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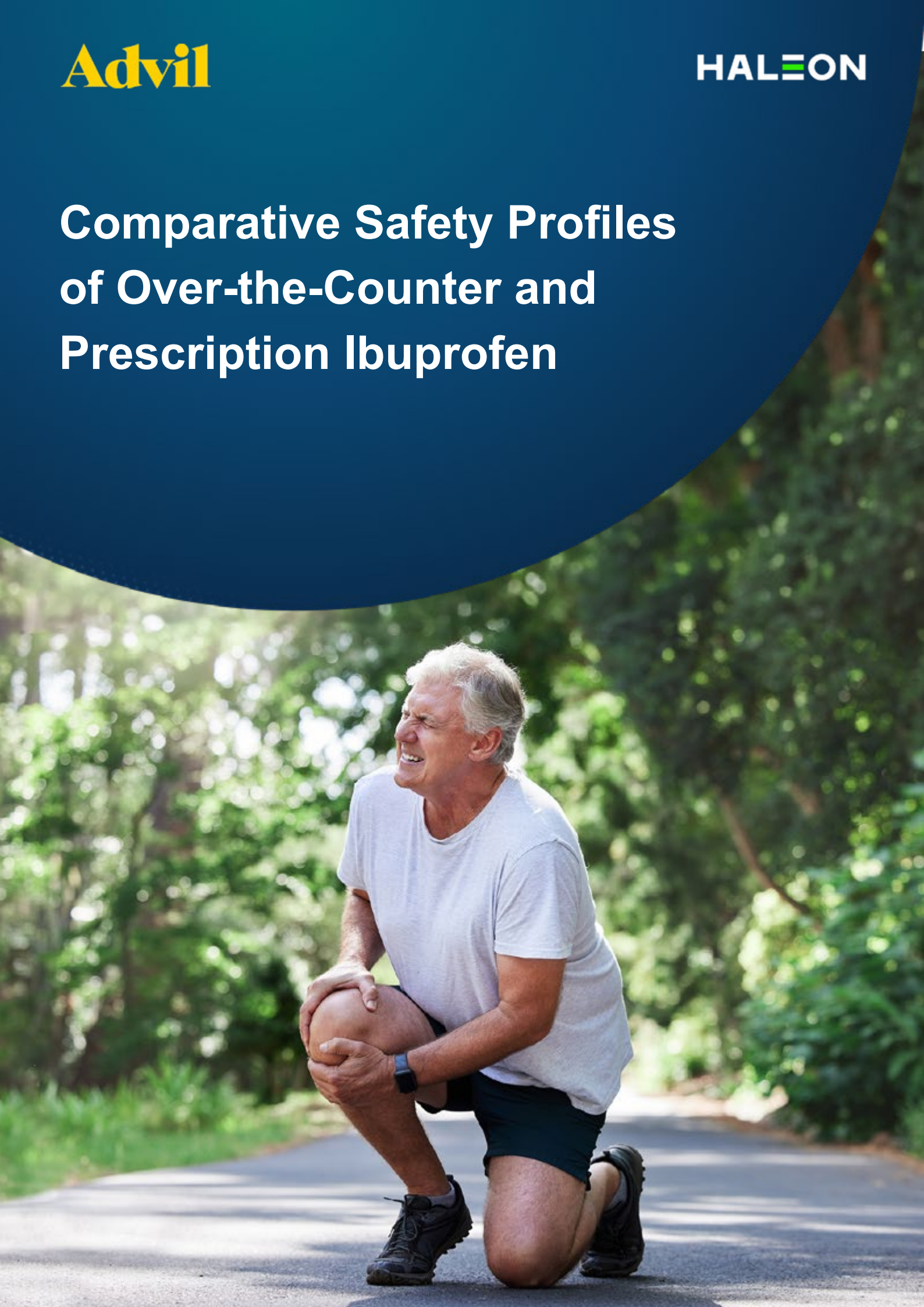
Comparative Safety Profiles of Over-the-Counter and Prescription Ibuprofen



