A brief overview of the evidence base for most popular medications in Ukraine

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Most drugs in the top-12 of sales in Ukraine have no proven efficacy.

Background

Ukraine - one of the few countries with very favorable conditions for the promotion of medicines. In particular, the following three items should be noted:

- Most medicines are sold without a prescription.
- Permission to advertise all registered OTC.
- No institution provides control of the information given on the drug’s packaging in accordance with the principles of evidence-based medicine.

In Ukrainian pharmaceutical market shows steady growth for the past 9 months. Thus, compared to the same period in the last year it demonstrates an increase in drugs sales by 9.3% and in monetary terms by 18.3%.

Of course, pharmaceutical companies are interested in the best possible sales of their products. For this purpose, in Ukraine, they have all needed possibilities, including an impact on the doctor's opinion and influence on the patient’s choice (by advertisements). If physicians can make the decision based on their knowledge and skills, objectively evaluate data for a given active substance, patients do not have such opportunity. In addition, the possibility of doctors for the clinical trials data analysis is also limited due to the language barrier (most guidelines and studies are published in English) and possible conflict of interest, which is not controlled by the public or government.

In this brief review, we have analyzed the evidence base for each drug, which is in the top 12 of sales in Ukrainian retail networks.

Methods and materials

Top-12 drug list was obtained from the newspaper "Pharmacy" (for the first 9 months of the 2017 year). For each brand was specified main active ingredient; several components, in case of combined medication. To understand whether the drug has sufficient evidence base, we analyzed the following points:

- The approved active ingredient (at least one brand), or combinations by the US Food and Drug Administration (FDA). Data searching was performed on the institution’s official website.
- The presence of the active ingredient in the clinical guidelines of the National Institute for Health and Clinical Excellence (NICE). Search was conducted on the official website of this organization.
- Published Cochrane Systematic Reviews on the active ingredient. Also, clinical significance of the results was analyzed, as well as authors’ conclusions regarding the substance.
Results

Results are presented in Table 1. As can be seen from the data, only 3 drugs from the top 12 have a sufficient evidence base for their use. Note that this short review does not aim any advertising purposes. We emphasize that it was based on evidence only for the active substance rather than the brand. As part of the analysis, we assume that the effectiveness of medications with different commercial names that have the same active ingredient is similar.

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Main active ingredient(s)</th>
<th>Presence of the active ingredient in the NICE guidelines</th>
<th>Approval by FDA</th>
<th>Presence in the Cochrane Reviews</th>
<th>Confirmed effectiveness in the Cochrane Reviews</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actovegin</td>
<td>Filtered extract obtained from calf blood</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Nurofen</td>
<td>Ibuprofen</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nimesil</td>
<td>Nimesulide</td>
<td>-</td>
<td>-</td>
<td>+ + (indirect review)</td>
<td>-</td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td>Sodium chloride</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nospanum</td>
<td>Drotaverine</td>
<td>-</td>
<td>-</td>
<td>+ + (labour)</td>
<td>-</td>
</tr>
<tr>
<td>Essentiale</td>
<td>Polynylphosphatid ycholine</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Reosoribact</td>
<td>Sorbitol</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Ringer's solution (sodium chloride, potassium chloride, etc.)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Citramon</td>
<td>Acetylsalicylic acid, paracetamol, caffeine</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Spasmalgon</td>
<td>Metamizole sodium</td>
<td>- (ban)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pityfenon</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Fenpiverinium bromide</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sinupret</td>
<td>Primula veris, Gentiana lutea, Sambucus nigra, etc.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tyvortin</td>
<td>Arginine hydrochloride</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cardiomaagnyl</td>
<td>ASA</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Magnesium hydroxide</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 1. Analysis of evidence for the medicinal products included in the top 12 by sales in Ukrainian retail networks.

Briefly about each medication with questionable evidence base:

- **The filtered extract obtained from calf blood.** We found no evidence for the use of the active substance in any medical condition.
- **Nimesulide.** This medication refers to NSAID class. It is not approved by FDA and mentioned in the NICE protocols. We have found several Cochrane review, but with no direct comparisons and conclusions on this drug. Although it was not the aim of this brief review, we have also conducted a search of decision by the European Medical Agency (EMA). According to the findings, the risks associated with this drug, far exceed its benefits. Its intake should be limited only for an acute pain and primary dysmenorrhea. Long-term intake, including osteoarthritis, is not recommended.
• **Drotaverine.** We have found one mention of the drug in the Cochrane Systematic Review, which analyzed antispasmodics effectiveness in labour («Antispasmodics for labour»). No definite conclusion on its effectiveness was stated. This substance is not approved by FDA.

• **Polyenylphosphatidylcholine.** This drug is not recommended by the FDA, is not mentioned in any of NICE guidelines and has not been studied as part of any Cochrane Systematic Review.

• **Combination: sorbitol + Ringer's solution.** This combination is not found among the solutions approved by the FDA, and not mentioned in NICE protocols or Cochrane Systematic Reviews. Of course, Ringer's solution is widely used in medicine and is one of the most extensively used solutions according to WHO. We found several substances that have a similar combination of active ingredients (containing sorbitol), but, again, they are only used in veterinary medicine (i.e., Dexolyte).

• **Combination: metamizole sodium + pitofenone + fenpiverinium bromide.** None of the components is mentioned in Cochrane Systematic Reviews or NICE protocols. Also, FDA has imposed a ban on a metamizole sodium because of side effects. Also, this drug is banned in the UK and 30 other countries. In most other countries its use is severely restricted: only by prescription, in limited quantities, with the pain that can't be controlled by other drugs.

• **Synupret®.** Extract of different herbs. According to the Ukrainian State Register it is listed as a medicine. This combination is not approved by FDA. Also, we haven’t found any recommendations for its use in NICE and Cochrane Systematic Reviews.

• **Arginine hydrochloride.** A similar situation.

• **ASC + magnesium hydroxide.** Of course, aspirin is an effective medication for the prevention of adverse cardiovascular events. This drug has an extensive evidence base in Cochrane Systematic Reviews, it is approved by FDA and is included in NICE guidelines. On the other hand, the combination of ASA and magnesium hydroxide is rather strange. First, magnesium hydroxide is used as a laxative (by the way, has a good evidence base in this area). Second, it reduces the effectiveness of ASA. Third, such a combination is not approved by FDA, NICE, and was not a subject for effectiveness evaluation in Cochrane Systematic Reviews.

**Additional information**

**Competing interests**

The author declares that no competing interests exist.

**References**

2. US Food and Drug Administration. Official site. Publisher Full Text