ISOPP CAPhO Collaborative Drug Shortages Webinar Q&A:

1. Etoposide injection by Medac is being discontinued -last batch expires NOV 2024. This is the only benzyl alcohol free option currently in UK. We require benzyl alcohol free for intrathecal administration and for IV in neonates. What do you use in your countries for etoposide intrathecal/intraventricular administration? Any experience of using Etoposide Phosphate for these situations.

   - [SHAUN]: Sorry I cannot comment on the etoposide phosphate - suggest ask as an ISOPP forum question as I don't work in paediatrics and have need for this formulation.
   - [MARC]: I do not have experience with Etopophos via those routes
   - [NIRACHORN]: Etopophos is not available in Thailand. I do not have experience with it.
   - [ANNEMERI]: I do not have experience with etoposide by other routes other than IV or oral

2. How can we create a more harmonized global regulatory framework for drug manufacturing and distribution to prevent shortages of essential anticancer medications?

   - [SHAUN]: This is a very tricky question - global harmonization needs to be first led by organisations such as FDA and regional/local variants such as TGA. I'm not sure that harmonization might create less shortages - the story of the last decade is concentration of manufacture to reduce costs increasing the vulnerability to black swan events such as we saw with BCG Connaught strain. There are a number of other factors that I will discuss later that affect this as well.
   - [MICHAL]: Completely agree with Shaun on this one- I also think WHO might need to be involved. I think that a more global approach would be good but difficult to manage with different laws/licenses etc. Think this may be for the nations governments to have an input in as well.
   - [MARC]: Agree with Shaun and Michal – no additional comments.
   - [NIRACHORN]: I do agree with Shaun, Michal and Marc
   - [ANNEMERI]: No additional comments

3. How do we predict or prevent drug shortage before this situation happens?

- [SHAUN]: Difficult as not enough information exists in a central database that could make sense of it. Would need to have access to:
    1. Knowing which companies manufactured drug and where it is registered and appropriate for use
    2. Manufacturers schedule, stock, interruptions and spare capacity to assist in shortages (all of which that may not want to share as commercial in confidence)
    3. Wholesalers and secondary distributors stores (again commercial in confidence issues)
    4. Health services stock on hand and ability to modify/reduce usage based on alternative protocols/products
    5. Changes over time in treatment trends (e.g. displacement of lines of treatment by newer therapies)
    6. Trends of secondary usage (e.g. if failures in region A, which region and stock is likely to be impacted as impacted health services reach out for stock)
    7. Abilities of non-current manufacturers to step into the space and produce usable medications

  Even if we could get all of this together, still difficult to predict what a minor bump in supply might be compared with a longer shortage due to uncertainty/changing nature of manufacturing issues etc. at pharma end (again see BCG - no-one predicted shut down of plant when it first started).

- [MICHAL]: Can we develop a system to monitor supply chains and detect potential shortages early? How to do that, I don't know. But someone who is IT savvy could? As this information can be freely available/accessible?
- [MARC]: I think manufacturers require to inform if there is a possibility of a drug shortage in advance. It would help sites be better prepared in the event there would be a shortage.
- [NIRACHORN]: Hospital level: Communication between purchasing team, pharmacy team and vendors (pharmaceutical manufacturers or distributors). Regional or Country level: change in treatment trends: new clinical practice guidelines, new agents approval, and change in reimbursement protocol from government
- [ANNEMERI]: Manufacturers are able to predict drug shortage according to the cause. They should be more transparent and advance information for hospitals. To prevent Drug shortages which are the result of lack of commercial interest would be necessary stricter laws, especially with drugs without generic substitutes.

4. When there are drug shortages, can we use alternative drug from another Company for a patient who has taken about three cycles of treatment.

- [SHAUN]: Yes, definitely for small molecules where there has been bioequivalence shown. Biosimilars appear to be moving towards interchangeability BUT this has not been proven to my knowledge and has changeover concerns. Need to consider risk/benefit of waiting (how long/chance of recurrence or treatment failure) vs treating with alternative (risk of treatment failure).
- [MARC]: Yes definitely if generics as these are interchangeable. As for biosimilars, it will depend on your country/Jurisdiction's policy regarding interchangeability of biosimilars. I would imagine in a world where the trade is not available and short, that physicians would want their patients to be treated with a biosimilar instead of no drug.
- [NIRACHORN]: Yes, alternative drug means same in generic name (same salt). I do agree with Shaun, Michal and Marc.

5. Can alternative therapies provide the same results as we providing them parent product. Are they effective can provide same efficacy, won't disturb patient's treatment Cycle. As, in our daily practice in Pakistan we do consider other options.

- [SHAUN]: Depends on the individual evidence for therapy - for some of our colleagues, they will make these decisions all the time based on what is available for treatment. Sometimes this can result in the selection of inferior treatments BUT again risk/benefit of waiting vs treatment now.
- [MICHAL]: Absolutely! If there is a drug shortage what is the second-best treatment? or is there a treatment of equivalent efficacy that can be used? Use published evidence, speak to colleagues in other centres, use ISOPP for advice.
- [MARC]: Agree with Michael and Shaun's comments. I think it depends a lot on tumor type and the evidence. Best to do literature search and connect with clinicians for their opinion.
- [NIRACHORN]: I do agree with Shaun, Michal and Marc. No additional comments.

6. If one option commonly stated as dealing with a shortage is to import licensed drug, are we in danger of creating other shortages in those markets?

- [SHAUN]: Yes definitely, I think this is a risk and has occurred with some drugs - might call this shortage contagion. However, this is a complex and multifaceted situation with other scenarios coming into play, like manufacturers being able to bring forward future production to somewhat meet demand etc. that may not happen if the shortage is strictly kept local. I don't have a good answer as to what the most ethical answer is to this question.
- [MICHAL]: Definitely, but it is difficult to predict and manage. But if all move to the second option it will relieve the pressure from the first and some of that shortage will be eased off. I suppose you want even distribution across all efficacious treatments.
- [MARC]: Yes there is.
- [NIRACHORN]: Yes, there is.

7. Regional procurement teams in the UK, can often see what drug available at some sites if their pharmacy systems are linked and try to mange shortages through mutual aid. With newer drugs that come direct from wholesalers that is more difficult to co-ordinate.

- [SHAUN]: Agreed - highly dependent on local systems. Other jurisdictions may want to see if this type of coordination is possible for them.
- [MARC]: Agreed.
- [NIRACHORN]: Agreed.

8. How dangerous are expired cytotoxic drugs.

- [SHAUN]: Good question. We are not allowed to extend expiries post what is listed in our country and I cannot recommend this.
- [MICHAL]: Difficult to answer and no blanket answer. I suppose members could speak to manufacturers on stability data and see if anything could be recommended or look at published evidence.
- [MARC]: Difficult to predict. We would not be allowed to use expired drugs in our jurisdiction
- [NIRACHORN]: Depends on type of cytotoxic agents, type of co-solvent and condition of storage. Some impurities occur during storage. (Uncontrolled temperature and humidity) most of them are unknown substances which may loss of potency or toxic to vital organs. To use an expired cytotoxic drugs need to be verified by manufacturers (Many pharmaceutical companies generate the worst case scenario or keep of range or generate in-use stability for submit to FDA to expand the expiry date on the label.)