Background

- Ibuprofen, clinically proven for alleviating various pain conditions, is recommended for temporary relief of minor aches and pains, such as headaches, toothaches, backaches, menstrual cramps, cold symptoms, muscular aches, and minor arthritis pain, as well as for reducing fever[1]
- Over-the-counter (OTC) doses range from 200–400 mg per dose, up to 1200 mg/day and is used for mild-to-moderate pain, fever, and menstrual cramps, while prescription doses range from 400–800 mg per dose, up to 3200 mg/day for chronic conditions like rheumatoid arthritis and osteoarthritis[2]
- A review by Moore et al. (2015) indicates that ibuprofen has a long history and proven safety profile at both prescription and OTC dosages[3]. Additionally, a meta-analysis showed that the overall incidence of adverse events among ibuprofen-treated subjects aged 65 years or older was equivalent to placebo, highlighting its excellent safety profile for both general and older populations[4]
- Extensive clinical data and regulatory guidance support that at recommended OTC doses for up to 7–10 days, ibuprofen has a favorable gastrointestinal and cardiovascular safety profile compared to prescription doses and other NSAIDs, with a positive benefit/risk profile when used as directed[1,5]
- Adverse reactions to ibuprofen appear to be dose and duration dependent. This document is aimed to distinguish the safety of OTC use of ibuprofen from its prescription use

Gastrointestinal (GI) safety profile

A combined analysis encompassing 40 clinical studies confirmed that lower OTC doses of ibuprofen have a significantly better GI profile and better tolerability compared to higher, prescription doses[6,7]

GI Bleeding[8] (OR)

1.1

4.6*

Prescription doses of ibuprofen have a greater risk of GI bleeding compared to OTC dose

GI Hospitalization[9] (Risk)

<0.2%

Greater risk

GI hospitalization are rare (<0.2%) at OTC doses

Mucosal injury[10]

Not significant (Degree of mucosal injury 0.46)

Evident (Degree of mucosal injury ranges from 1.24 to 1.80 at dose levels of 1600-4800 mg/day)

- **OTC dose: No significant increase in mucosal injury;**
- **Prescription dose: Dose-related mucosal damage**

