Ask RxSource

Direct-from-manufacturer or Open Market: what is the best way of sourcing a comparator?

Sourcing comparator drugs for Clinical Trials can be complicated. Even an experienced Procurement team can fall victim to unexpected complications. Having a good understanding of the market landscape will help reduce the risk of supply issues, and to develop plans to help mitigate against these.

There are four main strategies for sourcing comparator products/co-medications for clinical trials:

- Direct from the manufacturer
- Open-market sourcing (centralised or local/regional) via wholesalers
- Pharmacy supply (site or retail pharmacies)/reimbursement
- Hybrid approaches.

All approaches have positives and negatives, and the strategy chosen is dictated by the needs of each trial. A good partner will be able to support multiple approaches, and will collaborate with Sponsors to determine the best sourcing strategy for their trial. Provided of course the Sponsor is willing to share trial details with their partners, as opposed to just requesting a number of packs of comparator. Let's touch on some of the positives and negatives of each approach:

Direct from the manufacturer

Positives

- Fewer links in the supply chain – reduced handing/shipments & reduced risk of counterfeiting/ tampering.
- Best way to get required batch sizes, e.g. large single batches with maximum expiry.
- Access to supporting documentation, such as Certificates of Analysis.
- Manufacturers can plan additional demand into their production schedules, reducing the risk of an unplanned surge in demand from clinical trials leading to drug shortages in the wider market.

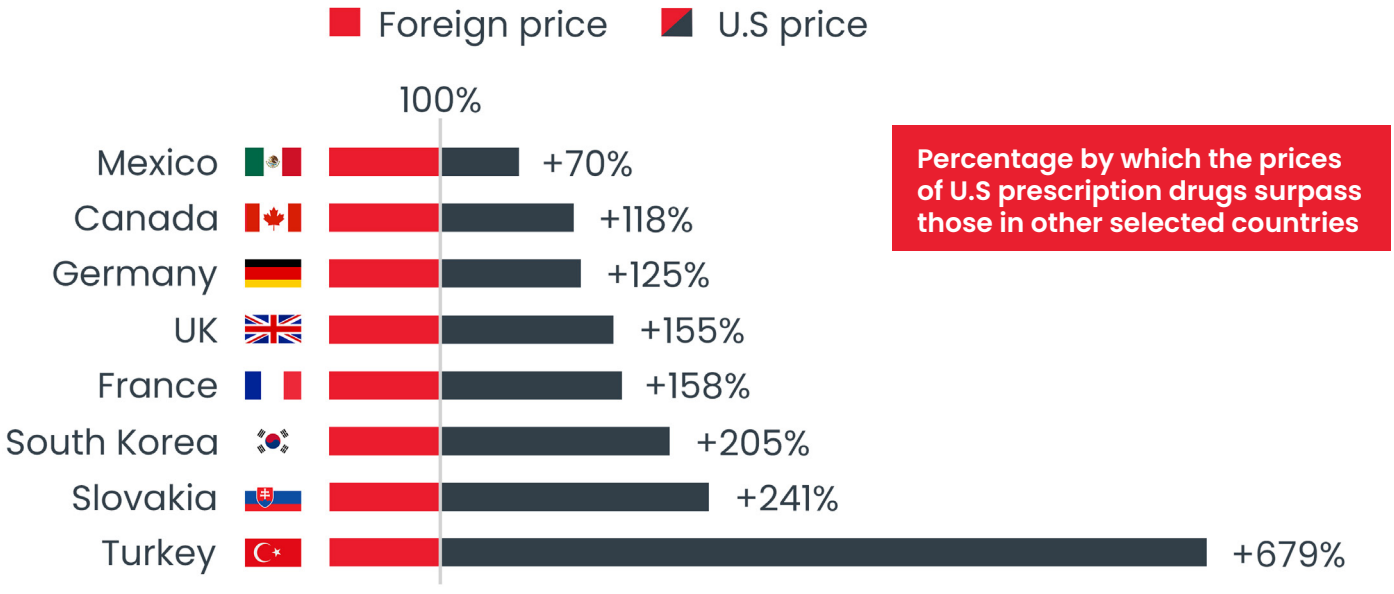
Negatives

- Manufacturers generally request clinical trial information before agreeing to supply; while the level of detail requested is usually

minimal, and is often available from public sources (e.g. clinicaltrials.gov), Sponsors are often reluctant to share this with manufacturers.
- Costs can be higher for this approach, compared with open market sourcing. In our experience, Manufacturers often apply a clinical trial price to sourced products more often than not, closer aligned to pricing in more expensive markets.
- Lead times can be longer, especially is the Manufacturer needs to schedule additional or larger manufacturing campaigns to accommodate increased demand.

