnicity, disability, or immigration status. In addition, although giving smaller children priority access to drugs that are dosed according to weight or body surface area might maximize lives saved per milligram of available drug, doing so would unjustifiably discriminate against older or larger children and should be impermissible.
10. Patients and families affected by drug shortages must be appropriately apprised of decisions about their treatment. Doing so respects patients and their caretakers as individuals who deserve to be informed and who may have something meaningful to contribute to current and future deliberations. We suggest that an institutional letter, explaining the situation and the process by which allocation decisions were reached, be shared with patients and their families.

Conclusions

Solving the drug shortage problem will ultimately require a major policy shift, one that is grounded in coordination and cooperation. Until that time comes, individuals and institutions that care for children with cancer must be prepared to make difficult decisions about allocating scarce life-saving chemotherapy. If shortages of CASCA persist despite mitigation strategies, prioritization should be based upon maximizing benefit according to total lives or life-years saved. Whenever possible, allocation decisions should be supported by evidence-based recommendations. “Curability,” prognosis, and the incremental importance of a particular drug to a given patient’s outcome are the critical factors to consider when deciding how to allocate scarce life-saving cancer drugs. Proven and standard-of-care uses of a drug should receive priority over promising but as yet unproven uses, and clinical trial participants should not be receive priority over non–trial participants. Lastly, patient and family representatives should be proactively engaged in decision-making about allocation as members of a DSC.

While healthcare rationing is inevitable, rationing life-saving chemotherapeutics and supportive agents raises many ethical challenges. Physicians lack sound guidance in making ethically appropriate decisions for allocating scarce drugs. In the absence of a much-needed national advisory statement on how best to allocate scarce drugs and until policymakers and stakeholders can prevent future shortages, the guidance articulated here supports reasoned decision-making in the face of an actual drug shortage and aims to minimize bias as might occur when individual clinicians or institutions are forced to make difficult, and at times tragic, rationing decisions for children with cancer.

Notes

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