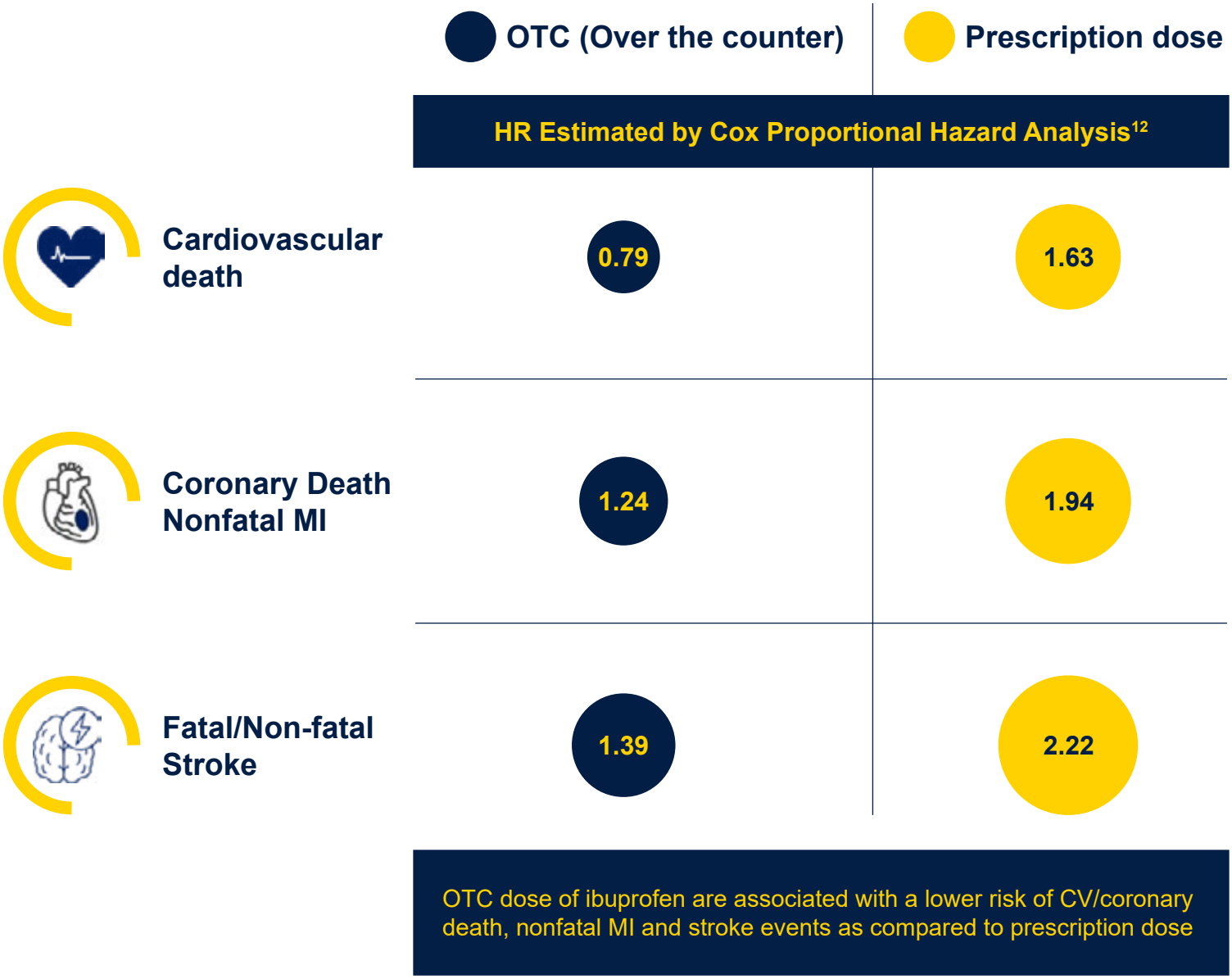
OTC (Over the counter) **Prescription dose**

Abbreviations: OR (Odds ratio)

Major GI safety concerns (GI bleeding, ulcer and risk of hospitalization), predominantly arise at the prescription dose, while OTC ibuprofen has a well-established safety profile, with GI side effects comparable to placebo in clinical studies[11]

Cardiovascular (CV) safety profile

OTC doses of ibuprofen demonstrated a lower CV risk of death, myocardial infarction, or stroke compared to prescription ibuprofen[12]



- A review of 38 studies found that 11 reported a dose-response relationship, with high doses of ibuprofen (≥1,200 mg/day) increasing cardiovascular risk by 78%[13]
- The European Medicines Agency (EMEA) underscored that high doses of ibuprofen (≥2,400 mg/day) are associated with slight increase in the risk of cardiovascular events, such as myocardial infarction and stroke, while doses up to 1,200 mg show no associated risk[14]

CV risk associated with Ibuprofen's is dose-dependent: OTC doses show minimal risk in clinical studies, while prescription doses significantly increase the risks of CV events particularly in patients with baseline conditions like hypertension, coronary artery disease, or diabetes[15]

Ibuprofen is generally well tolerated at recommended OTC doses (up to 1200 mg/ day) for up to 7–10 days; however, caution is always advised particularly with higher doses and extended use to minimize the risk of GI and CV complications

Conclusion

In clinical studies, patients without significant CV risk factors did not experience increased risk with OTC ibuprofen which can be used effectively when adhering to directions. However, it is advisable for people with prior health concerns or risk factors to take precautions. See the Warnings in ibuprofen product labels for more detail

References

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