Open Market Sourcing

Positives
- Product can be sourced from the open market which can be easier to facilitate from multiple options.
- Potential for shorter lead times – product may already be released and available in wholesaler inventories. However, for high demand products, and those in short supply at the time of request, some products may be tightly controlled by their Manufacturer. The result of this could be that each wholesaler is given a quota, and can only order up to the limit of that quota in a given time period.
- Potential for better pricing. Drug prices vary country-country as shown in the graph below. Open market sourcing gives Sponsors the ability to access comparators from lower cost markets. However, bear in mind that lower cost markets often have limited stocks, so we always recommend choosing a larger and potentially more expensive market as a back-up if seeking to include a low cost market as the main source for a trial.



Percentage by which the prices of U.S prescription drugs surpass those in other selected countries

2019 - 2021 analysis of 2018 prices
Source: Statista.com & Rand Corporation

Negatives

- Certificates of Analysis are not always available for products sourced from the open market. If this documentation is required, it should be specified at the time of inquiry, allowing sourcing partners to focus only on wholesalers able to provide this.
- Inconsistent supply of product with no guarantees of batch size.
- Shorter expiry dates compared with sourcing directly from manufacturers. Manufacturers may delay releasing new batches onto the market until existing inventories have been exhausted, which can result in shorter expiry dating on products sourced from the open market.
- Supply-and-demand factors can influence pricing. If demand is outstripping supply, prices to clinical trial users may increase…wholesalers are businesses after all.
- Sourcing from a lower cost market for a trial operating in the same region (e.g. sourcing from a low cost EU country for an EU trial) should not present any challenges. However, if a Sponsor plans to source comparator in a low cost country/region for a trial running in a different country/region (e.g. source EU product for use in a US trial), they discuss their plans up-front with regulators. In our experience, this is common practice provided Sponsors can justify their decision and/or can provide documentary evidence that product sourced from another market is equivalent to that approved in the trial country. Over the years, RxSource had built a library of 'equivalency statements' to support our clients in these discussions with regulators.

When sourcing from the open market, the most common approach we see is centralised sourcing, in which sourcing for the entire study is performed in a single market. This approach is especially common for trials in which comparator/co-medications are going to be re-packaged and re-labelled. Centralised sourcing reduces the number of batches and expiry dates that need to be managed over the course of the trial, simplifying inventory and expiry date management. It can also reduce the risk of waste compared with local sourcing – for example, if product is sourced locally for a specific country that then does not recruit any patients. Please be aware of the final bullet in the above list if adopting a centralised sourcing strategy globally!

We see local sourcing less frequently. This approach avoids the need to seek regulatory approval to use 'foreign' medicines in a trial. Also, if commercial packs are not going to be re-labelled, it can also avoid the need to translate patient information leaflets into local languages, should this be required. Finally, sourcing of small quantities from multiple markets may approve accessibility of products during shortages. However, sourcing from multiple markets can add complexity to downstream activities such as packaging (more batches of materials = more packaging operations, batch records, QA/QP release activities), inventory management, expiry date management and can generate waste is product is sourced from countries that do not recruit patients as anticipated.

Pharmacy Supply

Rather than ship comparator products or co-medications to clinical sites, Sponsors may ask that sites use their own inventory for patients, and reimburse sites for any product used. Alternatively, Sponsors may ask patients to collect commercial products from retail pharmacies, and either reimburse patients, or provide them with trial-specific 'pharmacy cards' to pay for medication.

Positives

- Potential for minimal waste. Drug does not need to be pre-bought by the Sponsor, and wasted if enrolment periods extend beyond the shelf life of sourced medication.
- Simplified inventory management, expiry date management and no re-labelling/over labelling of commercial products.
- Cost of shipping commercial products to clinical sites is eliminated.

Negatives

- Only suitable for open-label trials.
- Geographic limitations – requires partnership with a pharmacy chain covering most, if not all, countries in the trial. This can work in the US, but will it work in more fragmented retail pharmacy markets in other parts of the world.
- If site-supplied comparator/co-medications are used, site mark-ups on reimbursed products can be significantly higher than those applied by wholesalers.
- Additional administrative burden as a result of handling claims for reimbursement, although pharmacy cards can help reduce this.

Hybrid approaches

We have seen these used to attempt to capitalise on the strengths of the above strategies – especially for large global clinical trial, and those spanning multiple years. For example, a Sponsor may wish to source directly from a manufacturer, but delivery timelines offered by the manufacturer could delay their desired start date for their trial. To allow their trial to start when planned, the Sponsor may source from the open market initially to support the trial ahead of Manufacturer-supplied inventory becoming available.

To conclude

As described above, there is no perfect sourcing solution that will meet the needs of all trials. Clinical trial supply companies, and sourcing specialists, work closely with Sponsors to match their sourcing strategy closely to the needs of a trial. Combining this with their knowledge of product availability and pricing in global markets can help Sponsors to achieve cost effective reliable supply. At the end of the day, these service providers do this every day across multiple sponsors and trial designs, so their continued business depends on doing this right. In most cases, developing a successful sourcing strategy goes beyond the simple purchasing activity it is often seen as.

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